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Inflammatory Bowel Disease: A focus on the Role of Probiotics in Ulcerative Colitis

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Abstract

Inflammatory bowel disease (IBD) is a cluster of disorders of the gastrointestinal tract characterized by chronic inflammation and imbalance of the gut microbiota in a genetically vulnerable host. Crohn's disease and ulcerative colitis (UC) are well-known types of IBD, and due to its high prevalence, IBD has attracted the attention of researchers globally. The exact etiology of IBD is still unknown; however, various theories have been proposed to provide some explanatory clues that include gene-environment interactions and dysregulated immune response to the intestinal microbiota. These diseases are manifested by several clinical symptoms that depend on the affected segment of the intestine such as diarrhea, abdominal pain, and rectal bleeding. In this era of personalized medicine, various options are developing starting from improved intestinal microecology, small molecules, exosome therapy, to lastly stem cell transplantation. From another aspect, and in parallel to pharmacological intervention, nutrition, and dietary support have shown effectiveness in IBD management. There is an increasing evidence supporting the benefit of probiotics in the prophylaxis and treatment of IBD. There are several studies that have demonstrated that different probiotics alleviate UC. The present review summarizes the progress in the IBD studies focusing and exploring more on the role of probiotics as a potential adjunct approach in UC management.

Introduction

Inflammatory bowel disease (IBD) is a spectrum of chronic and recurring inflammatory disorders of the gastrointestinal tract that includes two distinct entities, Crohn's disease (CD) and ulcerative colitis (UC). These diseases are manifested by several clinical symptoms that depend on the affected segment of the intestine such as diarrhea, abdominal pain, rectal bleeding, and weight loss. To precisely establish IBD diagnosis, gastrointestinal sampling using endoscopic intervention as well as advanced radiography is routinely used. These techniques help to distinguish CD from UC. Although, the differentiation between these two diseases is challenging especially in severe cases when the colon is severely infected.

There are significant differences between CD from UC when considering histopathological changes. CD can influence the whole intestinal segment in any part of the gastrointestinal system, defined by injured areas mixed with healthy regions. The terminal ileum and colon are the most commonly affected; colonoscopy results involve skip lesions, cobblestoning, ulcerations, and strictures [1], [2]. In contrast, UC is characterized by rectal and colonic mucosal inflammation and is generally confined to the colon, and usually affects the mucosa and submucosa; pseudopolyps and continuous regions of inflammation are two of the most common colonoscopy results [1], [2]. In addition, it is characterized by the presence of abscesses in intestinal crypts and infiltrates of neutrophils, plasmocytes, and eosinophils.

The exact etiology of IBD is still unknown; however, various theories have been proposed to provide some explanatory clues that include gene-environment interactions, dysbiosis, mucosal barrier dysfunction, and dysregulated immune response to intestinal microbiota that is manifest as chronic inflammation [3], [4], [5]. Furthermore, many pharmacological approaches have been implemented over the years in managing IBD patients, with the primary aim to "treat to target," targeting complete endoscopic and clinical remission. These modalities contain

corticosteroids, aminosalicylates, immunomodulators, and biologics including pro-inflammatory cytokines inhibitors and integrin antagonists. Alternatively, patients with refractory disease, who do not respond to initial treatment motivate researchers to look into new therapeutic strategies. In the past few years, and in parallel to pharmacological intervention, scientists have examined the role of probiotics as a potential adjunct approach to IBD. Studies have shown that probiotics are essential for the regeneration of the intestinal mucosa [6], [7], [8]. The functions concerned with the probiotics' beneficial effects in the context of IBD include decreasing pathogenic, immune system modification, and synthesizing chemicals involved in cell proliferation and maturation, such as short-chain fatty acids (SCFAs) [6]. The present review summarizes the progress in the IBD research focusing and exploring more on the role of probiotics as a potential adjunct approach in UC management.

