

Microplastics, Gut Dysbiosis, and Inflammatory Pathways in Ulcerative Colitis

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Abstract: Microplastics (MPs) are pervasive environmental pollutants characterized by their widespread distribution. They can enter the human body through multiple routes, including inhalation and dietary intake, accumulate in the gastrointestinal tract, and subsequently disrupt intestinal microecological homeostasis, thereby contributing to digestive diseases. Ulcerative colitis (UC), a chronic inflammatory bowel disease of unclear etiology, has been closely associated with gut microbiota dysbiosis, which is considered one of its central pathogenic mechanisms. This review comprehensively review the fundamental characteristics of MPs and their interactions with the gut microbiota and microbial metabolites. It further elucidates the key mechanisms by which MPs mediate the initiation and progression of UC, with particular emphasis on intestinal mucosal barrier dysfunction and immune dysregulation. Mechanistically, MPs disrupt SCFAs-producing microbial networks and activate epithelial inflammatory pathways, particularly TLR4–NF-κB signaling, thereby amplifying mucosal inflammation in UC. This review is the first to completely connect the regulatory axis of MPs – gut microbiota – metabolites – intestinal barrier – immune inflammation, clarify the core pathological chain of UC induced by MPs, make up for the shortcomings of existing reviews that only conduct single-dimensional analysis and lack integration of complete mechanisms, and provide a new theoretical framework for this field. Additionally, current research limitations are discussed, and future research directions and potential intervention strategies are proposed, aiming to provide novel theoretical insights into the etiology and prevention of UC.

Keywords: gut microbiota, immunity, inflammatory, microplastics, ulcerative colitis

Introduction

Microplastics (MPs) are generally defined as plastic fibers, particles, or films with diameters ranging from 1 μm to 5 mm, and also include nanoplastics with sizes below 1 μm. MPs are generated through the physical, chemical, and biological degradation of plastic waste and are characterized by high persistence, widespread distribution, and ecological toxicity.¹ Based on their origin, MPs are classified into primary and secondary MPs. Primary MPs are intentionally manufactured at microscopic sizes, commonly used in personal care and cosmetic products, whereas secondary MPs arise from the degradation of larger plastic products through biological, physical, and chemical processes and represent the major source of environmental MPs.² Over recent decades, plastic pollution has emerged as a major global environmental challenge. Approximately 21% of plastic waste is recycled worldwide, whereas the remaining 79% is discarded into the environment.³ MPs are now ubiquitously present in aquatic systems, soils, and the atmosphere, as well as in food and drinking water. They can enter the human body through multiple exposure pathways, including ingestion, inhalation, and dermal contact, thereby posing substantial threats to human health and socioeconomic sustainability.⁴ The gastrointestinal tract is considered a principal target organ for MPs accumulation^{5,6} (the structural characteristics of MPs and their distribution in human tissues are illustrated in Figure 1). MPs have been detected in human blood, placenta, intestinal tissues, and other organs.⁷ Notably, accumulation has even been reported in the skeletal system, with a deposition abundance of 61.1±44.2 particles per gram identified in intervertebral discs, with an average particle size of 159.5±103.8 μm. In addition, MPs have been

