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Mini Review

# Micro- and Nanoplastics: A Paradigm Shift in the Pathogenesis of Inflammatory Bowel Disease

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## Abstract

Micro- and nanoplastics (MNPs) are pervasive environmental contaminants with growing recognition as potential contributors to human disease. Widespread human exposure occurs primarily through ingestion of contaminated food and water, and MNPs have been detected in multiple human tissues, including the gastrointestinal tract. Experimental evidence provides a plausible biological basis for disease associations, including impairment of intestinal barrier integrity, activation of mucosal immune pathways, and alteration of gut microbial communities caused by MNP exposure. Although human data remain limited, early studies demonstrate MNP detection in stool and suggest potential correlations with inflammatory biomarkers such as fecal calprotectin. These findings, together with mechanistic data from *in vitro* and animal models, raise concern that MNP exposure represents a paradigm shift in the pathogenesis or modulation of inflammatory bowel disease (IBD); however, methodological variability, small sample sizes, and contamination challenges currently limit definitive conclusions. The aim of this review is to evaluate the current understanding of MNP exposure and its impact on intestinal health, particularly in relation to IBD. We synthesize mechanistic and early clinical evidence linking MNPs to IBD and highlight critical research gaps. Future standardized exposure assessment, mechanistic validation in human systems, and longitudinal studies are essential to clarify causal relationships. Given the modifiable nature of environmental plastic exposure, advancing this field may offer new opportunities for IBD prevention and intervention.

## Introduction

Plastic pollution is a pervasive environmental challenge with increasing relevance to human health. Microplastics (MPs) and nanoplastics (NPs) are defined as plastic particles <5 mm and <100 nm, respectively.[1] To put this in perspective, a pencil eraser is approximately 5 mm, whereas a single human hair follicle is 80,000 nm wide. Recognizably, the composition of plastics primarily includes synthetic polymers, which are widely used across the spectrum of products in daily use (Table 1).[2] Although many plastic products are deemed "recyclable," in the United States less than 10% are actually recycled. Recognizably, global plastic production has increased exponentially, with annual global production projected to reach 1.1 billion tons in 2025, with a consequent effect resulting in over 12 billion tons of plastic waste accumulation in landfills.[3] As plastic waste degrades in landfills, is dumped into oceans, and is incinerated and aerosolized, these micro- and nanoplastics (MNPs) seep into every aspect of the environment, including water, soil, and air. The effect then is global, with uptake into every aspect of terrestrial life.

The chemical stability, persistence, and small size promote global dispersion and continuous human exposure through ingestion, inhalation, and dermal contact. Dietary exposure and gastrointestinal (GI) ingestion represent the dominant route, with MNPs documented in virtually all food products and liquids.[4,5] Given recognition of this burgeoning issue and the significantly increasing downstream human exposure, understanding the potential biological effects of MNPs has become increasingly urgent.

Growing evidence demonstrates that MNPs are not confined to the environment but accumulate within the human body. Analytical advances, including Raman and FTIR micro-spectroscopy, pyrolysis-GC/MS, and fluorescence-based detection, confirm the presence of MPs in human stool, blood, placenta, lung tissue, liver,

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**Table 1. Common polymers**

| Polymer | Common products |
|---|---|
| Polyethylene* | Plastic bags, bottles, cups, jars, packaging films |
| Polypropylene* | Food containers, rope, automotive parts, textiles |
| Polystyrene* | Disposable utensils, packaging materials, foam cups |
| Polyvinyl chloride | Pipes, vinyl flooring, synthetic leather, medical devices |
| Polyethylene terephthalate | Bottles, food packaging, textiles |
| Polymethyl methacrylate | Acrylic glass, lenses, signage |
| Polycarbonate | Bottles, glass, helmets, medical equipment |
| Nylon | Textiles, ropes, wound dressing, sutures, catheters, dental implants, packing material, automotive parts |
| Polytetrafluoroethylene | Nonstick cookware, electrical insulation, sutures, medical devices, industrial applications |

*Denotes polymers most commonly produced. Adapted from Johnson *et al.*,[2] with modification.

and even brain samples.[6–8] These findings support the ability of particles, particularly NPs, to cross biological barriers, interact with mucosal surfaces, and distribute systemically. The GI tract, as the primary entry site of exposure, is uniquely positioned at the interface between environmental particle load and host immune, microbial, and epithelial systems.

