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Gut Microbiota Dysbiosis and Probiotic Supplementation in IBD: A Narrative Review

Małgorzata Wandzel

Medical University of Silesia

Poniatowskiego 15, 40-055 Katowice

https://orcid.org/0009-0003-1151-3346

E-mail: gosiawandzel29@gmail.com

Daria Twardowska
Medical University of Silesia
Poniatowskiego 15, 40-055 Katowice
https://orcid.org/0009-0004-5807-4915
E-mail: daria.twardowska@interia.pl

Wiktoria Tłoczek
Medical University of Silesia
Poniatowskiego 15, 40-055 Katowice
https://orcid.org/0009-0004-7722-5037
E-mail: wiktoriatloczek10@interia.pl

Barbara Tomczak
Medical University of Silesia
Poniatowskiego 15, 40-055 Katowice
https://orcid.org/0009-0004-3113-4922
E-mail: basia.tom335@wp.pl

Kamil Topolski
Medical University of Silesia
Poniatowskiego 15, 40-055 Katowice
https://orcid.org/0009-0002-8552-8332
E-mail: kamil2158@op.pl

Dominika Żukowiecka-Sęga
Medical University of Silesia
Poniatowskiego 15, 40-055 Katowice
https://orcid.org/0009-0000-3426-7393
E-mail: dominikazukowiecka@gmail.com

Wiktoria Śliwa
Medical University of Silesia
Poniatowskiego 15, 40-055 Katowice
https://orcid.org/0009-0009-2406-853X
E-mail: wiki00727@gmail.com

Barbara Jelonek
Medical University of Silesia
Poniatowskiego 15, 40-055 Katowice
https://orcid.org/0009-0007-5238-0710
E-mail: jel.basia2000@gmail.com

Karolina Klubikowska
Medical University of Silesia
Poniatowskiego 15, 40-055 Katowice
https://orcid.org/0009-0002-7893-3081
E-mail: k.klubikowska@gmail.com

Dagmara Porada
Medical University of Silesia
Poniatowskiego 15, 40-055 Katowice
https://orcid.org/0009-0000-5326-3996
E-mail: dagmaraporada15@gmail.com

Corresponding Author
Małgorzata Wandzel, e-mail: gosiawandzel29@gmail.com

ABSTRACT

Background. Inflammatory bowel diseases (IBD) are chronic, multifactorial disorders with yet unclear etiopathogenesis. The incidence of this illness continues to rise. Growing amounts of evidence suggest environmental factors, particularly diet, as important for the onset and

progression of IBD. Diet affects the function and composition of the gut microbiota which has been implicated in its pathophysiology. Therefore, interest is growing in the therapeutic potential of microbiota-modulating therapies, including probiotics. Although the latter one is considered adjunct therapy in managing IBD, evidence regarding their effectiveness are inconsistent.

Aim. The aim of this study is to review the role of microbiota disorders in the etiopathogenesis of IBD, as well as to consider the validity of using probiotics in the management of the above.

Material and Methods. A narrative review was conducted using PubMed, Cochrane Library and Google Scholar, focusing on Randomized Controlled Trials (RCTs), systematic reviews, and meta-analyses published between 2017 and 2025. Twenty-eight high-quality sources were selected for analysis.

Results. Patients with IBD exhibit alterations in gut microbiota composition, including depletion of beneficial short-chain fatty acid (SCFA)–producing bacteria, alongside enrichment of pro-inflammatory taxa. Experimental and clinical data indicate that probiotics can influence key pathogenic mechanisms by enhancing epithelial barrier integrity, increasing tight-junction protein expression, promoting SCFA production, and modulating immune responses. Clinical trials show modest but measurable benefits in ulcerative colitis, particularly in maintaining remission, whereas outcomes in Crohn's disease remain inconsistent. Additionally, emerging preclinical studies on engineered probiotics demonstrate targeted antioxidant, immunomodulatory, and microbiota-reshaping effects, highlighting their therapeutic potential.