Epidemiology

IBD impacts people of all age groups, commonly in early adulthood, with a peak incidence between the ages of 15 and 30 years [9]. The incidence of IBD has swiftly progressed over the last few decades with the greatest relative increase seen in emerging and recently developed nations [9], [10]. The estimated incidence of pediatric IBD in Asia and the Middle East ranges from 0.5 to 11.4 (per 100,000 person-years), which is relatively less than the comparable values in Northern and Western Europe 0.5–23 (per 100,000 person-years) and North America 1.1–15.2 (per 100,000 person-years [11]. Another study on adult IBD estimated the disease occurrence was 1.74 per 100,000 persons per year in China [12]. In western countries, although the morbidity remains stable, the disease burden is high as the prevalence exceeds 0.3% [10]. Furthermore, family history of IBD and people relocating to countries with high IBD incidence tends to acquire IBD, especially their first-generation kids [1]. This reflects that IBD is a global disease that not only seriously affects human health, but has drastic economic, psychological, and occupational domains burden on individuals, families, and societies.

Etiology

The exact etiology of IBD is still unknown; however, various theories have been proposed to provide some explanatory clues that include gene-environment interactions, dysbiosis, mucosal barrier dysfunction, and dysregulated immune response to intestinal microbiota that is manifest as chronic inflammation [3], [4], [5]. A decrease in bacterial diversity was noted in the IBD patients, with a marked decline in the number of common anaerobic bacteria including Bacteroides, Eubacteria, and Lactobacilli. Moreover, mucosal inflammation has been closely linked with the loss of these normal anaerobic bacteria [13]. This inflammation is a physiological process occurred as a defense response of an organism. It can be triggered by internal factors such as body cells, or by association with external factors such as infections or exposures to inflammatory agents. This response is mainly initiated to limit and remove any harmful internal and external agents and protect tissues from further damage [14].

The genetic profile of the mucosa seems to react with the gut microflora. According to Magnusson *et al*. [15], this interaction was not observed in UC patients, suggesting that some bacterial activities, such as butyrate synthesis, can influence the genetic expression of the mucosa. Lepage *et al*. [16] found that individuals with UC have various gene expression patterns in the intestinal mucosa, fewer bacterial species, and large amounts of aerobic bacteria than healthy individuals. The intolerance to change toward the gut microflora leads to the stimulation of macrophages and T cells and cytokine synthesis, an increase in adhesion molecules and chemokines, accompanied by the recruiting of neutrophils eosinophils, and monocytes. These effector cells pass through the mucosa and create abscesses in the crypts, deactivating the function of the epithelial barrier. This mechanism allows bacteria more access to the mucosa, enhancing the inflammatory response [17].

The triggers that contribute to IBD include diet, smoking, alcohol, and medications (such as nonsteroidal anti-inflammatory drugs and oral contraceptives [2]. It is also recognized that our food influences the composition of our gut microflora. Many researchers have associated the composition of the diet with the development of IBD, with data indicating that nutrition appears to be significant in the majority of cases with IBD. Westernized diets in wealthy societies are characterized by high levels of animal protein (a risk factor) and low levels of dietary fiber (a preventative factor). According to recent studies, westernized diets are related to decreased gut microbial diversity (dysbiosis), which may raise susceptibility to IBD and other prevalent chronic illnesses [18] while great microbial diversity is attributed to plant-based diets high in dietary fiber.

The intestinal barrier is composed of four-part; physical, made up of the epithelial layer of the cell, the chemical barrier of secreted mucus on the luminal surface of the epithelium, immunological barriers consisting of immune cells found in the lamina propria, and microbiological barriers, consisting of commensal bacteria, in the intestinal lumen and outer mucus layer. The intestinal barrier is comprised of the intestinal tract,

and it prevents harmful materials from entering the intestines [19], [20].

Intestinal Microbiota and Inflammatory Bowel Diseases

The intestinal microbial population that lives in the human intestine counts more than 10^{14} commensal micro-organisms of about 1000 species harboring in the human gut, with higher density and variety from the stomach to the rectum [21].