Geographic, socioeconomic, and lifestyle factors further modify MP exposure, creating substantial variability across populations. Urbanization, industrial density, and waste-management infrastructure strongly influence environmental MNP concentrations, with higher airborne and waterborne levels documented in densely populated and industrialized regions.[1] Coastal proximity and local seafood consumption patterns further affect ingestion-based exposure.[2] Individual behaviors such as bottled-water use, reliance on packaged foods, and indoor MNP inhalation from household dust contribute additional variability.[1,9] Emerging environmental-health assessments also highlight marked differences in MP contamination of drinking water, soil, and air across countries and income levels, reflecting socioeconomic inequities in plastic production, use, and waste-management systems.[10] Together, these disparities underscore that exposure is neither uniform nor random and emphasize the need for region-specific environmental monitoring capable of linking exposure hotspots with GI health outcomes.[7]

Mechanistic work from GI, respiratory, vascular, and placental models provides strong biological plausibility for MNP-induced injury. MPs have been shown to disrupt mucus membrane architecture, weaken epithelial tight junctions, induce oxidative stress and mitochondrial dysfunction, alter cytokine signaling, and impair host–microbe interactions.[11] In the gut specifically, experimental data demonstrate decreased microbial diversity, shifts in key bacterial taxa, accumulation of potentially pathogenic organisms, and enhanced inflammatory signaling. Additionally, MPs have the capacity to adsorb environmental chemicals, plasticizers, and microbial products, with delivery of these to organ systems, with potent effects on epithelial permeability and immune activation.[12,13]

These mechanisms parallel established pathways in inflammatory bowel disease (IBD), where genetic susceptibility, epithelial barrier dysfunction, dysbiosis, and dysregulated immune responses drive chronic inflammation. Patients with IBD exhibit baseline defects in mucus composition, tight junction integrity, and microbial homeostasis and thus may be especially vulnerable to environmental insults such as MP exposure. Early translational evidence supports this concern: a recent case–control study demonstrated higher fecal MP concentrations in patients with IBD compared with healthy controls, with correlations between MP burden and disease activity.[6] Although causality has not been established, the convergence of mechanistic plausibility, tissue-level detection, and emerging human data suggests that MP exposure may represent a novel modifier of intestinal inflammation.

Given the ubiquity of exposure and the GI tract's central role in ingested substance processing, understanding how MNPs interact with mucosal biology is a critical area of investigation. Clarifying these relationships may illuminate new environmental contributors to IBD onset and flares, identify susceptible patient subgroups, and inform strategies to mitigate exposure-related disease burden. Taken together, these findings suggest that MNPs represent more than passive environmental contaminants and may constitute a previously underrecognized focus of intestinal inflammation. Recognizing MNPs as such represents a paradigm shift in IBD research, away from models predominantly focused on genetic susceptibility and building upon those centered around chronic, low-level environmental exposures capable of damaging intestinal barrier health, disrupting the gut microbiome, and dysregulating intestinal immune response (Fig. 1). Within this paradigm, MNPs may influence IBD not only by modifying disease activity in susceptible hosts but potentially by contributing to disease initiation, flare dynamics, and variability in treatment response. Recognizing MP exposure as a modifiable environmental factor has implications for mechanistic investigation, prevention strategies, and translational efforts aimed at mitigating environmentally driven intestinal inflammation. This review synthesizes current evidence on MNP exposure, mechanistic pathways relevant to gut inflammation, and emerging clinical data.

## Mechanistic evidence: Biological basis for MNP and IBD

### *MNP-induced disruption of intestinal barrier integrity*

Within this conceptual framework, MNPs are best understood not as inert environmental byproducts, but as biologically active exposures capable of perturbing epithelial barrier integrity, reshaping the gut microbiota, and amplifying mucosal immune signaling, core processes central to IBD pathophysiology. The intestinal barrier is a multilayered and complex defense system composed of the mucus layer, epithelial cells connected by tight junctions, and underlying immune structures. Together, these components form

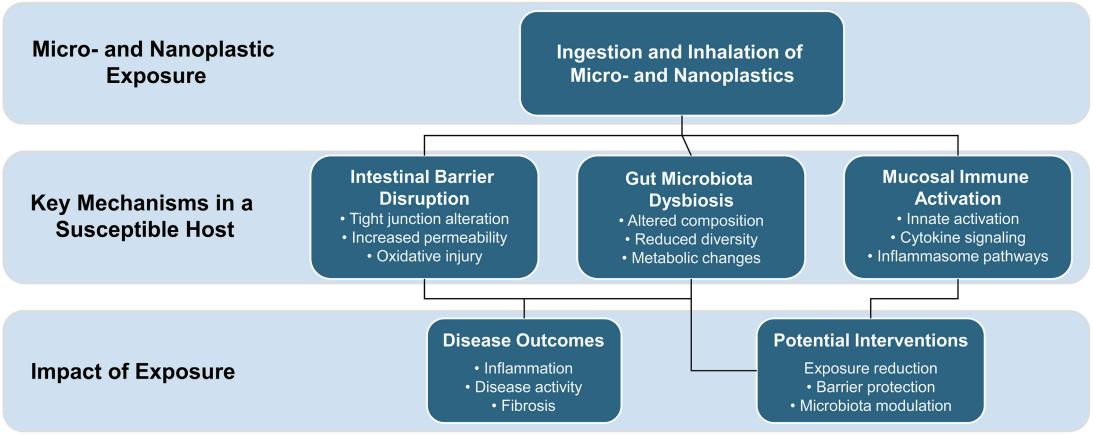


**Fig. 1. The emerging paradigm by which MNP exposure may contribute to IBD through effects on epithelial barrier integrity, microbiota composition, and mucosal immune activation.** IBD, inflammatory bowel disease; MNP, micro- and nanoplastic.