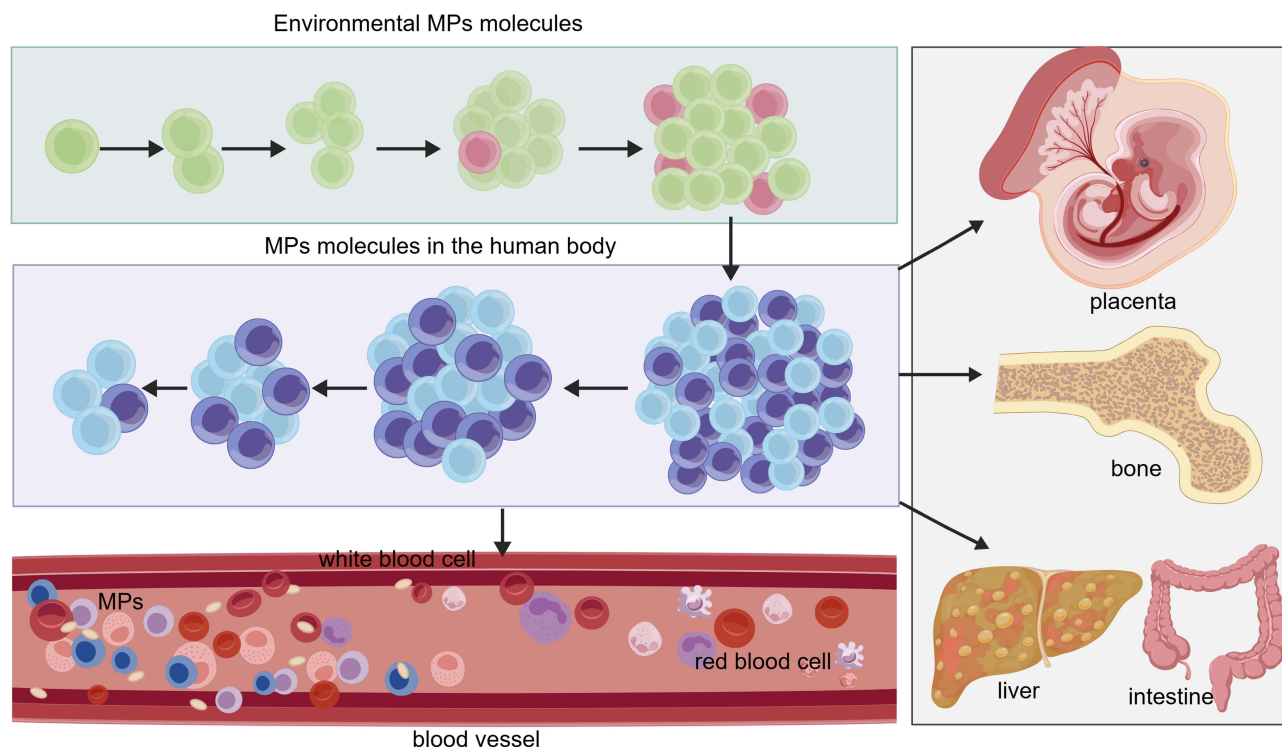


Figure 1 Environmental MPs enter the human body and accumulate in the bloodstream, where they interact with blood cells (including red blood cells and white blood cells). Subsequently, circulating MPs can translocate to and accumulate in multiple organs and tissues, such as the placenta, bone, liver, and intestine.

detected in the human stomach.⁸ Analysis of gastric contents from 26 cadavers revealed widespread MPs presence, predominantly fibers (52.04%), followed by fragments (39.80%) and films (8.16%), underscoring the potential health risks associated with MPs exposure. The impacts of MPs on intestinal homeostasis, digestive and respiratory systems, and immune function have become a multidisciplinary research focus spanning environmental science, microbiology, and medicine.⁹ Existing studies have confirmed that MPs exposure can induce tissue injury through multiple pathways, including physical irritation, adsorption of pathogenic bacteria and toxins, release of harmful substances such as plasticizers and heavy metals, and disruption of the *in vivo* microecological balance.^{10,11} However, most current studies only focus on the environmental toxicity of MPs or a single pathogenesis of intestinal inflammation, lacking systematic integration of the complete regulatory axis of MPs exposure–gut microbiota dysbiosis–microbial metabolite imbalance–intestinal barrier damage–immune inflammation activation. Meanwhile, the core pathological chain underlying the progression of ulcerative colitis (UC) mediated by MPs remains unclear. Based on the above evidence, this review proposes a scientific hypothesis that MPs can disrupt intestinal microecological balance, damage the intestinal mucosal barrier, and trigger intestinal immune disorder, thereby driving the onset and progression of UC. This paper aims to comprehensively summarize the physicochemical characteristics, environmental exposure and human accumulation patterns of MPs, and elaborate the interactions between MPs, gut microbiota and microbial metabolites, providing novel theoretical evidence for the etiological exploration and clinical prevention and treatment of UC.

UC is a chronic, nonspecific inflammatory bowel disease primarily involving the rectal and colonic mucosa and submucosa, with an etiology that remains incompletely understood. Clinically, it is characterized by persistent or recurrent abdominal pain, diarrhea, and mucopurulent bloody stools.¹² UC is typically marked by a protracted course and a high rate of relapse. In severe cases, it may lead to adverse outcomes such as intestinal perforation and malignant transformation. Recent data indicate that among 667 patients with UC who received standard therapy over a five-year period, nearly 57.0% experienced new disease progression, 5.4% required colectomy, and 2.1% were diagnosed with malignancy,¹³ underscoring its status as a major global threat to gastrointestinal health. Current evidence suggests that UC pathogenesis arises from the interplay of genetic susceptibility, environmental exposures, gut microbiota dysbiosis,

and immune dysregulation. Among these factors, disruption of gut microbial homeostasis has been identified as a central driving mechanism. A decline in beneficial commensals accompanied by overgrowth of pathogenic bacteria not only compromises the integrity of the intestinal mucosal barrier but also triggers aberrant immune responses, resulting in an imbalance between pro-inflammatory and anti-inflammatory mediators. This process establishes a vicious cycle of “microbiota dysbiosis-mucosal barrier disruption-immune dysregulation” that perpetuates intestinal inflammation.¹⁴ In recent years, accumulating evidence has linked environmental pollutant exposure to an increased risk of UC. A meta-analysis encompassing 32 human studies demonstrated significant associations between inflammatory bowel disease risk and exposure to heavy metals, air pollutants, per- and polyfluoroalkyl substances, and pesticides.¹⁵ As emerging environmental contaminants, MPs disturb the composition and metabolic function of gut microbiota, sharply decrease the abundance of SCFAs-producing beneficial bacteria and trigger gut dysbiosis. The subsequent microbial imbalance further impairs the integrity of intestinal mucosal barrier, activates classic inflammatory signaling pathways including TLR4-NF- κ B, induces excessive secretion of pro-inflammatory cytokines and immune dysfunction, and consequently provokes persistent mucosal inflammatory damage to facilitate UC progression. However, their precise mechanistic roles have not yet been systematically elucidated. Accordingly, this review comprehensively examines the mechanisms by which MPs regulate the gut microbiota to mediate UC development and progression, with the aim of providing theoretical support for etiological research and the optimization of preventive and therapeutic strategies for UC.

Exposure Pathways and Accumulation Characteristics of MPs

The mechanistic schematic illustrating the exposure pathways and accumulation characteristics of MPs is presented in Figure 2.

