



International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Operating Publisher
SciFormat Publishing Inc.
ISNI: 0000 0005 1449 8214

2734 17 Avenue SW,
Calgary, Alberta, T3E0A7,
Canada
+15878858911
editorial-office@sciformat.ca

ARTICLE TITLE	MICRO- AND NANOPLASTICS IN INFLAMMATORY BOWEL DISEASE: FROM EXPERIMENTAL MODELS TO HUMAN EVIDENCE
----------------------	---

DOI	https://doi.org/10.31435/ijitss.4(52).2026.6481
------------	---

RECEIVED	20 August 2026
-----------------	----------------

ACCEPTED	19 October 2026
-----------------	-----------------

PUBLISHED	28 October 2026
------------------	-----------------

LICENSE



The article is licensed under a **Creative Commons Attribution 4.0 International License**.

© The author(s) 2026.

This article is published as open access under the Creative Commons Attribution 4.0 International License (CC BY 4.0), allowing the author to retain copyright. The CC BY 4.0 License permits the content to be copied, adapted, displayed, distributed, republished, or reused for any purpose, including adaptation and commercial use, as long as proper attribution is provided.

MICRO- AND NANOPLASTICS IN INFLAMMATORY BOWEL DISEASE: FROM EXPERIMENTAL MODELS TO HUMAN EVIDENCE

Magdalena Kowalczyk

Students' Scientific Association at the Department of Normal, Clinical and Imaging Anatomy, Medical University of Lublin, Lublin, Poland
ORCID ID: 0009-0005-7613-0826

Maciej Kolasa

Students' Scientific Association at the Department of Normal, Clinical and Imaging Anatomy, Medical University of Lublin, Lublin, Poland
ORCID ID: 0009-0000-2122-6293

Filip Kuca

Students' Scientific Association at the Department of Normal, Clinical and Imaging Anatomy, Medical University of Lublin, Lublin, Poland
ORCID ID: 0009-0005-7536-9501

Mateusz Gawiński

Students' Scientific Association at the Department of Pediatric Pneumonology and Rheumatology, Medical University of Lublin, Lublin, Poland
ORCID ID: 0009-0003-4614-5336

Kacper Kraśnik (Corresponding Author, Email: kacper.krasnik@gmail.com)

Students' Scientific Association at the Department of Normal, Clinical and Imaging Anatomy, Medical University of Lublin, Lublin, Poland
ORCID ID: 0009-0009-3223-1026

Piotr Kuchciak

Students' Scientific Association at the Department of Pediatric Pneumonology and Rheumatology, Medical University of Lublin, Lublin, Poland
ORCID ID: 0009-0004-2131-6730

Szymon Kurus

Students' Scientific Association at the Department of Pediatric Pneumonology and Rheumatology, Medical University of Lublin, Lublin, Poland
ORCID ID: 0009-0002-4453-3792

ABSTRACT

Research objectives: Micro- and nanoplastics (MNPs) are pervasive environmental contaminants that may affect gastrointestinal health. This narrative review aimed to evaluate current mechanistic, experimental, and human evidence concerning the potential relationship between MNP exposure and inflammatory bowel disease (IBD), including ulcerative colitis and Crohn's disease.

Methods: PubMed, Scopus, and Google Scholar were searched for human, animal, and in vitro studies investigating MNP exposure in IBD, experimental colitis, ileitis, intestinal inflammation, or mechanisms relevant to IBD pathogenesis. Studies addressing epithelial barrier dysfunction, mucus alterations, oxidative stress, immune activation, dysbiosis, and epithelial cell death were included. The evidence was synthesized descriptively because of substantial methodological heterogeneity.

Key findings: Experimental studies indicate that MNPs can impair the intestinal mucus layer and epithelial junctions, increase permeability, promote oxidative and mitochondrial stress, activate inflammatory pathways, alter the gut microbiota and microbial metabolites, and disturb epithelial regeneration. In healthy animals, these effects were generally mild, subclinical, or inconsistent, and MNP exposure alone did not reliably produce an IBD-like phenotype. In contrast, most chemically induced colitis models showed greater mucosal injury, inflammation, permeability, delayed healing, fibrosis, or colitis-associated tumorigenesis after MNP exposure. Human studies reported higher fecal microplastic concentrations in IBD and associations with disease activity and Crohn's disease-related fibrosis, but evidence remains limited.

Conclusions: MNPs should currently be regarded as potential environmental modifiers of IBD rather than established etiological agents. Prospective studies using standardized exposure assessment and separate analyses of ulcerative colitis and Crohn's disease are required to clarify causal relationships.

KEYWORDS

Microplastics, Nanoplastics, Inflammatory Bowel Disease, Ulcerative Colitis, Crohn's Disease

CITATION

Kowalczyk, M., Kolasa, M., Kuca, F., Gawiński, M., Kraśnik, K., Kuchciak, P., & Kurus, S. (2026). Micro- and nanoplastics in inflammatory bowel disease: From experimental models to human evidence. *International Journal of Innovative Technologies in Social Science*, 4(52). [https://doi.org/10.31435/ijitss.4\(52\).2026.6481](https://doi.org/10.31435/ijitss.4(52).2026.6481)

COPYRIGHT

© The author(s) 2026. This article is published as open access under the Creative Commons Attribution 4.0 International License (CC BY 4.0), allowing the author to retain copyright. The CC BY 4.0 License permits the content to be copied, adapted, displayed, distributed, republished, or reused for any purpose, including adaptation and commercial use, as long as proper attribution is provided.

Introduction

The rapid increase in plastic production over recent decades has rendered plastic pollution one of the most widespread environmental challenges globally. Approximately 8.3 billion metric tons of virgin plastics were produced worldwide between 1950 and 2015. Of the estimated 6.3 billion metric tons of plastic waste generated during this period, only about 9% was recycled [1]. The degradation of plastic products leads to the formation of microplastics (MPs), defined as plastic particles smaller than 5 mm, and nanoplastics (NPs), which constitute a smaller and potentially more bioavailable fraction capable of interacting with biological structures [2,3]. Collectively termed micro- and nanoplastics (MNPs), these particles are widely distributed across water, food, soil, and air, resulting in virtually unavoidable human exposure [3].

The gastrointestinal tract constitutes a primary route of human exposure to MNPs. Detection of MPs particles in human stool provides direct evidence of ingestion and transit through the digestive system [4]. A recent dietary intervention study identified MPs in all analyzed stool samples and indicated that plastic use during food packaging and preparation, as well as consumption of highly processed foods, may increase oral exposure [5]. Plastic particles have also been identified in human blood [6] and vascular tissue [7], indicating that some particles may traverse biological barriers and enter systemic circulation. Nevertheless, the clinical implications of their presence in human tissues remain unclear, and methodological limitations related to particle detection and sample contamination must be acknowledged.

Inflammatory bowel disease (IBD), encompassing ulcerative colitis (UC) and Crohn's disease (CD), consists of chronic, relapsing inflammatory disorders of the gastrointestinal tract. The pathogenesis of IBD involves complex interactions among genetic susceptibility, dysregulated immune responses, alterations in the intestinal microbiota, impairment of the epithelial barrier, and environmental exposures. The global burden of IBD has risen substantially, with prevalence exceeding 0.3% in many countries in Europe, North America, and Oceania, and incidence continuing to increase in newly industrialized regions [8]. According to the Global

Burden of Disease Study, approximately 6.8 million individuals were living with IBD worldwide in 2017 [9]. The concurrent rise in IBD incidence and industrialization has intensified interest in environmental factors that may contribute to disease development or influence its clinical course [10].

MNPs are of particular relevance to IBD because the intestinal mucosa is directly and repeatedly exposed to ingested particles. Environmental factors are increasingly recognized as important modifiers of disease initiation, activity, progression, and treatment response in IBD [11]. Experimental studies indicate that MNPs can interact with the intestinal mucus layer, disrupt epithelial tight junctions, increase intestinal permeability, induce oxidative and mitochondrial stress, activate inflammatory signaling pathways, and alter the composition and metabolic activity of the gut microbiota [12]. These mechanisms overlap with those implicated in the pathogenesis of UC and CD. Furthermore, an inflamed or permeable intestinal barrier may facilitate particle retention or translocation, suggesting a potentially bidirectional relationship between MNP exposure and intestinal inflammation.

However, the current body of evidence is heterogeneous and is derived primarily from in vitro experiments and animal models employing various polymers, particle sizes, doses, and exposure durations. Human studies remain limited and do not yet clarify whether MNP exposure contributes to the development or exacerbation of IBD, or whether intestinal inflammation itself promotes particle accumulation and excretion. Therefore, this narrative review aimed to summarize and critically evaluate the available mechanistic, experimental, and human evidence regarding the potential relationship between MNP exposure and IBD, with particular emphasis on intestinal barrier dysfunction, oxidative stress, immune activation, microbiota alterations, epithelial injury, and differences between UC and CD.

Methodology

A narrative literature search was performed using PubMed, Scopus, and Google Scholar. The search strategy incorporated terms related to MNPs, such as “microplastic”, “microplastics”, “nanoplastic”, “nanoplastics”, “micro- and nanoplastics”, and “MNPs”, in combination with terms associated with inflammatory bowel disease and experimental intestinal inflammation, including “inflammatory bowel disease”, “IBD”, “ulcerative colitis”, “Crohn’s disease”, “colitis”, “ileitis”, “intestinal inflammation”, “animal model”, “DSS-induced colitis”, and “TNBS-induced colitis”.

Human, animal, and in vitro studies were included if they directly investigated the relationship between MNP exposure and IBD, intestinal inflammation, or experimental models of colitis and ileitis. Studies examining mechanisms relevant to IBD pathogenesis, including epithelial barrier dysfunction, oxidative stress, immune activation, dysbiosis, mucus alterations, and epithelial cell death, were also considered. Articles were excluded if they were not relevant to the gastrointestinal effects of MNPs, did not provide sufficient information on the investigated outcomes, or focused exclusively on environmental detection methods without assessing biological effects.

A total of 23 studies directly examining MNPs in IBD, intestinal inflammation, or related experimental models were included as the primary evidence base. An additional 20 mechanistic studies not directly focused on IBD were incorporated to provide supporting evidence and enhance understanding of the potential biological pathways linking MNP exposure with IBD development or exacerbation. Owing to the narrative nature of the review and considerable methodological heterogeneity among the included studies, the evidence was synthesised descriptively without a meta-analysis.