a highly selective interface permitting nutrient absorption while preventing exposure of luminal microbiota and dietary antigens to the mucosal immune system. Integrity of this barrier is paramount for proper immune system regulation, and disruption triggers and perpetuates intestinal inflammation, a hallmark of IBD.[11,12] Overall, epithelial barrier dysfunction and altered mucus barrier in IBD facilitate increased penetration of luminal antigens and microbes, perpetuating inflammation. Environmental pollutants, including MNPs, likely exacerbate these defects by penetrating mucus and impairing epithelial cells, contributing to the pathogenesis and severity of IBD.[14–17] While TEER is commonly used to assess epithelial integrity *in vitro*, more sensitive impedance-based approaches may capture additional aspects of barrier function and detect subtler perturbations.

The integrity of the epithelial barrier is maintained by several key components, including the mucus layer and underlying epithelial tight junctions. The mucus layer, primarily composed of the MUC2 mucus-secreting protein, serves as a first defense by physically separating bacteria from the epithelial cells. In IBD, defects in this mucus layer allow bacteria to penetrate and contact the epithelium, which is associated with disease severity and ongoing inflammation. The normally dense, stratified inner colonic mucus layer becomes damaged and thinner, contributing to immune activation and epithelial injury.[13]

The epithelial tight junctions act to further regulate permeability and prevent paracellular passage of luminal contents. At the molecular level, tight junction integrity is maintained by transmembrane and scaffolding proteins, including occludin and zonula occludens-1, both of which are disrupted in inflammatory states. Experimental models demonstrate that MNP exposure can downregulate tight junction protein expression and alter junctional organization, leading to increased paracellular permeability. These effects appear to be mediated, in part, by oxidative stress and pro-inflammatory cytokine signaling, mechanisms that overlap with established pathways of barrier dysfunction in IBD.[18] In IBD, these junctions are functionally impaired due to cytokine-mediated disruption, particularly tumor necrosis factor-α, interleukin (IL)-6, and IL-17, oxidative stress, microbial metabolites, and genetic susceptibility.[11,19,20] Microbial components such as bacterial flagellins also drive immune activation by stimulating innate and adaptive immune responses through receptors such as Toll-like receptor 5, contributing to chronic inflammation in genetically susceptible hosts.[21] Mononuclear phagocytes, including macrophages and dendritic cells, normally help maintain barrier integrity and immune balance but have been shown to contribute to chronic inflammation in IBD and may be especially influenced by environmental factors like MPs.[22]

Collectively, insults to barrier integrity and promotion of inflammation contribute to increased intestinal permeability, or "leaky gut." This permeability exposes the immune system to luminal contents such as microbial products and dietary antigens, fueling dysregulated immune responses. Signaling pathways such as IL-6/gp130/STAT3 normally function to maintain epithelial integrity during inflammation by regulating tight junction protein expression and epithelial survival. Dysregulation of these pathways contributes to barrier breakdown in colitis models and IBD, which MP-induced epithelial stress could potentially aggravate.[23] Therapeutic approaches like anti-tumor necrosis factor-α agents can reduce inflammation and restore barrier function to some extent, underscoring the importance of epithelial integrity in disease control.[24]

Although direct evidence linking MNPs to IBD-specific epithelial and mucus barrier dysfunction is still emerging, environmental pollutants are known to impair epithelial barrier integrity, harm the mucus layer, and promote gut dysbiosis, thereby exacerbating barrier dysfunction and inflammation. These mechanisms offer opportunities to contribute to disease risk and progression in susceptible individuals with IBD.[18] While specific effects of MNPs on mucus layer properties and intestinal permeability in IBD require further research, similarities with heavy metals and other pollutants suggest a plausible detrimental role via mucus penetration and barrier disruption. Notably, MPs have been shown to act as adjuvants or carriers of microbial components and toxins, potentially enhancing mucosal immune activation and barrier disruption analogous to bacterial antigens.[25] Potentially, this would exacerbate the inflammatory milieu by increasing immune cell activation, cytokine release, and epithelial permeability, similar to mechanisms observed in bacterial–mucosal interactions that provoke aberrant immune responses in IBD.[26]

### *Microbiota dysbiosis and metabolic consequences*

The dynamic between the mucosal immune system and gut microbiota is critical for maintaining intestinal homeostasis, and any perturbation by MPs might induce dysbiosis, further amplifying