Human Exposure Pathways of MPs

MPs can enter the human body through multiple exposure pathways. With the advent of the “fast-food era”, dietary intake has become the predominant route of exposure. MPs have been detected in takeaway food containers, food packaging materials, drinking water (including bottled and tap water), seafood (such as fish and shellfish), processed foods (eg, chips and candies), and various other packaging products. Regular consumption or use of these items may therefore result in the ingestion of measurable quantities of MPs.¹⁶ A dietary exposure assessment conducted in Qingdao, China, reported an average intake abundance of 1.17 ± 1.07 particles per person, with fibrous MPs accounting for 91.5% of the detected particles.¹⁷ Inhalation represents another important exposure route. Atmospheric MPs can be inhaled into the respiratory tract, and some particles may subsequently deposit in the gastrointestinal tract and accumulate in the intestine. It has been reported that the substantial increase in face mask consumption during the COVID-19 pandemic may have markedly elevated human exposure to MPs, thereby posing additional health risks.¹⁸ In addition, dermal contact-through cosmetics and textile fibers-constitutes a potential exposure pathway. MPs may penetrate the skin barrier, enter the systemic circulation, and subsequently distribute to organs such as the gastrointestinal tract and lungs. Collectively, although multiple exposure routes exist, MPs primarily exert systemic pathological effects through the gut-systemic axis. This further underscores the critical role of interactions between MPs and the intestinal microecological environment in the pathogenesis of digestive diseases.

Accumulation and Metabolic Characteristics of MPs in the Intestine

As the primary site of MPs accumulation in the human body, the intestine exhibits deposition patterns closely associated with exposure dose, particle size, and polymer type. Smaller MPs are more likely to penetrate the intestinal mucosal barrier, enter the systemic circulation, and subsequently distribute to extraintestinal organs. A study investigating the systemic toxicity of polystyrene MPs of different sizes in C57BL/6J mice demonstrated that smaller particles exhibited greater organ distribution. However, larger particles (5 μ m) are associated with more pronounced intestinal mucosal barrier dysfunction and microbial dysbiosis.¹⁹ Within the intestinal environment, MPs exert toxic effects through multiple mechanisms, including physical irritation, chemical degradation, and biotransformation. Evidence indicates that MPs can enhance copper accumulation in the liver, pancreas, and intestine, thereby triggering severe oxidative stress responses.²⁰ Additionally, biofilm-developed MPs have been shown to induce intestinal oxidative reactions and disrupt gut microbial

