Revista ARACÊ
ISSN: 2358-2472

GUT MICROBIOTA MODULATION AS PREVENTION AND TREATMENT STRATEGIES FOR INTESTINAL INFLAMMATORY DISEASES

https://doi.org/10.56238/arev7n12-209

Date of submission: 11/18/2025 **Date of publication:** 12/18/2025

Larissa Lopes Santos[1], Rafael de Freitas Juliano[2], Alexandre de Castro Keller[3], Izabel Cristina Rodrigues da Silva[4], Sonia Gómez-Martínez[5], João Paulo Martins do Carmo[6]

ABSTRACT

The intestinal microbiota represents a functional extension of the host genome, providing non-encoded enzymes and proteins essential for metabolism and physiological regulation. Dysbiosis and the consequent disruption of intestinal barrier are key contributors to the onset and progression of inflammatory bowel diseases (IBD), including Crohn's disease (CD) and ulcerative colitis (UC). Beyond conventional therapies, gut microbiota modulation has emerged as a promising strategy for IBD managing. However, its succes depends on a clear understanding of underlying mechanisms, potential risks and therapeutic benefits, to ensure informed decision making by both clinicians and patients. This study aimed to conduct a comprehensive and systematic literature review on microbiota-targeted interventions in adult patients with CD and UC. Twenty-one studies were analyzed: six focusing on CD and 15 on UC. The interventions included fecal microbiota transplantation (FMT), dietary supplementation with probiotics, probiotic-derived fractions, prebiotics, synbiotics, and plant-based diets. The most frequent outcomes were clinical remission and symptom reduction, with adverse effects generally mild and well tolerated. Across studies, microbiota modulation was associated with increased beneficial bacteria genera, higher short-chain fatty acid (SCFA) levels, and reduced pro-inflammatory cytokines. In summary, gut microbiota modulation appears to restore mucosal barrier integrity, alleviate dysbiosis, and attenuate intestinal inflammation, supporting its potential as viable therapeutic strategy for preventing and managing IBD, particularly CD and UC.

Keywords: Intestinal Inflammatory Diseases. Environmental Factors. Microbiota. Treatment. Food and Water Security.

[1] Bachelor of Pharmacy, Pharmacy School, Goiás State University (UEG). Universitary Unity (UnU) Itumbiara, Goiás (GO), Brazil. E-mail: larissalosa33@gmail.com Orcid: https://orcid.org/0009-0001-9443-8323 Lattes: http://lattes.cnpq.br/3583286498279909
[2] Professor, Ph.D. UEG, UnU Itumbiara, GO, Brazil. E-mail: rafreju@ueg.br Orcid: https://orcid.org/0000-0003-2371-7429 Lattes: http://lattes.cnpq.br/0875219054249716
[3] Associated Professor, Ph. D. Escola Paulista de Medicina. Federal University of São Paulo (UNIFESP), São Paulo, SP, Brazil. E-mail: ackeller@unifesp.br Orcid: https://orcid.org/0000-0002-7827-0292 Lattes: http://lattes.cnpq.br/9264244341601758
[4] Professor, Ph.D. Department of Molecular Pathology. Universidade de Brasília (UnB), Ceilândia, Distrito Federal (DF), Brazil. E-mail: belbiomedica@gmail.com Orcid: https://orcid.org/0000-0002-6836-3583 Lattes: http://lattes.cnpq.br/9808053066757132
[5] Professor, PhD. Department of Nutrition and Food Science, Faculty of Pharmacy, Complutense University of Madrid, 28040, Madrid, Spain. E-mail: songom03@ucm.es Orcid: https://orcid.org/0000-0002-3281-0118
[6] Professor, Ph.D. UEG, UnU Itumbiara, GO, Brazil. E-mail: joao.carmo@ueg.br Orcid: https://orcid.org/0000-0003-3961-8732 Lattes: http://lattes.cnpq.br/4477605272205779

Revista ARACÊ
ISSN: 2358-2472

MODULAÇÃO DA MICROBIOTA INTESTINAL COMO ESTRATÉGIA DE PREVENÇÃO E TRATAMENTO DE DOENÇAS INFLAMATÓRIAS INTESTINAIS

RESUMO

A microbiota intestinal representa uma extensão funcional do genoma do hospedeiro, fornecendo enzimas e proteínas não codificadas por ele, essenciais para o metabolismo e a regulação fisiológica. A disbiose e a consequente ruptura da barreira intestinal são fatores determinantes no início e na progressão das doenças inflamatórias intestinais (DII), como a doença de Crohn (DC) e a retocolite ulcerativa (RCU). Além das terapias convencionais, a modulação da microbiota intestinal tem emergido como estratégia promissora no manejo dessas doenças. No entanto, sua eficácia depende de uma compreensão aprofundada dos mecanismos subjacentes, bem como de seus potenciais riscos e benefícios terapêuticos. O presente estudo apresenta uma revisão sistemática da literatura sobre intervenções direcionadas à microbiota em pacientes adultos com DC e RCU. Foram analisados vinte e um estudos, sendo seis focados em DC e 15 em RCU. As intervenções incluíram transplante de microbiota fecal (TMF), probióticos, frações derivadas de probióticos, prebióticos, simbióticos e dietas à base de plantas. O TMF foi a estratégia mais frequentemente relatada. Os desfechos mais frequentemente relatados foram remissão clínica e redução dos sintomas, com efeitos adversos leves e bem tolerados. Em geral, a modulação da microbiota esteve associada a aumento de gêneros bacterianos benéficos, níveis mais elevados de ácidos graxos de cadeia curta (AGCC) e redução de citocinas pró-inflamatórias. Em síntese, a modulação da microbiota intestinal contribui para a restauração da integridade da mucosa intestinal, a correção da disbiose e a atenuação da inflamação intestinal, configurando-se como estratégia terapêutica viável e potencialmente eficaz para a prevenção e manejo das DIIs, espcialmente da DC e RCU.

Palavras-chave: Doenças Inflamatórias Intestinais. Microbiota. Fatores Ambientais. Tratamento. Segurança Hídrica e Alimentar.

MODULACIÓN DE LA MICROBIOTA INTESTINAL COMO ESTRATEGIAS DE PREVENCIÓN Y TRATAMIENTO DE LAS ENFERMEDADES INFLAMATORIAS INTESTINALES

RESUMEN

La microbiota intestinal representa una expansión funcional del genoma del huésped, proporcionando enzimas y proteínas no codificadas por este, esenciales para el metabolismo y la la regulación fisiológica. La disbiosis y la consecuente alteración de la la barrera intestinal constituyen fatores claves en la aparición y progresión de las enfermedades inflamatorias intestinales (EII), como la enfermedad de Crohn (EC) y la colitis ulcerosa (CU). Mas allá de las terapias convencionales, la modulación de la microbiota intestinal ha surgido como una estrategia prometedora para el manejo de las EII. No obstante, su eficacia depende de una comprensión clara de los mecanismos subjacentes, así como de los possibles riesgos y benefícios terapéuticos. El presente estudio realiza una revisión sistemática de la literatura sobre intervenciones dirigidas a la microbiota en pacientes adultos con EC y colitis ulcerosa. Se analizaron veintiún estudios, de los cuales seis se centraran en EC y quince en CU. Las intervenciones incluyeron transplante de microbiota fecal (TMF), probióticos, fracciones derivados de probióticos, prebióticos, simbióticos y dietas baseadas en plantas. Los

Revista ARACÊ
ISSN: 2358-2472

resultados más frecuentes fueron remisión clínica y reducción de los síntomas, con efectos adversos generalmente leves y bien tolerados. En conjunto, la modulación de la microbiota se asoció con un aumento de géneros bacterianos beneficiosos, mayores niveles de ácidos grasos de cadena corta (AGCC) y reducción de citocinas proinflamatórias. En conclusión, la modulación de la microbiota intestinal favorece la restauración de la integridad de la barrera mucosa, mejora la disbiosis y atenúa la inflamación intestinal, lo que respalda su potencial como estratégia terapéutica viable para la prevención y el tratamiento de las EII, particularmente la EC y la CU.

Palabras clave: Enfermedades Inflamatorias Intestinales. Microbiota. Factores Ambientales. Tratamiento. Seguridad Hídrica y Alimentaria.

Revista ARACÊ
ISSN: 2358-2472

1 INTRODUCTION

The human microbiome comprises a vast community of organisms, including viruses, protozoa, fungi, archaea, and bacteria. More than 70% of these microbes reside in the gastrointestinal tract, where they maintain a mutually beneficial relationship with its host (PASCALE *et al.*, 2018; KHO; LAL, 2018). Microbial cells also colonize the oral cavity, genital organs, respiratory tract, and skin, but the colon harbors the largest population, approximately $3.8x10^{13}$ bacteria (MIYAUCHI *et al.*, 2023).

This remarkable diversity represents a functional extension of the host genome, contributing enzymes and proteins not coded by human DNA and playing an essential role in metabolism and physiological regulation. The predominant bacteria phyla in the gut are Firmicutes and Bacteroidetes. The beneficial relationship of the intestinal microbiota with its host is mediated by a complex network of metabolites that act as signaling molecules, regulating the neuroimmune axis and modulating inflammatory responses (KHO; LAL, 2018; PADHI *et al.*, 2022; TAN *et al.*, 2024; VAN DE WOUW *et al.*, 2018).

Among these metabolites, short-chain fatty acids (SCFA) - acetate, butyrate, and propionate – are particularly important. They promote the synthesis of glucagon-like peptide 1 - GLP-1, support intestinal gluconeogenesis, exert immunomodulatory effects, and activate dendritic cells. The microbiota also synthesizes vitamins such as thiamine (B1), pyridoxine (B6), and cobalamin (B12), providing energy to the host and proliferation of regulatory immune cells (HAASE *et al.*, 2018; HANTSOO; ZEMEL, 2021; PADHI *et al.*, 2022; VAN DE WOUW *et al.*, 2018; YADAV *et al.*, 2022).

Beyond GLP-1, several gastrointestinal hormones communicate with the brain to regulate appetite and body weight. Ghrelin function as an orexigenic hormone, while glucose-dependent insulinotropic peptide (GIP), cholecystokinin (CCK), postprandial peptide YY (PYY) and oxyntomodulin (OXM) exhibit anorexigenic effects (HONG & CHOY, 2024). Incretins, such as GIP and GLP-1, secreted postprandially by intestinal cells, stimulate insulin release by pancreatic b-cells and influence lipid metabolism, gastric emptying, appetite, and overall energy balance. The gut microbiota plays a critical role in modulating these processes by interacting with enteroendocrine cells that regulate incretin secretion. Microbial metabolites, including SCFA and indoles, directly stimulate incretin release from colonic enteroendocrine cells, thereby influencing satiety and food intake. Moreover, Milhouse *et al* (2025) demonstrated in murine models that gut microbiota downregulates genes involved in appetite suppression, modulates G-protein coupled receptors (GPCR) linked to gut hormone

Revista ARACÊ
ISSN: 2358-2472

secretion, and contributes to leptin resistance (ANGELINI; RUSSO; MINGRONE, 2024; DA SILVA *et al.*, 2022; MILHOUSE *et al.*, 2025; TAN *et al.*, 2024).