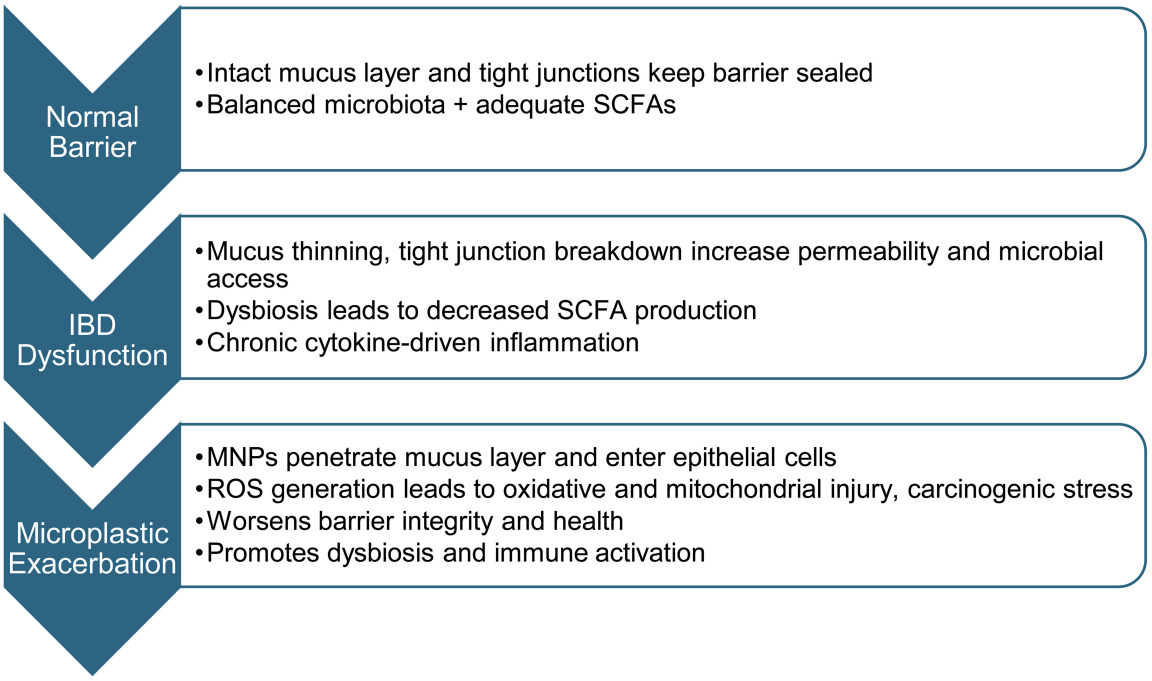


**Fig. 2. Plausible effects of MNP-associated damage.** IBD, inflammatory bowel disease; MNPs, micro- and nanoplastics; ROS, reactive oxygen species; SCFA, short-chain fatty acid.

abnormal immune stimulation and cytokine cascade disruptions associated with IBD.[27,28] MNP-induced dysbiosis has already been linked to systemic sequelae such as neurodegenerative disease, further supporting the widespread effects.[29] Although some studies show modest overall compositional changes, correlations have been identified between specific MP polymers and bacterial genera including *Roseburia*, *Clostridium*, and *Prevotella*, as well as alteration in the Firmicutes:Bacteroidetes ratio, a key component of immune regulation.[9,25] Additionally, MPs contribute to dysbiosis through biofilm formation and antimicrobial resistance, acting as a nidus for bacterial proliferation and promoting the spread of genes involved in antimicrobial resistance and plastic breakdown.[26,30–32] Chronic exposure-induced dysbiosis has been associated with reduction in short-chain fatty acids, including butyrate, a metabolite essential for epithelial barrier integrity and immune regulation. Impaired production of short-chain fatty acids has been linked to increased mucosal cytokine production and dysregulation of immune activity (Fig. 2).[33] Exposure duration is a key factor in driving these harmful changes, with chronic exposure producing more pronounced dysbiosis and identifying taxa that serve as biomarkers of MP toxicity.[9]

### *Immune activation, oxidative stress, and inflammation*

Finally, particle size plays a significant role in determining the impact of MNPs on the gut, exhibiting increased mobility, bioavailability, and toxicity. The smaller size of NPs affords ease of access through biological barriers, absorption across the gut epithelium, and systemic distribution, including accumulation in the liver, leading to both local and distant inflammation via the gut–liver axis.[18,34,35] MNPs disrupt gut microbiota, impair epithelial homeostasis, and interact directly with cellular components, causing oxidative stress, immune activation, and cellular injury. While larger MPs typically produce localized mechanical irritation since they remain confined to the lumen, chronic ingestion of either form reduces microbial diversity and promotes intestinal inflammation. However, the deeper tissue penetration and higher reactivity seen with NPs compared to MPs lead to more severe effects.[10] NPs carry adsorbed toxic pollutants and leach plastic additives, provoking inflammation by direct chemical toxicity to gut tissues and microbes, amplifying their inflammogenic potential. These mechanisms illustrate why NPs generate more severe intestinal injury and inflammatory responses than larger MP particles, raising particular concern for individuals with pre-existing barrier defects such as IBD.[10,18,31]