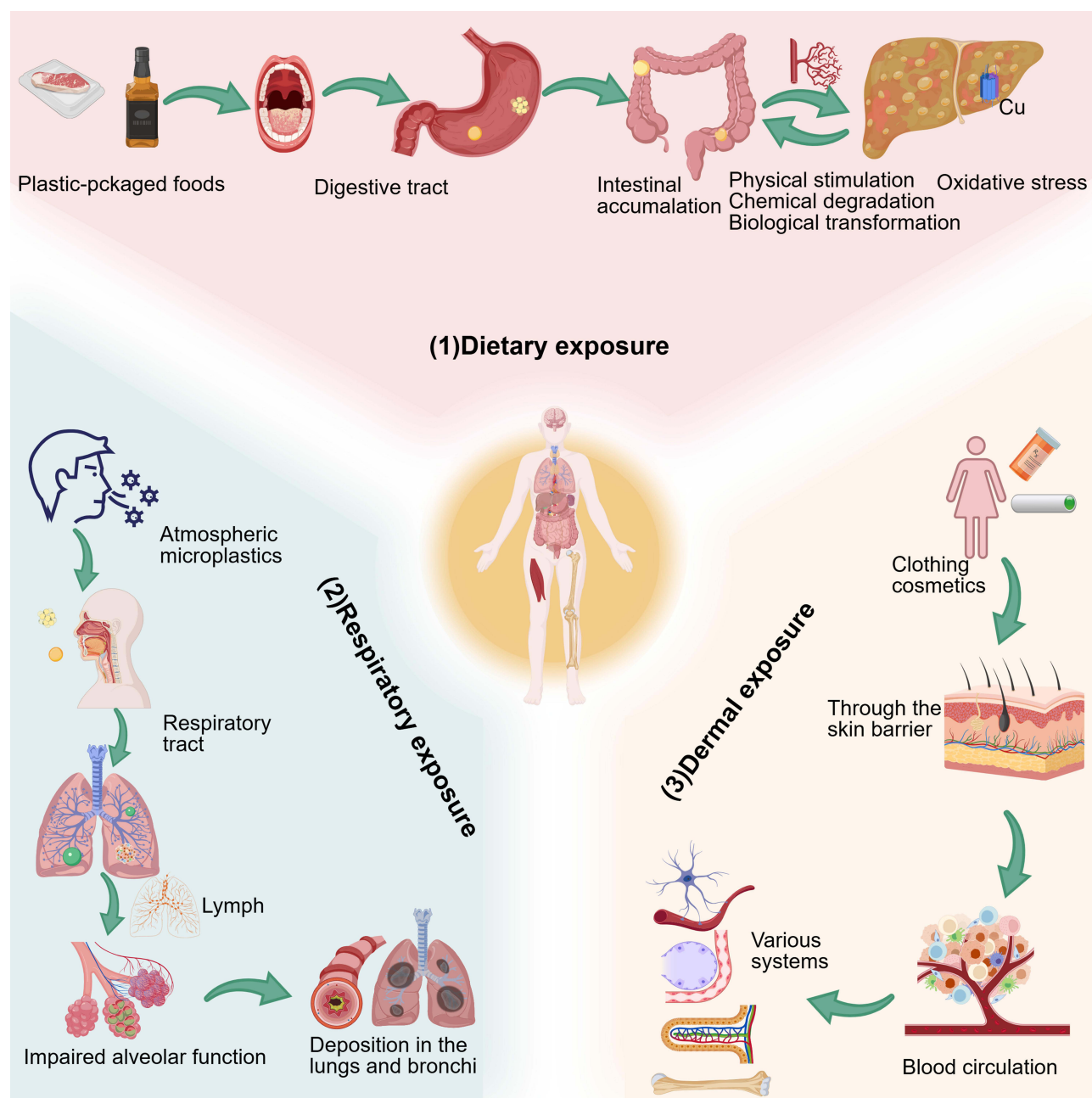


Figure 2 Humans are exposed to MPs via three primary routes: (1) dietary exposure through plastic-packaged foods, leading to intestinal accumulation and triggering physical stimulation, chemical degradation, biological transformation, and oxidative stress; (2) respiratory exposure via atmospheric MPs, resulting in deposition in the lungs/bronchi, impaired alveolar function, and systemic distribution through the lymphatic system; and (3) dermal exposure through clothing, cosmetics, and personal care products, enabling MPs to cross the skin barrier, enter blood circulation, and accumulate in multiple tissues.

homeostasis.²¹ Regardless of the specific mechanism, disturbance of gut microbiota equilibrium represents a central event in MPs-associated intestinal pathology. Consistent with findings reported by Xia et al²² continuous exposure to polyethylene MPs for 21 days resulted in significant alterations in intestinal histomorphology and pronounced microbial dysbiosis. These effects exhibited a dose-dependent trend across three MPs concentrations (1, 5, and 10 mg/L). Specifically, microbial diversity indices were markedly reduced, with the Chao index decreasing from 429 to 326 and the Shannon index declining from 7.05 to 6.02. Moreover, the relative abundance of Proteobacteria was significantly increased. The expansion of such potentially pathogenic taxa may suppress beneficial microbial populations, thereby promoting intestinal oxidative stress and impairing epithelial barrier integrity. Although existing studies have clarified the

damaging mechanism of MPs on the intestine, most of them are based on animal experiments, which differ from the actual human exposure scenario, and the clinical transformation value of the research results still needs further verification.

Core Mechanisms by Which MPs Regulate the Gut Microbiota to Mediate the Initiation and Progression of Ulcerative Colitis

The core mechanisms by which MPs regulate the gut microbiota to mediate the initiation and progression of UC can be summarized into four principal aspects: remodeling of microbial community structure, disruption of microbial metabolic functions, impairment of intestinal mucosal barrier integrity, and dysregulation of intestinal immune homeostasis. A schematic overview of these mechanisms is presented in Figure 3. The following sections provide a detailed discussion of each of these four key mechanisms.

MPs-Mediated Remodeling of Gut Microbial Community Structure

Homeostasis of the gut microbiota is fundamental for maintaining intestinal health, requiring a balanced abundance of beneficial and potentially harmful bacteria. Exposure to MPs can disrupt this microbial equilibrium through both physical and chemical mechanisms, thereby creating conditions conducive to the initiation and progression of UC. On the physical level, MPs can exert mechanical stimulation within the intestine, adhere to gut bacteria, and alter the local microenvironment, ultimately affecting microbial growth and proliferation. For instance, studies have shown that oral administration of polystyrene MPs in bees significantly reduced overall body weight and survival rate by impacting the gut microbiota, particularly in the rectum. Scanning electron microscopy revealed that 1 μm and 10 μm MPs tightly adhered to intestinal