The intestinal barrier, positioned between the external environment and the host's internal milieu, consists of a mucus layer and epithelial cells connected by tight junction proteins that preserve barrier integrity and regulate permeability. When this barrier is disrupted, commensal microorganisms, microbial products, and luminal components can translocation across the epithelium, triggering abnormal immune activation. Such dysregulation promotes inflammation, allergic responses, and autoimmune disorders through mechanisms involving molecular mimicry and impaired T-lymphocyte responses (LAWLEY; WALKER, 2013; PADHI *et al.*, 2022; PANDA; PATTNAIK; AICH, 2025).

Maintaining intestinal homeostasis depends on the delicate balance between regulatory T lymphocytes (Tregs) and T helper 17 (Th17) cells, which enables the immune system to distinguish pathogens from commensal microorganisms, and establishes tolerance toward beneficial species. Commensal bacteria such as *Bacteroides fragilis*, *Bifidobacterium infantis*, and members of the *Firmicutes* phylum promote the expansion of Tregs expressing the *FOXP3* gene, which encodes a hallmark anti-inflammatory protein responsible for interleukin-10 (IL-10) production. This cytokine suppresses pathological inflammation driven by aberrant T-cell activation and further reinforces intestinal barrier function (CHENG; YANG; CHU, 2022; DA SILVA *et al*., 2022; LAWLEY; WALKER, 2013).

Numerous disorders have been associated with disruptions in the normal functioning of the intestinal microbiota. Factors such as antibiotic use, dietary composition, exposure to microplastic and nanoplastics through water and food, psychological and physical stress, and individual host characteristics can induce dysbiosis. This imbalance promotes the proliferation of opportunistic or virulent microbial strains and the production of harmful metabolites. Inflammatory bowel diseases (IBD) are marked by an overrepresentation of virulent *Bacteroides fragilis*, mucolytic *Ruminococcus* spp., and members of the *Enterobacteriaceae* family, along with a reduction of butyrate-producing species, such as *Faecalibacterium prausnitzii* and *Roseburia hominis*. Furhtermore, during the COVID-19 pandemic, evidence indicated that a shift toward a pro-inflammatory gut microbiome and reduced anti-inflammatory bacterial activity might have been associated with severe clinical outcomes (ALI *et al*., 2025; CHEN *et al*., 2023; GAO *et al*., 2025; KHO; LAL, 2018; PANDA; PATTNAIK; AICH, 2025; REINOLD *et al*., 2021; SMITH *et al*., 2022).

Revista ARACÊ
ISSN: 2358-2472

Disruption of the intestinal barrier represents a crucial event in the initiation of inflammation underlying IBD. Throughout the gastrointestinal tract (GIT), the intestinal microbiota must be tolerated by the immune system while remaining protected against dysbiosis and the proliferation of opportunistic pathogens. The intestinal epithelium is essential for preserving this equilibrium, serving both as a physical barrier and a source of antimicrobial compounds (ALI *et al*, 2025; CHEN *et al*, 2023; GAO *et al*, 2025; SHALAPOUR; KARIN, 2020).

IBD encompasses chronic inflammatory disorders of the GIT, primarily Chron's disease (CD) and ulcerative colitis (UC). These conditions differ from other intestinal inflammatory diseases, such as diverticulitis, appendicitis, radiation- or drug-induced enteritis, intestinal vasculitis, and infectious processes, as they represent chronic and relapsing diseases that occur in genetically predisposed individuals with incompletely understood etiologies. Nonetheless, interaction between host genetic factors and gut microbiota play a pivotal role in their pathogenesis. Both UC and CD present with diarrhea, abdominal pain, and hematochezia, but differ in the distribution and depth of inflammation. CD causes discontinuous, transmural inflammation that may involve any segment of the digestive tract, from the mouth to the anus, whereas UC is characterized by continuous inflammation limited to the mucosa and superficial submucosa, primarily affecting the colon and rectum (CARVALHO *et al.*, 2022; CORRIDONI; ARSENEAU; COMINELLI, 2014; FERREIRA; DEUS; ANTANACCI JUNIOR, 2021; SANTOS, 2013).

Genetic susceptibility is an important determinant of IBD, but additional environmental and lifestyle factors contribute substantially to disease risk. These include smoking, diet, medication use, psychosocial stress, microbial exposures, and - more recently – ingestion of microplastics and nanoplastics through food and water. Studies indicate that a Western-style diet increases the risk of CD and UC, while the use of non-steroidal anti-inflammatory drugs (NSAIDs) can aggravate IBD progression. These drugs compromise the intestinal mucosa and disturb the balance between commensal microbiota and host defense mechanisms, influencing both the onset and persistence of inflammatory processes (ALI *et al.*, 2025; CHEN *et al.*, 2023; CHICCO *et al.*, 2021; CORRIDONI; ARSENEAU; COMINELLI, 2014; GAO *et al.*, 2025; PERLER; FRIEDMAN; WU, 2022; PILEGGI *et al.*, 2019; SINGH *et al.*, 2023).

Current therapeutic strategies for IBD primarily involve anti-inflammatory biologics, including monoclonal antibodies targeting Tumor Necrosis Factor – alpha (TNF-a), IL-12, and IL-23, as well as small molecules such as α4β7 integrin antagonists. Although these

Revista ARACÊ
ISSN: 2358-2472

treatments are among the most effective options currently available, they are often associated with significant adverse effectts and disease reccurrence over time. Consequently, there is a growing interest in developing safer, microbiota-targeted strategies for maintaining intestinal health in patients with CD and UC, either as standalone approaches or as adjuncts to biologic therapies (HVAS *et al.*, 2018; KHO; LAL, 2018; KIM; AHN; PARK, 2021; STERLIN; GOROCHOV, 2021).

A comprehensive understanding of the mechanisms underlying microbiota-based interventions is essential for their effective clinical implementation. Such knowledge clarifies the benefits and potential risks of these therapies, supports informed decision-making for patients, and provides a foundation for exploring synergistic effects between microbiota modulation and biological therapies to optimize outcomes in Crohn's disease and ulcerative colitis.

2 THE GUT MICROBIOTA: COMPOSITION AND FUNCTIONAL STATES

2.1 STRUCTURAL AND CELLULAR COMPONENT

The human gut microbiota comprises a vast diversity of microorganisms that play essential roles in digestion, substrate fermentation, immune system regulation, and the synthesis of vitamins and enzymes. The metabolic activity of this microbial ecosystem is so extensive that it is often referred to as a “virtual organ”. Despite representing an immunological challenge, the intestinal microbiota is fundamental for the lymphoid tissues development and maturation, as well as for the intestinal immunity maintenance and modulation (PAREKH *et al.*, 2015; SOMMER; BÄCKHED, 2013).

The intestinal epithelium, including the crypts of the small and large intestines, contains specialized cells that perform distinct physiological roles. Enterocytes absorb nutrients and water; goblet cells secrete mucins that compose the mucus layer; enteroendocrine cells release hormones; Paneth cells produce antimicrobial peptides (AMPs); and intestinal stem cells ensure continuous epithelial renewal. Paneth cells, found exclusively in the small intestine, secrete α-defensins, lysozymes, ribonucleases (such as angiogenin-4), and secretory phospholipase A_2 only in the small intestine (ALLAIRE *et al.*, 2018; SIMPSON *et al.*, 2025).

Paneth cells, restricted to the small intestine, produce a-defensins, lysozymes, ribonucleases such as angiogenin-4, and secretory phospholipase A_2. Enterocytes, found in both the small and large intestines, express REG3γ and REG3β, while epithelial cells in

Revista ARACÊ
ISSN: 2358-2472

general secrete β-defensins and cathelicidins. In the large intestine, goblet cells are more abundant and produce RELMβ, ANG4, REG3γ, and REG3β. These cells are connected by tight junction proteins, including occludins, claudins, zonula occludens (ZO), and junctional adhesion molecules, that regulate intestinal permeability and prevent microbial translocation. The expression is modulated by external stimuli such as cytokines. Intestinal epithelial cells directly interact with the microbiota express pattern recognition receptors (PRRs), including Toll-like receptors (TLRs). These receptors activate NF-κB and interferon regulatory factors (IRFs) through the MyD88 and TRIF signaling, initiating cascades that recruit additional adaptor proteins, and activate the NLRP3 inflammasome, which coordinates downstream inflammatory responses (ALLAM-NDOUL; CASTONGUAY-PARADIS; VEILLEUX, 2020; BOWCUTT *et al.*, 2014; JAHROMI; RAZI; REZAEI 2024; LAVELLE *et al.*, 2010; ROWART, 2018; VINCENZO *et al.*, 2024).

2.2 HOMEOSTASIS AND INFLAMMATORY TRANSITIONS

The gut-liver axis represents a key anatomical and functional link between the intestine and liver, mediated by the biliary tract and the portal vein. This connection allows bile acids synthesized by the liver to reach the GIT, while the liver receives blood enriched with nutrients microbial metabolites for filtration and detoxification. Approximately 75% of the liver's blood supply is derived from the portal vein, which drains the mesenteric venous system (MILOSEVIC *et al.*, 2019; PABST *et al.*, 2023).

Under homeostatic conditions, specialized antigen-presenting myeloid cells capture luminal antigens, migrate to mesenteric lymph nodes, and present them to naïve T cells in the presence of TGF-β and retinoic acid. This promotes Treg cell differentiation specific to dietary and bacterial antigens. IL-10 further promotes Treg proliferation and induces IgA class switching in B cells, a process also regulated by TGF-β. Secretory IgA is transcytosed across the epithelial barrier via the polymeric immunoglobulin receptor and released into the intestinal lumen, where it regulates antigen entry from food and commensal microbes. Along with Tregs, IgA contributes to systemic tolerance to dietary and microbial antigens. A balanced diet promotes microbial diversity and increases SCFA and tryptophan metabolite production, which inhibit pro-inflammatory pathways such as NF-κB and NLRP3, enhance tight junction protein expression and sustain epithelial cell homeostasis (DZUTSEV *et al.*, 2017; MACPHERSON *et al.*, 2018; PABST *et al.*, 2023).

Revista ARACÊ
ISSN: 2358-2472

During inflammation, bacteria or microbial products that breach the intestinal barrier activate local myeloid cells to produce IL-23. This cytokine amplifies IL-17-mediated inflammatory pathways while inhibiting Treg differentiation, thereby affecting not only the intestine but also the liver, pancreas, and other organs. When the intestinal barrier becomes compromised, the liver is among the first organs to encounter microbial components that penetrate the submucosa, initiating immune activation. Overnutrition, alcohol abuse, and indiscriminate antibiotic use can exacerbate this process, leading to chronic inflammation and contributing to both non-alcoholic and alcoholic steatohepatitis development. Barrier disruption also reduces microbial diversity and SCFA levels while activating NF-κB and NLRP3, perpetuating inflammation in both intestinal and hepatic tissues (CIAULA *et al.*, 2020; MANNON, 2019; MILOSEVIC *et al.*, 2019; PABST *et al.*, 2023; PANDA; PATTNAIK; AICH, 2025; SMITH *et al.*, 2022).