The most prevalent bacterial genera in the human microbiota are *Bacteroides* spp., *Faecalibacterium* spp., and *Bifidobacterium* spp. [22]. Advances in molecular biology methods have resulted in a much better knowledge of stomach bacteria. The types of microbial populations vary depending on geographical area, ethnicity, age range, and dietary preferences [23]. These organisms, known as commensal microbiota, live in symbiotic relationships with the human host. It plays a significant role in host metabolism by generating vitamins and other metabolites necessary to the host's physiology [24]. The gut microbiome performs several essential roles in the body, including pathogen resistance, immune system modulation, digestion and metabolism, and epithelial cell proliferation and differentiation [25].

Many gut microbiota members perform important roles in the fermentation of dietary components that cannot be absorbed or digested by the small intestine. For example, gut bacteria ferment dietary fibers to SCFAs, including acetic, propionic, and butyric acids, which have anti-cancer, anti-inflammatory, and antioxidant properties, hence aid in the development of host defense and immunity [26], [27].

Research has indicated the significant impact of gut mutualistic bacterial populations on human health [28]. Numerous agents can alter gut microbiota, such as host genetic, mode of delivery, gender, age, height, weight, diet, immune system, bacterial infections, antibiotic treatment, lifestyle, surgery, and diet [29], [30], [31]. The microbiota of UC patients alters quantitatively and qualitatively, with a substantial decrease in population diversity.

A study performed by Noor *et al*. [32], discovered a substantial variation in microbiota composition between healthy people and those with UC or irritable bowel syndrome. There observed a reduction in *Bacteroides* spp. in both diseases, which might be attributed to a decrease in the protective role of this genus during inflammation [13], [32]. On the other hand, some pathogens bacteria are capable of inflicting a host injury through particular virulence factors such as the generation of toxins. These characteristics allow adhesion to and penetration of epithelial cells [33]. The mucosal immune system needs to support a commensal microbiota while fighting against pathogenic bacteria. Microbial population concurrently with immune system development influences gut function [31]. For these causes, significant changes in the structure and function of intestinal bacteria, known as gut microbiota dysbiosis, are linked to gastroenteric diseases and neurologic, respiratory, metabolic, hepatic, and cardiovascular diseases [24].

Management

IBD is characterized by the aggravation and remission stage and one of the treatment aims is to preserve the potentially lengthy remission rates. The paucity of research and the spread of these diseases contributes to diagnostic delays and higher morbidity [34], [35]. Many pharmacological approaches have been implemented over the years in managing IBD patients, with the primary aim to "treat to target," targeting complete endoscopic and clinical remission. These modalities contain corticosteroids, aminosalicylates, immunomodulators, and biologics including pro-inflammatory cytokines inhibitors and integrin antagonists.

In this sense, choosing an appropriate therapy is critical for enhancing the quality of life of IBD patients. Aminosalicylates, particularly 5-aminosalicylic acid, is thought to be beneficial for IBD patients [36]. Corticosteroids, particularly prednisone, hydrocortisone, and budesonide, have been effective in the treatment of IBD, quickly suppressing inflammation and, as a result, alleviating symptoms [3]. However, long-term usage of this drug might lead to additional illnesses such as hypertension, cataract, and metabolic issues [35], [37] affecting the treatment efficacy. In 20% of patients with IBD, the therapies mentioned above do not respond positively, requiring the institution of immunosuppressive therapy, administering azathioprine, methotrexate, and cyclosporine [38].

Alternatively, patients with refractory disease, who do not respond to initial treatment or develop disease' related complications, experience severe colitis or have a high risk of malignant transformation, surgery may be indicated for permanent cure [39]. In this era of personalized medicine, various options are developing starting from improved intestinal microecology, small molecules, exosome therapy, to lastly stem cell transplantation. In the past few years, and in parallel to pharmacological and surgical interventions, guidelines have suggested that enteral feeding is preferred over the parenteral nutrition in adult patients, but to not be used exclusively in treating acute flares of the disease [40]. However, others

recommended that exclusive enteral nutrition may be useful in pediatric CD patients to induce remission alternative to corticosteroids use [41]. Scientist also examined the role of probiotics as a potential adjunct approach in UC management.