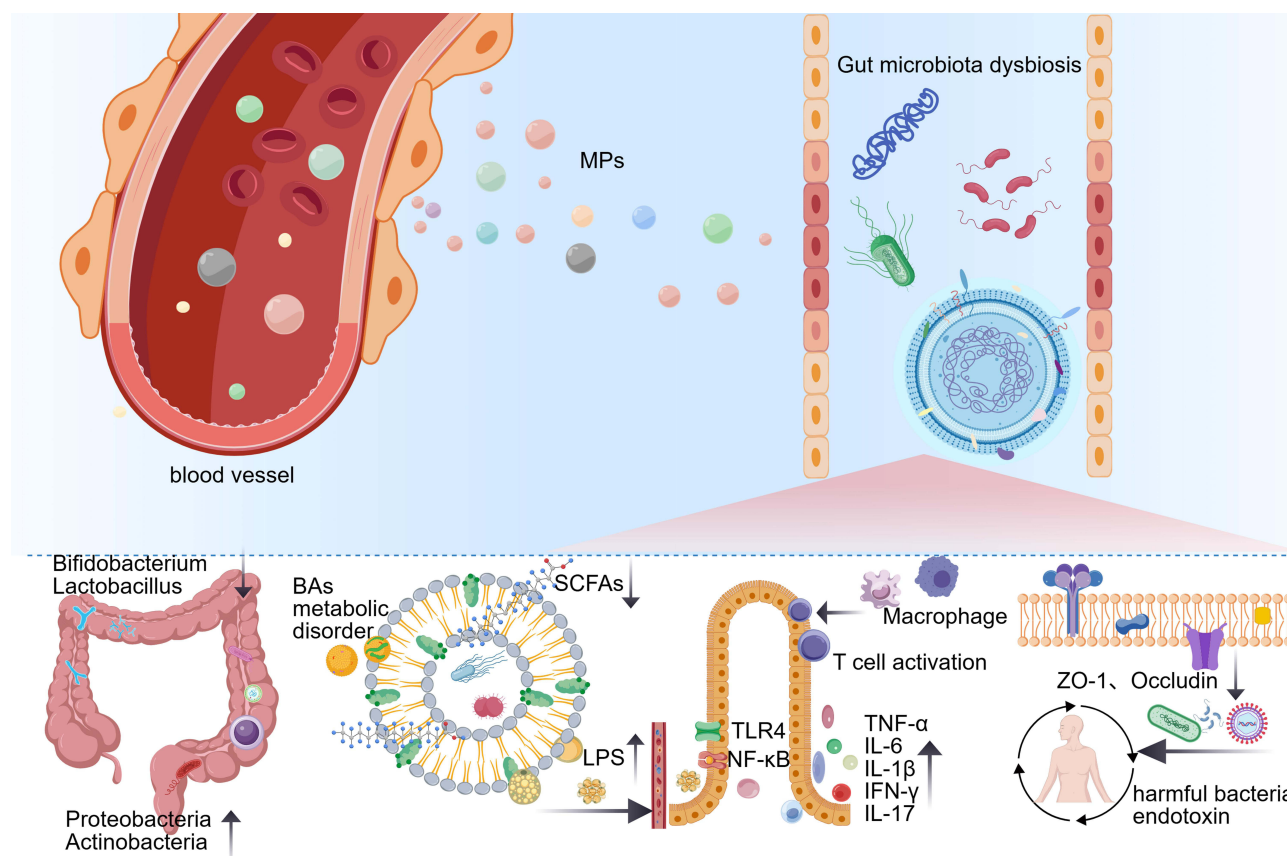


Figure 3 MPs translocate into the intestine and trigger gut microbiota dysbiosis, characterized by reduced beneficial bacteria (eg, *Bifidobacterium*, *Lactobacillus*) and increased pathogenic bacteria (eg, *Proteobacteria*, *Actinobacteria*). This dysbiosis impairs microbial metabolic function (including reduced short-chain fatty acids (SCFAs) and disrupted bile acids (BAs) metabolism), promotes lipopolysaccharide (LPS) release, and activates the TLR4/NF- κ B pathway, leading to intestinal immune imbalance (macrophage and T cell activation, elevated pro-inflammatory cytokines). Additionally, MPs disrupt the intestinal mucosal barrier by downregulating tight junction proteins (eg, ZO-1, Occludin), increasing permeability to harmful bacteria and endotoxins, and exacerbating intestinal inflammation and dysfunction.

bacteria, and microbial analysis showed a marked decrease in beneficial bacteria such as *Lactobacillus* and *Bifidobacterium*, accompanied by an increase in pathogenic bacteria, leading to disrupted microbial community structure.²³ Similarly, Jiang et al reported that the abundance of *Actinobacteria* increased from 0.72% in controls to 3.74% in the MPs group, while the relative abundance of *Firmicutes* decreased from 36.17% to 30.90%. At the genus level, MPs significantly reduced populations of *Lactobacillus*, *Bacteroides*, and *Blautia*, confirming the substantial impact of MPs on gut microbial composition.²⁴ A meta-analysis of 28 studies further indicated that MPs exposure enriches taxa such as *Clostridia*, *Proteobacteria*, and *Chlamydiae*, while reducing *Bacteroidetes*, thereby promoting intestinal inflammatory infiltration.²⁵ On the chemical level, MPs can adsorb pathogenic bacteria and toxins from the environment, introducing them into the intestine and triggering inflammation and microbial dysbiosis. MPs themselves may undergo enzymatic degradation, generating small molecules that selectively inhibit beneficial bacteria while promoting pathogenic bacterial growth. MPs have been shown to carry and release heavy metals and persistent organic pollutants (POPs), which stimulate the release of pro-inflammatory cytokines such as TNF- α and IL-6, damage the intestinal mucosa, and exacerbate oxidative stress and inflammation. When MPs accumulate beyond a certain threshold, they further disrupt the balance between beneficial and harmful bacteria, aggravating intestinal inflammation.²⁶ Additionally, a significant proportion of foodborne micro- and nanoplastics (MNPs) has been detected in human intestinal and fecal samples. MNPs can alter gut microbial composition and metabolic function, being degraded by a series of enzymatic reactions-including biotransformation, fragmentation, and assimilation-into small molecules such as N₂, CH₄, and CO₂, which create an environment favorable for pathogenic bacteria while inhibiting beneficial bacteria.^{27,28} Collectively, these studies indicate that MPs can mediate structural remodeling of the gut microbiota, reduce intestinal anti-inflammatory and antioxidant capacity, and increase susceptibility to intestinal inflammation. Notably, particle size plays a critical role: smaller MPs exert stronger effects on microbial composition, likely due to their greater ability to penetrate the intestinal mucosa and adhere to bacteria.²⁹