1. Biological Mechanisms Linking MNPs with Intestinal Inflammation

Studies identified in this review showed that MNPs influence gut homeostasis, specifically toward IBD or its animal models, through numerous mechanisms. These mechanisms could be categorized into groups: 1. interaction with the intestinal mucus layer, 2. intestinal epithelial barrier dysfunction, 3. oxidative stress and mitochondrial dysfunction, 4. immune activation, 5. the gut microbiota and microbial metabolites, and 6. abnormal epithelial regeneration and cell death. Below, we review each of these mechanisms individually.

1.1. Interaction with the intestinal mucus layer

The intestinal mucus layer serves as the primary barrier that separates luminal particles and microorganisms from the epithelial surface. MUC2, the major structural component of this layer, is secreted by goblet cells. Consequently, alterations in mucin production, goblet-cell differentiation, or mucus composition can increase epithelial exposure to MPs.

Research in healthy mice has generally demonstrated reduced mucus secretion following oral exposure to polystyrene microplastics (PS-MPs) or polyethylene microplastics (PE-MPs) [13–15]. Lu et al. [13] reported decreased Alcian blue–periodic acid–Schiff (AB-PAS) - positive mucus and reduced expression of Muc1 and Klf4, while Muc2 exhibited only a non-significant downward trend [13]. Jin et al. identified broader transcriptional changes: Muc1 and Klf4 were downregulated at both exposure levels, and high-dose exposure further reduced Muc2 and Retnlb; Muc3 and Meprin- β also tended to decrease [14]. In contrast, Sun et al. observed a significant reduction in mucin density despite a non-significant increase in MUC2 mRNA [15]. These findings indicate that histological mucus depletion does not always correspond to reduced Muc2 transcription and may result from impaired mucin processing, secretion, or increased degradation.

The impact of MPs may also extend to alterations in mucus composition and goblet-cell function. Zolotova et al. found that PS-MPs increased the content of highly sulfated mucins in healthy mice, without significantly affecting neutral mucins or goblet-cell abundance, although a downward trend in goblet-cell numbers was noted [16]. This increase in sulfated mucins may represent an adaptive response, as these mucins are more resistant to bacterial degradation. Conversely, Xie et al. [17] reported a reduction in goblet-cell number, which was associated with excessive crypt-cell proliferation and activation of the Notch pathway, suggesting disrupted differentiation of epithelial progenitor cells into mucus-producing goblet cells [17].

These alterations are particularly significant in the context of colitis. In models of dextran sulfate sodium (DSS) - induced acute and chronic colitis, additional PS-MP exposure exacerbated mucus-layer damage and reduced mucin coverage, whereas MPs alone caused relatively limited intestinal changes [18]. Sung et al. [19] reported that the group receiving both DSS and high-dose MP supplementation exhibited lower Muc2 levels compared to the DSS-only group [19]. Similarly, Xie et al. [17] associated goblet-cell depletion and impaired epithelial renewal with a more severe course of experimental colitis [17]. Zolotova et al. [16] observed that both DSS groups had fewer goblet cells, but MPs did not significantly intensify this reduction relative to DSS alone. However, neutral mucin content was significantly lower in the MP-plus-DSS group, while highly sulfated mucins remained unchanged [16].

In summary, MPs may compromise the mucus barrier by reducing mucus secretion [13–15,18], altering the expression of Muc1, Muc2, Klf4, and other mucus-associated genes [13,14], disrupting goblet-cell differentiation [17], and modifying mucin composition [16]. However, the findings are not entirely consistent, particularly with respect to Muc2 expression and goblet-cell abundance. The consequent functional weakening of the mucus layer may facilitate contact between particles and the epithelium, although direct penetration of MPs through colonic mucus was not evaluated in the studies reviewed.

1.2. Intestinal epithelial barrier dysfunction

Experimental studies demonstrate that MNPs impair the intestinal epithelial barrier by altering tight junction proteins and increasing paracellular permeability. In healthy mice, exposure to polystyrene nanoplastics (PS-NPs) or PS-MPs reduces the expression of zonula occludens-1 (ZO-1), occludin, and claudin-1, resulting in epithelial injury and increased intestinal permeability [20–22]. These effects are generally dose-dependent. However, at the lowest PS-NPs concentration, Li et al. [20] observed a reduction only in occludin, while ZO-1 and claudin-1 remained unchanged [20]. Chen et al., at the lowest PS-NPs concentration, showed

a reduction only in claudin-1 [22]. Additionally, Zeng et al. reported that 5- μ m particles caused greater junctional damage than smaller particles, indicating that toxicity is not determined solely by particle size [21].

The underlying mechanism involves oxidative stress and activation of the nuclear factor kappa B (NF- κ B)/NLRP3/ interleukin-1 β (IL-1 β)/ myosin light-chain kinase (MLCK) pathway, which promotes disruption of tight junctions and increases epithelial permeability [21,22]. Chen et al. [22] further demonstrated that reduced expression of ZO-1, occludin, and claudin-1 is associated with increased serum lipopolysaccharide (LPS), indicating enhanced translocation of bacterial products through the compromised barrier [22].

These effects are particularly relevant in IBD. In DSS-induced acute and chronic colitis, PS-MPs further reduced claudin-1 and occludin expression, increased intestinal permeability and serum LPS, and aggravated both epithelial and histological damage [18]. However, in this study, PS-MPs alone produced only minor effects in healthy mice [18], contrasting with other experiments that demonstrated clear barrier injury in the absence of pre-existing colitis [20–22]. This discrepancy may be attributable to differences in particle size, dose, exposure duration, or the specific intestinal segment assessed.

Sung et al. similarly demonstrated that PE-MPs aggravated DSS-induced colitis and decreased ZO-1 and occludin protein levels [19]. The authors also observed reduced E-cadherin expression, suggesting that MPs may impair both tight junctions and adherens junctions [19]. Notably, changes in mRNA and protein expression were not always consistent. ZO-1 protein levels decreased despite the absence of a significant additional reduction in its mRNA, indicating that post-transcriptional mechanisms may contribute to junctional damage [19].

Collectively, the available evidence indicates that MNPs weaken the epithelial barrier by downregulating or dysregulating ZO-1, occludin, claudin-1, and E-cadherin, resulting in increased intestinal permeability. In IBD, the presence of an already compromised barrier may heighten susceptibility to plastic particles, while additional junctional disruption may facilitate the translocation of LPS and other luminal antigens, thereby amplifying intestinal inflammation [16,18,19,22].

1.3. Oxidative stress and mitochondrial dysfunction

Oxidative stress is considered a principal mechanism underlying micro- and nanoplastic (MNP)-induced intestinal toxicity. In healthy mice, polystyrene (PS) particles increased reactive oxygen species (ROS) production throughout the duodenum, jejunum, ileum, and colon, with 50-nm particles generally exerting stronger effects than 500-nm particles. Co-exposure to both particle sizes further enhanced ROS generation and epithelial apoptosis. Antioxidant treatment reduced ROS levels, apoptosis, and intestinal permeability, supporting a causal relationship between oxidative stress and barrier injury [23].

Comparable effects were observed following exposure to polypropylene microplastics (PP-MPs). PP-MPs increased malondialdehyde (MDA) levels, indicating enhanced lipid peroxidation, and reduced glutathione (GSH), superoxide dismutase (SOD), glutathione peroxidase (GSH-Px), and catalase levels. These biochemical changes were accompanied by mitochondrial swelling, vacuolisation, loss of matrix, and disorganisation of mitochondrial cristae in colonic epithelial cells [24]. Smaller 8- μ m PP particles generally induced greater oxidative and mitochondrial damage than 70- μ m particles [24]. Furthermore, PP-MPs activated the mitochondrial apoptotic pathway, as evidenced by increased Bax, cleaved caspase-9, and cleaved caspase-3 levels, together with reduced Bcl-2 expression [24]. In human intestinal organoids, PS particles similarly increased ROS levels, reduced mitochondrial membrane potential, induced deoxyribonucleic acid (DNA) damage and epithelial-cell death, and impaired epithelial proliferation and maturation. Nanoscale particles were more toxic than microscale particles [25].

The relevance of these mechanisms to IBD is supported by studies employing inflamed or IBD-like intestinal models. In DSS-induced acute and chronic colitis, PS-MPs alone produced limited effects in healthy mice but significantly aggravated epithelial injury, inflammation, and intestinal permeability in animals with pre-existing colitis [18]. Although this study did not directly measure ROS, lipid peroxidation, or mitochondrial function, the findings suggest that an already inflamed intestine may be particularly susceptible to MNP-associated cellular stress [18].

More direct evidence was obtained using a model of Crohn's ileitis-like injury. Approximately 100-nm PS-NPs accumulated in mitochondria, increased mitochondrial ROS, reduced mitochondrial membrane potential, and caused membrane rupture, cristae disruption, and mitochondrial vacuolization [26]. Mitochondrial damage activated PTEN-induced kinase 1 (PINK1)/Parkin-dependent mitophagy. However,

lysosomal deacidification impaired autophagosome–lysosome fusion, resulting in increased autophagosome formation, reduced autolysosome formation, and accumulation of damaged mitochondria [26]. Restoration of mitophagic flux with rapamycin reduced epithelial-cell necrosis, indicating that mitophagy initiation may be protective, whereas failure to complete mitochondrial degradation promotes cell death [26].

The reported forms of epithelial-cell death varied between studies. Liang et al., Jia et al., and Xue et al. predominantly observed apoptosis associated with ROS production and mitochondrial dysfunction [23–25], whereas Xu et al. [26] found that PS-NPs primarily induced receptor-interacting serine/threonine-protein kinase 3 (RIPK3)/mixed lineage kinase domain-like pseudokinase (MLKL) - dependent necroptosis rather than apoptosis [26]. These findings are not necessarily contradictory and may reflect differences in particle size, polymer type, surface functionalisation, intestinal segment, exposure conditions, and experimental model. Collectively, the available evidence supports a mechanism in which MNP-induced ROS production, impaired antioxidant defence, lipid peroxidation, and mitochondrial damage result in defective mitochondrial quality control and epithelial-cell death. In the context of IBD, these processes may amplify pre-existing oxidative and inflammatory injury and further compromise the intestinal barrier [18,23–26].