Conclusion. IBD is a multifactorial disease, and one of the contributing factors may be microbiota disorders. Probiotics may be used as supportive treatment in selected patients with ulcerative colitis; however, they are not advised as first-line or primary therapy. In Crohn's disease, clinical guidelines do not recommend their routine use due to lack of sufficient evidence. Nevertheless, probiotics can still be considered as a complementary option in UC management, given their safety profile. Engineered probiotics are a possible future therapy, but further high-quality research is needed to establish long-term efficacy. Overall, current evidence supports a biologically plausible role for microbiota-directed interventions in IBD, though their clinical effectiveness varies by disease subtype and formulation.

Keywords: Inflammatory Bowel Disease, IBD, Crohn's disease, Ulcerative colitis, Probiotics, Microbiota

Content

1. INTRODUCTION

Inflammatory bowel diseases (IBD), with principal forms of ulcerative colitis and Crohn's disease, have complex etiology involving chronic intestinal inflammation, caused by nuanced interaction of genetic, immune, microbial, and environmental factors (Yang & Zhang, 2025). They are becoming more common each year, with higher rising trends in newly industrialized countries, while in many Western countries, incidence appears to plateau at high levels (Ng et al., 2017).

A systematic review conducted by Siew C Ng et al. analyzed 147 population-based studies (119 on incidence, 69 on prevalence) of Crohn’s disease (CD) and ulcerative colitis (UC) published from 1990 to 2016. It found that the highest prevalence of IBD was reported in Europe and North America, exceeding 0.3% of the population in many countries. In North America and Europe, data shows incidence rates that are stable or even decreasing for both UC and CD. In contrast, since 1990, incidence rates have been increasing significantly in newly industrialized

regions of Africa, Asia, and South America (e.g., Brazil and Taiwan), with annual percent changes showing growing trends for both diseases (Ng et al., 2017).

A recent systematic review and meta-analysis held by Heydari et al. of 215 population-based studies reported a global IBD incidence of approximately 9.7 per 100 000 person-years, with Crohn's disease at about 4.0 and ulcerative colitis at 5.0 per 100 000 person-years. The highest incidence of UC was seen in North America (≈9.8 per 100 000 person-years), and Oceania exhibited the highest overall incidence rates for IBD and CD, indicating that although Western regions continue to bear a high burden, incidence in other regions is rising as well (Heydari et al., 2025).

While one cannot influence the genetic factors, it is possible to try to avoid triggers that cause the disease. Although numerous review articles have examined environmental factors in IBD, there is still no agreement on which specific factor plays the most significant role in initiating the disease. However, diet has gained particular attention due to its influence on the microbiota (Shivashankar & Lewis, 2017). Recent studies indicate that Western-style diets are linked to decreased diversity of the gut microbiota (dysbiosis), which may increase vulnerability to IBD (Chiba et al., 2019). Since microbiota disorders can be considered one of the factors causing disease, the conclusion suggests itself that probiotics can be considered as part of the treatment. Most commonly used probiotics in IBD include *Bifidobacterium* and *Lactobacillus* species, *Enterococcus faecium, Saccharomyces boulardii, Bacillus* spp., *Pediococcus* spp., and non-pathogenic *E. coli* Nissle 1917 (Estevinho et al., 2024; Hijová, 2025; Weingarden & Ko, 2024). They may benefit IBD through several mechanisms, such as enhancing mucosal barrier, providing anti-inflammatory effects by increasing production of anti-inflammatory cytokines, like IL-10, and decreasing pro-inflammatory cytokines (e.g., TNF-α, IL-8) (Weingarden & Ko, 2024; Zakerska-Banaszak et al., 2024).

2. MATERIALS AND METHODS

This narrative review was conducted through a comprehensive examination of the available scientific evidence concerning the involvement of the gut microbiota in the pathogenesis of inflammatory bowel disease and the therapeutic role of probiotics in its management. To ensure clinical applicability and methodological rigor, a structured literature search was performed across major electronic databases, including PubMed, Google Scholar, and the Cochrane Library, covering the period from 2017-2025.

Search Strategy

The literature search strategy incorporated a combination of predefined keywords and Medical Subject Headings terms, including “IBD,” “inflammatory bowel disease,” “microbiome,” “microbiota,” “probiotics,” “antibiotics,” “breastfeeding,” and “therapy.” Boolean operators (AND, OR) were systematically employed to optimize and refine the retrieval process (e.g., “probiotics AND therapy”).