2.3 TREATMENTS FOR CROHN'S DISEASE (CD) AND ULCERATIVE COLITIS (UC)

Among inflammatory bowel diseases (IBD), CD and UC present exhibit highly heterogeneous clinical manifestations, making it difficult to categorize patients into broad clinical groups. Each case requires individualized characterization based on its clinical, radiological and histopathological presentations, which often do not align perfectly. This multifactorial nature explains the wide variability in therapeutic approaches. CD can affect any segment of the digestive tract, from the mouth to the anus, in a focal, asymmetrical, and transmural pattern. It may present as inflammatory, fistulizing, and fibrostenotic forms, predominantly involving the ileum, colon, and perianal region. Diagnosis relies on a combination of clinical, imaging, and histopathological findings, and intestinal transit studies are useful both for diagnostic confirmation and for excluding other GIT diseases (CHA *et al.*, 2017; PARAMSOTHY *et al.*, 2018; SANTOS, 2013; SOUZA *et al.*, 2021; SU *et al.*, 2018; YANTISS; ODZE, 2006).

In contrast, UC primarily affects the mucosa, and alterations in the mucus layer are believed to play a central role in its pathogenesis. Intestinal mucus, mainly composed of mucins, protects the epithelial surface by forming a selective barrier that regulates bacterial colonization. Its selectivity depends on biochemical properties that allow adhesion only of specific bacterial species. In refractory UC – characterized by severe bleeding, toxic megacolon, or significant dilation – surgical management through colectomy with terminal ileostomy may be indicated. Similarly, CD patients with recurrent or persistent obstruction,

Revista ARACÊ
ISSN: 2358-2472

hemorrhage, perforation, or neoplastic transformation may require surgical intervention (BARROS *et al.*, 2020; CORRIDONI *et al.*, 2014; SANTOS, 2013; SU *et al.*, 2018).

IBD management relies primarily on anti-inflammatory and immunomodulatory therapies aimed at alleviating symptoms, prolonging remission, delaying the need for surgery, and improving patient's quality of life. Nutritional correction is also a critical component of care, while surgical procedures are generally reserved for disease-related complications. Hanauer *et al* (2019) proposed a “treatment pyramid” for IBD, incorporating both step-up and top-down strategies, depending on disease severity. While treatment protocols for CD and UC differ slightly, their overarching goals and therapeutic rationale remain similar (CHA *et al.*, 2017; CHICCO *et al.*, 2021; CORRIDONI *et al.*, 2014; HANAUER *et al.*, 2009; PARAMSOTHY *et al.*, 2018; SANTOS, 2013; SOUZA *et al.*, 2021; SCHNUR *et al.*, 2022; SU *et al.*, 2018).

2.4 ANTI-INFLAMMATORY AND IMMUNOMODULATORY THERAPIES

Anti-inflammatory drugs include corticosteroids and aminosalicylates which reduce intestinal inflammation and prevent tissue injury. Aminosalicylates, such as mesalazine (5-aminosalicylic acid, 5-ASA) inhibit cyclooxygenase 1 and 2 enzymes, and reduce prostaglandins and pro-inflammatory cytokine production, thereby decreasing leukocyte chemotaxis. These are considered first-line agents for inducing and maintaining remission in mild-to-moderate UC. Sulfasalazine, with combined anti-inflammatory and antibacterial activity, has shown greater efficacy in certain CD presentations (PILEGGI *et al.*, 2019; SCHNUR *et al.*, 2022; SHANG *et al.*, 2023).

In more severe UC cases, corticosteroids are used to induce remission, although many patients develop steroid dependence and long-term therapy provides limited benefits (BAIMA *et al.*, 2022). However, they are not indicated for maintenance of remission. Ileal-release budesonide has demonstrated similar efficacy to prednisone for inducing remission in perianal perianal CD. The most common adverse effects include fluid retention, lipodystrophy, hyperglycemia, osteoporosis, and myopathy (SILVA *et al.*, 2020).

Antibiotics such as ciprofloxacin and metronidazole are effective in short-term management of active, fistulizing, or perianal CD. They can be administered for extended periods with relatively few adverse effects – though tendon rupture (ciprofloxacin) and peripheral neuropathy (prolonged metronidazole use) have been reported. When combined with corticosteroids, anti-inflammatories, and biologic agents, antibiotics may increase the

Revista ARACÊ
ISSN: 2358-2472

risk of secondary infections. Purine analogues, including azathioprine and 6-mercaptopurine, are commonly used in corticosteroid-dependent CD. They inhibit ribonucleotide synthesis and immune cell proliferation, helping maintain remission while reducing corticosteroid cytotoxicity. However, these agents carry risk of hepatic and pancreatic toxicity, requiring regular laboratory monitoring (JHA *et al.*, 2024; KONSTANTINIDIS *et al.*, 2020; PANDA; PATTNAIK; AICH, 2025; PINTO, 2010; SMITH *et al.*, 2022).

Methotrexate, an immunomodulator that inhibits dihydrofolate reductase, suppresses DNA synthesis and decreases interleukin production. Administered intramuscularly or subcutaneously, it is typically used at 25 mg/week for remission induction and 15 mg/week for maintenance. Adverse effects include leukopenia and hepatic fibrosis, while hypersensitivity pneumonitis remains a rare but serious complication (SU *et al.*, 2019; AMEEL; SULAIS; RAINE, 2022).

Cyclosporine, a lipophilic peptide that inhibits both cellular and humoral immune responses, blocks IL-2 production by helper T lymphocytes and inhibits calcineurin, preventing T- and B-cell activation. Although effective, it can cause nephrotoxicity, hypertension, gingival hyperplasia, hypertrichosis, paresthesia, tremors, headaches, and electrolyte disturbances. Opportunistic infections such as pneumocystosis may occur, and prophylaxis is advised. Tacrolimus, a macrolide antibiotic with similar properties but greater potency and oral bioavailability, has demonstrated efficacy in severe UC (GHUSN *et al.*, 2025; TRINDADE; MORCERF; ESPASANDIN, 2019).

2.5 BIOLOGIC THERAPIES

Biological agents offer targeted modulation of key inflammatory mediators and are used in moderate-to-severe or refractory disease. They are indicated for fistulizing CD or steroid-resistant CD and for UC unresponsive to corticosteroid therapy (DANESE; VUITTON; PEYRIN-BIROULET, 2015). The most widely used class consists of TNF-α antagonists. Infliximab, a chimeric monoclonal antibody, was the first approved biologic for IBD treatment and remains highly effective in both CD and UC (GHUSN *et al.*, 2025; PARAMSOTHY *et al.*, 2018). Although biologic therapy has achieved significant success in controlling disease activity and prolonging remission, caution is required when determining which patients should initiate immunotherapy. Immunosuppression increases susceptibility to opportunistic and non-opportunistic infections and may be associated with higher risk of malignancy (CHA *et al.*, 2017).

Revista ARACÊ
ISSN: 2358-2472

3 OBJECTIVE

This review aims analyze and synthesize current scientific evidence on the therapeutic use of intestinal microbiota modulation in managing adult patients with Crohn's disease and ulcerative colitis.

4 METHODOLOGY

This study is an integrative review, deisgned to meet the objectives of the proposed topic. It involved a comprehensive and systematic analysis of the scientific literature compile, analyze, and synthesize evidence from multiple studies, enhancing understanding and supporting broader conclusions on the subject (MENDES; SILVEIRA; GALVÃO, 2008).

4.1 DATA SOURCES AND SEARCH STRATEGY

Data collection was carried out in the PubMed and ScienceDirect databases. Descriptors were selected from the DeCS/MeSH system (Health Sciences Descriptors/Medical Subject Headings) system and combined using the Boolean operators "AND" and "OR". The main search terms were "*Crohn's disease*", "*ulcerative colitis*", *"prebiotic"*, *"probiotic"*, *"dietary intervention"*, and *"fecal microbiota transplantation"*. The guiding research question was: *"how have modifications of the intestinal microbiota been applied to improve treatment outcomes in adult patients with Crohn's disease or ulcerative colitis?"*. The following descriptor combinations were used in both databases: *Crohn's disease* AND *dietary intervention*; *Crohn's disease* AND *probiotic*; *Crohn's disease* AND *prebiotic*; *Crohn's disease* AND *fecal microbiota transplantation*; *ulcerative colitis* AND *dietary intervention*; *ulcerative colitis* AND *probiotic*; *ulcerative colitis* AND *prebiotic*; *ulcerative colitis* AND *fecal microbiota transplantation*.