1.4. Immune activation

Experimental studies indicate that MNPs can activate intestinal immune responses, although the magnitude of this effect varies considerably. In healthy rats, prolonged exposure to PS-MPs increased inflammatory-cell infiltration and colonic levels of IL-1 β , IL-6, and tumor necrosis factor alpha (TNF- α) through activation of the Toll-like receptor 4 (TLR4)/ myeloid differentiation primary response 88 (MyD88)/NF- κ B/ cyclooxygenase-2 (COX-2) pathway [27]. PS-MPs were also shown to induce oxidative stress and inflammation through the ROS-dependent NF- κ B/NLRP3/IL-1 β /MLCK pathway, with antioxidant treatment and inhibition of NLRP3 or MLCK attenuating these effects [21]. Thus, despite differences in upstream signalling, NF- κ B appears to be a central mediator of MP-induced intestinal inflammation [21,27].

However, immune activation in healthy animals was not consistently observed. Xie et al. reported only modest increases in colonic IL-1 β and IL-6, without comparable changes in the jejunum or liver [17]. Similarly, long-term exposure to polymethyl methacrylate nanoplastics (PMMA-NPs) did not induce spontaneous colonic inflammation in healthy mice [28]. These discrepancies may reflect differences in polymer type, particle size, dose, exposure duration, and tissue accumulation [17,21,27,28].

Direct macrophage activation has nevertheless been demonstrated in vitro. PMMA-NPs and PS-NPs were internalized by bone-marrow-derived macrophages and increased the expression of *Tnfa*, *Il6*, and *Il12b*, while changes in *Cd80* and *Cd86* depended on particle size and exposure duration [28]. These findings indicate that NPs can directly modify macrophage function, although such responses do not necessarily translate into overt intestinal inflammation in vivo [28].

The immunological effects of MNPs were more pronounced in animals with pre-existing intestinal injury. PS-MPs aggravated DSS-induced colitis, increasing weight loss, diarrhoea, bloody stools, histological damage, and inflammatory responses [17]. In acute and chronic colitis, exposure increased the expression of *Il1b*, *Il6*, *Tnfa*, *Tgfb*, *Mcp1*, *Nfkb*, *Nos2*, *Cox2*, *Tlr4*, *Il17a*, and *Il22* [18]. Acute colitis was associated with more pronounced systemic cytokine changes, whereas chronic exposure predominantly resulted in persistent local immune activation, including elevated serum LPS and colonic *Il17a* and *Il22* expression [18].

In chronic colitis, 100-nm PS-NPs increased inflammatory-cell infiltration, enhanced *Tnfa* expression, reduced *Il10*, and activated the mitogen-activated protein kinase (MAPK) pathway through phosphorylation of extracellular signal-regulated kinases 1 and 2 (ERK1/2), c-Jun N-terminal kinase (JNK), and p38 [29]. These findings suggest that MAPK signalling may act alongside NF- κ B- and NLRP3-dependent pathways [21,27,29].

Macrophage recruitment and polarization may also contribute to MNP-associated inflammation. Exposure to mixed PS particles increased colonic murine macrophage marker F4/80-positive macrophages and pro-inflammatory inducible nitric oxide synthase (iNOS) - positive cells, while Arg1-positive cells remained largely unchanged [30]. Proteomic analysis identified enrichment of M1 macrophage and neutrophil signatures [30]. In human peripheral blood mononuclear cells (PBMCs) -derived macrophages, smaller PS-NPs were internalized more efficiently, reduced cluster of differentiation 206 (CD206) and programmed death-ligand 1 (PD-L1), and increased the pro-inflammatory marker 4-1BBL [30]. Together with the findings of Schwarzfischer et al., these results suggest that MNPs may promote a pro-inflammatory macrophage phenotype [28,30].

Evidence concerning adaptive immunity remains limited. Increased IL17a and IL22 expression and the presence of lymphocytes in inflammatory infiltrates suggest possible involvement of IL-17- and IL-22-producing cells [18,30]. However, direct effects on Th1, Th2, Th17, regulatory T cells, or B cells have not been established.

Most studies indicate that MNPs intensify inflammation in DSS-induced or IBD-like models [17,18,29–31]. Nevertheless, long-term PMMA-NP exposure did not exacerbate acute DSS colitis despite pro-inflammatory macrophage responses in vitro [28], while Kopatz et al. observed macrophage infiltration and polarization but only a non-significant increase in overall histological severity [30]. Therefore, MNP-induced immune activation is not universal and depends on particle properties, exposure conditions, and the severity of underlying intestinal inflammation [17,18,28–31]. Overall, MNPs may amplify inflammation in susceptible intestines through TLR4/NF- κ B/COX-2, NF- κ B/NLRP3/IL-1 β , and MAPK signalling, accompanied by cytokine production and pro-inflammatory macrophage polarization [18,21,27,29,30].

1.5. Gut microbiota and microbial metabolites

Experimental studies indicate that MNPs can alter the composition and metabolic activity of the gut microbiota. In healthy mice, PS-MPs affected microbial diversity and the abundance of multiple bacterial taxa [13,14,32–34]. However, the direction of these changes was inconsistent. Lu et al. reported decreased Firmicutes, Oscillospira, and Anaerostipes, with increased Bifidobacterium [13], whereas Jin et al. observed reductions in Actinobacteria, Bifidobacterium, Lachnospira, and Blautia [14]. Tu et al. found increased Firmicutes, Lachnospiraceae, and microbial diversity [34], while other studies reported reduced diversity or no change in α -diversity [32,33,35]. These discrepancies may reflect differences in particle characteristics and exposure conditions.

Despite heterogeneous taxonomic findings, MNP exposure frequently reduced bacteria involved in short-chain fatty acid (SCFA) production, including Lachnospiraceae_NK4A136_group, Roseburia, Butyricicoccus, Anaerotruncus, and Ruminiclostridium [32,33]. PS-MPs also decreased fecal acetate, propionate, butyrate, and isobutyrate concentrations [34]. Notably, reduced SCFA levels occurred despite increased abundance of some SCFA-producing taxa, indicating that bacterial abundance may not directly reflect metabolic activity [34].

MNPs may also disrupt bile acid and lipid metabolism. PS-MPs exposure altered hepatic bile acid accumulation and the concentrations of taurocholic and muricholic acids [32–34]. However, results were inconsistent: Cyp7a1 expression was increased in one study [14] but inhibited in another, together with increased CYP8B1 and CYP27A1 expression and reduced bile acid transport through multidrug resistance-associated protein 2 and 3 (MRP2 and MRP3), and bile salt export pump (BSEP) [32]. Similarly, fecal taurocholate was increased by Tu et al. [34] but decreased by Jiang et al. [32]. PS-MPs also altered triglyceride and cholesterol concentrations and lipid-synthesis-related genes, although a causal link between dysbiosis and these systemic effects has not been established [13,32,34].

The relevance of these alterations to IBD was demonstrated by Zhai et al. Polydisperse PS-MPs reduced Lachnospiraceae_NK4A136_group and butyrate concentrations, inhibited peroxisome proliferator-activated receptor gamma (PPAR γ) signalling, and impaired mucus homeostasis without causing overt inflammation in healthy mice. However, they exacerbated DSS-induced colitis, while microbiota depletion eliminated this effect. Fecal microbiota transplantation transferred susceptibility to colitis, whereas butyrate supplementation attenuated inflammation through PPAR γ activation [36]. These findings support a causal microbiota–butyrate–PPAR γ pathway linking MP exposure with increased susceptibility to intestinal inflammation.

Environmentally derived polyvinyl chloride (PVC) fragments also aggravated chronic DSS-induced colitis and fibrosis. These effects were associated with increased Parasutterella, Clostridium sensu stricto 1, Colidextribacter, and Dubosiella, reduced Lactobacillus, and enrichment of a predicted isopropanol biosynthesis pathway [35]. However, the causal roles of these taxa and metabolites have not been confirmed. Overall, MNPs produce heterogeneous changes in microbial composition but may consistently disturb SCFA, bile acid, and lipid metabolism, potentially increasing susceptibility to microbiota-dependent inflammation in IBD [35,36].

1.6. Abnormal epithelial regeneration and cell death

MNPs may disrupt intestinal epithelial renewal by altering the balance between crypt-cell proliferation and differentiation. In healthy mice, exposure to 5- μ m PS-MPs increased crypt number and depth, as well as the expression of intestinal stem-cell markers, proliferating cell nuclear antigen (PCNA), and c-Myc, while reducing goblet-cell numbers. Organoid experiments attributed these effects to excessive Notch activation, which suggests a shift toward epithelial overproliferation and impaired secretory differentiation [17].

The relevance of this mechanism to IBD is complex because Notch signaling can have both harmful and protective effects. Increased Notch activity, enhanced epithelial proliferation, and goblet-cell depletion have been observed in DSS colitis models and in the crypts of patients with UC [37]. In contrast, inhibition of Notch signaling during the regenerative phase exacerbated colitis by impairing epithelial repair, while deletion of the epithelial *Rbpj* gene halted crypt-cell turnover, increased bacterial translocation, and induced chronic colitis [37,38]. Therefore, excessive or prolonged Notch activation may promote abnormal proliferation, whereas insufficient signaling impairs effective epithelial regeneration [17,37,38].

NPs may also increase epithelial cell loss via RIPK3/MLKL-dependent necroptosis. Exposure to approximately 100-nm PS-NPs induced Crohn's ileitis-like lesions in mice and activated RIPK3 and MLKL in ileal epithelial cells and Caco-2 cells. Necrosis increased without a corresponding rise in apoptosis, particularly following exposure to aminated PS-NPs [26]. Mechanistically, NPs accumulated in mitochondria and lysosomes, induced mitochondrial damage, and inhibited mitophagic flux. Treatment with rapamycin partially reduced epithelial necrosis [26].

This mechanism is relevant to IBD, as increased levels of RIPK3 and phosphorylated MLKL (MLKL) have been detected in inflamed intestinal biopsies from patients with CD and UC. Activation of RIPK3/MLKL increased the expression of IL-1, IL-8, IL-33, high-mobility group box 1 (HMGB1), NF- κ B signaling, and NLRP3 inflammasome activity, while reducing the levels of E-cadherin, occludin, and ZO-1. Administration of necrostatin-1 attenuated these effects, supporting a role for necroptosis in sustaining inflammation and barrier dysfunction [39].