Inclusion and Exclusion Criteria

The primary focus was placed on articles published between 2017 and 2025 to capture the most recent advancements in the field.

The inclusion criteria were:

1. Randomized controlled trials (RCTs),
2. Systematic reviews and meta-analyses,
3. Full-text articles published in English or Polish,
4. Studies involving human subjects.

Exclusion criteria included non-peer-reviewed articles, case reports with insufficient clinical data, and studies published before 2016, unless they provided fundamental data.

Data Synthesis and Analysis

Following the initial screening process, 28 studies meeting predefined relevance criteria were included for comprehensive analysis. Data were synthesized using a qualitative approach, structured around three core thematic domains: (1) the contribution of intestinal microbiota dysbiosis to the pathogenesis of inflammatory bowel disease, (2) the clinical efficacy and applicability of probiotic interventions, and (3) the therapeutic potential of engineered probiotics as an emerging treatment modality. Each included study was critically appraised with respect to methodological design, sample size adequacy, and clinical validity to ensure a rigorous, balanced, and evidence-informed synthesis.

3. RESULTS

3.1 Etiology of IBD

Inflammatory bowel disease arises from interactions between genetic susceptibility and environmental triggers (Bai et al., 2025). Genome-wide studies have identified about 200 IBD-

associated loci, mainly affecting three areas: innate immunity and autophagy (e.g., *nod2, atg16l1*), adaptive immunity including interleukin-23/17 and IL-10 signaling (e.g., *il23r*, *il10*), and epithelial barrier function (e.g., *ecm1, cdh1*). The first is mainly linked to Crohn's disease, the third to ulcerative colitis, and the second to both (Chiba et al., 2019).

Host genetics can also influence the composition and abundance of gut microbial communities, which in turn affect inflammatory processes relevant to IBD. Different strains of bacteria play various roles in the intricate process of disease pathogenesis—some are beneficial, while others may contribute to the development of IBD. Beneficial microbes include *Bacteroides fragilis, Faecalibacterium prausnitzii, Lactobacillus rhamnosus, Bifidobacterium longum, Clostridium leptum*, and *Ruminococcus bromii*, which support barrier function and immune regulation. Harmful taxa enriched in IBD include adherent-invasive *Escherichia coli* and *Mycobacterium avium* subsp. paratuberculosis, which promotes epithelial damage and inflammation (Chiba et al., 2019; Heydari et al., 2025; Khan et al., 2019; Shivashankar & Lewis, 2017; Yang & Zhang, 2025). Host genetics shapes these microbial patterns. Variants in glycosylation genes (*fut2, galc, manba*) alter mucosal glycans, leading to reduced protective microbes like Ruminococcaceae and increased harmful taxa such as *Bilophila* and *Escherichia*. Autophagy-related genes (*nod2, atg16l1, irgm, card9*) also influence microbiota: for example, *nod2* variants are linked to increased Proteobacteria and decreased Firmicutes, while *atg16l1* variants reduce *Akkermansia muciniphila* and favor pathobionts. Immune-regulating genes (*il10, il23r*) further modulate microbiota, with some bacteria stimulating pro-inflammatory cytokines (e.g., *Klebsiella pneumoniae* induces IL-1β, TNF-α) and others, like *Bifidobacterium adolescentis*, showing protective effects (Zakerska-Banaszak et al., 2024).

However, it is believed that genetic factors explain less than one-third of IBD heritability (Jans & Cleynen, 2023), so the rapid rise in incidence in developing countries may be connected to environmental changes. Westernization of lifestyle is likely a major contributor (Chiba et al., 2019). Westernized diets, high in animal protein, fat, processed foods, and low in fiber, are strongly associated with gut microbial dysbiosis, a key factor in IBD pathogenesis. Such diets are linked to reduction of beneficial bacteria, including *Faecalibacterium prausnitzii, Roseburia, Bifidobacterium*, and *Prevotella*, which produce short-chain fatty acids (SCFAs) that maintain epithelial integrity and regulate immune responses. On the contrary, harmful taxa such as *Fusobacterium, Enterobacter*, and adherent-invasive *Escherichia coli* are enriched, promoting inflammation. Mechanisms include reduced microbial diversity, expansion of mucin-degrading bacteria like *Bacteroides thetaiotaomicron* and *Akkermansia muciniphila*, and

increased pro-inflammatory *Proteobacteria*. In contrast, fiber-rich plant-based foods support microbial diversity and SCFA production, enhancing barrier function and anti-inflammatory signaling (Chiba et al., 2019).