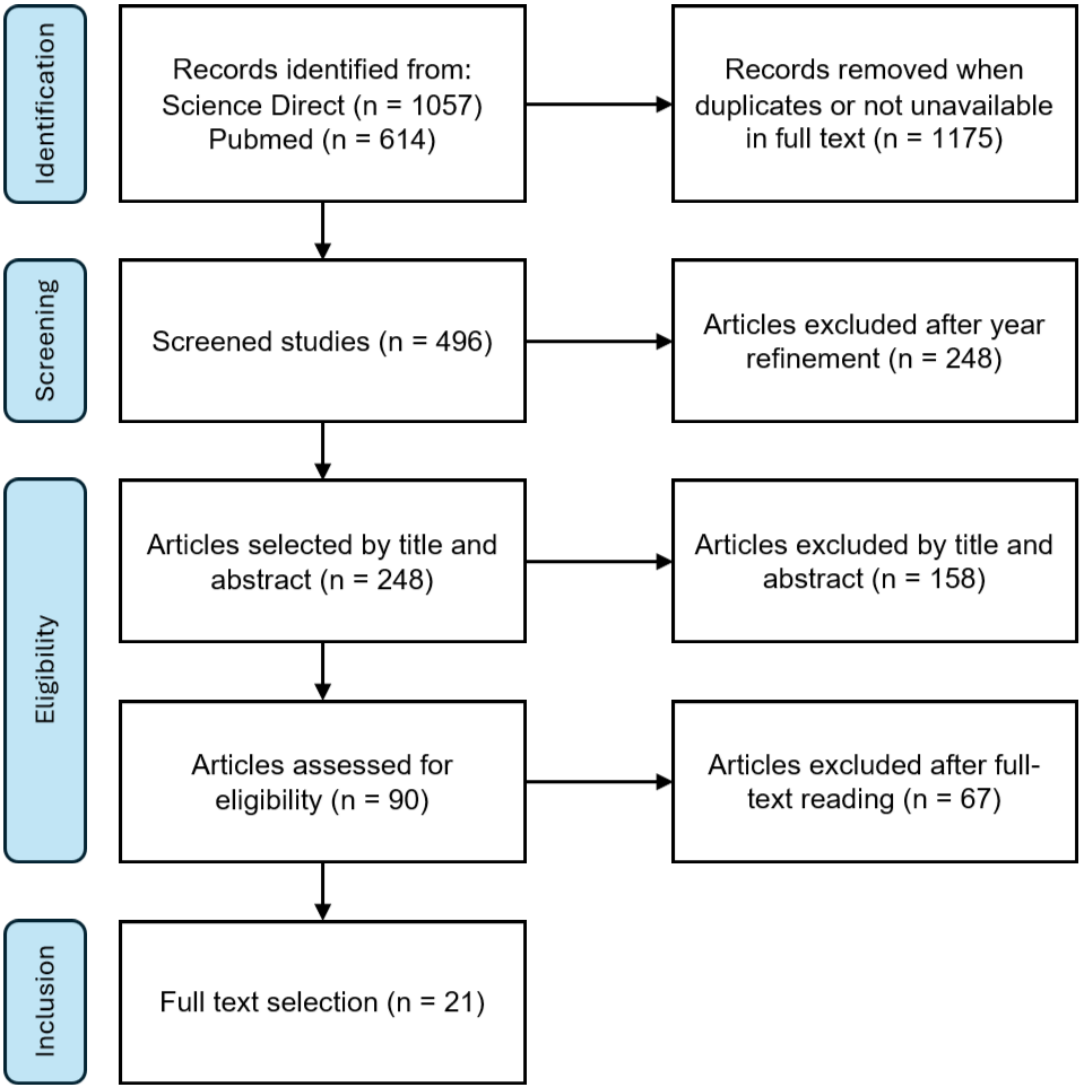
4.2 ELIGIBILITY CRITERIA

Inclusion criteria comprised studies published between 2018 and 2023; focused on the proposed theme, written in English, Portuguese, or Spanish and available in full-text online. Exclusion criteria were publications prior to 2018; studies involving pediatric populations; research unrelated to IBD; duplicate records; and studies excluded after abstract screening due to lack of relevance or misalignment with the study objectives.

Revista ARACÊ
ISSN: 2358-2472

Figure 1

Flowchart of the number of articles found and selected after applying the inclusion and exclusion criteria based on the PRISMA model.



Source: Prepared by the authors, adapted from Paige (2020).

4.3 STUDY SELECTION

The initial search yielded 1,671 articles – 1,057 from PubMed and 614 from ScienceDirect. After removing duplicates, excluding studies without full-text access, and refining results to the 2018-2023 period, the remaining records were screened according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines (PAGE *et al.*, 2021). Title and abstract screening resulted in the exclusion of 158 articles, leaving 90 for full-text assessment. Following detailed evaluation, 21 studies met all inclusion

Revista ARACÊ
ISSN: 2358-2472

criteria and were selected for final synthesis and discussion. A PRISMA-based flow diagram summarizing the selection process and inclusion/exclusion steps is shown in Figure 1.

5 RESULTS AND DISCUSSION

The studies selected based in the inclusion and exclusion criteria are summarized in Table 1. The methodology adopted was adequate for addressing the proposed objective, covering the most relevant literature on the topic. Among the 21 articles analyzed, most reported significant improvements in the management of CD and UC when intervertions targeting intestinal microbiota were used, either as adjuncts to standard treatment or integrated into therapeutic protocols. Of the studies included, seventeen involved *in vivo* research in humans; one was conducted *in vitro*, one combined *ex vivo* assays in piglets combined with *in vitro* analyses. The main microbiota-related interventions identified for each IBD are summarized in Table 2.

Table 1

Strategies used for intestinal microbiota modification in the treatment of Chron's disease (CD) and ulcerative colitis (UC).

Authors / Year	Title	Subset/Method	Results
ALTUN; YILDIZ; AKIN, 2019.	Effects of synbiotic therapy in mild-to-moderately active ulcerative colitis: A randomized placebo-controlled study	Human *in vivo* Group: n= 40 patients with mild to moderately active UC Method: randomized placebo-controlled study, versus synbiotic therapy. Groups were assessed for acute-phase reactants, clinical and endoscopic disease activities. Time: baseline and after 8 weeks of therapy.	In the synbiotic group, C-reactive protein: ↓ significantly: (CRP) and erythrocyte sedimentation rate (ESR) levels. Both groups: statistically significant ↑ in clinical and endoscopic activities. However, the symbiotic group exhibited significantly greater improvement in clinical activity compared to the control group.
CALVETE-TORRE *et al.*, 2023.	Fecal microbiota cooperative metabolism of pectins derived from apple pomace: A functional metagenomic study.	Human *in vitro*. Method: batch fecal fermentations were performed using samples from healthy donors (HD) and CD patients in the presence of apple pomace and	Apple pomace / pectins ↑ key taxa generally underrepresented in CD patients but are attributed with anti-inflammatory properties, with *Faecalibacterium*, *Ruminococcaceae*, and

Revista ARACÊ
ISSN: 2358-2472

		pectins with different structural properties	*Akkermansia* members being particularly notable.
CHEN *et al.*, 2023.	Specific fungi associated with response to capsulized fecal microbiota transplantation in patients with active ulcerative colitis	Human *in vivo*. Group: patients with active UC (n= 22) and HD (n=9) according to the criteria. Method: Patients received encapsulated FMT 3x / week. Metagenomic analysis of fecal samples collected before and during follow-up visits after encapsulated FMT.	Encapsulated FMT: ↑fungal diversity and altered fungal composition; ↓fungal diversity in samples from UC who achieved remission following encapsulated FMT, resembling samples collected from HD. UC who achieved remission after encapsulated FMT showed specific ↑ of *Kazachstania naganishii*, *Pyricularia grisea*, *Lachancea thermotolerans*, and *Schizosaccharomyces pombe* compared to those who did not achieve remission
CHIBA *et al.*, 2019.	Relapse Prevention by Plant-Based Diet Incorporated into Induction Therapy for Ulcerative Colitis: A Single-Group Trial	Human *in vivo* Group: 92 UC Patients hospitalized Treatment: Plant-based Diet (PBD) + medication Method: PBD	↓↓↓Relapse rates in UC VS previously reported conventional therapy
CHIBA *et al.*, 2020.	High Remission Rate with Infliximab and Plant-Based Diet as First-Line (IPF) Therapy for Severe Ulcerative Colitis: Single-Group Trial	Human *in vivo* Group: Patients with severe UC. Method: standard induction therapy + infliximab (5.0 - 7.5 mg/kg) at 0/2/6 weeks plus PBD during the hospitalization period to receive infusions and a questionnaire with dietary guidelines.	The remission rate was 76% (13/17) and the colectomy rate was 6% (1/17) in the induction phase. ↓↓↓ CRP values and ESR decreased at week 6, from 9.42 to 0.33 mg/dL and from 59 to 17 mm/h, respectively. Cumulative relapse rate: 25% at the 1-year follow-up. No additional cases of colectomy.
CHIBA *et al.*, 2022.	Relapse-Free Course in Nearly Half of Crohn's Disease Patients with Infliximab and Plant-Based Diet as First-Line Therapy: A Single-Group Trial	Human *in vivo*. Group: 24 newly diagnosed adult CD patients during hospitalization Method: induce remission by 3 standard infliximab infusions + PBD. Patients were instructed to continue the diet after discharge.	No relapse: 13 cases. The relapse-free rates assessed by Kaplan–Meier survival analysis at 1, 2, 3, and 4 years were 79%, 66%, 57%, and 52%, respectively. The relapse-free rate with normal CRP levels at 1–2 and 3–10 years was 57% and 52%, respectively.

Revista ARACÊ
ISSN: 2358-2472

CHICCO *et al.*, 2021.	Multidimensional Impact of Mediterranean Diet on IBD Patients	Human *in vivo*. Group: Patients with IBD, both CD and UC. Method: Mediterranean Diet. Parameters analyzed: BMI, body tissue composition, steatosis and liver function, serum lipid profile, clinical disease activity, and inflammatory biomarkers (CP and fecal calprotectin) collected at the beginning of the study and compared with those obtained after 6 months to assess the impact of the diet.	Patients who adhered to the diet improved their BMI and waist circumference. ↓↓↓ number of patients affected by hepatic steatosis of any degree after dietary intervention in both groups. After 6 months of diet, < patients with stable therapy presented with disease and ↑ inflammatory biomarkers. The diet improved the quality of life. Serum lipid profile and liver function: not modified.
DAY *et al.*, 2022.	Therapeutic Potential of the 4 Strategies to Sulfide-Reduction (4-SURE) Diet in Adults with Mild to Moderately Active Ulcerative Colitis: An Open-Label Feasibility Study	Human *in vivo*. Group: 28 adults with mild to moderately active UC. Method: ↑ intake of fermentable fibers, restrict total and sulfur-containing proteins, and avoid specific food additives for 8 weeks (SURE Diet).	The clinical response occurred in 46% of the participants and endoscopic improvement in 36%. Two participants (7%) worsened. Fecal excretion of SCFAs increased by 69%, while the proportion of branched-chain fatty acids relative to SCFAs was suppressed by 27%.
HIDALGO-CANTABRANA *et al.*, 2020.	The extracellular proteins of *Lactobacillus acidophilus* DSM 20079T display anti-inflammatory effect both in piglets, healthy human donors and Crohn's Disease patients	Animal *in vivo*. Method: Daily administration of *L. acidophilus* DSM 20079 T was given to healthy piglets to verify cytokine production and the PBMC pro-inflammatory response from CD patients and HD to probe the homeostatic effect mediated by the extracellular protein fraction.	↑ anti-inflammatory cytokine IL-10 and extracellular protein A, demonstrating the immunomodulatory effect. The strain was able to activate innate immune pathways in dendritic cells (DCs) and ↓ the pro-inflammatory cytokine production of in both CD4+ and CD8+ T cell subsets in HDs and CD patients.
HUANG *et al.*, 2022.	Fecal microbiota transplantation versus glucocorticoids for the induction of remission in mild to moderate ulcerative colitis	Human *in vivo*. Group: Patients with mild to moderate active UC recruited for the prospective single-center cohort study. Method: 62 treated with FMT and 60 with	Achieved the clinical remission endpoint: FMT group: 34 (54.8%). GC group: 29 (48.3%). Adverse events in GC group (58.3%) >>> FMT group (22.6%). ↓↓↓TNF-α and IL-6 levels significantly (FMT responder group); ↓↓↓IL-10 (non-responders).