Repeated cycles of epithelial cell death followed by compensatory proliferation may establish a microenvironment that promotes chronic inflammation and neoplastic transformation [40]. In an azoxymethane (AOM)/DSS model, exposure to PS-MPs increased tumor number, tumor prevalence, and local inflammatory infiltration [41]. However, PS-MPs did not significantly affect Mki67 or Bax expression [41], which contrasts with the epithelial overproliferation reported by Xie et al. [17]. These differences may result from distinct models, exposure durations, intestinal regions, and measured endpoints. Consequently, although MNPs may contribute to colitis-associated carcinogenesis, direct evidence linking them to altered proliferation or apoptosis remains limited and partially inconsistent [40,41].

Taken together, the available evidence suggests that MNPs can disrupt intestinal homeostasis in previously healthy models, but their adverse effects are generally more pronounced in the presence of pre-existing inflammation or IBD-like injury. A comparative summary of these effects across the six discussed mechanisms is presented in Table 1.

Table 1. Comparative effects of MNPs on intestinal homeostasis in healthy models and models with pre-existing intestinal inflammation

Comparative effects of MNPs in healthy and IBD-like intestinal models		
Mechanism	Healthy intestinal models	IBD-like/inflamed models
Mucus layer	Reduced mucus secretion and altered mucin expression or goblet-cell function.	Greater mucus depletion and reduced mucin coverage.
Epithelial barrier	Decreased ZO-1, occludin and claudin-1; increased permeability.	Further junctional damage, LPS translocation and epithelial injury.
Oxidative stress	Increased ROS, lipid peroxidation and mitochondrial dysfunction.	Stronger mitochondrial injury, impaired mitophagy and epithelial-cell death.
Immune activation	Usually mild or variable cytokine and NF- κ B/NLRP3 activation.	Pronounced cytokine production, inflammatory infiltration and macrophage activation.
Gut microbiota	Dysbiosis and reduced SCFA-producing bacteria and metabolites.	Microbiota-dependent worsening of colitis, including disruption of the butyrate-PPAR γ axis.
Regeneration and cell death	Abnormal crypt proliferation, impaired differentiation and apoptosis.	Impaired epithelial repair, necroptosis and possible promotion of colitis-associated carcinogenesis.

Abbreviations: IBD, inflammatory bowel disease; LPS, lipopolysaccharide; ROS, reactive oxygen species; SCFA, short-chain fatty acid

2. Evidence from Experimental Models

2.1. Effects of MNPs in animals without pre-existing intestinal inflammation

Studies in animals without pre-existing intestinal inflammation provide inconsistent evidence that MNPs alone can induce clinically significant intestinal disease. Reported effects include dysbiosis, mucus and barrier impairment, histological injury, and inflammatory-cell infiltration. However, most studies did not observe the full phenotype of experimental colitis, including substantial weight loss, diarrhoea, rectal bleeding, colon shortening, ulceration, or extensive crypt destruction [13,14,21,33,35,42–44]. Thus, MNPs appear more likely to disturb intestinal homeostasis and induce low-grade inflammation than to independently cause an IBD-like condition.

In healthy mice, PS-MPs reduced mucus secretion and altered microbial composition without inducing overt colitis [13]. Similar exposure produced mucus depletion, dysbiosis, and metabolic abnormalities, with stronger effects on MUC2 expression and intestinal transport at higher concentrations [14]. Nevertheless, neither study demonstrated clinical or histological changes comparable to DSS-induced colitis [13,14]. Dose was an important determinant: PE-MPs caused microbiological and immunological alterations at several exposure levels, whereas significant colonic and duodenal inflammation was primarily observed at the highest dose [42].

Particle characteristics also influenced toxicity. Aminated PS particles caused greater gastrointestinal injury than carboxylated or pristine particles, indicating that surface reactivity may be as important as polymer type or particle size [33]. Exposure duration was similarly relevant. Long-term PS-MPs administration produced dysbiosis, increased permeability, and tissue inflammation [44], whereas a comparison of 14- and 28-day exposures showed that barrier dysfunction, mucin and claudin-1 depletion, leukocyte infiltration, and immune abnormalities became more pronounced over time [45]. These findings suggest that prolonged exposure may overcome initially limited or compensatory responses [44,45].

The relationship between particle size and intestinal toxicity was not linear. Although smaller particles produced stronger effects in some experiments [45], 5- μ m PS-MPs caused greater barrier damage and

inflammatory infiltration than 0.2- or 1- μ m particles in another study [21]. Different effects were also observed for 0.5- and 50- μ m particles without a consistent size-dependent pattern [13]. Particle number, surface area, aggregation, retention, and surface chemistry may therefore be more informative than size alone [13,21,33,45].

Several studies reported little or no intestinal injury despite particle uptake. Long-term exposure to 50-nm or 1- μ m PS particles resulted in translocation and accumulation in distant organs but did not impair intestinal health [43]. Similarly, a mixture of differently sized PS particles caused no overt histopathological damage after short-term administration [30]. These findings contrast with studies demonstrating barrier dysfunction or inflammation [21,33,45]. Environmentally derived PVC fragments also increased oxidative and inflammatory markers without producing clear colonic histomorphological lesions, showing that molecular stress does not necessarily translate into overt disease [35].

The biological importance of these subclinical changes becomes clearer in animals with pre-existing intestinal injury. PS-MPs caused only minor effects in healthy mice but markedly aggravated colon shortening, mucus loss, permeability, inflammation, and histological damage in acute and chronic DSS colitis [18]. Similarly, exposure produced only mild cytokine changes in healthy animals but substantially worsened clinical and histological colitis after DSS treatment [17]. Subtle alterations in mucins and lamina propria cellularity also progressed to more extensive inflammation and ulceration following DSS administration [16]. Environmentally derived PVC fragments aggravated chronic colitis, fibrosis, and neutrophil recruitment [35], while mixed PS particles produced increased macrophage infiltration and a non-significant trend toward greater histological severity [30].

Overall, most studies indicate that MNPs can exacerbate DSS-induced disease [16–18,35], although long-term PS exposure did not affect colitis severity in one study and another demonstrated only a non-significant aggravating trend [30,43]. These discrepancies likely reflect differences in polymer type, surface modification, dose, administration route, exposure duration, DSS protocol, and animal microbiota. Current evidence therefore does not support MNPs as sufficient independent initiators of IBD. Instead, they may induce dysbiosis, barrier dysfunction, and subclinical inflammation, particularly after high-dose or prolonged exposure [13,14,21,33,35,42,44,45], thereby reducing intestinal resilience and increasing susceptibility to subsequent inflammatory injury [16–18,30,35,43].

2.2. Effects of MNPs in experimental models of IBD and related intestinal complications

Research in healthy animal models demonstrates that exposure to MNPs typically does not induce overt colitis. Most studies report no significant body-weight loss, ulceration, or severe histological inflammation. However, subclinical abnormalities affecting goblet cells, mucus production, epithelial renewal, inflammatory markers, and gut microbiota have been observed [16,17,30,35,36,41]. For instance, polydisperse PS-MPs reduced Muc2 expression without causing inflammation under basal conditions [36], while environmentally sourced PVC-MPs increased colonic myeloperoxidase activity and altered inflammatory gene expression in the absence of visible tissue injury [35]. In contrast, long-term exposure to PS or polymethacrylate nanoparticles did not significantly affect intestinal morphology, permeability, or homeostasis in two studies [28,43]. Collectively, these findings suggest that MNPs are more likely to increase intestinal susceptibility to subsequent injury rather than independently induce IBD-like inflammation.

2.2.1. Acute experimental colitis

The majority of studies indicate that MNP exposure exacerbates acute DSS-induced colitis. Prior exposure to 5- μ m PS-MPs resulted in increased body-weight loss, diarrhea, rectal bleeding, histopathological injury, and inflammation following DSS administration [17]. Comparable results were observed with both 5- μ m PS-MPs and a polydisperse mixture of 5–200- μ m particles, which did not induce overt inflammation in healthy animals but heightened the severity of subsequent colitis [16,36].

Simultaneous administration of MNPs and DSS generally intensified intestinal injury. PS-MPs led to increased colon shortening, histological damage, inflammatory responses, mucus loss, and intestinal permeability [18]. PE-MPs fragments elevated disease activity and caused dose-dependent epithelial, crypt, and goblet-cell injury, although they did not further reduce colon length [19]. In mice with DSS-induced intestinal immune imbalance, PS-MPs accumulation was substantially increased and associated with more severe mucosal injury, heightened inflammatory cytokine expression, and disruptions in microbial and metabolic profiles [46]. A mixture of differently sized PS particles also mildly aggravated DSS-induced colitis,

resulting in greater accumulation in inflamed tissues and changes in macrophage populations and gut microbiota [30].

However, some studies did not corroborate these findings. Schwarzfischer et al. found that PS-NPs and PS-MPs traversed the intestinal barrier but did not exacerbate either acute or chronic DSS-induced colitis [43]. Likewise, six months of PMMA nanoparticle exposure did not alter intestinal histology, epithelial permeability, colon length, or disease severity following DSS administration [28]. These inconsistencies may be attributable to variations in polymer type, particle size, surface characteristics, dosage, tissue accumulation, and timing of exposure.

In summary, the majority of evidence indicates that MNPs can exacerbate acute DSS-induced colitis; however, this effect is not universal and cannot be explained solely by particle size or exposure duration [16–19,28,30,36,43,46].

2.2.2. Chronic and recurrent colitis

Repeated DSS cycles have been employed to evaluate the effects of MNPs during recurrent intestinal injury. Luo et al. demonstrated that 5- μ m PS-MPs increased histopathological damage, local inflammatory responses, mucus loss, and epithelial permeability, as well as delayed recovery from chronic colitis [18]. Similarly, 100-nm PS-NPs aggravated colonic epithelial injury, elevated TNF- α expression, and reduced IL-10 expression in mice subjected to three DSS cycles [29].

Prolonged administration of 5- μ m PS-MPs also increased the prevalence of pathological lesions, ulcers, and crypt abscesses in chronic colitis [41]. However, the degree of inflammatory infiltration, goblet-cell volume, mucin content, epithelial proliferation markers, and serum cytokines did not differ significantly between DSS-treated mice with and without PS-MPs [41]. These findings suggest that MNPs may increase the extent of intestinal lesions without consistently affecting all inflammatory or molecular endpoints.

Environmentally sourced particles elicited similar or more pronounced effects. Irregular PVC fragments increased body-weight loss, epithelial injury, inflammatory infiltration, and neutrophil recruitment in chronic DSS colitis [35]. A mixture of environmental PP, PET, PS, and PE fragments also exacerbated colonic inflammation, particularly at the medium exposure dose [47]. Nonetheless, one study reported no aggravation of chronic DSS colitis following long-term PS exposure [43].