3.2 Link between antibiotic therapy in childhood, microbiota disorders and IBD

A microbiome-related factor which may be linked to IBD etiopathogenesis is the use of antibiotics in early childhood (Dar et al., 2023). A systematic review and meta-analysis conducted by Størdal et al, indicates that antibiotic use in childhood is associated with a significantly increased risk of developing inflammatory bowel disease later in life, likely through long-term effects on the developing gut microbiome (Størdal et al., 2026). This meta-analysis pooled data from 10 cohort and case-control studies involving 2,783 IBD cases and compared children exposed to antibiotics with those who were not. The results showed that children exposed to antibiotics had a 42% higher risk of subsequent IBD (pooled risk ratio [RR] 1.42; 95% confidence interval [CI], 1.23–1.66) compared with unexposed peers, a statistically significant association ($p < .05$). When the analysis was stratified by disease type, the association was even stronger for Crohn's disease, with a 59% increased risk (RR 1.59; 95% CI, 1.39–1.81; $p < .05$), and a smaller but still significant increased risk was found for ulcerative colitis (RR 1.23; 95% CI, 1.08–1.40; $p < .05$). The explanation for these associations lies in the effect of antibiotics on the gut microbiome, which plays a critical role in immune system development and intestinal homeostasis. Antibiotics, especially when administered early in life, can disrupt normal microbial colonization and reduce microbial diversity. Such disruptions are thought to have a negative influence on immune education and tolerance, potentially driving chronic inflammatory responses typical to IBD (Juhl et al., 2025; Størdal et al., 2026).

3.3. Protective impact of breastfeeding

Breastfeeding is increasingly recognized as an important early-life factor which influences gut microbiota and immune development, with potential implications for inflammatory bowel disease risk. Breast milk provides important components, including human milk oligosaccharides, immunoglobulins, and microbial metabolites, that shape infant's intestinal ecosystem and promote colonization by beneficial taxa such as *Bifidobacterium* and Lactobacillus, which support epithelial barrier integrity and immune tolerance (Bertin et al., 2023). Prospective studies indicate that infants born to mothers with IBD exhibit altered gut microbiota, with reduced quantity of protective bacteria and breast milk protein profiles that correlate with microbial differences (Sabino et al., 2023). Experimental evidence further shows that breastfed infants harbor *Limosilactobacillus* and other microbes capable of modulating

intestinal immune responses and producing anti-inflammatory metabolites, which may reduce susceptibility to chronic intestinal inflammation (Huang et al., 2024).

3.4. How probiotics work

Following the analysis of gut microbiota dysbiosis in IBD pathogenesis, probiotics have emerged as a potential therapeutic strategy. Probiotics are defined as live microorganisms that, when administered in adequate amounts, confer health benefits to the host through multiple mechanisms, including modulation of immune responses, enhancement of intestinal barrier function, production of antimicrobial substances, competitive exclusion of pathogenic bacteria, and suppression of pro-inflammatory cytokine production while augmenting anti-inflammatory mediators like interleukin-10 (Kaur et al., 2020; Vaghela et al., 2026).