In addition to particle size, studies demonstrate that potential harm from MPs varies substantially by polymer type, surface chemistry, and degradation behavior. Polystyrene NPs, in particular, have driven much of the available mechanistic insight to date, though findings vary across experimental systems, particle sizes, and exposure conditions. They have been shown to reduce microbial diversity and exacerbate intestinal inflammation primarily via dysbiosis.[10] Plastics such as polystyrene and polyethylene consistently induce high levels of intracellular reactive oxygen species (ROS), mitochondrial depolarization, lipid peroxidation, and antioxidant depletion, all of which lead to oxidative and cellular damage.[36] Polyethylene terephthalate and polyvinyl chloride particles also show similar oxidative damage, though to a lesser degree. Similar to the potential for increased microbial disruption, the smaller size of NPs carries the potential for more severe oxidative damage due to their high surface area-to-volume ratio, increased cellular uptake, and adsorption capacity. Oxidative stress is a well-recognized amplifier of the intestinal inflammation often seen in IBD. ROS destabilize and weaken the intestinal barrier and activate ROS-sensitive inflammatory pathways such as mitogen-activated protein kinase.[33] These changes perpetuate the chronic inflammation characteriz-

ing IBD and reflect the numerous opportunities for MNP exposure to influence disease activity.

## MNPs and IBD: Current literature and evidence

### *Human observational evidence*

The body of research on MNPs and their impact on IBD is sparse; however, current studies suggest potential associations between MNP exposure and disease activity, as summarized in Table 2. In IBD specifically, an observational study by Yan *et al*.[9] demonstrated higher concentrations of MPs in feces in patients with IBD compared to stool samples from patients without IBD. Furthermore, their study suggests an association between fecal MP concentration and disease severity, as indicated by the Harvey-Bradshaw Index or Mayo score.[9] Another observational study by Linares *et al*.,[37] evaluating patients with Crohn's disease, found that patients with active Crohn's have significantly higher levels of bisphenol A (BPA), a chemical commonly used in plastic manufacturing. The study also found that BPA levels were associated with serum inflammatory markers and decreased levels of beneficial gut metabolites. Furthermore, they found that patients with colonic disease had higher BPA levels compared to those with ileal disease, suggesting a region-specific and anatomical impact of MNP-associated additives.[37] Recent human tissue-based analyses have demonstrated direct accumulation of MPs within fibrotic ileal segments and adjacent mesenteric adipose tissue in patients with Crohn's disease. MP burden was higher in fibrotic tissue and positively correlated with histologic severity of fibrosis, supporting an association between tissue-level MP accumulation and severity of disease.[38]

### *Preclinical and experimental evidence*

The underlying pathophysiology of this association between MNPs and IBD is not yet fully understood. Several animal and experimental studies point to potential explanations, including oxidative stress, alterations to the gut microbiome, and disruption of intestinal barrier function.[39–41] In analyses of the human gut microbiome, patients with IBD are noted to have significant degrees of dysbiosis and decreased microbial diversity. A study aimed at evaluating MP exposure on the infant gut microbiome with an *in vitro* colon model demonstrated increased growth of pathobionts in the gut microbiome and lower butyrate production, a metabolite of intestinal bacteria with anti-inflammatory properties thought to be protective in IBD.[42,43] Additional evidence supporting the impact of MPs on the gut microbiome comes from a quasi-experimental study evaluating thermal exposure to disposable plastic tableware, which demonstrated significant increases in fecal MPs and marked shifts in gut microbial composition in healthy adults.[44] In these patients, there was an increase in pro-inflammatory genera such as *Proteobacteria* and *Dorea*, as well as a reduction in beneficial genera *Faecalibacterium* and *Roseburia*. *Faecalibacterium* and *Roseburia* are both important in the production of butyrate, and decreased abundance has been associated with IBD.[42]

### *Carcinogenesis and long-term risk (preclinical evidence)*

Current evidence linking MNP exposure to carcinogenesis in IBD is derived primarily from preclinical models, and its relevance to human disease remains to be established. Chronic inflammation in IBD already confers an increased risk of colorectal cancer (CRC), and emerging evidence suggests that MNP exposure may further potentiate this risk. Murine models of colitis-associated CRC have demonstrated that polystyrene NPs exacerbate tumor formation through pathways such as induction of oxidative stress, mitochondrial dysfunction, and lipid peroxidation.[45] These particles disrupt DNA repair checkpoints, promote genomic instability, and activate oncogenic signaling pathways such as phosphatidylinositol 3-kinase, AKT, and mammalian target of rapamycin, all of which are highly relevant to IBD-associated carcinogenesis.[43] Given that patients with IBD already experience cycles of epithelial damage and repair, the addition of MNP-driven genotoxic stress may create a biologically synergistic environment that could potentiate neoplastic progression. While human data remain limited, these preclinical findings underscore the urgent need to evaluate whether chronic MNP exposure modifies CRC risk in IBD. These effects appear most pronounced for NPs, given their high surface area and adsorption capacity, underscoring the importance of particle size, polymer composition, and co-adsorbed contaminants in shaping long-term biological risk.