Overall, the majority of studies indicate that MNPs exacerbate recurrent colitis, although results regarding mucus, systemic cytokines, and epithelial markers remain inconsistent [18,29,35,41,43,47].

2.2.3. CD-like ileitis and fibrosis

Evidence specifically addressing CD is limited. Xu et al. demonstrated that approximately 100-nm PS-NPs induced ileal structural injury, neutrophil accumulation, increased inflammatory mediators, and epithelial necroptosis in otherwise healthy mice [26]. Surface-modified PS-COOH and PS-NH₂ particles produced more pronounced effects than unmodified particles [26]. The authors characterized these abnormalities as Crohn's ileitis-like; however, the model did not replicate the full phenotype of CD, such as transmural inflammation, granulomas, strictures, or fistulas.

Evidence for intestinal fibrosis primarily derives from a chronic DSS study utilizing environmental PVC fragments. PVC exposure increased the expression of extracellular matrix remodeling genes and type III collagen deposition in the colon [35]. However, these results were obtained in the context of colonic DSS injury rather than a model of stricturing ileal CD. Consequently, the role of MNPs in fibrostenotic complications remains uncertain.

2.2.4. Colitis-associated carcinogenesis

Three studies have assessed MNP exposure in azoxymethane/DSS models of colitis-associated cancer. PS-NPs increased tumor number, Ki-67 expression, oxidative stress, and DNA damage [48]. Similarly, long-term exposure to 5- μ m PS-MPs elevated tumour number, tumour prevalence, and local inflammatory infiltration, although serum cytokines and several epithelial gene markers remained unchanged [41]. A realistic mixture of environmental PP, PET, PS, and PE fragments also increased tumor burden and the expression of Cyclin D1 and MYC, particularly at the highest dose [47].

Collectively, all available AOM/DSS studies indicate that MNPs can promote the progression of inflammation-associated colorectal cancer [41,47,48]. However, these models do not establish that MNPs independently initiate carcinogenesis, as all animals were exposed to both a carcinogen and DSS.

Animal studies generally suggest that MNPs do not independently induce overt colitis in healthy animals but may cause subclinical disturbances that increase susceptibility to intestinal injury. Most DSS-based studies have reported more severe inflammation, epithelial damage, ulceration, or delayed recovery following MNP exposure, although some studies found no aggravating effect [16–19,28–30,35,36,41,43,46,47]. The evidence is strongest for colon-dominant DSS-induced inflammation and colitis-associated carcinogenesis, while data regarding CD-like ileitis, fibrosis, and stricturing complications remain limited [26,35,41,47,48]. At present, MNPs should be regarded as potential modifiers of intestinal inflammation rather than established independent causes of IBD.

3. Evidence from Human Studies

Evidence from human studies linking MNPs to IBD remains limited. Existing research includes direct measurements of MPs in stool or intestinal tissue, alongside transcriptomic and computational analyses that do not directly assess exposure. Furthermore, current clinical investigations focus on MPs, and direct evidence regarding NPs in IBD is currently unavailable.

MPs are frequently detected in individuals without gastrointestinal disease. In a cohort of 24 healthy young men, MPs were identified in 23 stool samples, with concentrations ranging from 1 to 36 particles per gram of wet stool. Polypropylene was the most prevalent polymer, and MPs abundance correlated with consumption of packaged water and beverages [49]. These results suggest that dietary habits and plastic packaging significantly influence fecal MPs concentrations and should be accounted for when interpreting studies of IBD.

3.1. Studies involving mixed IBD populations

Yan et al. conducted a direct comparison of stool samples from 52 patients with IBD and 50 healthy controls. Mean MPs concentrations were significantly higher in the IBD group than in controls, measuring 41.8 and 28.0 particles per gram of dry stool, respectively. Patients with IBD exhibited a greater proportion of particles smaller than 50 μm . PET and polyamide were the most frequently detected polymers, with PET representing a higher proportion of particles in IBD patients compared to healthy participants [50].

In patients with complete clinical data, fecal MPs concentration showed a positive correlation with the Harvey–Bradshaw Index in CD and the Mayo score in UC. However, MPs concentrations and polymer profiles were not reported separately for CD and UC, which precludes direct comparison between the two diseases [50].

Both Yan et al. and Zhang et al. associated fecal MPs abundance with consumption of plastic-packaged beverages. Yan et al. further reported higher concentrations among participants who consumed takeaway food or experienced frequent dust exposure [49,50]. Therefore, variations in diet, packaging use, and living conditions may partially account for the increased MPs burden observed in IBD.

Caution is warranted when comparing the numerical results of these studies. Zhang et al. reported concentrations per gram of wet stool and utilized Fourier-transform infrared spectroscopy, while Yan et al. analyzed dry stool using micro-Raman spectroscopy and detected smaller particles [49,50]. As a result, differences in absolute particle counts and dominant polymers may arise from methodological rather than biological variation.

3.2. UC

Direct evidence specific to UC is primarily limited to the positive correlation between fecal MPs concentration and Mayo score reported by Yan et al. [50]. To date, no dedicated UC cohort has directly quantified MNPs in blood or intestinal biopsies, nor examined their relationship with calprotectin, C-reactive protein, histological activity, or endoscopic severity.

Yang et al. integrated public transcriptomic datasets from patients with UC with predicted PET-related targets, machine learning, single-cell analysis, and molecular docking. Four genes - cathepsin K (CTSK), N-acyl ethanolamine acid amidase (NAAA), PDE4B, and PFKFB3 - were identified as potential links between PET-MPs and UC. CTSK, PDE4B, and PFKFB3 were upregulated, while NAAA was downregulated in UC samples [51]. These expression patterns were subsequently validated in a DSS-induced mouse model, where PET-MPs exacerbated colitis compared to DSS treatment alone [51].

Ye et al. performed a separate computational analysis and identified 17 potential PET-associated targets in UC and 14 final hub genes across IBD [52]. These targets showed limited overlap with those reported by Yang et al. [51,52]. This inconsistency likely reflects differences in datasets, target-prediction methods, and machine-learning approaches, rather than conflicting clinical observations. Notably, neither study measured PET-MPs in patient samples; thus, their findings should be regarded as hypothesis-generating rather than evidence of human exposure [51,52].

3.3. CD

In the fecal study conducted by Yan et al., MPs concentration correlated positively with the Harvey–Bradshaw Index, indicating an association with CD activity [50]. More direct tissue-level evidence was provided by Wu et al., who examined intestinal and mesenteric adipose tissue from ten patients undergoing surgery for complicated CD [53].

MPs were detected in involved ileal segments, adjacent uninvolved ileum, creeping fat, and mesenteric adipose tissue. Their abundance was greater in fibrotic lesions than in surrounding tissues and correlated positively with fibrosis severity. Approximately one-third of the detected particles measured 20–50 μm [53]. These results suggest that MPs may be retained not only in the intestinal lumen but also within the intestinal wall and adjacent mesentery.

The findings of Yan et al. and Wu et al. are directionally consistent, as both studies associated a greater MPs burden with more severe CD [50,53]. However, the studies evaluated different outcomes: fecal MPs excretion and clinical activity in one, and tissue accumulation and fibrosis in the other. The tissue study was further limited to patients requiring surgery, lacked a healthy intestinal control group, and included only ten individuals [53].

Wu et al. also associated frequent invasive gastrointestinal examinations with increased tissue MPs accumulation [53]. This finding may reflect procedure-related exposure; however, patients with more severe disease typically undergo more investigations. Consequently, confounding by disease severity cannot be excluded.

Discussion:

The available evidence indicates a biologically plausible relationship between micro- and nanoplastic exposure and intestinal inflammation. Experimental studies demonstrate that MNPs may disrupt the mucus layer and epithelial junctions, increase intestinal permeability, induce oxidative and mitochondrial stress, activate inflammatory signalling pathways, alter the gut microbiota, and impair epithelial regeneration. Importantly, these effects are generally more pronounced in animals with pre-existing intestinal injury than in healthy animals. In most studies, MNP exposure alone caused mild, subclinical, or inconsistent abnormalities, whereas additional exposure during chemically induced colitis resulted in greater mucosal damage, inflammatory infiltration, permeability, delayed healing, and, in some models, fibrosis or tumour development [16–19,26,29,35,36,41,47,48]. These observations support the interpretation that MNPs may act primarily as environmental modifiers that reduce intestinal resilience and amplify existing inflammatory processes rather than as independent and sufficient causes of IBD.

Human findings are directionally consistent with this interpretation, although the evidence remains considerably more limited. Yan et al. reported higher fecal MPs concentrations in patients with IBD than in healthy controls and demonstrated positive correlations with the Harvey–Bradshaw Index in CD and the Mayo score in UC [50]. Wu et al. subsequently detected MPs in involved and macroscopically uninvolved ileal tissue, creeping fat, and mesenteric adipose tissue obtained from patients undergoing surgery for complicated CD. Particle abundance was greater in fibrotic lesions and correlated with the severity of fibrosis [53]. Together,

these studies suggest that MPs burden may be associated with both inflammatory activity and structural intestinal complications. However, they evaluated different biological compartments and outcomes. Fecal particle concentration reflects luminal exposure and elimination, whereas tissue detection may indicate retention, penetration, or translocation. Consequently, the results cannot be interpreted as measurements of a single, uniform “body burden” of MPs.

A central limitation is the inability to establish the direction of the observed associations. Greater dietary or environmental exposure to MNPs may promote barrier dysfunction, microbial dysbiosis, immune activation, and disease exacerbation. Conversely, active IBD may itself facilitate particle accumulation or alter fecal MP concentrations. Increased epithelial permeability, ulceration, mucus disruption, and inflammatory tissue remodelling may allow particles to penetrate more deeply into the intestinal wall or adjacent mesentery. Altered intestinal transit, diarrhoea, reduced absorptive capacity, and changes in stool water content may also influence the number of particles measured per gram of stool. Therefore, a high fecal MP concentration may represent greater ingestion, altered intestinal elimination, or both. Similarly, the accumulation of MPs within fibrotic CD tissue may contribute to persistent inflammation and extracellular matrix remodelling, but established fibrosis and impaired tissue clearance may also promote the secondary retention of particles [12,50,53]. The current relationship should therefore be considered potentially bidirectional rather than unidirectional.