There are several specific mechanisms of action. One of them is the effect on lactate production and SCFAs. Many probiotic strains, particularly Lactobacillus and Bifidobacterium species, ferment dietary carbohydrates to produce lactate, which serves as a metabolic substrate for cross-feeding commensal bacteria capable of generating SCFAs, including acetate, propionate, and especially butyrate (Estevinho et al., 2024; Weingarden & Ko, 2024). Butyrate is of particular importance in inflammatory bowel diseases, as it represents the primary energy source for colonocytes and plays a central role in maintaining and repairing the intestinal epithelium. Beyond this, butyrate mediates additional molecular mechanisms: it inhibits histone deacetylases (HDACs), thereby regulating transcription of genes involved in barrier function and immune modulation; activates G-protein-coupled receptors GPR43 and GPR109A on epithelial and immune cells to enhance anti-inflammatory signaling; and stimulates AMP-activated protein kinase (AMPK) pathways, promoting tight-junction assembly and epithelial energy homeostasis (Estevinho et al., 2024; Hijová, 2025; Weingarden & Ko, 2024). Butyrate also promotes epithelial cell survival and regeneration, enhances the expression of tight-junction proteins such as ZO-1 and occludin, stimulates mucin production by goblet cells, and reduces intestinal permeability. These actions collectively strengthen mucosal barrier integrity, limiting microbial translocation and preventing excessive immune activation. Through these interconnected mechanisms — metabolic support of colonocytes, reinforcement of tight-junction architecture, enhancement of mucus layer protection, and immune modulation — probiotic-mediated SCFA production contributes directly to mucosal healing and immune homeostasis, processes that are fundamentally impaired in IBD (Estevinho et al., 2024; Hijová, 2025; Iyer & Corr, 2021; Y. Ma et al., 2024; Weingarden & Ko, 2024). In addition to SCFA-

mediated effects, probiotics exert direct immunomodulatory actions on both innate and adaptive immune responses. These include downregulation of pro-inflammatory cytokines such as TNF-α and IL-6, upregulation of anti-inflammatory mediators including IL-10, enhancement of secretory IgA production, and modulation of Th1/Th2 balance toward a more regulatory phenotype. Certain probiotic strains also activate aryl hydrocarbon receptor (AhR) pathways, which further support epithelial stability and mucosal immune equilibrium. Moreover, some strains reduce oxidative stress markers and increase antioxidant enzyme activity, such as superoxide dismutase, thereby limiting reactive oxygen species–mediated mucosal injury and contributing to overall barrier preservation (Y. Ma et al., 2024; Weingarden & Ko, 2024).

3.5. Clinical applicability

Evidence from systematic reviews, meta-analyses, and randomized controlled trials consistently indicates that probiotics are more effective in ulcerative colitis than in Crohn's disease. A systematic review of Crohn's disease identified 2 randomized controlled trials (46 participants), and 0 of 2 trials demonstrated a statistically significant benefit of probiotics for induction of remission (Limketkai et al., 2020). In contrast, a systematic review of ulcerative colitis included 14 randomized controlled trials (865 participants), of which 6 trials demonstrated a statistically significant increase in remission rates, particularly with multi-strain formulations and *Escherichia coli* Nissle 1917 (Kaur et al., 2020). These effects were often observed when probiotics were combined with standard therapies such as 5-aminosalicylic acid (5-ASA), suggesting a potential synergistic benefit (Kaur et al., 2020).

Meta-analyses demonstrate that probiotics significantly increase the likelihood of achieving clinical remission in ulcerative colitis, with a pooled odds ratio (OR) of 2.00 (95% CI 1.28–3.11) (Kaur et al., 2020). In contrast, evidence in Crohn's disease does not demonstrate a statistically significant benefit, with a reported risk ratio of 1.06 (95% CI 0.65–1.71) (Limketkai et al., 2020). Also, multi-strain probiotic formulations consistently outperform single strains, highlighting the importance of microbial diversity in therapeutic effects (Vakadaris et al., 2023). Specific probiotics, such as VSL#3 and *Escherichia coli* Nissle 1917, have shown potential to improve clinical activity or maintain remission in ulcerative colitis, but results are strain-specific and not consistently replicated. Systematic reviews highlight heterogeneity in study design and effect size, and current guidelines do not recommend probiotics as standard maintenance therapy (Kaur et al., 2020). In CD, however, trials using *Saccharomyces boulardii* or other probiotic formulations generally failed to demonstrate significant clinical benefit (Limketkai et al., 2020; Vakadaris et al., 2023).