MPs-Mediated Disruption of Gut Microbial Metabolic Functions

The metabolic products of the gut microbiota are central to its physiological functions. MPs can disrupt these metabolites by altering microbial community structure, with key products including short-chain fatty acids (SCFAs), lipopolysaccharides (LPS), and bile acids (BAs), all of which play critical roles in UC pathogenesis. SCFAs, produced by beneficial bacteria such as *Bifidobacterium*, act as a bridge between the intestinal microecology and host intestinal homeostasis. They suppress intestinal inflammation through activation of G-protein-coupled receptors, promote mucosal barrier repair, and feedback to regulate microbial homeostasis, making them essential for intestinal health.³⁰ Exposure to MPs reduces the abundance of beneficial bacteria, directly decreasing SCFAs synthesis. This results in insufficient energy supply for intestinal epithelial cells, impaired mucosal barrier repair, weakened anti-inflammatory effects, and heightened susceptibility to intestinal inflammation. Polylactic acid MPs, commonly found in food packaging or disposable containers, have been shown to increase the abundance of *H. muridarum* and *Helicobacter japonicus* by more than 1000-fold, while populations of *Prevotella* sp. MGM1 and *Bacteroides bouchesdurhonensis* decreased significantly. Isotope-tracing studies revealed that partially degraded polylactic acid MPs fragments entered epithelial cell tricarboxylic acid (TCA) cycles, altering intestinal metabolism. SCFAs levels, the primary energy source for epithelial cells, were significantly reduced: acetate and propionate decreased by 20% and butyrate by 4%, leading to barrier disruption.³¹ Other studies indicate that oral MPs exposure may not always change SCFAs levels but can still alter natural killer (NK) cell populations and microbial composition, inducing severe intestinal inflammation. MPs-exposed mice exhibited more than double the number of NK cells compared to controls, with NK cells secreting IFN- γ and TNF- α , thereby exacerbating inflammation. Microbial shifts included a marked decrease in *Bacteroides* and an increase in inflammation-associated *Allobaculum* and *Firmicutes*.³² LPS, a cell wall component of Gram-negative bacteria, is normally present at low levels in the intestine, with the mucosal barrier preventing systemic entry.³³ MPs promote the overgrowth of pathogenic bacteria, thereby increasing intestinal LPS levels. LPS can penetrate the mucosal barrier, enter circulation, and activate TLR4/NF- κ B signaling pathways, triggering excessive secretion of pro-inflammatory cytokines such as TNF- α , IL-6, and IL-1 β , thereby aggravating intestinal inflammation and promoting UC. For example, mice exposed to MPs for 21 days displayed acute inflammation by histopathology and blood tests, with activation of the NF- κ B/NLRP3

pathway, neutrophil and macrophage infiltration, increased intestinal permeability, and elevated LPS levels, which further amplified TLR4/NF- κ B/NLRP3-mediated inflammation.³⁴ MPs also affect microbial BAs metabolism, disrupting primary and secondary BAs levels, exacerbating microbial dysbiosis and inflammation. MPs have been shown to regulate BAs synthesis and transport-related gene expression, altering the ratio of primary to secondary BAs in feces and impairing normal BAs metabolism, which leads to intestinal barrier and liver damage.³⁵ Multi-omics analyses further indicated that MPs-mediated microbial dysbiosis disturbs BAs metabolism: 16S rRNA sequencing revealed a reduction in *Bacteroides* and *Proteobacteria* and enrichment of *Actinobacteria*. Conjugated BAs in the colon increased approximately 1.5–2 times relative to controls, with a positive correlation between BAs levels and *Actinobacteria*, and a negative correlation with *Proteobacteria*.³⁶ These findings suggest that MPs may exacerbate colonic inflammation by disrupting specific microbial–BAs interactions.

MPs-Gut Microbiota Axis-Mediated Impairment of Intestinal Mucosal Barrier Function

The intestinal mucosal barrier is a critical defense system that maintains gut health, encompassing physical and chemical, including epithelial cells and tight junction proteins. Its integrity is essential, and barrier disruption is a key pathological event in UC. MPs can act on the gut microbiota to form MPs–microbiota axis, impairing mucosal barrier function through multiple mechanisms. Physical barrier: MPs-mediated microbial dysbiosis increases the production of harmful metabolites such as reactive oxygen species (ROS), which damage intestinal epithelial cells by promoting apoptosis, reducing proliferation, and downregulating tight junction proteins such as ZO-1 and Occludin. This loosens epithelial cell connections, increases intestinal permeability, and allows pathogenic bacteria and endotoxins to enter systemic circulation, triggering systemic inflammation. For example, polystyrene MPs have been shown to disrupt the physical barrier in quail ceca, alter microbial diversity, and damage ultrastructures, including microvilli breakage and rearrangement, with marked reductions in ZO-1 and Occludin expression.³⁷ Similarly, exposure of *Cipangopaludina cathayensis* to polystyrene MPs and roxithromycin (ROX) resulted in mucosal damage, villus atrophy, epithelial cell shedding, and disrupted microbial structure; transcriptomic data also indicated oxidative stress and epithelial injury.³⁸ Chemical barrier: Dysbiosis reduces mucus secretion and thickness, weakening the barrier against pathogen–epithelial contact and exacerbating mucosal injury. Polystyrene MPs exert dose-dependent intestinal and hepatic barrier injury by modulating the gut microbiota, reducing beneficial bacteria such as *Firmicutes*, *Bifidobacterium*, and *Akkermansia*, while increasing *Proteobacteria* and *Bacteroidota*. In treated groups (200 ppb and 500 ppb), mucus secretion decreased by 44.67% $\pm$ 0.52% and 49.50% $\pm$ 0.71%, respectively. Histology revealed significant reductions in goblet cell numbers, elevated iFABP (276.50 $\pm$ 10.73 pg/mL), and decreased sIgA (0.60 $\pm$ 0.03 mg/g), indicating increased intestinal permeability and chemical barrier disruption.³⁹ Notably, bacterial biofilms on MPs can further modify their physical and chemical properties, influencing mucosal integrity. The intestinal mucosal barrier is a key link in the pathogenesis of UC. MPs can damage the intestinal mucosal barrier function from three dimensions (physical and chemical) by regulating the intestinal flora: at the physical level, they damage intestinal epithelial cells and the expression of tight junction proteins, increasing intestinal mucosal permeability; at the chemical level, they reduce intestinal mucus secretion and weaken the protective effect of the barrier.