Several behavioural and clinical factors may additionally confound this association. Patients with active or complicated IBD frequently modify their diet and may consume greater amounts of bottled water, packaged beverages, takeaway food, processed products, or specialised enteral nutrition. Each of these exposures may increase contact with plastic packaging. Hospitalisation, medication packaging, diagnostic procedures, endoscopy, surgery, and other medical interventions may represent additional sources of exposure. Wu et al. observed an association between frequent invasive gastrointestinal examinations and tissue MP accumulation [53]. However, patients with more severe disease are also more likely to undergo repeated examinations, making it difficult to distinguish procedure-related exposure from confounding by disease severity. Other factors, including age, place of residence, occupational or household dust exposure, smoking, medication use, socioeconomic status, and dietary patterns, have not been comprehensively controlled in the available studies.

Methodological heterogeneity further limits the interpretation and comparison of human findings. Studies differ in sample collection and preparation, digestion procedures, contamination control, analytical platforms, particle-size detection thresholds, polymer identification, and reporting units. For example, fecal concentrations have been expressed per gram of wet or dry stool, while Fourier-transform infrared spectroscopy and micro-Raman spectroscopy differ in their ability to detect smaller particles [49,50]. Consequently, variation in particle counts and dominant polymer types may partly reflect analytical differences rather than true biological variation. Moreover, existing clinical studies have focused almost exclusively on MPs, while direct evidence regarding NPs in patients with IBD is currently unavailable.

Overall, the findings support an association between MPs, IBD activity, and CD-related fibrosis, but they do not establish causality. Small sample sizes, cross-sectional designs, selected surgical populations, incomplete exposure assessment, and the absence of prospective pre-diagnostic data prevent definitive conclusions. At present, MNPs should be regarded as potential environmental modifiers of intestinal inflammation and disease progression rather than confirmed etiological agents of UC or CD. A simplified overview of the experimental and human evidence, together with the principal limitations affecting its interpretation, is presented in Figure 1.

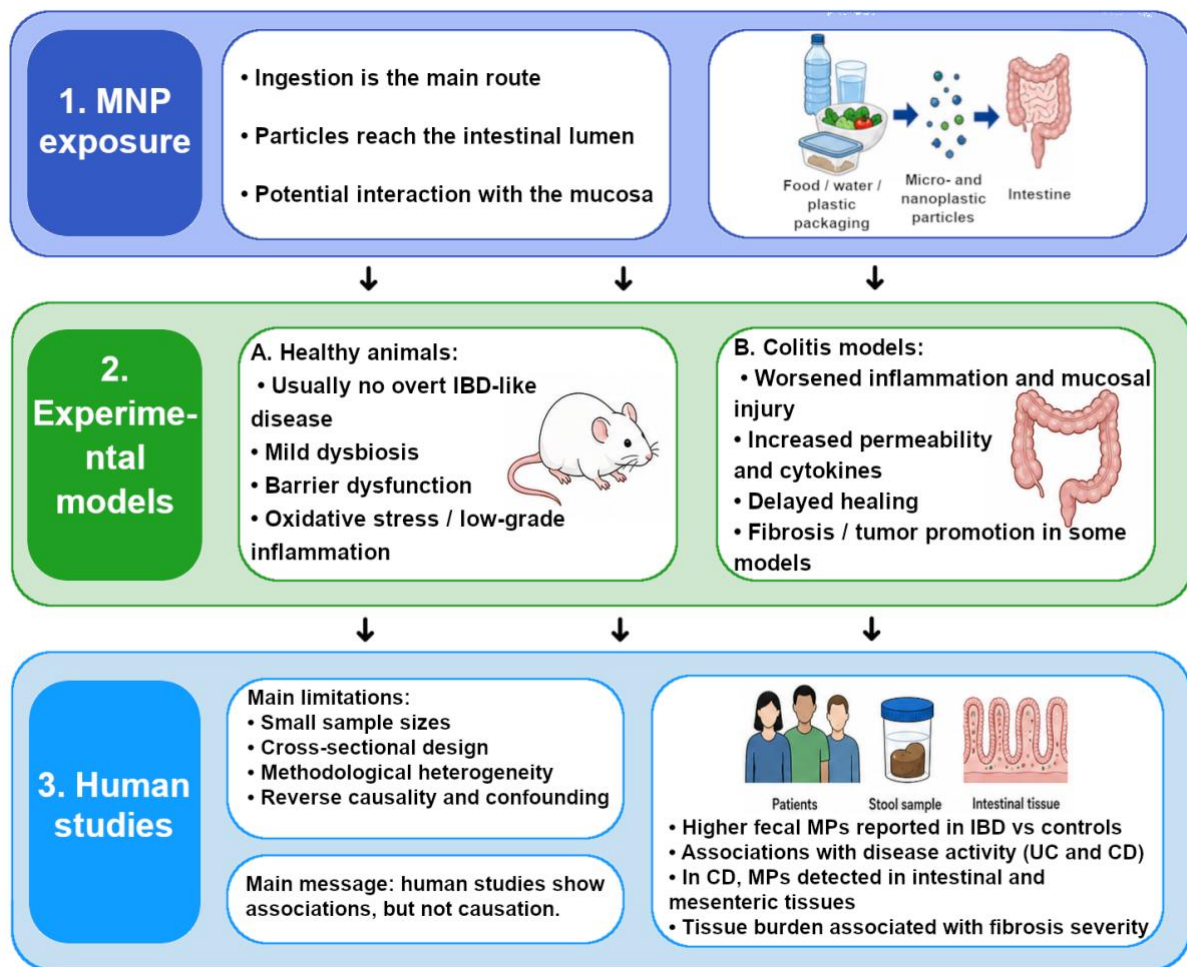


Fig. 1. Micro-and Nanoplastics in IBD: Simplified overview of experimental and human evidence linking MNPs with IBD.

Research Gaps and Future Directions

Current evidence on the relationship between MNPs and IBD remains limited. Large prospective cohorts, particularly studies conducted before IBD diagnosis, are needed to clarify whether MNP exposure precedes disease development or results from altered intestinal permeability, diet, treatment, and disease activity.

Future studies should analyze UC and CD separately and account for CD location and behavior, including inflammatory, stricturing, and penetrating phenotypes. Pediatric populations also require greater attention.

A major limitation is the lack of standardized methods for sample collection, preparation, detection, and reporting. Laboratory contamination, differences in analytical techniques, particle-size thresholds, doses, and reporting units substantially reduce comparability between studies.

Experimental research relies excessively on pristine PS spheres, which poorly reflect real-world exposure. Future models should include irregular, secondary, environmentally weathered particles, mixed polymers, fibers, additives, and surface contaminants, using exposure ranges relevant to humans.

Finally, studies should evaluate whether reducing plastic exposure influences IBD activity or progression. Diet, medication, smoking, hospitalization, medical procedures, packaged food consumption, and lifestyle factors should be carefully considered as potential confounders.

Conclusions

MNPs can affect several mechanisms relevant to IBD, including mucus and epithelial barrier disruption, oxidative stress, immune activation, dysbiosis, and abnormal epithelial regeneration.

Animal studies generally indicate that MNPs aggravate intestinal damage and inflammation in organisms with pre-existing susceptibility or experimental colitis. However, evidence that MNPs independently induce IBD-like disease remains considerably weaker.

Human studies have identified associations between MP burden, IBD activity, and fibrosis in CD, but their cross-sectional design, small sample sizes, confounding factors, and possible reverse causality prevent causal conclusions.

MNPs should therefore currently be regarded as potential environmental modifiers of IBD rather than confirmed causes of the disease.

Conflict of Interest: The authors declare that they have no conflicts of interest.

Abbreviations

AB-PAS, Alcian blue-periodic acid-Schiff
AOM, azoxymethane
BSEP, bile salt export pump
CD, Crohn's disease
CD206, cluster of differentiation 206
COX-2, cyclooxygenase-2
CTSK, cathepsin K
DNA, deoxyribonucleic acid
DSS, dextran sulfate sodium
ERK1/2, extracellular signal-regulated kinases 1 and 2
GSH, reduced glutathione
GSH-Px, glutathione peroxidase
HMGB1, high-mobility group box 1
IBD, inflammatory bowel disease
IL, interleukin
iNOS, inducible nitric oxide synthase
JNK, c-Jun N-terminal kinase
LPS, lipopolysaccharide
MAPK, mitogen-activated protein kinase
MDA, malondialdehyde
MLCK, myosin light-chain kinase
MLKL, mixed lineage kinase domain-like pseudokinase
MNPs, micro- and nanoplastics
MPs, microplastics
mRNA, messenger RNA
MRP2, multidrug resistance-associated protein 2
MRP3, multidrug resistance-associated protein 3
MyD88, myeloid differentiation primary response 88
NAAA, N-acyl ethanolamine acid amidase
NF- κ B, nuclear factor kappa B
NPs, nanoplastics
PBMCs, peripheral blood mononuclear cells
PCNA, proliferating cell nuclear antigen
PD-L1, programmed death-ligand 1
PE, polyethylene
PET, polyethylene terephthalate
PDE4B, phosphodiesterase 4B

PFKFB3, 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase 3
 PINK1, PTEN-induced kinase 1
 PMMA, polymethyl methacrylate
 PP, polypropylene
 PPAR γ , peroxisome proliferator-activated receptor gamma
 PS, polystyrene
 PVC, polyvinyl chloride
 RIPK3, receptor-interacting serine/threonine-protein kinase 3
 ROS, reactive oxygen species
 SCFA, short-chain fatty acids
 SOD, superoxide dismutase
 Th, T helper
 TLR4, Toll-like receptor 4
 TNF- α , tumor necrosis factor alpha
 UC, ulcerative colitis
 ZO-1, zonula occludens-1