Current clinical guidelines prioritize established pharmacologic therapies for induction and maintenance of ulcerative colitis, including aminosalicylates, corticosteroids, immunomodulators, and biologics. Although some small trials have evaluated probiotics—such as multi-strain formulations and *Escherichia coli* Nissle 1917—for remission induction or maintenance, evidence is limited and heterogeneous, and there is insufficient evidence to recommend probiotics for routine use in UC (Rubin et al., 2025). Similarly, for Crohn's disease, probiotics are not recommended due to lack of proven efficacy (Limketkai et al., 2020). Nevertheless, probiotics are generally considered safe and may be used as a complementary approach in select UC patients.

3.6. Engineered probiotics as a possible future treatment

The growing understanding of inflammatory bowel disease as a disorder involving dysregulated host–microbiota interactions has accelerated the development of microbiome-targeted therapies (Khan et al., 2019; Yang & Zhang, 2025). Beyond conventional probiotics, recent research has explored engineered probiotics—microorganisms genetically or structurally modified to deliver specific therapeutic functions (Y. Ma et al., 2024; Zhou et al., 2022). These next-generation strategies aim not only to restore microbial balance but also to directly modulate inflammatory pathways, oxidative stress, epithelial barrier integrity, and neuro-immune signaling (Y. Ma et al., 2024; Zhou et al., 2022). Emerging preclinical evidence suggests that engineered probiotics may represent a promising future direction for precise IBD therapy (Y. Ma et al., 2024; Zhou et al., 2022).

In a study conducted by Zhou et al., researchers developed a genetically modified strain of *Escherichia coli* Nissle 1917 (EcN) engineered to overexpress the antioxidant enzymes catalase and superoxide dismutase (SOD) (Zhou et al., 2022). The rationale behind this approach stems from the well-established role of oxidative stress in IBD pathogenesis, where excessive reactive oxygen species (ROS) contribute to epithelial injury and perpetuate mucosal inflammation. By enhancing the antioxidant capacity directly within the intestinal lumen, the engineered strain—designated ECN-pE—was designed to neutralize ROS at sites of inflammation. To improve gastrointestinal survival, the probiotic was encapsulated using a chitosan and sodium alginate layer-by-layer coating system. In murine dextran sulfate sodium (DSS)-induced colitis models, oral administration of the encapsulated engineered strain significantly reduced disease severity, as evidenced by lower disease activity indices and improved histopathological scores (Zhou et al., 2022). This treatment was associated with downregulation of pro-inflammatory cytokines such as TNF-α and IL-6, along with restoration of tight-junction proteins including ZO-1 and

occludin, indicating improved epithelial barrier integrity. The study further demonstrated reduced epithelial apoptosis and enhanced mucosal repair. Importantly, microbiota analysis revealed increased abundance of beneficial taxa such as *Lachnospiraceae_NK4A136* and *Odoribacter*, organisms linked to short-chain fatty acid production and mucosal homeostasis. Thus, the therapeutic effects were mediated through a dual mechanism: direct attenuation of oxidative stress and secondary reshaping of the gut microbial community (Zhou et al., 2022).

Complementing this antioxidant-focused strategy, a study conducted by Ma et al. explored the use of engineered probiotics as targeted delivery vehicles for endogenous gasotransmitters (T. Ma et al., 2025). In this investigation, EcN was loaded with a gas-releasing copolymer (POSR) capable of delivering carbon monoxide (CO) and hydrogen sulfide (H_2S), two molecules known for their potent anti-inflammatory and cytoprotective properties. Because systemic administration of these gasotransmitters is limited by toxicity and lack of tissue specificity, the authors engineered a probiotic-based system (POSR@EcN) to enable localized release directly within inflamed intestinal tissue. In murine models of colitis, this engineered construct significantly reduced inflammatory cytokine production and improved epithelial barrier function (T. Ma et al., 2025). CO and H_2S are known to inhibit NF-κB activation, suppress pro-inflammatory mediator release, and enhance antioxidant defenses, thereby limiting mucosal injury. In this study, probiotic-mediated delivery not only reduced intestinal inflammation but also altered gut microbiota composition in favor of SCFA-producing bacteria. Notably, the intervention increased levels of metabolites such as indoleacetic acid and γ-aminobutyric acid (GABA), linking microbial modulation to gut–brain axis signaling. Behavioral assessments in treated mice showed reductions in anxiety- and depression-like features, suggesting that engineered probiotics may also exert systemic neuro-immune benefits beyond local mucosal repair (T. Ma et al., 2025).