Role of Probiotics in Ulcerative Colitis Management

One of the possible methods for preventing/treating IBD is gut modulation by probiotics, which can result in favorable changes in the composition and operations of the gut microbiota and either temporarily or permanently repair it [25]. Bacteria known to be protective in IBD include *Lactobacillus, Bifidobacterium,* and *Enterococcus*. Probiotics may assist in correcting intestinal microbiota imbalances, promote the microecological community, intestinal mucosal barrier effectiveness, and decrease gastrointestinal infections [42].

Over the previous two decades, many articles have been published on the function of probiotics in the course of IBD, using various experimental models, cell lines [43], [44], animal models of colitis in both murine and rat models [45], and clinical study [46]. Probiotics have been investigated in the sickness therapy, protection, and recovery of illnesses. Even if the results are similar, they vary, most likely due to the study techniques and the bacterial strain used. In the animal model for colitis induction, dextran sulfate sodium (DSS) or 2,4,6-trinitrobenzene sulfonic acid (TNBS) is the most popular. DSS is commonly employed by its strong, rapid, and dose-dependent UC-like action [7]. At the same time, TNBS is usually used to induce CD-like colitis [7]. However, these models may not fully represent the actual human IBD. Still, until now, these are the most well-known colitis stimuli.

Some lactobacilli can attach to mammalian tissues, enabling adaptation to the gastrointestinal tract, interaction with the host, and competitive pathogen exclusion. Once the intestinal barrier is well, it enables selective paracellular transport of nutrients, regulates solute and water fluxes, and also acts as a defense mechanism against pathogen/toxin entry. When barrier function is disrupted, permeability and function change, leading to irritable bowel syndrome [47], food allergies, and obesity [48]. In this context, the role of probiotics involves the beneficial alteration in the composition of the intestinal microbiota, pathogenic micro-organism reduction, modulation of the immune response, and creation of compounds that help the regeneration of the gut mucosa [3].

The dose of probiotics required for bacteria varies based on the strain and the product. In general, to provide health benefits, products containing probiotic micro-organisms must include the lowest quantity of live cells with proven effectiveness (through human experiments), estimated between 10^6 and 10^8 CFU/g of the final product or 10^8-10^{10} CFU/day (taking into account 100 g or 100 mL of food [49]. A few years ago, there has been tremendous progress in understanding the processes underlying distinct types of probiotics and how they relate to IBD [6].

Several mechanisms have been hypothesized to explain the therapeutic impact of probiotics in patients with IBD, including a decrease of pathogenic organisms by competition and synthesis of antimicrobial molecules (lactic and acetic acids, hydrogen peroxide, and bacteriocins); activation of the immune system-related with epithelial cells, resulting in the generation of anti-inflammatory interleukins such as IL-10; enhancement of intestinal barrier function; and production of SCFAs and polyamines [50], [51], [52]. Understanding the mode of action of probiotic micro-organisms, especially in the case of IBD, will allow the establishment of criteria for selecting the appropriate probiotic strain for each type of disease, finding the most effective dosages and administration times, in addition to allowing for synergistic mixtures of various bacterial species [50].

Different bacteria, including pathogens and commensals, can influence intestinal barrier function either directly or indirectly. For instance, *Lactobacillus rhamnosus, Escherichia coli*, and a commercial combination of *lactobacilli* and *bifidobacteria* have been proven to prevent “leaky gut” by improving mucosal and lowering barrier permeability [8]. Martín *et al*. [53] demonstrated that *L. rhamnosus* CNCM I-3690 avoids the increased intestinal permeability caused by moderate inflammation. Furthermore, this strain protects against oxidative stress in *Caenorhabditis elegans* [53], [54]. Many studies have found that the beneficial impacts of probiotics can only be acquired by ingesting various strains and that probiotic characteristics can be greatly influenced by the metabolic activity of the strains [45]. Much research on the IBD and probiotics has shown promising outcomes utilizing bacteria strains from the genera *Lactobacillus* spp. and *Bifidobacterium* spp. using animal models (Table 1).