Studies with mouse models of IBD suggest worse outcomes with MP exposure, evidenced by shorter colon length with histopathologic evidence of injury and inflammation, decreased mucus secretion, and increased permeability of the colon compared to healthy controls.[46] Further research is necessary to better understand the impact of MNPs on IBD, including standardization of methodological practices, quantifying MNP exposure, and longitudinal monitoring of patient outcomes.

## Future directions, challenges, and outlook

### *Future directions in MNPs and IBD pathogenesis*

The investigation of environmental triggers such as MNPs in the pathogenesis of IBD represents an emerging but increasingly important frontier that intersects mucosal immunology, toxicology, and environmental health. Although current models of IBD emphasize the interplay of genetic susceptibility, epithelial barrier dysfunction, microbiome alterations, and dysregulated immune responses, the contribution of MNP exposure remains under-characterized. Future work must integrate MNPs into existing multifactorial frameworks to clarify how chronic exposure influences disease onset, flares, and progression. Mechanistic studies already suggest that MNPs can disrupt barrier integrity, alter mucus structure, modulate immune pathways, and drive dysbiosis, but translational data remain limited. Multi-omics approaches, including genomics, transcriptomics, proteomics, lipidomics, and microbiome profiling, may help reveal exposure-related molecular signatures, identify susceptibility phenotypes, and uncover novel biomarkers of MP-induced epithelial and immune stress.[47,48]

### *Key research challenges and opportunities*

Addressing key knowledge gaps at the intersection of MNP exposure and IBD will require integration of emerging analytical and computational approaches. Multi-omics profiling, including microbiome, metabolome, and host transcriptomic analyses, may help link environmental exposure to functional epithelial and immune perturbations, enabling identification of exposure-associated molecular signatures. Advanced causal modeling frameworks that integrate compositional microbiome data with clinical phenotyping could further clarify pathways connecting MNP exposure, dysbiosis, and disease activity. In parallel, nanomedicine-based strategies, including barrier-protective formulations or targeted antioxidant delivery, may offer opportunities to mitigate MP-induced epithelial and immune stress. Together, these approaches provide a

**Table 2. Human studies evaluating MNP exposure in IBD**

| Study | Population | Sample size | Study design | MNP evaluated | Specimen type and detection method | Reporting units | Contamination controls | Disease activity metrics | Key strengths | Key limitations |
|---|---|---|---|---|---|---|---|---|---|---|
| Yan *et al.*, 2021[9] | Adult patients with IBD and healthy controls in China | 52 IBD patients, 50 healthy controls | Observational case-control study | Microplastics and polymer types | Chemical digestion, micro-Raman spectroscopy of fecal samples | Fecal MP concentration (items/g dm) | Plastic free study materials, Quality control sample analysis with ultrapure water | HBI, Mayo score | Prospective study design comparing IBD patients with healthy controls | -Evaluates IBD disease severity by questionnaire data and self-reporting -Lack of endoscopic evaluation |
| Linares *et al.*, 2021[37] | Adult patients with CD in Spain | 200 Crohn's patients – 140 in remission and 60 with active disease | Prospective observational cohort study | Endocrine-disrupting chemicals –BPA, EtPB, MePB, PrPB, BuPB, BzP-1 and -3 | Quantification based on prior study techniques, analysis by DLLME and UHPLC-MS/MS of serum samples | Serum concentration (μM) | Controlled environmental measures and study materials to avoid external contamination | CDAI, clinical symptoms of relapse | Multidimensional biomarker assessment, inclusion of genotype data, prospective study design | -Single serum sample evaluation -Evaluation of chemicals used in microplastic manufacturing rather than true microplastic exposure |
| Wu *et al.*, 2025[38] | Adult patients with CD and associated complications requiring surgical resection in China | 10 patients with CD | Observational cross-sectional study | Microplastics, 12 different types identified including CPE, ACR, flurorubber, PE | Laser infrared imaging spectrometry of resected ileal segments and mesenteric adipose tissue | Tissue MP concentration (particles/g) | Labware cleaning with ultrapure water and microscopic inspection prior to use, reagent filtration to reduce contamination, inclusion of blank control group | Not directly measured however study samples taken from surgeries required for complications of CD | Study design utilizing human tissue samples from patients with CD | -Lack of comparison to healthy controls without IBD -Extrapolation of disease severity based on requirement of surgery |

ACR, acrylate copolymer; BPA, bisphenol-A; BuPB, butylparaben; BzP, benzophenones; CD, Crohn's disease; CDAI, Crohn's disease activity index; CPE, chlorinated polyethylene; DLLME, dispersive liquid–liquid microextraction; EtPB, ethylparaben; HBI, Harvey-Bradshaw Index; IBD, inflammatory bowel disease; MePB, methylparaben; MNP, micro- and nanoplastic; PE, polyethylene; PrPB, propylparaben; UHPLC-MS/MS, ultra-high-performance liquid chromatography with tandem mass spectrometry detection.