Revista ARACÊ
ISSN: 2358-2472

		glucocorticoids for 3 days	
LI *et al.*, 2021.	Supplemental bifid triple viable capsule treatment improves inflammatory response and T cell frequency in ulcerative colitis patients	Human *in vivo*. Method: Bifid triple viable bacterial capsules were administered orally, 420 mg each time, 3 times a day for 2 months in 130 patients with UC hospitalized in a hospital.	↓ IL-6, IL-8, CRP, and TNF-α plasma levels decreased in both groups after treatment and were lower in the experimental than in the control group. $CD4^+$ levels and the CD4/CD8 ratio increased and were higher in the experimental group than in the control group.
MARKANDEY *et al.*, 2023.	Fecal microbiota transplantation refurbishes the crypt-associated microbiota in ulcerative colitis	Human *in vivo*. Group: UC patients before and after FMT with an anti-inflammatory diet (FMT-AID) Method: laser capture microdissection coupled with 16S amplicon sequencing to characterize crypt-associated microbiota (CAM). Compositional differences in CAM and its interactions with mucosa-associated microbiota were compared between non-IBD controls and UC patients pre- and post-FMT (n = 26).	CAM exhibited UC-associated dysbiosis and showed restoration after FMT-AID. The positive effects of FMT-AID further extended to the renewal of CAM–mucosa-associated microbiota interactions, which were disrupted in UC. The taxa restored by FMT were negatively correlated with disease activity in patients.
MILAJERDI *et al.*, 2020.	A randomized controlled trial investigating the effect of a diet low in fermentable oligosaccharides, disaccharides, monosaccharides, and polyols on the intestinal microbiome and inflammation in patients with ulcerative colitis: Study protocol for a randomized controlled trial	Human *in vivo*. Group: 30 patients with mild to moderately active UC. Method: Random treatment with a low FODMAP diet (n = 15) or to continue their usual diet as a control (n = 15) for 4 weeks.	The consumption of a low FODMAP diet can ↓ systemic and intestinal inflammation, alter the bacterial population in the intestine, and modulate clinical symptoms in patients with UC.
OH *et al.*, 2021.	Therapeutic Potential of *Escherichia coli* Nissle 1917 (EcN) in Clinically Remission-attained	Human *in vivo* hospital-based coort study. Group: UC patients. Method: Retrospective review based on	After 3 months of treatment, there was no significant change in FC. On the other hand, the partial Mayo score significantly ↓ from 0.085 to 0.014, and body weight,

Revista ARACÊ
ISSN: 2358-2472

	Ulcerative Colitis Patients: A Hospital-based Cohort Study	medical records of EcN administration after clinical remission for more than 3 months at Kosin University Gospel Hospital between 2013-2018.	BMI, hemoglobin, and cholesterol levels increased. One patient experienced severe AE, and 14 patients discontinued EcN due to AEs.
PAGNINI *et al.*, 2018	Mucosal adhesion and anti-inflammatory effects of *Lactobacillus rhamnosus* GG in the human colonic mucosa: A proof-of-concept study	Human *ex vivo* and experimental model. Patients group: n=68 Control: n= 30 Treatment group: LGG-conditioned medium; *in vivo*, total: 42 patients (20 with UC and 22 controls). Method: colon biopsies from healthy individuals who consumed a commercial LGG formulation for 7 days before the colonoscopy and control biopsies from patients who did not consume it.	Proof-of-concept study demonstrating that LGG adheres to human colonic mucosa and exerts anti-inflammatory effects, at the double dose (DD). UC patients + DD LGG ↑ [bacteria] in the mucosa and ↓ TNF-α and IL-17 expression compared to patients who consumed the regular dose (↓ of 48% and 40%, respectively).
SHANG *et al.* (2023).	The Impacts of Fecal Microbiota Transplantation from Same Sex on the Symptoms of Ulcerative Colitis Patients.	Human *in vivo*. Group and method: FMT performed by transferring the gut microbiota from healthy adolescent male or female donors to same-sex patients via gastroscope three times (once every three weeks), with a placebo group receiving an equal volume of saline. Abdominal pain, diarrhea, bloody thick stools, intestinal mucosal injury, and Mayo scores were assessed, along with changes in gut flora detected through 16S rRNA sequencing.	FMT ↓ diarrhea scores, abdominal pain, mucosal injury, and Mayo scores. *Clostridiales* and *Desulfovibrionaceae* were dominant in the gut microbiota of male patients and ↓ after FMT; *Prevotella*, *Lactobacillus*, and *Bifidobacterium* ↑ in the group. Female patients: ↑↑ abundance of *Escherichia-Shigella*, *Desulfovibrionaceae*, and *Staphylococcaceae* before FMT, which was ↓ after treatment; *Prevotella*, *Lactobacillus* *Porphyromonadaceae*, and *Bifidobacterium* ↑ in the female group.
SMITH *et al.* (2022)	Strain-resolved analysis in a randomized trial of antibiotic pretreatment and maintenance dose delivery	Human *in vivo*. Group: 22 patients with mild to moderate UC. Method: The effects of antibiotic pretreatment	Of the patients who received antibiotic pretreatment, 6/11 achieved remission after 6 weeks of treatment, compared to 2/11 in the non-pretreated group.

Revista ARACÊ
ISSN: 2358-2472

	mode with fecal microbiota transplant for ulcerative colitis	were tested, and two modes of maintenance dose administration - capsules versus enema - were compared in a 2 × 2 factorial, randomized, open-label pilot study.	Microbiome renewal was extensive and significantly more pronounced in the pretreated patients. Associations were also revealed between taxonomic turnover and changes in the composition of primary and secondary bile acids.
SOKOL *et al.* (2020)	Fecal microbiota transplantation to maintain remission in Crohn's disease: A pilot randomized controlled study	Human *in vivo*. Group and method: Patients enrolled during crises received oral corticosteroids. Once in clinical remission, they were randomized to receive FMT or a control transplant during colonoscopy. Corticosteroids tapered, and a 2nd colonoscopy was performed in week 6. The primary outcome was the donor microbiota engraftment in week 6.	The clinical remission rate without steroids at 10 and 24 weeks was 44.4% (4/9) and 33.3% (3/9) in the control transplant group and 87.5% (7/8) and 50.0% (4/8) in the FMT group. The Crohn's Disease Endoscopic Severity Index ↓ 6 weeks after FMT, but not after the control transplant. No safety signals were identified.
VALCHEVA *et al*. (2019)	Inulin-type fructans improve active ulcerative colitis associated with microbiota changes and increased short-chain fatty acids levels	Human *in vivo* pilot exploratory study. Group: Patients (n=25) with mild to moderately active UC. Method: 7.5g (n=12) or 15g (n=13) daily of oral inulin enriched with oligofructose (Orafti®Synergy1) for 9 weeks.	The fructans significantly ↓ UC in the high-dose group: 77% clinical response versus 33% in the low-dose group. The fructans ↑ colonic butyrate production at the dose of 15 g/d, and fecal butyrate levels were negatively correlated with the Mayo score.
WANG *et al*., 2018	The Safety of Fecal Microbiota Transplantation for Crohn's Disease: Findings from A Long-Term Study	Human *in vivo.* Method: 184 FMT frequencies via mid-gut for mild to severe CD in a single-protocol trial with 139 patients. Years: from October 2012 to December 2016. Possible factors with AE and efficacy after FMT were recorded prospectively.	No AEs beyond 1 month were observed. Therefore, a 1-month limit could be suggested to define short- and long-term FMT AEs.
XIANG *et al*., 2020.	Efficacy of faecal microbiota transplantation in Crohn's disease: a new target treatment?	Group: 146 CD patients Method: FMT value in treating clinical targets related to CD was	One month after FMT, 72.7% (101/139), 61.6% (90/146), 76% (19/25), and 70.6% (12/17) of patients showed improvement in abdominal pain, diarrhea,

Revista ARACÊ
ISSN: 2358-2472

		evaluated based on 7 therapeutic targets: fever, abdominal pain, hematochezia, diarrhea, enterocutaneous fistula, steroid dependence, and active perianal fistula.	hematochezia, and fever, respectively; while 50% (10/20) of steroid-dependent patients achieved steroid-free remission after FMT.

Source: Prepared by the authors (2025), based on data extracted from the literature review (2018-2023)

Table 2

Main changes in gut microbiota observed in the treatment of CD and UC

Disease in treatment	Method used for Intestinal Microbiota Modulation	Adverse Effects (AE)	Authors
Crohn's Disease (CD)	Fecal Microbiota Transplantation (FMT)	AEs: 13,6% (mild, during 1 month after FMT) included ↑ defecation frequency, fever, flatulence, hematochezia, vomituring, abdominal pain and distension, and herpes zoster.	WANG *et al.*, 2018; XIANG *et al.*, 2020; SOKOL *et al.*, 2020.
	Fraction derived from the probiotic *Lactobacillus acidophilus* DSM 20079	No AE reported. However, tolerogenic, anti-inflammatory and regulatory effects were reported.	HIDALGO-CANTABRANA *et al.*, 2020.
	Combined treatment with infliximab and a plant-based diet (PBD)	No AE reported, and the authors state that "patients are free from the worry associated with the AE of medication".	CHIBA *et al.*, 2022.
	Prebiotic pectin	No AE reported, since this study was performed *in vitro*.	CALVETE-TORRE *et al.*, 2023.
Ulcerative Colitis (UC)	Probiotic *Lactobacillus rhamnosus* GG	The authors did not exclude the possibility of AE, but neither mentioned which of them were present or absent.	PAGNINI *et al.*, 2018.
	Synbiotic preparation composed of probiotics: *Enterococcus faecium, Lactobacillus plantarum, Streptococcus thermophilus, Bifidobacterium lactis, Lactobacillus acidophilus, Bifidobacterium longum* and a prebiotic: frutooligossacaride	No AE reported.	ALTUN; YILDIZ; AKIN, 2019.
	Prebiotic inulin-type fructans	Mild to moderate gastro-intestinal sensations as flatulence and bloating	VALCHEVA *et al.*, 2019.
	Incorporation of a PBD into conventional pharmacological treatment	All patients ate PBD, and none experienced a serious AE suspected of being caused by a PBD.	CHIBA *et al.*, 2019.
	Infliximab in combination with a PBD	No patient experienced AEs.	CHIBA *et al.*, 2020.

Revista ARACÊ
ISSN: 2358-2472

	Incorporation of a low-FODMAP diet (low in fermentable oligosaccharides, disaccharides, monosaccharides, and polyols).	No AE reported.	MILAJERDI *et al.*, 2020.
	Use of a triple probiotic composed of *Enterococcus, Lactobacillus acidophilus* and *Bifdobacterium.*	During the course of treatment, 2 cases of abdominal discomfort and 1 case of rash occurred in the experimental group, with an AE rate of 4.62% (3/65); 3 cases of abdominal discomfort and 2 cases of rash occurred in the control group, with an AE rate of 7.69% (5/65).	LI *et al.*, 2021.
	Administration of *Escherichia coli* Nissle (EcN)1917.	No unexpected or novel side effects of EcN in this study	OH *et al.*, 2021.
	Sulfide-reducing dietary strategy (SURE diet).	No AE reported.	DAY *et al.*, 2022.
	Fecal Microbiota Transplantation (FMT).	CHEN *et al.* (2023), MARKANDEY *et al.* (2023), and SHANG *et al.* (2023) did not report any AE. HUANG *et al.* (2022) reported that FMT was as effective as GCs to be a remission induction therapy with fewer adverse events. Although SMITH *et al.* (2022) did not report AE directly, the authors stated they could not distinguish if the AE observed were derived from the patients themselves or FMT donors.	CHEN *et al.*, 2023. HUANG *et al.*, 2022; MARKANDEY *et al.*, 2023; SHANG *et al.*, 2023; SMITH *et al.*, 2022.
CD and UC	Mediterranean diet	No AE reported.	CHICCO *et al.*, 2021.