MPs-Gut Microbiota Axis-Mediated Dysregulation of Intestinal Immune Homeostasis

The intestinal immune system is closely linked to the gut microbiota. Under normal conditions, the microbiota mediates immune tolerance through three interconnected pathways, maintaining immune homeostasis: (1) establishing a foundational microbial community through birth mode and diet, (2) dynamic microbiota–immune interactions that guide tolerance programming, and (3) direct stimulation of lymphoid tissue maturation and T cell differentiation by microbial antigens. Disruption at any of these steps can lead to immune deficiencies and compromise intestinal immunity.⁴⁰ MPs can disrupt this balance by modulating the gut microbiota, breaking intestinal immune tolerance, and promoting the initiation and progression of UC. An integrated analysis of 118 experimental studies revealed that even when the microbiota possesses partial capacity to degrade MPs, MPs still exert a significant impact on intestinal microecology and indirectly influence the immune system.⁴¹ MPs promote the proliferation of pathogenic bacteria and enhance LPS release. LPS, a major component of the bacterial outer membrane, triggers cascades of interleukin-mediated

responses by activating antigen-presenting cells such as macrophages and dendritic cells, leading to the secretion of pro-inflammatory cytokines. Simultaneously, Th1 and Th17 cells are activated, producing IFN- γ and IL-17, further aggravating intestinal inflammation. For example, in MPs-exposed mice, the abundance of harmful bacteria such as *Desulfovibrio* increased, accompanied by elevated serum levels of LPS, CRP, TNF- α , and CEA compared to controls. The expression of pro-inflammatory cytokines, including IL-1 β and TNF- α , was significantly upregulated in the ileum and colon, contributing to inflammation initiation.⁴² Microbial dysbiosis activates the gut mucosal immune system, causing abnormal activation of lymphocytes and macrophages, immune imbalance, and exacerbation of inflammation and barrier injury, forming a vicious cycle of “microbiota dysbiosis-immune dysregulation-inflammatory stimulation” that drives UC pathology. Polystyrene MPs alter microbial composition, reducing the *Firmicutes/Bacteroidetes* ratio and increasing harmful bacteria such as *Escherichia-Shigella* and *Enterobacteriaceae*. Longer exposure times further increased pathogenic bacterial abundance. ELISA and flow cytometry analyses demonstrated significant downregulation of sIgA and suppressed T lymphocyte differentiation under high-concentration MPs, with reductions in CD4⁺ and CD8⁺ T cells becoming evident after 28 days. The first 14 days, during which beneficial bacteria temporarily compensate, showed minimal immune changes, indicating a strong correlation between microbial shifts and immune alterations. High-throughput sequencing and PCR-DGGE analyses indicated pronounced dysbiosis, including increased *α-Proteobacteria* and *Actinobacteria*, and significant reductions in *Clostridium* (2–3 times lower than controls) and *Bacteroides* (4 times lower than controls), both of which are crucial for immune system development and pathogen defense.⁴³ These findings highlight the critical role of the MPs-microbiota axis in impairing the intestinal mucosal barrier and promoting UC-related inflammation. MPs also alter microbial composition and LPS metabolic pathways: *Firmicutes* abundance decreased, *Bacteroides* increased, LPS downstream genes ERK1 and NF- κ B mRNA were downregulated, and immunoglobulin levels were elevated, collectively mediating intestinal immune responses.⁴⁴ These findings demonstrate that MPs, via the MPs-microbiota axis, can profoundly disturb intestinal immune homeostasis, creating a pro-inflammatory environment that contributes to UC pathogenesis.

Gut Microbiota-Mediated Metabolism of MPs and Attenuation of UC Progression

Currently, environmental protection measures aim to reduce plastic and MPs usage at the source. However, in the “fast-food era”, the widespread use of plastics and MPs is inevitable due to convenience. Therefore, strategies to accelerate MPs metabolism in the body and minimize their harmful effects are of critical importance.