REFERENCES

1. Geyer, R., Jambeck, J. R., & Law, K. L. (2017). Production, use, and fate of all plastics ever made. *Science Advances*, 3(7), e1700782. <https://doi.org/10.1126/sciadv.1700782>
2. Hartmann, N. B., Hüffer, T., Thompson, R. C., Hassellöv, M., Verschoor, A., Daugaard, A. E., Rist, S., Karlsson, T., Brennholt, N., Cole, M., Herrling, M. P., Hess, M. C., Ivleva, N. P., Lusher, A. L., & Wagner, M. (2019). Are we speaking the same language? recommendations for a definition and categorization framework for plastic debris. *Environmental Science & Technology*, 53(3), 1039–1047. <https://doi.org/10.1021/acs.est.8b05297>
3. Vethaak, A. D., & Legler, J. (2021). Microplastics and human health. *Science*, 371(6530), 672–674. <https://doi.org/10.1126/science.abe5041>
4. Schwabl, P., Köppel, S., Königshofer, P., Bucsics, T., Trauner, M., Reiberger, T., & Liebmann, B. (2019). Detection of various microplastics in human stool. *Annals of Internal Medicine*, 171(7), 453–457. <https://doi.org/10.7326/M19-0618>
5. Hartmann, C., Lomako, I., Schachner, C., El Said, E., Abert, J., Satrapa, V., Kaiser, A.-M., Walch, H., & Köppel, S. (2024). Assessment of microplastics in human stool: A pilot study investigating the potential impact of diet-associated scenarios on oral microplastics exposure. *Science of The Total Environment*, 951, 175825. <https://doi.org/10.1016/j.scitotenv.2024.175825>
6. Leslie, H. A., Van Velzen, M. J. M., Brandsma, S. H., Vethaak, A. D., Garcia-Vallejo, J. J., & Lamoree, M. H. (2022). Discovery and quantification of plastic particle pollution in human blood. *Environment International*, 163, 107199. <https://doi.org/10.1016/j.envint.2022.107199>
7. Marfella, R., Prattichizzo, F., Sardu, C., Fulgenzi, G., Graciotti, L., Spadoni, T., D'Onofrio, N., Scisciola, L., La Grotta, R., Frigé, C., Pellegrini, V., Municinò, M., Siniscalchi, M., Spinetti, F., Vigliotti, G., Vecchione, C., Carrizzo, A., Accarino, G., Squillante, A., ... Paolisso, G. (2024). Microplastics and nanoplastics in atheromas and cardiovascular events. *New England Journal of Medicine*, 390(10), 900–910. <https://doi.org/10.1056/NEJMoa2309822>
8. Ng, S. C., Shi, H. Y., Hamidi, N., Underwood, F. E., Tang, W., Benchimol, E. I., Panaccione, R., Ghosh, S., Wu, J. C. Y., Chan, F. K. L., Sung, J. J. Y., & Kaplan, G. G. (2017). Worldwide incidence and prevalence of inflammatory bowel disease in the 21st century: A systematic review of population-based studies. *The Lancet*, 390(10114), 2769–2778. [https://doi.org/10.1016/S0140-6736\(17\)32448-0](https://doi.org/10.1016/S0140-6736(17)32448-0)
9. Alatab, S., Sepanlou, S. G., Ikuta, K., Vahedi, H., Bisignano, C., Safiri, S., Sadeghi, A., Nixon, M. R., Abdoli, A., Abolhassani, H., Alipour, V., Almadi, M. A. H., Almasi-Hashiani, A., Anushiravani, A., Arabloo, J., Atique, S., Awasthi, A., Badawi, A., Baig, A. A. A., ... Naghavi, M. (2020). The global, regional, and national burden of inflammatory bowel disease in 195 countries and territories, 1990–2017: A systematic analysis for the global burden of disease study 2017. *The Lancet Gastroenterology & Hepatology*, 5(1), 17–30. [https://doi.org/10.1016/S2468-1253\(19\)30333-4](https://doi.org/10.1016/S2468-1253(19)30333-4)

10. Kaplan, G. G., & Windsor, J. W. (2021). The four epidemiological stages in the global evolution of inflammatory bowel disease. *Nature Reviews Gastroenterology & Hepatology*, 18(1), 56–66. <https://doi.org/10.1038/s41575-020-00360-x>
11. Ananthakrishnan, A. N., Gerasimidis, K., Ho, S.-M., Mayer, E., Pollock, J., Soni, S., Wu, G. D., Benyacoub, J., Ali, B., Favreau, A., Smith, D. E., Oh, J., Heller, C., Hurtado-Lorenzo, A., Moss, A., & Croitoru, K. (2024). Challenges in IBD research 2024: Environmental triggers. *Inflammatory Bowel Diseases*, 30(Supplement_2), S19–S29. <https://doi.org/10.1093/ibd/izae085>
12. Agrawal, M., Vianello, A., Picker, M., Simon-Sánchez, L., Chen, R., Estevinho, M. M., Weinstein, K., Lykkemark, J., Jess, T., Peter, I., Colombel, J.-F., Allin, K. H., & Vollertsen, J. (2024). Micro- and nano-plastics, intestinal inflammation, and inflammatory bowel disease: A review of the literature. *Science of The Total Environment*, 953, 176228. <https://doi.org/10.1016/j.scitotenv.2024.176228>
13. Lu, L., Wan, Z., Luo, T., Fu, Z., & Jin, Y. (2018). Polystyrene microplastics induce gut microbiota dysbiosis and hepatic lipid metabolism disorder in mice. *Science of The Total Environment*, 631–632, 449–458. <https://doi.org/10.1016/j.scitotenv.2018.03.051>
14. Jin, Y., Lu, L., Tu, W., Luo, T., & Fu, Z. (2019). Impacts of polystyrene microplastic on the gut barrier, microbiota and metabolism of mice. *Science of The Total Environment*, 649, 308–317. <https://doi.org/10.1016/j.scitotenv.2018.08.353>
15. Sun, H., Chen, N., Yang, X., Xia, Y., & Wu, D. (2021). Effects induced by polyethylene microplastics oral exposure on colon mucin release, inflammation, gut microflora composition and metabolism in mice. *Ecotoxicology and Environmental Safety*, 220, 112340. <https://doi.org/10.1016/j.ecoenv.2021.112340>
16. Zolotova, N., Dzhalilova, D., Tsvetkov, I., & Makarova, O. (2023). Influence of microplastics on morphological manifestations of experimental acute colitis. *Toxics*, 11(9), 730. <https://doi.org/10.3390/toxics11090730>
17. Xie, S., Zhang, R., Li, Z., Liu, C., Chen, Y., & Yu, Q. (2023). Microplastics perturb colonic epithelial homeostasis associated with intestinal overproliferation, exacerbating the severity of colitis. *Environmental Research*, 217, 114861. <https://doi.org/10.1016/j.envres.2022.114861>
18. Luo, T., Wang, D., Zhao, Y., Li, X., Yang, G., & Jin, Y. (2022). Polystyrene microplastics exacerbate experimental colitis in mice tightly associated with the occurrence of hepatic inflammation. *Science of The Total Environment*, 844, 156884. <https://doi.org/10.1016/j.scitotenv.2022.156884>
19. Sung, M., Lee, Y.-J., Sung, S.-E., Kang, K.-K., Park, J. W., Lee, Y., Kim, D., Lee, S., Choi, J.-H., & Lee, S. (2025). Exacerbation of polyethylene microplastics in animal models of DSS-induced colitis through damage to intestinal epithelial cell junctions. *Current Research in Toxicology*, 8, 100217. <https://doi.org/10.1016/j.crttox.2025.100217>
20. Li, L., Lv, X., He, J., Zhang, L., Li, B., Zhang, X., Liu, S., & Zhang, Y. (2024). Chronic exposure to polystyrene nanoplastics induces intestinal mechanical and immune barrier dysfunction in mice. *Ecotoxicology and Environmental Safety*, 269, 115749. <https://doi.org/10.1016/j.ecoenv.2023.115749>
21. Zeng, G., Li, J., Wang, Y., Su, J., Lu, Z., Zhang, F., & Ding, W. (2024). Polystyrene microplastic-induced oxidative stress triggers intestinal barrier dysfunction via the NF-κB/NLRP3/IL-1β/MCLK pathway. *Environmental Pollution*, 345, 123473. <https://doi.org/10.1016/j.envpol.2024.123473>
22. Chen, X., Xuan, Y., Chen, Y., Yang, F., Zhu, M., Xu, J., & Chen, J. (2024). Polystyrene nanoplastics induce intestinal and hepatic inflammation through activation of NF-κB/NLRP3 pathways and related gut-liver axis in mice. *Science of The Total Environment*, 935, 173458. <https://doi.org/10.1016/j.scitotenv.2024.173458>
23. Liang, B., Zhong, Y., Huang, Y., Lin, X., Liu, J., Lin, L., Hu, M., Jiang, J., Dai, M., Wang, B., Zhang, B., Meng, H., Lelaka, J. J. J., Sui, H., Yang, X., & Huang, Z. (2021). Underestimated health risks: Polystyrene micro- and nanoplastics jointly induce intestinal barrier dysfunction by ROS-mediated epithelial cell apoptosis. *Particle and Fibre Toxicology*, 18(1), 20. <https://doi.org/10.1186/s12989-021-00414-1>
24. Jia, R., Han, J., Liu, X., Li, K., Lai, W., Bian, L., Yan, J., & Xi, Z. (2023). Exposure to polypropylene microplastics via oral ingestion induces colonic apoptosis and intestinal barrier damage through oxidative stress and inflammation in mice. *Toxics*, 11(2), 127. <https://doi.org/10.3390/toxics11020127>
25. Xue, Z., Cheng, S., Liu, X., Zhang, Y., Huang, Y., Du, S., Chen, X., Zhang, Z., Yang, X., Xu, M., & Huang, J. (2026). Evaluation of intestinal toxicity of polystyrene micro/nanoplastics using intestinal organoids. *Chemico-Biological Interactions*, 432, 112060. <https://doi.org/10.1016/j.cbi.2026.112060>