5.1 TARGETED MODIFICATIONS IN GUT MICROBIOTA FOR THE TREATMENT OF CROHN'S DISEASE (CD)

FMT appears to be a safe therapeutic option for CD. In the study by Wang *et al*. (2018), few adverse events (AEs) were reported, mostly during the first week, and they resolved spontaneously. Many AEs were attributed to manual preparation of the transplant material. Xiang *et al.* (2020) similarly reported no severe AEs during the trial.

FMT was associated with clinical improvement in key CD symptons such as abdominal pain, diarrhea, and hematochezia, as well as in patients with fever and steroid dependence prior to the procedure (XIANG *et al.*, 20220). These improvements contributed to better quality of life and treatment adherence.

Revista ARACÊ
ISSN: 2358-2472

Sokol *et al.* (2020) examined the optimal timing for FMT, highlighting that performing the intervention early in the course of clinical deterioration, or during the transition toward an exacerbation, helps maintain remission more effectively. Although the small sample size limited statistical significance, the authors observed that donor microbiota colonization varied among patients. Immediately after FMT, alpha diversity temporarily increased but gradually returned toward baseline within weeks, whereas beta diversity remained stable for several months, indicating a lasting structural effect on the microbiota.

Probiotic subunits also showed therapeutic potential. Extracellular proteins from *Lactobacillus acidophilus* demonstrated immunomodulatory activity, reducing pro-inflammatory cytokines and increasing anti-inflammatory responses in CD patients (HIDALGO-CANTABRANA *et al.*, 2020). This approach may allow the use of probiotic-derived molecules without exposing patients to high microbial loads.

Chiba *et al.* (2022) proposed a combined protocol including a plant-based diet (PBD) with infliximab administration. Incorporation of PBD after remission induction was associated with lower relapse rates, supported by a follow-up period of at least 12 months, which confirmed sustained dietary benefits. No AEs led participants to withdraw from the study.

Calvete-Torre *et al.* (2023) reported that pectin metabolism modified microbiota composition in CD samples, increasing the production of SCFAs. *Akkermansia muciniphila* and *Ruminococcus* species, typically reduced in CD, increased after *in vitro* pectin fermentation. These fiber-degrading bacteria correlated positively with SCFA production (isobutyric, valeric, isovaleric, caproic acids), and showed synergistic interactions with other gut taxa, contributing to improved dysbiosis.

5.2 TARGETED MODIFICATIONS IN GUT MICROBIOTA FOR THE TREATMENT OF ULCERATIVE COLITIS (UC)

The most frequently reported therapeutic approach was fecal microbiota transplantation (FMT), investigated across both inflammatory bowel diseases (IBD). FMT is recognized as promising strategy, particularly for UC, where clinical and endoscopic remission represent its most relevant outcomes (SMITH *et al.*, 2022; HUANG *et al.*, 2022; SHANG *et al.*, 2023).

SMITH *et al.* (2022) demonstrated that antibiotic pretreatment may optimize FMT effectiveness in UC, with most pretreated patients classified as responders. Improvements included endoscopic healing, clinical remission, and greater transfer of donor microbiota and

Revista ARACÊ
ISSN: 2358-2472

microbial functions. Another study evaluated the administration of *Escherichia coli* to modulate intestinal inflammation, reporting symptom improvement but also notable adverse events (AEs) and reduced tolerability (OH *et al.*, 2021).

In the comparative analysis by HUANG *et al.* (2022), FMT was applied during the remission induction phase – traditionally managed with corticosteroids in patients intolerant or unresponsive to 5-ASA. Microbiota modulation proved more effective than corticosteroids and was associated with fewer AEs. This approach also improved several clinical signs and symptoms, such as abdominal discomfort, hematochezia, mucosal lesions, and overall mental health (SCHNUR *et al.*, 2022; SHANG *et al.*, 2023).

Another key therapeutic goal of FMT is increasing microbial taxa associated with reduced disease activity. SHANG *et al.* (2023) found distinct microbial signatures in male and female patients prior to treatment. In men, taxa such as *Bacteroidetes*, *Clostridiales*, *Desulfovibrionaceae*, *Enterobacteriaceae*, *Megamonas*, *Erysipelotrichaceae*, *Eubacterium*, *Romboutsia*, *Roseburia*, and *Saccharibacteria* predominated. Post-FMT samples showed increased abundance of *Prevotella*, *Lactobacillus*, *Bifidobacterium*, *Coprococcus*, *Faecalibacterium*, *Veillonella*, *Ruminococcaceae*, *Blautia*, *Clostridiales*, and *Alloprevotella*. Among women, higher baseline levels of *Desulfovibrionaceae*, *Escherichia-Shigella*, *Lachnospiraceae*, *Staphylococcaceae*, *Megamonas*, *Veillonella*, *Erysipelotrichaceae*, *Enterobacteriaceae*, *Citrobacter*, and *Porphyromonadaceae* were identified. After FMT, dominant taxa included *Porphyromonadaceae*, *Prevotella*, *Bifidobacterium*, *Firmicutes*, *Lactobacillus*, *Akkermansia*, *Streptococcus*, *Anaerostipes*, *Coprococcus*, and *Rumbococcus*.

As for AEs associated with FMT, the most frequent were gastrointestinal discomfort and fever (HUANG *et al.*, 2022), along with self-limiting abdominal pain, constipation, diarrhea, vomiting, flatulence, and fever (SMITH *et al.*, 2022). In both studies, AEs were infrequent and resolved quickly.

MARKANDEY *et al.* (2023) evaluated the combined effect of FMT and a Mediterranean anti-inflammatory diet on crypt- and mucosa-associated microbiota. In UC, they observed a reduction in several beneficial genera - *Faecalibacterium*, *Prevotella*, *Roseburia*, *Lachnospira*, *Bifidobacterium*, *Catenibacterium*, *Coprococcus*, *Gemmiger*, *Dialister*, *Eubacterium*, *Ruminococcus*, *Megasphaera*, *Ligilactobacillus*, among others - and an expansion of pathobionts (*Anoxybacillus*, *Halomonas*, *Acinetobacter*, *Burkholderia*, *Pseudomonas*, *Brevundimonas*, *Staphylococcus*, *Corynebacterium*, *Thermus*, *Brevibacillus*, *Methylobacterium*, *Escherichia*, and others). According to the authors, these changes reflect

Revista ARACÊ
ISSN: 2358-2472

dysbiosis driven by inflammation, weakened competitive exclusion of pathogenic species, and reduced antimicrobial defenses typical of UC.

Consistent with previous studies, FMT remodeled key microbial communities of the mucosa and intestinal crypts – structures often damaged or depleted during active inflammation. This remodeling contributed to restoring local architectural integrity, reducing dysbiosis, and mitigating inflammation (SMITH *et al.*, 2022; SHANG *et al.*, 2023). In addition, fungal communities associated with clinical remission were also reestablished following FMT, indicating a therapeutic role for microbiota modulation (CHEN *et al.*, 2023).

Specific dietary strategies for IBD treatments have also been extensively investigated and may be used for relapse prevention, in combination with biological agents, or in the management of severe UC. Recent advances in biotechnology have expanded the therapeutic arsenal, leading to the development of biological agents and small-molecule targeted drugs that act on immune components such as T cells, cytokines, and autoantibodies. These agents modulate inflammatory pathways by blocking immune responses, thereby suppressing inflammation and protecting the gastrointestinal mucosa. Anti-tumor necrosis factor alpha (anti-TNF-a) therapy remains the first-line treatment for moderate to severe IBD. Anti-integrin antibodies have also become key therapeutic options; vedolizumab, for instance, is often used in patients who do not respond to anti-TNF-a or who are intolerant to other treatments. Additional biological agents are under evaluation in clinical trials at various stages of development (ATIA *et al.*, 2025; XUE *et al.*, 2025).

Biological agents are indicated for moderate to severe cases. In the treatment protocol combining PBD with infliximab, the authors proposed replacing intravenous corticosteroids as the first-line therapy. This combined approach resulted in lower relapse and colectomy rates, as well as higher remission rates, compared with expected outcomes from intensive corticosteroid therapy or rescue treatment for corticosteroid-refractory patients (CHIBA *et al.*, 2020).

In another study, CHIBA *et al*. (2019) reported that patients who adhered to the PBD – characterized by prioritizing plant-based foods, unprocessed ingredients, low fat, reduced animal protein and sugar, and high fiber intake - during induction therapy (remission phase) showed lower relapse rates compared with those documented for conventional therapy (FAUBION *et al.*, 2001; KORNBLUTH; SABAR, 2010). Despite the difficulty many UC patients face in maintaining the PBD outside the hospital setting, the authors suggest that in-hospital adherence serve as a starting point for long-term dietary re-education (CHIBA *et al.*, 2019).

Revista ARACÊ
ISSN: 2358-2472

The low-FODMAP diet ("Fermentable Oligosaccharides, Disaccharides, Monosaccharides, and Polyols") has demonstrated prebiotic effects and improvement of various gastrointestinal symptoms. However, the fermentation of these carbohydrates increases SCFA production, a key factor in modulating inflammation in UC and other IBDs (MILAJERDI *et al.*, 2020). The 4-SURE diet ("4 Strategies for Sulfite Reduction") expands upon the low-FODMAP approach by also managing protein intake, aiming for more specific outcomes such as symptom reduction and mucosal healing (DAY *et al.*, 2022).

Reduction of proinflammatory cytokines through gut modulation was a consistent finding across the studies. PAGNINI *et al.* (2018) demonstrated decreased mucosal TNF-α levels following *Lactobacillus rhamnosus* GG consumption. Synbiotic therapy combining probiotics (live microorganisms preparation) was composed of six probiotic strains (3×10^9 CFU) - *Enterococcus faecium, Lactobacillus plantarum, Streptococcus thermophilus, Bifidobacterium lactis, Lactobacillus acidophilus, Bifidobacterium longum*) - with prebiotics (frutooligossaccharide, 225mg/tablet, after breakfast and dinner) - further enhanced clinical benefits, with most patients shifting from moderate to mild disease activity by the end of treatment (ALTUN; YILDIZ; AKIN, 2019).

Studies on probiotic supplementation - when used alongside with pharmacological therapy (mesalazine plus somatostatin), also demonstrated significant improvements in inflammatory regulation and T-cell modulation, supporting the incorporation of dietary interventions into UC treatment protocols (LI *et al.*, 2021). Prebiotics such as inulin-type fructans were similarly evaluated in isolation; higher-dose administration (15g; n=13) modified microbiota functions associated with inflammation reduction. Although some patients experienced AEs such as increased flatulence and abdominal bloating, these effects were mild, transient, and decreased over time (VALCHEVA *et al.*, 2019).

5.2.1 Western Diet vs. Mediterranean Diet in CD and UC

Intestinal dysbiosis not only worsens inflammation in IBD but also negatively affects quality of life, by contributing to excess weight, obesity, undernutrition, and metabolic comorbidities. Adherence to the Mediterranean diet – rich in vegetables, fruits, legumes, whole grains, nuts, olive oil; moderate in fish, dairy, and wine; and low in red meat and sweets – was associated with improved anthropometric indicators and reduced disease activity indices in IBD patients (CHICCO *et al.*, 2021).