Several investigations showed that various *Lactobacillus* and *Bifidobacterium* species exhibit anti-inflammatory characteristics, enhance innate and adaptive immune responses, and promote the production of anti-inflammatory cytokines [55], [56]. According to Yan *et al*. [57], the strain of *Bifidobacterium longum* YS108R induces the production of IL-10, which can be used to control IBD (Table 1). Other research has demonstrated the efficiency of probiotics in improving colon cells and repairing the intestinal barrier function [55], [58], [59]. Other studies also concluded that the administration of *Lactobacillus plantarum* YS-3 and *Lactobacillus bulgaricus* to Mouse induced 1% Oxazolone promotes an anti-colitis by decreasing

Table 1: The effect of probiotics on inflammatory bowel diseases, particularly ulcerative colitis in animal models

Type of probiotic	Dose and period	Research model	Induced chemical and period	Result	References
L. acidophilus XY27	1×10^9 CFU/mL (21 days)	(Animal model) mouse	3% DSS-induced colitis (7 days)	Symptom reduction and colitis prevention in mice with DSS-induced ulcerative colitis Repaired the intestinal barrier function Relieving the symptoms of colitis Abilities of antioxidant Restoring the gut barrier Achieving equilibrium between gene expression and inflammatory agent secretion	[59]
B. longum Bif10, Bif11 and Bif16	2×10^{10} CFU/animal (25 days)		2.5% DSS-induced colitis (7 days)	Protection against DSS-induced colitis Improved SCFA levels Prevented shortening of the colon ↓ Produce the level of LPS-induced NO and pro-inflammatory cytokines ↓ The amounts of IL-1β, 6, TNF-α, and Lipocalin ↓ The DAI of IBD	[62]*
B. longum 5 (1A)	10^9 CFU/mL (7 days) (10 days)		3.5% DSS-induced colitis (7 days)	↓ In intestinal permeability ↓ IL-1β, MPO ↓ Eosinophil peroxidase levels ↓ The impact of the inflammatory response and its implications for the epithelial layer of the gut	[63]*
B. longum YS108R	10^9 CFU/mL (21 days)		2.5% DSS-induced colitis (7 days)	Reduce the DSS-induced inflammation and its symptoms ↑ IL-10 ↓ The pro-inflammatory cytokine IL-6 and IL-17A levels ↓ TNF-α, MPO, IL-1β Keep the mucosal barrier genes expression levels constant Keeping the mucosal barrier in its normal state and reversal of the altered microbiota	[57]*
B. longum and VSL#3	4×10^9 CFU/dose (7 days)		2.5% TNBS-induced colitis (4 days)	↓ *High mobility group box 1* protein Improved intestinal inflammation Fecal microbiota balance ↑ Expression of zonula occludins-1, occludin, and claudin-1 in colon tissues	[64]*
E. faecalis (EF-2001)	Group (a): 2 mg/kg Group (b): 17 mg/kg (16 days)		4% of DNBS (2 days)	↓ Symptoms of IBD Preventing the pathological shortening of the colon's length ↓ The weight of mesenteric lymph nodes ↓ Proinflammatory cytokine expression in the colon Enhance the colon's health ↓ Inflammation associated with colitis	[65]