In parallel to genetically engineered systems, interest has also grown in leveraging specific commensal organisms with defined barrier-supporting and immunomodulatory properties. A comprehensive review examining *Akkermansia muciniphila* highlights its relevance as a next-generation probiotic candidate in IBD (Zheng et al., 2023). In this review, reduced abundance of *A. muciniphila* is consistently reported in patients with active ulcerative colitis and Crohn's disease, suggesting its depletion may contribute to dysbiosis and impaired mucosal protection (Zheng et al., 2023). Unlike traditional probiotics that primarily ferment dietary carbohydrates, *A. muciniphila* resides within the mucus layer and directly interacts with host epithelial cells.

Mechanistically, *A. muciniphila* promotes mucus turnover and stimulates goblet cell function, thereby reinforcing the physical barrier separating luminal antigens from the immune system (Zheng et al., 2023). Its outer membrane protein Amuc_1100 and derived extracellular vesicles have been shown in experimental models to modulate immune responses, promoting regulatory T cell differentiation and reducing pro-inflammatory macrophage infiltration. Furthermore, supplementation in animal models of colitis has been associated with decreased inflammatory cytokine expression and improved epithelial integrity. Interestingly, both live and pasteurized forms demonstrate immunomodulatory effects, suggesting structural microbial components may be sufficient to trigger beneficial signaling pathways (Zheng et al., 2023). Although clinical data remain limited, *A. muciniphila* appears to be an example of a bacterial species that could be harnessed or potentially engineered to restore mucosal homeostasis.

Taken together, these studies show that engineered probiotics can work in several complementary ways. They may help reduce oxidative stress, decrease inflammation, deliver specific therapeutic molecules directly to affected areas, strengthen the intestinal barrier, and improve imbalances in the gut microbiota. Instead of acting solely as passive supplements, these modified strains function more like active therapeutic tools that can interact with the immune and metabolic systems in a more targeted way.

Although most of the available evidence comes from preclinical studies, the results so far suggest that engineered probiotics could become a promising new option in the treatment of inflammatory bowel disease. By combining synthetic biology, biomaterials, and microbiome research, these approaches aim to provide more targeted, local therapy with potentially fewer systemic side effects than traditional immunosuppressive drugs. However, further clinical studies are still needed to confirm their safety, determine optimal dosing, and evaluate long-term effectiveness. Even so, engineered probiotics appear to be a promising and rapidly developing direction in future IBD therapy. (T. Ma et al., 2025; Zheng et al., 2023; Zhou et al., 2022).

4. DISCUSSION

This review emphasizes the multifactorial nature of inflammatory bowel disease, arising from complex interactions between genetic susceptibility, environmental factors, immune dysregulation, and gut microbiota alterations. Although genome-wide association studies have identified numerous susceptibility loci linked to immune regulation and epithelial barrier function, genetic factors account for only a portion of disease heritability. The increasing global

incidence of IBD therefore highlights the importance of environmental and lifestyle-related contributors (Chiba et al., 2019; Heydari et al., 2025; Shivashankar & Lewis, 2017; Yang & Zhang, 2025).

The gut microbiota represents a central interface between host genetics and environmental exposure. Variants in genes such as NOD2, ATG16L1, and IL23R influence immune responses and microbial composition, supporting the concept of impaired host–microbe interactions in IBD. Dysbiosis—characterized by reduced diversity, depletion of beneficial short-chain fatty acid –producing bacteria, and expansion of pro-inflammatory taxa—appears to contribute to sustained mucosal inflammation rather than just reflecting it (Chiba et al., 2019; Zakerska-Banaszak et al., 2024).