Revista ARACÊ
ISSN: 2358-2472

Conversely, the Western dietary pattern, characterized by high intake of processed, refined, sugary, and ultra-processed foods such as fast food, snacks, and soft drinks – was associated with increased intestinal inflammation. Dietary modification let to reductions in promoting adiposity elevate pro-inflammatory cytokines such as IL-6, IL-8, and TNF-α, which aggravate the intestinal inflammatory process in CD and UC. Dietary modification led to reductions in hepatic steatosis prevalence, lower C-reactive protein (CRP) levels, and decreased fecal calprotectin, highlighting clinical improvement (CHICCO *et al.*, 2021).

6 FINAL CONSIDERATIONS

The absence of a definitive causal relationship between the numerous risk factors associated with CD and UC continues to pose challenges for effective treatment. Both conditions are marked by chronic, progressive inflammation and significantly impair patient's quality of life. Nonetheless, several therapeutic strategies are currently being widely investigated, with evidence indicating their potential to reduce disease activity, improve comorbidities, and alleviate key clinical symptoms.

Gut microbiota modulation has emerged as a promising approach to restore dysbiosis and prevent the escalation of intestinal inflammation. These interventions may help reestablish mucosal barrier integrity or at least improve its functional capacity. Among such strategies, fecal microbiota transplantation (FMT) is one of the most promising options, with encouraging results in both major forms of IBDs. However, because FMT involves biological material with inherent risks of contamination, strict safety protocols are essential. Although FMT is generally associated with few adverse events, treatment adherence may vary, and the influence of concomitant medications of underlying health conditions requires further investigation to clarify causality.

Dietary interventions were well tolerated and provided benefits that extended beyond disease-specific outcomes, including the reduction of inflammatory conditions that may contribute to CD or UC onset. Despite the challenge of maintaining long-term dietary changes, these interventions can complement conventional therapies, helping prevent relapses and reduce the burden of associated chronic conditions.

Prebiotics also represent a viable alternative for modulating intestinal homeostasis, particularly because they are widely accepted, accessible, and safe. Evidence indicates that probiotic supplementation can modulate inflammatory pathways and contribute to clinical improvement. In addition, emerging studies on probiotic-derived fractions, such as

Revista ARACÊ
ISSN: 2358-2472

extracellular proteins, suggest an expanding research avenue for patients who may not tolerate live microorganisms or who present impaired mucosal permeability. These molecular approaches may reduce risks related to microbial load while preserving immunomodulatory benefits.

The ongoing development of therapies targeting the gut microbiota is expected to remain central in IBD management, given the strong association between clinical remission, balanced immune responses, and maintenance of intestinal homeostasis. Advances in microbial culture sequencing, metagenomics, and bioinformatics continue to refine our understanding of host-microbe interactions, offering increasingly precise and personalized strategies capable of improving patient's quality of life.

ACKNOWLEDGMENTS

To the State University of Goiás (UEG), which funded the execution of this research and other works, through the "Convocatória UEG nº 20/2023 and Convocatória UEG nº 04/2024 – Plataforma Institucional de Pesquisa e Inovação em Segurança Hídrica", resulting in the publication of this paper.

REFERENCES

ALLAIRE, J. M., *et al*. The Intestinal Epithelium: Central Coordinator of Mucosal Immunity. **Trends Immunol**. v. 39; n .9. p. 677-696, set. 2018.

AMEEL, A. T.; SULAIS A. E.; RAINE, T. Methotrexate in inflammatory bowel disease: A primer for gastroenterologists. **Saudi J Gastroenterol.**, v. 28, n. 4, p. 250-260, 2022.

ALLAM-NDOUL, B.; CASTONGUAY-PARADIS, S.; VEILLEUX, A. Gut Microbiota and Intestinal Trans-Epithelial Permeability. **Int J Mol Sci.**, v. 21, n. 17, p. 6402, 2020.

ALTUN, H. K.; YILDIZ, E. A.; AKIN, M. Effects of symbiotic therapy in mild-to-moderately active ulcerative colitis: A randomized placebo-controlled study. **Turk J Gastroenterol**, v. 30, n. 4, p. 313-20, 2018.

ANGELINI, G.; RUSSO, S.; MINGRONE, G. Incretin hormones, obesity and gut microbiota. Peptides, v. 178, p. 171216, 2024.

ATIA, O. *et al.* Maintenance treatment with vedolizumab in paediatric inflammatory bowel disease (VEDOKIDS): 54-week outcomes of a multicentre, prospective, cohort study. **Lancet Gastroenterology and Hepatology**, v. 10, n. 3, p. 234-247, 2025.

Revista ARACÊ
ISSN: 2358-2472

BAIMA, J. P. *et al*. Second Brazilian consensus on the management of ulcerative colitis in adults: a consensus of the Brazilian Organization for Crohn's Disease And Colitis (Gediib). **Arquivos de Gastroenterologia**, v. 59, p.51–84, 2022.

BARROS, G. V. N. *et al*. Métodos diagnósticos e terapêuticos das doenças inflamatórias intestinais. **Pará Research Medical Journal**,, v. 4, p. 1-6, 2020.

CALVETE-TORRE, I. *et al*. Fecal microbiota cooperative metabolism of pectins derived from apple pomace: a functional metagenomic study. **Lwt,** v. 187, p. 115362, 2023.

CARVALHO, A. T. P. Terapia biológica. **Revista do Hospital Universitário Pedro Ernesto**, UERJ, Ano 11, Out/Dez, 2012.

CARVALHO, L. C. *et al*. Doenças inflamatórias intestinais: uma abordagem geral. **Revista Eletrônica Acervo Médico**, v. 2, p. e9650, fev. 2022.

CHA, J. M. *et al.* Physicians should provide shared decision-making for anti-TNF therapy to inflammatory bowel disease patients. **J Korean Med** Sci, v.32, n. 1, p. 85-94, 2017.

CHEN, Q. *et al*. Specific fungi associated with response to capsulized fecal microbiota transplantation in patients with active ulcerative colitis. **Frontiers in Cellular and Infection Microbiology**, v. 5, n. 12, p. 2023.

CHENG, Z.; YANG, L.; CHU, H. The Gut Microbiota: A Novel Player in Autoimmune Hepatitis. **Frontiers in Cellular and Infection Microbiology**, v. 12, p. 947382, 2022.

CHIBA, M. *et al*. High Remission Rate with Infliximab and Plant-Based Diet as First-Line (IPF) Therapy for Severe Ulcerative Colitis: Single-Group Trial. **The Permanente Journal.** v. 24, n. 5, p. 40-53, 2020.

CHIBA, M. *et al*. Relapse Prevention by Plant-Based Diet Incorporated into Induction Therapy for Ulcerative Colitis: A Single-Group Trial. **The Permanente Journal,** v. 26, n. 2, p. 40-53, jun. 2019.

CHIBA, M., *et al*. Relapse-Free Course in Nearly Half of Crohn's Disease Patients With Infliximab and Plant-Based Diet as First-Line Therapy: A Single-Group Trial. **The Permanente Journal.** Vol. 26, N. 2, jun., 2022.

CHICCO, F. *et al.*, Multidimensional Impact of Mediterranean Diet on IBD Patients. **Inflammatory Bowel Diseases**, v. 27, n. 1, p. 1-9, 2021.

CORRIDONI, D.; ARSENEAU, K. O.; COMINELLI, F. Inflammatory bowel disease. **Immunology Letters**, v. 161, n. 2, p. 231-235, out. 2014.

DA SILVA, E. M. *et al*. Crosstalk between incretin hormones, Th17 and Treg cells in inflammatory diseases. **Peptides**, v. 155, p. 170834, set. 2022.

Revista ARACÊ
ISSN: 2358-2472

DANESE, S.; VUITTON, L.; PEYRIN-BIROULET, L. Biologic agents for IBD: practical insights. **Nature Reviews Gastroenterology & Hepatology**, v. 12, n. 9, p. 537-45, set. 2015.

DAY, A. S. *et al*. Therapeutic Potential of the 4 Strategies to SUlfide-REduction (4-SURE) Diet in Adults with Mild to Moderately Active Ulcerative Colitis: An Open-Label Feasibility Study. **The Journal of Nutrition**, v. 152, n. 7, p. 1690-1701, 2022

DZUTSEV, A. *et al*. Microbes and cancer. **Annu. Rev. Immunol**, v.35, n. 1, p. 199–228, 2017.

FAUBION, W. A. *et al*. The natural history of corticosteroid therapy for inflammatory bowel disease: A population-based study. **Gastroenterology,** v. 121, n. 2, p. 255–60, 2001.

FERREIRA, G. S.; DEUS, M. H. de.; ANTONACCI JUNIOR, E. Fisiopatologia e etiologias das doenças inflamatórias intestinais: uma revisão sistemática de literatura. **Brazilian Journal of Health Review**, Curitiba, v. 4, n. 4, p. 17061-17076, 2021.

FLAIG, B. *et al*. Treatment of Dyslipidemia through Targeted Therapy of Gut Microbiota. **Nutrients**, v 15, n. 1, p. 228, jan. 2023.

GHUSN, W. *et al*. The Use of Immunomodulators, Biologic Therapies, and Small Molecules in Patients With Inflammatory Bowel Disease and Solid Organ Transplant. **J. Clin. Gastroenterol.**, v. 59, n. 1, p. 24-35, 2025.

HAASE, S. *et al*. Impacts of microbiome metabolites on immune regulation and autoimmunity. **Immunology,** v. 154, n. 2, p. 230-238, jun. 2018.

HANTSOO, L.; ZEMEL, B. S. Stress gets into the belly: Early life stress and the gut microbiome. **Behavioural Brain Research**, v. 414, p.113474, set. 2021.

HIDALGO-CANTABRANA, C. *et al*. The extracellular proteins of *Lactobacillus acidophilus* DSM 20079T display anti-inflammatory effect in both in piglets, healthy human donors and Crohn's Disease patients. **Journal Of Functional Foods**, v. 64, p. 103660, 2020.

HONG, S. H; CHOI, K. M. Gut hormones and appetite regulation. **Curr Opin Endocrinol Diabetes Obes**, v. 31, n. 3, p. 115-121, 2024.

HUANG, C. *et al*. Fecal microbiota transplantation versus glucocorticoids for the induction of remission in mild to moderate ulcerative colitis. **Journal of Translational Medicine**, v. 2022, n. 354, 2022.

JAHROMI, G. G; RAZI, S.; REZAEI, N. NLRP3 inflammatory pathway. Can we unlock depression? **Brain Res.**, v. 1, n. 1822, p. 148644, 2024.

JHA, D. K; MISHRA, S.; DUTTA, U.; SHARMA V. Antibiotics for inflammatory bowel disease: Current status. **Indian J Gastroenterol.**, v. 43, n. 1, p. 145-159, 2024

KHO, Z. Y.; LAL S. K. The Human Gut Microbiome – A Potential Controller of Wellness and Disease. **Frontiers in Microbiology**, v. 14, n. 9, p. 1835, 2018.