26. Xu, D., Ma, Y., Peng, C., Gan, Y., Wang, Y., Chen, Z., Han, X., & Chen, Y. (2023). Differently surface-labeled polystyrene nanoplastics at an environmentally relevant concentration induced Crohn's ileitis-like features via triggering intestinal epithelial cell necroptosis. *Environment International*, 176, 107968. <https://doi.org/10.1016/j.envint.2023.107968>
27. Feng, X., Zhang, M., Zhao, T., Cui, J., Ye, H., Zhou, C., Ye, L., & Zhou, L. (2025). Polystyrene microplastics trigger colonic inflammation in rats via the TLR4/NF- κ B/COX-2 pathway and modulation of intestinal microbiota. *Toxicology*, 513, 154090. <https://doi.org/10.1016/j.tox.2025.154090>
28. Schwarzfischer, M., Ruoss, T. S., Niechcial, A., Lee, S. S., Wawrzyniak, M., Laimbacher, A., Atrott, K., Manzini, R., Wilmink, M., Linzmeier, L., Morsy, Y., Lang, S., Rogler, G., Kaegi, R., Scharl, M., & Spalinger, M. R. (2024). Impact of nanoplastic particles on macrophage inflammation and intestinal health in a mouse model of inflammatory bowel disease. *Nanomaterials*, 14(16), 1350. <https://doi.org/10.3390/nano14161350>
29. Ma, J., Wan, Y., Song, L., Wang, L., Wang, H., Li, Y., & Huang, D. (2023). Polystyrene nanobeads exacerbate chronic colitis in mice involving in oxidative stress and hepatic lipid metabolism. *Particle and Fibre Toxicology*, 20(1), 49. <https://doi.org/10.1186/s12989-023-00560-8>
30. Kopatz, V., Resch, U., Draganic, K., Horvath, A., Pfneissl, J., Kabiljo, J., Mödl, B., Timelthaler, G., Wallner, J., Mirzaei, Z., Beratlyte, S., Schleder, M., Sarbu, S., Laslau, S., Hollóczki, O., Raigel, M., Gruber, E. S., Widder, J., Kufferath, I., ... Kenner, L. (2025). Polystyrene micro- and nanoplastics in a colitis mouse model – effects on biodistribution, macrophage polarization, and gut microbiome. *Microplastics and Nanoplastics*, 6(1), 9. <https://doi.org/10.1186/s43591-025-00160-7>
31. Li, G., Rong, J., Xu, X., Kwak, E., Wang, S., Qu, G., Lin, S., & Peng, G. (2025). Distinct effects between polystyrene micro- and nanoplastics: Exacerbation of adverse outcomes in inflammatory bowel disease-like zebrafish and mice. *ACS Nano*, 19(15), 15081–15099. <https://doi.org/10.1021/acsnano.5c02307>
32. Jiang, P., Yuan, G., Jiang, B., Zhang, J., Wang, Y., Lv, H., Zhang, Z., Wu, J., Wu, Q., & Li, L. (2021). Effects of microplastics (MPs) and tributyltin (TBT) alone and in combination on bile acids and gut microbiota crosstalk in mice. *Ecotoxicology and Environmental Safety*, 220, 112345. <https://doi.org/10.1016/j.ecoenv.2021.112345>
33. Qiao, J., Chen, R., Wang, M., Bai, R., Cui, X., Liu, Y., Wu, C., & Chen, C. (2021). Perturbation of gut microbiota plays an important role in micro/nanoplastics-induced gut barrier dysfunction. *Nanoscale*, 13(19), 8806–8816. <https://doi.org/10.1039/D1NR00038A>
34. Tu, P., Xue, J., Niu, H., Tang, Q., Mo, Z., Zheng, X., Wu, L., Chen, Z., Cai, Y., & Wang, X. (2023). Deciphering gut microbiome responses upon microplastic exposure via integrating metagenomics and Activity-Based metabolomics. *Metabolites*, 13(4), 530. <https://doi.org/10.3390/metabo13040530>
35. Djouina, M., Waxin, C., Caboche, S., Dehaut, A., Himber, C., Balesdent, C., Beury, D., Hot, D., Vignal, C., Launay, D., Dubuquoy, L., Duflos, G., & Body-Malapel, M. (2025). Ingestion of environmentally sourced polyvinyl chloride microplastic fragments increases colon inflammation and fibrosis in mice. *Environmental Research*, 285, 122621. <https://doi.org/10.1016/j.envres.2025.122621>
36. Zhai, Z., Yang, Y., Xu, Y., Fu, Q., Chen, S., & Wu, Z. (2026). Polydisperse polystyrene microplastics exacerbate colitis through gut microbiota-butyrate-PPAR γ axis disruption in mice. *Journal of Hazardous Materials*, 507, 141722. <https://doi.org/10.1016/j.jhazmat.2026.141722>
37. Okamoto, R., Tsuchiya, K., Nemoto, Y., Akiyama, J., Nakamura, T., Kanai, T., & Watanabe, M. (2009). Requirement of Notch activation during regeneration of the intestinal epithelia. *American Journal of Physiology-Gastrointestinal and Liver Physiology*, 296(1), G23–G35. <https://doi.org/10.1152/ajpgi.90225.2008>
38. Obata, Y., Takahashi, D., Ebisawa, M., Kakiguchi, K., Yonemura, S., Jinnohara, T., Kanaya, T., Fujimura, Y., Ohmae, M., Hase, K., & Ohno, H. (2012). Epithelial Cell-Intrinsic Notch signaling plays an essential role in the maintenance of gut immune homeostasis. *The Journal of Immunology*, 188(5), 2427–2436. <https://doi.org/10.4049/jimmunol.1101128>
39. Negroni, A., Colantoni, E., Pierdomenico, M., Palone, F., Costanzo, M., Oliva, S., Tiberti, A., Cucchiara, S., & Stronati, L. (2017). RIP3 AND pMLKL promote necroptosis-induced inflammation and alter membrane permeability in intestinal epithelial cells. *Digestive and Liver Disease*, 49(11), 1201–1210. <https://doi.org/10.1016/j.dld.2017.08.017>
40. Bruno, A., Dovizio, M., Milillo, C., Aruffo, E., Pesce, M., Gatta, M., Chiacchiaretta, P., Di Carlo, P., & Ballerini, P. (2024). Orally ingested micro- and Nano-Plastics: A hidden driver of inflammatory bowel disease and colorectal cancer. *Cancers*, 16(17), 3079. <https://doi.org/10.3390/cancers16173079>

41. Zolotova, N., Kirillova, M., Dzhililova, D., Tsvetkov, I., Fokichev, N., & Makarova, O. (2025). Microplastics' impact on the development of AOM/DSS-Induced Colitis-Associated colorectal cancer in mice. *International Journal of Molecular Sciences*, 26(23), 11511. <https://doi.org/10.3390/ijms262311511>
42. Li, B., Ding, Y., Cheng, X., Sheng, D., Xu, Z., Rong, Q., Wu, Y., Zhao, H., Ji, X., & Zhang, Y. (2020). Polyethylene microplastics affect the distribution of gut microbiota and inflammation development in mice. *Chemosphere*, 244, 125492. <https://doi.org/10.1016/j.chemosphere.2019.125492>
43. Schwarzfischer, M., Niechcial, A., Lee, S. S., Sinnet, B., Wawrzyniak, M., Laimbacher, A., Atrott, K., Manzini, R., Morsy, Y., Häfliger, J., Lang, S., Rogler, G., Kaegi, R., Scharl, M., & Spalinger, M. R. (2022). Ingested nano- and micro-sized polystyrene particles surpass the intestinal barrier and accumulate in the body. *NanoImpact*, 25, 100374. <https://doi.org/10.1016/j.impact.2021.100374>
44. Deng, Y., Chen, H., Huang, Y., Zhang, Y., Ren, H., Fang, M., Wang, Q., Chen, W., Hale, R. C., Galloway, T. S., & Chen, D. (2022). Long-Term exposure to environmentally relevant doses of large polystyrene microplastics disturbs lipid homeostasis via bowel function interference. *Environmental Science & Technology*, 56(22), 15805–15817. <https://doi.org/10.1021/acs.est.1c07933>
45. Zhang, Z., Xu, M., Wang, L., Gu, W., Li, X., Han, Z., Fu, X., Wang, X., Li, X., & Su, Z. (2023). Continuous oral exposure to micro- and nanoplastics induced gut microbiota dysbiosis, intestinal barrier and immune dysfunction in adult mice. *Environment International*, 182, 108353. <https://doi.org/10.1016/j.envint.2023.108353>
46. Liu, S., Li, H., Wang, J., Wu, B., & Guo, X. (2022). Polystyrene microplastics aggravate inflammatory damage in mice with intestinal immune imbalance. *Science of The Total Environment*, 833, 155198. <https://doi.org/10.1016/j.scitotenv.2022.155198>
47. Djouina, M., Pichavant, M., Waxin, C., Dehaut, A., Loison, S., Driencourt, E., Deborgher, A., Balesdent, C., Launay, D., Dubuquoy, L., Duflos, G., & Body-Malapel, M. (2026). Ingestion of a human-relevant mixture of environmentally sourced microplastics promotes inflammation and tumorigenesis in the mouse colon. *Environmental Pollution*, 395, 127794. <https://doi.org/10.1016/j.envpol.2026.127794>
48. Tian, S., Li, R., Li, J., & Zou, J. (2025). Polystyrene nanoplastics promote colitis-associated cancer by disrupting lipid metabolism and inducing DNA damage. *Environment International*, 195, 109258. <https://doi.org/10.1016/j.envint.2025.109258>
49. Zhang, N., Li, Y. B., He, H. R., Zhang, J. F., & Ma, G. S. (2021). You are what you eat: Microplastics in the feces of young men living in Beijing. *Science of The Total Environment*, 767, 144345. <https://doi.org/10.1016/j.scitotenv.2020.144345>
50. Yan, Z., Liu, Y., Zhang, T., Zhang, F., Ren, H., & Zhang, Y. (2022). Analysis of microplastics in human feces reveals a correlation between fecal microplastics and inflammatory bowel disease status. *Environmental Science & Technology*, 56(1), 414–421. <https://doi.org/10.1021/acs.est.1c03924>
51. Yang, X., Yan, B., Zhao, Y., Zhou, L., Liu, M., Chen, G., Shen, L., & Deng, T. (2026). Polyethylene terephthalate microplastics exposure enhances the risk of ulcerative colitis: Insights from multiomics integration, machine learning, and molecular docking reveal intestinal toxicity mechanisms. *International Journal of Surgery*, 112(1), 735–750. <https://doi.org/10.1097/JS9.00000000000003476>
52. Ye, J., Lu, Q., Wang, H., Chen, Z., & Ran, S. (2026). Investigation of the molecular network underlying PET-MPs-induced inflammatory bowel disease via integrated machine learning and molecular docking approaches. *Scientific Reports*. <https://doi.org/10.1038/s41598-026-57094-0>
53. Wu, F., Wu, F., Liu, X., Xie, W., Liang, Y., Ye, Y., Xiao, X., Sun, K., Bai, L., Liu, S., & Liu, Z. (2025). Microplastic accumulation in fibrotic intestinal tissue and mesenteric adipose tissue in Crohn's disease patients. *Environmental Research*, 271, 121077. <https://doi.org/10.1016/j.envres.2025.121077>