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roadmap for translating mechanistic insights into actionable exposure assessment and intervention strategies.

A major priority for future research is to define dose–exposure and temporal dynamics of MNP accumulation. Exposure begins early in life, is continuous, and varies across dietary patterns, water sources, and environments. Early-life exposure is particularly relevant because neonatal and pediatric intestinal barriers remain comparatively immature and more permeable, potentially increasing susceptibility to MP penetration and immune priming.[12,13] Long-term cumulative exposure may also interact with age-related changes in mucus thickness, epithelial turnover, and immune regulation, which could partly explain differential vulnerability across the lifespan.[12,13] Animal and ecotoxicology models consistently demonstrate dose–response relationships between increasing MP load and worsening epithelial injury, oxidative stress, and dysbiosis, but human thresholds for clinically meaningful risk are unknown.[12,13] Longitudinal cohorts that integrate environmental exposure data, dietary intake, and detailed IBD phenotyping will be essential to move from association toward causality.

Clarifying whether polymer type and particle chemistry influence toxicity is another important direction. Different polymers, such as polystyrene, polyethylene, polypropylene, polyvinyl chloride, and polyamide, exhibit distinct degradation behavior, surface chemistries, and capacities to adsorb environmental pollutants and microbial products. Polystyrene NPs, in particular, have been shown in preclinical models to exacerbate colitis, induce epithelial injury, and promote microbial dysbiosis.[10] Other work highlights the role of leached additives, including plasticizers and stabilizers, and the intrinsic cellular toxicity of NPs, which can induce oxidative stress, mitochondrial dysfunction, and genotoxicity in gut and hepatic tissues.[31,32] Future research should determine whether certain polymers or additive combinations confer disproportionate risk for mucosal injury or immune dysregulation, which could inform regulatory policy and consumer-level exposure mitigation.[31,32]

A third major challenge is accurately quantifying MPs in the human GI tract. Current methodologies, including Raman and FTIR micro-spectroscopy, pyrolysis–GC/MS, and fluorescent dye–based imaging, each carry limitations related to particle-size detection, contamination risk, and polymer misclassification.[49] Stool-based measurements provide a practical, noninvasive index of luminal exposure and have already been used to correlate fecal MP burden with IBD status in case–control designs, but they do not capture mucosal retention or systemic translocation.[6] Tissue-based analyses and advanced imaging approaches capable of detecting NPs remain technically demanding and lack standardization. A major barrier to progress is the absence of harmonized reference materials, such as standardized particle-size distributions, polymer compositions, and laboratory controls, as well as unified reporting metrics across studies.[6,46] Establishing consensus standards will be essential for reproducibility, cross-study comparison, and the development of clinically meaningful exposure biomarkers.[46]

### *Host susceptibility and therapeutic opportunities*

Emerging research should also address host factors that may modify vulnerability to MNP-induced intestinal injury. Genetic variants linked to epithelial integrity, mucin production, autophagy pathways, or innate immune signaling may influence how individuals respond to chronic MP exposure, paralleling known susceptibility pathways in IBD.[12,16,22] Dietary components such as fiber, emulsifiers, and high-fat content may alter MP aggregation, transit, or absorption, potentially modifying inflammation risk, consistent with emerging data on diet–microbiome–barrier interactions in IBD.[14,30] Medications used in IBD, such as corticosteroids and JAK inhibitors, alter epithelial permeability and immune response and could, in theory, interact with MP exposure to worsen barrier dysfunction, although this remains hypothetical and has not yet been directly studied in MP models.[50,51] These intersections between host biology, environment, and therapeutics represent fertile ground for biomarker discovery and personalized exposure–risk prediction.

These mechanistic and methodological insights create opportunities for therapeutic innovation. Nanomedicine strategies, including orally delivered nanocarriers and polymer-based drug delivery systems, are being developed to target inflamed gut segments and may also be leveraged to counteract oxidative stress and immune activation triggered by MNP exposure.[52] Modulating the gut microbiota through targeted probiotics, prebiotics, synbiotics, or live biotherapeutic products may help mitigate MP-induced dysbiosis, restore barrier integrity, and dampen mucosal immune activation.[53] Incorporating environmental exposure metrics, including MP burden, into emerging precision-medicine frameworks for IBD may allow identification of patients who are particularly susceptible to MP-associated inflammatory exacerbations.[40]