Recent studies indicate that certain probiotic strains in the gut can enhance MPs degradation, providing a potential intervention avenue. Probiotic supplementation has been shown to restore microbiota balance and improve intestinal barrier function, preventing unnecessary immune activation and thereby reducing MPs toxicity in vivo.⁴⁵ Some probiotics can adsorb MPs in the intestine and facilitate their excretion via feces, effectively reducing intestinal accumulation. For instance, an assessment of 784 bacterial strains revealed that *Lactobacillus paracasei* DT66 and *Lactiplantibacillus plantarum* DT88 achieved the highest MPs adsorption, increasing fecal excretion of polystyrene MPs in mice by 34% and reducing residual intestinal MPs by 67%, concurrently alleviating intestinal inflammation.⁴⁶ Similarly, lactic acid bacteria efficiently adsorb polypropylene, polyethylene, and polyvinyl chloride MPs, with adsorption rates of 78.57%, 71.59%, and 66.57%, respectively.⁴⁷ *Clostridium dalinum* has also been shown to promote toxin clearance and restore intestinal barrier function by regulating metabolites, increasing ZO-1 and Occludin expression to ~97% (approximately 70% higher than MPs-exposed groups) and suppressing TLR4/NF- κ B signaling to mitigate inflammation.⁴⁸ Engineered strains, such as *Escherichia coli* Nissle 1917, can reduce MPs absorption by intestinal cells, thereby protecting mucosal barrier integrity.⁴⁹ Collectively, these studies demonstrate that various probiotics can promote MPs metabolism and ameliorate UC-related intestinal pathology, though research in this area remains limited and warrants further investigation. Table 1 summarizes the mechanisms by which probiotics promote MPs metabolism or regulate gut microbiota to alleviate the progression of UC.

Table I The Mechanisms by Which Probiotics Promote MPs Metabolism or Regulate Gut Microbiota to Alleviate the Progression of UC

Probiotics	Mechanism of Action on MPs	Mechanism of Action on UC	Significance	References
Probiotics (eg, <i>Lactobacillus</i> and <i>Bifidobacterium</i>)	Bind to MPs and interfere with their toxicokinetics	Increase intestinal mucus secretion, reduce damage to tight junction proteins, correct gut dysbiosis, and alleviate inflammatory responses	Avoid activating the immune system	[43]
<i>Lactobacillus paracasei</i> DT66 and <i>Lactiplantibacillus plantarum</i> DT88	Strong MPs adsorption, accelerate MPs excretion, and reduce residual intestinal MPs	Mitigate intestinal inflammation and improve gut immunity	Alleviate the toxic effects of MPs	[44]
Probiotic <i>Lactobacillus</i>	Adsorb MPs and promote their fecal excretion	Restore gut microbial homeostasis, protect intestinal mucosal barrier, and reduce inflammation	Alleviate the toxic effects of MPs	[45]
<i>Clostridium dalinum</i>	Promote MPs excretion	Upregulate mucosal barrier protein expression and inhibit TLR4/NF- κ B inflammatory signaling	Protect the intestinal mucosal barrier	[46]
Engineered <i>Escherichia coli</i> Nissle 1917	Reduce intestinal cellular uptake of MPs	Activate NF- κ B pathway in Caco-2 cells while reducing inflammation; alleviate intestinal barrier permeability	Protect the intestinal mucosal barrier	[47]

Conclusion and Perspectives

MPs, as an emerging environmental pollutant, can enter the human body through multiple routes such as dietary intake and inhalation, and accumulate in the intestine. They contribute to gut microbiota dysbiosis and metabolic disturbances, impair intestinal mucosal barrier function, and disrupt intestinal immune homeostasis, forming a pathological pathway of “MPs exposure $\rightarrow$ gut microbiota dysbiosis $\rightarrow$ mucosal barrier damage $\rightarrow$ immune imbalance”, which plays a critical role in the pathogenesis and progression of UC. This review summarizes the core mechanisms by which MPs promote UC development, aiming to provide insights into additional etiological factors of UC. Notably, Most studies suggest that MPs are related to UC via multifaceted regulation of gut microbiota composition; however, whether MPs can serve as a modeling agent for UC in future experimental studies remains unclear, and classical UC modeling systems are still lacking. Future research could evaluate the efficacy of MPs combined with dextran sulfate sodium (DSS) in constructing UC models so as to establish an experimental system integrating MPs exposure with classical UC animal models, thereby more accurately elucidating the role of MPs in the onset and progression of UC.

Furthermore, most current studies are focused on animal experiments, including fish, shrimp, and birds, with data demonstrating correlations between MPs exposure levels, gut microbiota characteristics, and disease severity. However, clinical studies in humans are still limited, there are significant interspecies differences in intestinal structure, gut microbiota composition, and immune regulation between experimental animals and humans, limiting the direct extrapolation of animal findings to human pathogenesis. In addition, a marked discrepancy exists between the high exposure doses used in animal studies and the lower levels encountered in real-world human exposure. Therefore, current high-dose experiments mainly serve to elucidate the potential toxic mechanisms of MPs and should not be directly interpreted as reflecting UC risk in the general population. Consequently, the actual role of MPs in human UC pathogenesis and the dose–response relationship remain uncertain. Large-scale, multicenter clinical studies are needed to clarify the association between MPs exposure and UC risk or disease progression, and conduct studies using environmentally relevant low-dose and dose-gradient exposure models to establish dose–response relationship, providing evidence for the potential role of MPs in UC. Finally, current preventive strategies against MPs are largely limited to environmental protection measures. Given the unavoidable use of plastics in the contemporary convenience-oriented society, future interventions could focus on accelerating MPs metabolism in vivo by leveraging the interaction between MPs and gut microbiota. In

summary, continued research on the interactions between MPs and gut microbiota is expected to open new avenues for intestinal health protection and the prevention and treatment of inflammatory bowel diseases.

Data Sharing Statement

Data sharing is not applicable to this article as no data were created or analyzed in this study.

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Author Contributions

Yalong Chen: Investigation, Visualization, Writing-original draft, Writing – review and editing; Xudong Tian: Conceptualization, Supervision, writing-review & editing. All authors gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that there are no conflicts of interest.

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