Three strains: *L. paracasei* subsp. *paracasei* NTU 101 (lyophilized powdered)	Half dose: 2.3×10^9 CFU/kg Full dose: 4.5×10^9 CFU/kg (25 days)		DSS (7 days)	Improved antioxidant capacity ↓ Pro-inflammatory cytokine ↑ Anti-inflammatory cytokine Reduce the DSS-induced colitis and its symptoms	[56]
L. plantarum CQPC07 (*LP*)	Low dose: 1.0×10^8 CFU/kg High dose: 1.0×10^9 CFU/kg (35 days)		2% DSS (on the 21st day) 4% DSS (on the 35th day)	Prevent the colon's length from reducing and its weight-to-length ratio Prevent DSS-induced oxidative damage in colon tissue Inhibit DSS-induced colitis in mice (inhibit colitis) ↓ The ET and SP concentrations ↑ The concentrations of SS and VIP in mice with colitis ↑ The level of IL-2 and ↓ the level of IL-10 in serum Upregulated the expression of nNOS, eNOS, c-Kit, and SCF mRNA	[66]*
L. plantarum YS-3 (LP-YS3) *L. bulgaricus*	Low concentration: 1×10^8 CFU/mL High concentration: 1×10^9 FU/mL (26 days) 1×10^9 CFU/mL (26 days)		1% oxazolone (on the 20th, 22nd and 25th days)	Enhanced the ratio of colonic weight/colon length and prevented the future loss of colonic length due to colitis ↓ DAI in colitis mice ↓ The contents of MPO, NO, MDA, and IL-10 in colonic tissues ↓ The expression of iNOS, IL-8, and CXCR2 in colonic tissues ↑ The content of GSH and the serum level of IL-2 ↑ The expression of nNOS, eNOS, c-Kit, and SCF Prevent oxazolone-induced colitis	[61]*
L. plantarum YS-4 (LP-YS4)	Low concentration: 1×10^8 CFU/mL High concentration: 1×10^9 CFU/mL (35 days)		2% DSS (in weeks 3) 4% DSS (in weeks 5)	Improve the levels of IL-2 cytokines Suppress the DSS-induced oxidative stress response Inhibit DSS-induced colitis ↓ ET, SP level ↓ IL-10 levels in serum ↓ MPO and MDA activity in colonic tissues of mice with colitis ↓ The expression of iNOS, IL-8, and CXCR2 in the colon of colitis mice ↑ GSH, superoxide dismutase activity ↑ The expression of nNOS, eNOS, c-Kit, SCF mRNA	[67]
B. longum LC67	2×10^9 CFU/animal (3 days)		2.5% TNBS-induced colitis	↓ NF-κB, MPO ↓ Pro-inflammatory factors (IL-1031, TNF-α)	[68]
L. plantarum YS2 (LPYS2) *L. bulgaricus*	Low concentration: 1×10^8 CFU/mL High concentration: 1×10^9 CFU/mL (26 days) 1×10^9 CFU/mL (26 days)		1% oxazolone (on the 20th day)	A good anti-colitis effect ↓ DAI score ↓The MPO, NO, MDA levels in colon tissues ↓ iNOS, IL-8, and CXCR2 expressions Improve the levels of IL-2 cytokines ↑ Length of the colon following colitis induction in mice ↑ The proportion of colon weight to colon length in mice with colitis ↑ nNOS, eNOS, c-kit, SCF mRNA expressions	[60]*

(Contd...)