Early-life factors further shape this risk. Antibiotic exposure during childhood has been associated with increased IBD incidence, likely through disruption of microbial colonization and immune maturation. In contrast, breastfeeding may confer protective effects by promoting beneficial microbial communities and supporting immune tolerance. Together, these findings emphasize the importance of early microbial programming in disease susceptibility (Bertin et al., 2023; Huang et al., 2024; Sabino et al., 2023; Størdal et al., 2026).

Probiotic therapy is supported mechanistically by evidence showing enhancement of epithelial barrier integrity, increased short-chain fatty acid production, modulation of cytokine profiles, and activation of pathways such as HDAC inhibition and GPR signaling (Iyer & Corr, 2021; Khan et al., 2019; Yang & Zhang, 2025). Clinically, benefits are more consistently observed in ulcerative colitis, where certain probiotics have shown modest effects in maintaining remission (Estevinho et al., 2024; T. Ma et al., 2025; Weingarden & Ko, 2024). In contrast, evidence for Crohn’s disease remains insufficient to support routine probiotic use (Limketkai et al., 2020). These differences likely reflect distinct pathogenic mechanisms between the two conditions (Yang & Zhang, 2025).

Engineered probiotics represent a promising future direction, aiming to deliver targeted bioactive molecules directly to inflamed mucosa. While preclinical results are encouraging, larger and longer-term clinical trials are required to determine their definitive role. Overall, microbiota-directed therapies offer biologically plausible adjunctive strategies, though their clinical application must remain evidence-based and disease-specific (T. Ma et al., 2025; Zheng et al., 2023; Zhou et al., 2022).

5. CONCLUSIONS

The analysis of current scientific literature (2017-2025) supports the following conclusions:

1. Inflammatory bowel disease is a complex, multifactorial disorder resulting from interactions between genetic susceptibility, environmental exposures, immune dysregulation, and alterations in gut microbiota composition. It is not possible to identify a single, specific cause of the disease.
2. Host genetic variants influence both immune pathways and microbial communities, reinforcing the concept of IBD as a disorder of impaired host–microbiota equilibrium.
3. Early-life environmental factors, particularly antibiotic exposure and feeding practices, significantly shape microbiota development and may alter long-term IBD risk. Antibiotic exposure in childhood is associated with an increased risk of disease, while breastfeeding appears to exert protective effects through microbiome and immune modulation.
4. Probiotics exert biologically plausible therapeutic effects through SCFA production, enhancement of epithelial barrier integrity, immune modulation, and reduction of oxidative stress.
5. Clinical evidence supports the adjunctive use of selected probiotic formulations in ulcerative colitis. However, probiotics are not recommended as first-line therapy and have not demonstrated consistent efficacy in Crohn's disease.
6. Engineered probiotics represent a promising future direction in IBD treatment, offering targeted delivery of bioactive molecules and precise modulation of inflammatory pathways. Nevertheless, further high-quality clinical trials are required to establish long-term safety, optimal dosing strategies, and definitive therapeutic benefit.

Disclosure

Authors Contributions:

Conceptualization: Małgorzata Wandzel, Kamil Topolski, Barbara Jelonek, Dominika Żukowiecka-Sęga, Karolina Klubikowska, Barbara Tomczak

Methodology: Małgorzata Wandzel, Daria Twardowska, Wiktoria Tłoczek, Wiktoria Śliwa

Software: Dagmara Porada, Daria Twardowska

Check: Wiktoria Śliwa, Małgorzata Wandzel

Formal analysis: Barbara Jelonek, Karolina Klubikowska, Dagmara Porada

Investigation: Karolina Klubikowska, Wiktoria Tłoczek, Kamil Topolski

Research: Dagmara Porada, Barbara Tomczak, Małgorzata Wandzel

Resources: Wiktoria Śliwa, Dominika Żukowiecka-Sęga

Writing- rough preparation: Dominika Żukowiecka-Sęga, Wiktoria Tłoczek

Writing- review and editing: Daria Twardowska, Kamil Topolski, Barbara Jelonek

Visualization: Małgorzata Wandzel, Barbara Tomczak, Daria Twardowska

Supervision: Wiktoria Tłoczek, Kamil Topolski

Project administration: Małgorzata Wandzel

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