Revista ARACÊ
ISSN: 2358-2472

KONSTANTINIDIS T, *et al.* Effects of Antibiotics upon the Gut Microbiome: A Review of the Literature. **Biomedicines**, v. 8, n. 11, p. 502, Nov. 2020.

KORNBLUTH, A.; SACHAR, D. B. Practice Parameters Committee of the American College of Gastroenterology. Ulcerative Colitis Practice Guidelines in Adults: American College of Gastroenterology, Practice Parameters Committee. **The American Journal of Gastroenterology**, v. 105, n. 3, p. 501–523, 2010.

LAWLEY, T. D.; WALKER, A. W. Intestinal colonization resistance. **Immunology**, v. 1, n. 138, p. 1-11, 2013.

LI, S. *et al*. Supplemental bifid triple viable capsule treatment improves inflammatory response and T cell frequency in ulcerative colitis patients. **BMC Gastroenterology**, v. 21, n. 1, p. 314, 2021.

MACPHERSON, A. J. *et al.* IgA function in relation to the intestinal microbiota. **Annu. Rev. Immunol**, v. 36, n. 1, p. 359–81, 2018.

MARKANDEY, M. *et al*. Fecal microbiota transplantation refurbishes the crypt-associated microbiota in ulcerative colitis. **iScience**, v. 26, n. 5, 2023.

MENDES, K. D. S.; SILVEIRA, R. C. C. P.; GALVÃO, C. M.. Revisão integrativa: método de pesquisa para a incorporação de evidências na saúde e na enfermagem. **Texto contexto – enfermagem**, v. 17, n. 4, p. 758-764, 2008.

MILAJERDI, A. *et al*. A randomized controlled trial investigating the effect of a diet low in fermentable oligosaccharides, disaccharides, monosaccharides, and polyols on the intestinal microbiome and inflammation in patients with ulcerative colitis: study protocol for a randomized controlled trial. **Trials Journal**, v. 21, n. 201, 2020.

MILHOUSE, W. *et al.* Microbiome affects mice metabolic homeostasis via differential regulation of gene expression in the brain and gut. **Physiol Rep.,** v. 13, n. 10, p. e70373, 2025.

MILOSEVIC, I.; *et al.* Eixo Intestino-Fígado, Microbiota Intestinal e Sua Modulação no Tratamento de Doenças do Fígado: Uma Revisão da Literatura. **Int. J. Mol.** ciência 2019, 20, 39milo

MIYAUCHI, E. *et al*. The impact of the gut microbiome on extra-intestinal autoimmune diseases. **Nature Reviews Immunology**, v. 23, n. 1, p. 9-23, 2023.

OH, G. M. *et al*. Therapeutic Potential of *Escherichia coli* Nissle 1917 in Clinically Remission-attained Ulcerative Colitis Patients: A Hospital-based Cohort Study. **The Korean Journal of Gastroenterology**, v. 77, n. 1, p. 12-21, 2021.

PABST, O. Gut-liver axis: barriers and functional circuits. **Nat Rev Gastroenterol Hepatol.**, v. 20, n. 7, 447-461, 2023

Revista ARACÊ
ISSN: 2358-2472

PADHI, P. *et al*. Mechanistic Insights Into Gut Microbiome Dysbiosis-Mediated Neuroimmune Dysregulation and Protein Misfolding and Clearance in the Pathogenesis of Chronic Neurodegenerative Disorders. **Frontiers in Neuroscience**, v. 16, p. 836605, 2022.

PAGE, M. J. *et al*. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews, **BMJ**, v. 372, n. 71, 2021.

PAGNINI, C. *et al*. Mucosal adhesion and anti-inflammatory effects of *Lactobacillus rhamnosus* GG in the human colonic mucosa: A proof-of-concept study. **World Journal of Gastroenterology**, v. 24, n. 41, p. 4652-4662, 2018.

PANDA, S. S; PATTNAIK, T; AICH, P. Antibiotic Cocktail: An Excellent Tool to Probe Physiology by Perturbing Gut Microbiota: A Mice Model. **Curr Microbiol.**, v. 82, n. 10, p. 457, 2025.

PARAMSOTHY, S. *et al*. The current state of the art for biological therapies and new small molecules in inflammatory bowel disease. **Mucosal Immunology**, v. 11, n. 6, p. 1558-1570, 2018.

PAREKH, P. J. *et al.* The Influence of the Gut Microbiome on Obesity, Metabolic Syndrome and Gastrointestinal Disease. **Clin Transl Gastroenterol**, v. 6, n. 6, e91, 2015.

PASCALE, A. *et al*. Microbiota and metabolic diseases. **Endocrine**, v. 61, n. 3, p. 357-371, set. 2018.

PERLER B. K., FRIEDMAN E. S., WU G. D. The Role of the Gut Microbiota in the Relationship Between Diet and Human Health. **Annual Review of Physiology**, v. 85, 2023.

PILEGGI, G. S., *et al*. Recomendações brasileiras sobre a segurança e eficácia da vacinação contra a febre amarela em pacientes com doenças inflamatórias crônicas imunomediadas. **Avanços em Reumatologia**, v. 59, n.17, 2019.

PINTO, A. L. T. **Azatioprina no tratamento de pacientes com doença de Crohn corticodependente: resultados no longo prazo e fatores preditivos de resposta**. 2010. 38 f. Tese (Doutorado em Saúde). Faculdade de Medicina, Universidade Federal de Juiz de Fora, Juiz de Fora, 2010.

REINOLD, J. *et al*. A Pro-Inflammatory Gut Microbiome Characterizes SARS-CoV-2 Infected Patients and a Reduction in the Connectivity of an Anti-Inflammatory Bacterial Network Associates With Severe COVID-19. **Frontiers in Cellular and Infection Microbiology**, v. 11, p. 747816, nov. 2021.

ROWART, P. Implications of AMPK in the Formation of Epithelial Tight Junctions. **International Journal Molecular Sciences**. V.19, n. 7, 2040, 2018 Jul

SANTOS, S. M. R. **Doença de Chron: etiopatogenia, aspectos clínicos, diagnóstico e tratamento**. 2013. 91 f. Monografia (Mestrado) - Curso de Ciências Farmacêuticas, Universidade Fernando Pessoa, Porto, 2013

Revista ARACÊ
ISSN: 2358-2472

SCHNUR, S., *et al*. Inflammatory bowel disease addressed by Caco-2 and monocyte-derived macrophages: an opportunity for an in vitro drug screening assay. **In vitro Models,** v. 1, p. 365–383, 2022.

SHALAPOUR, S.; KARIN, M. Cruel to Be Kind: Epithelial, Microbial, and Immune Cell Interactions in Gastrointestinal Cancers. **Annual Review of Immunology**, v. 38, p. 649-671, fev. 2020.

SHANG, S. *et al*. The Impacts of Fecal Microbiota Transplantation from Same Sex on the Symptoms of Ulcerative Colitis Patients. **Polish Journal of Microbiology**, v. 72, n. 3, p. 247-268, set. 2023.

SINGH, R. *et al*. An IBD-associated pathobiont synergises with NSAID to promote colitis which is blocked by NLRP3 inflammasome and Caspase-8 inhibitors. **Gut Microbes**, v. 15, n. 1., p. 2163838, 2023.

SIMPSON, H. L. *et al*. Human organoids and organ-on-chips in coeliac disease research. **Trends Mol Med.**, v. 31, n. 2. p. 117-137, 2025.

SMITH, B. J. *et al*. Strain-resolved analysis in a randomized trial of antibiotic pretreatment and maintenance dose delivery mode with fecal microbiota transplant for ulcerative colitis. **Scientific Reports**, v. 12, n. 1, p. 5517, abr. 2022.

SOKOL, H. *et al*. Fecal microbiota transplantation to maintain remission in Crohn's disease: a pilot randomized controlled study. **Microbiome**, [S.L.], v. 8, n. 1, 2020.

SOMMER, F.; BÄCKHED, F. The gut microbiota — masters of host development and physiology. **Nature Reviews Microbiology**, v. 11, n. 4, p. 227–238, fev. 2013.

SOUZA F. G, *et al*. Adesão ao tratamento farmacológico em pacientes com doenças inflamatórias intestinais: uma revisão integrativa da literatura. **Revista Eletrônica Acervo Saúde**, v. 13, n. 2, p. e4601, 2021.

STERLIN, D.; GOROCHOV, G. When Therapeutic IgA Antibodies Might Come of Age. **Pharmacology,** v. 106, n. 1-2, p. 9-19. fev. 2021.

SU, H. J. *et al*. Inflammatory bowel disease and its treatment in 2018: Global and Taiwanese status updates. **J Formos Med Assoc.**, v. 118, n. 7, p. 1083-1092, 2018.

TAN, S. *et al*. Interaction between the gut microbiota and colonic enteroendocrine cells regulates host metabolism. **Nat Metab.**, v. 6, n. 6, p. 1076-1091, 2024.

TRINDADE, M.; MORCERF, C. C. P.; ESPASANDIN, V. L. Terapia biológica na doença de Crohn: quando iniciar? **Sociedade Brasileira de Clínica Médica**, v. 17, n. 1, p. 41-46, jan. 2018.

VALCHEVA, R. *et al*. Inulin-type fructans improve active ulcerative colitis associated with microbiota changes and increased short-chain fatty acids levels. **Gut Microbes**, v. 10, n. 3, p. 334–357, 2018.

Revista ARACÊ
ISSN: 2358-2472

VAN DE WOUW, M. *et al*. Short-chain fatty acids: microbial metabolites that alleviate stress-induced brain-gut axis alterations. **The Journal of Physiology**, v. 596, n. 20, p. 4923-4944, out. 2018.

WALKER, A. W.; LAWLEY, T. D. Therapeutic modulation of intestinal dysbiosis. **Pharmacological Research**, vol. 69, p. 75-86. 2013).

WANG, H., *et al*. The Safety of Fecal Microbiota Transplantation for Crohn's Disease: findings from a long-term study. **Advances In Therapy**, [S.L.], v. 35, n. 11, p. 1935-1944, 16 out. 2018.

XIANG, L. *et al*. Efficacy of faecal microbiota transplantation in Crohn's disease: a new target treatment? **Microbial Biotechnology**, [S.L.], v. 13, n. 3, p. 760-769, 20 jan. 2020.

XUE, J. C. *et al.* Biological agents as attractive targets for inflammatory bowel disease therapeutics. **Biochim Biophys Acta Mol Basis Dis.,** v. 1871, n. 3, p. 167648, 2025.

YADAV, S. *et al*. Therapeutic potential of short-chain fatty acid production by gut microbiota in neurodegenerative disorders. **Nutrition Research**, v. 106, p. 72-84, 2022.

YANTISS, R. K., ODZE, R. D. Diagnostic difficulties in inflammatory bowel disease pathology. **Histopathology**.; v. 48, n. 2, p. 116-32, 2006.