Table 1: ***(Continued)***

Type of probiotic	Dose and period	Research model	Induced chemical and period	Result	References
L. fermentum HY01 (LF-HY01)	Low concentration: 1×10^{9} CFU/kg High concentration: 1×10^{10} CFU/kg (35 days)		2% DSS (in weeks 3) 4 % DSS (in weeks 5)	Improving colon cells, length damage ↓ Pro-inflammatory factors (INF-γ, IL-12, TNF-α, and IL-6) ↑ The protein levels of IκBα ↓ The protein levels of NF-κB p65, iNOS, and cyclooxygenase-2	[58]*
B. longum LC67	1×10^{9} CFU/animal (3 days)		6 mL ethanol-induced gastritis (3 h)	Reduce the liver damage and gastritis that ethanol causes ↓ Ethanol-induced hemorrhagic ulcerative lesions area ↓ NF-κB, TNF, Platelet factor 4 (CXCL4) ↓ MPO activity ↓ Inflammatory responses ↑ ADH and, ALDH activities	[69]
B. longum ssp. *longum* CCM 7952 (BI 7952) and CCDM 372 (BI 372)	2×10^{8} CFUs (10 days)		2.5 % DSS-induced colitis (7 days)	Improved intestinal barrier function ↑ Pro- and anti-inflammatory cytokines ↓ Clinical signs and maintained tight junction protein expression ↓ Decrease FITC-dextran concentration in serum Maintain the disruption of tight connections proteins linked to the pathogenesis of ulcerative colitis	[55]*
L. casei	10^{8} CFU/mL (10 days)	(Animal model) Rat	5% TNBS (the first day)	Reduction in colitis symptoms as measured by pathology scores ↓ MPO activity ↓ Colon oxidative stress markers	[70]
L. reuteri	10^{8} CFU/day (14 days)		3% DSS (7 days)	↓ Severity of colitis (clinically and histologically) ↓ Inflammation markers MPO, IL-1β, IL-6, and mKC ↑ The firmly adherent mucus thickness ↑ Expression of the tight junction proteins occludin and ZO-1	[71]

*CFU/mL: Colony-forming unit per millilite, DSS: Dextran sulfate sodium, UC: Ulcerative colitis, SCFA: Short-chain fatty acids, LPS: Lipopolysaccharide, TNF-α: Tumor necrosis factor alpha, DAI: Disease activity index, IBD: Inflammatory bowel disease, MPO: Myeloperoxidase, TNBS: 2,4,6-Trinitrobenzene sulfonic acid, mg/kg: Milligrams per kilograms, ET: Endothelin, SP: Substance P, SS: Somatostatin, VIP: Vasoactive intestinal peptide, GSH: Glutathione, MDA: Malondialdehyde, nNOS: Neuronal nitric oxide synthase, eNOS: Endothelial nitric oxide synthase, SCF: Stem cell factor, mRNA: Messenger RNA, iNOS: Inducible nitric oxide synthase, CXCR2: C-X-C motif chemokine receptor 2, NO: Nitric oxide, NF-κB: Nuclear factor kappa B, INF-γ: Interferon gamma, FITC dextran: Fluorescein isothiocyanate dextran, IL-1β: Interleukin-1β, IL-6: Interleukin 6, IL-17A: Interleukin-17, IL-10: Interleukin 10, IL-8: Interleukin 8, IL-12: Interleukin 12,IL-2: Interleukin-2, L. acidophilus: *Lactobacillus acidophilus*, *B. longum*: *Bifidobacterium longum*, *E. faecalis*: *Enterococcus faecalis*, *L. paracasei*: *Lactobacillus paracasei*, *L. plantarum*: *Lactobacillus plantarum*, *L. bulgaricus*: *Lactobacillus bulgaricus*, *L. fermentum*: *Lactobacillus fermentum*, *L. casei*: *Lactobacillus casei*, *L. reuteri*: *Lactobacillus reuteri*, DNBS: Dinitrobenzene sulfonic acid, ADH: Alcohol dehydrogenase, ALDH: Acetaldehyde dehydrogenase, mKC: Mouse keratinocyte chemoattractant, ZO-1: Zonula occludens-1. ↑ : Increase, ↓ : Decrease

disease activity index score in colitis mice and increases the colon length after the mice induced colitis [60], [61].

Conclusion

Despite the fact that the etiology of IBD is still unknown, it is becoming increasingly evident that many factors such as genetics, environment, immunology, and gut microbiota interact and contribute to disease symptoms and severity. Recently, researchers' effort has focused primarily on factors that influence the diagnosis and management of IBD. Probiotics have played a significant role in UC management. Although more research is needed to support this therapeutic effect, this discovery could represent a viable strategy for IBD patients due to its mild to non-existent side effects, as well as it is simply being introduced into patients' daily diet.

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