In summary, the intersection of MNP exposure and IBD pathogenesis presents substantial scientific and methodological challenges, but at present, there is clearly a need to recognize what we know and what we do not know (Fig. 3a and b). Addressing key gaps, including dose thresholds and timing, polymer-specific toxicity, standardized quantification methods, host susceptibility factors, and longitudinal human data, will be essential for defining the clinical relevance of MNPs in IBD.[6,10,46]

## Limitations

While this review provides an overview of the potential links between MNPs and IBD, several limitations should be acknowledged. First, the current body of evidence primarily consists of observational studies and experimental models, with a lack of large-scale, longitudinal human studies that could establish definitive causal relationships. Furthermore, methodological variability, such as differences in exposure quantification methods, particle characterization, and contamination controls, limits the comparability of results across studies. The small sample sizes in many human studies also hinder the ability to draw broad conclusions. Additionally, while experimental models have provided valuable mechanistic insights, they may not fully capture the complexity of human exposure or the long-term effects of MNPs in real-world conditions. Finally, the lack of standardized protocols for MP detection and characterization remains a significant barrier to reproducibility and to the development of clinically relevant biomarkers for exposure.

## Conclusions

MNPs represent a pervasive and biologically active class of environmental exposures with plausible relevance to IBD. Experimental evidence demonstrates that MNPs can disrupt epithelial barrier integrity, promote dysbiosis, induce oxidative stress, and amplify mucosal immune activation—mechanisms that closely parallel established pathways in IBD pathogenesis. Emerging human data, including detection of MPs in stool and intestinal tissue and associations with inflammatory markers and disease severity, further support the need for focused investigation, although causality has not yet been established.

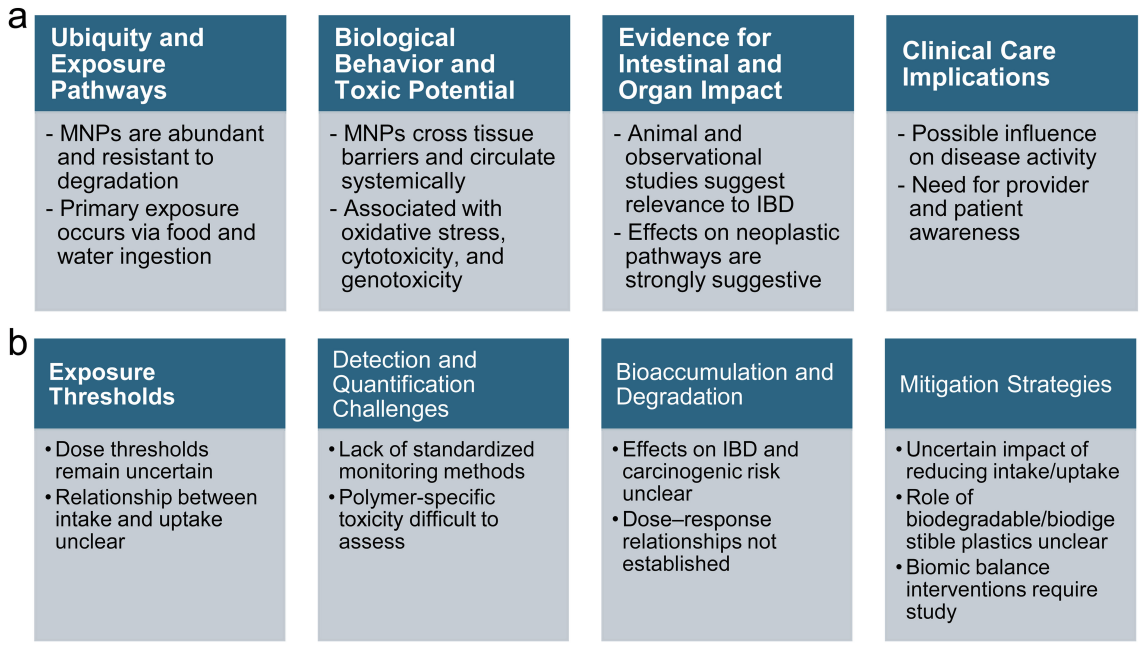


**Fig. 3. What we know (a) and do not know (b) about MNPs in IBD.** IBD, inflammatory bowel disease; MNPs, micro- and nanoplastics.

At present, substantial methodological and translational gaps remain, including standardized exposure quantification, clarification of polymer- and size-specific toxicity, and longitudinal human studies capable of defining dose–response relationships and clinical impact. Given the ubiquity of exposure and the modifiable nature of plastic contamination, advancing this field holds implications not only for mechanistic understanding but also for prevention, risk stratification, and environmentally informed disease management. Integrating environmental exposure science into IBD research frameworks may ultimately broaden our understanding of disease drivers and support more comprehensive approaches to patient care.

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No conflicts of interest or disclosures were reported by any of the authors.

## Author contributions

Study design (MS, DJ), manuscript writing (MS, PD, GH, DJ), and critical revision (EO, DJ). All authors have made significant contributions to this study and have approved the final manuscript.

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