Synbiotics in Inflammatory Bowel Diseases

Subjects: Immunology | Nutrition & Dietetics | Gastroenterology & Hepatology

Contributor: Tanvi Shinde , Kent Taylor

Inflammatory bowel disease (IBD) is a group of chronic relapsing gastrointestinal disorders that are characterized by inflammation of the gastrointestinal tract. The involvement of three distinct recurrent inflammatory features that sustains the chronic inflammation in IBD have been clearly identified that includes, disturbances in the gut microbiota, dysregulated immune response and altered colonic epithelial integrity. Dietary components such as prebiotic dietary fibres (DF) and probiotics due to their potential in modulating immune functions and influencing microbiota are promising strategies in the context of IBD. In this entry, we review the recent evidence from in-vivo studies to support the application of synergistic synbiotic carrying whole-plant complex prebiotic fibre and probiotic in resolving in the inflammatory cycle in IBD.

Probiotic Prebiotic Inflammation Gut Health Synbiotic Microbiome Sugarcane Dietary Fibre IBD Short Chain Fatty Acid Gut Barrier

1. Introduction

Inflammatory bowel disease (IBD) is a group of chronic relapsing gastrointestinal tract (GIT) disorders including ulcerative colitis (UC) and Crohn's disease (CD) that are characterized by inflammation of the gastrointestinal tract and dysbiosis of the gut microbiota[1]. The incidence of CD and UC is rising globally[2]. The adoption of "Westernised" diet low in fruits and vegetables has been blamed as a potential factor for the recent rise in IBD incidence[3][4]. Despite current medical treatments that focus primarily on immunosuppression[5], overall 20% of patients with CD still require surgery and over 10% of UC patients still require colectomy[6]. This highlights the urgent need for research into prevention and management of these complex pathologies to avoid debilitating complications and the need for substantial medical interventions.

2. Three-part inflammatory cycle in IBD

Although, the etiopathology of IBD remains largely unknown, emerging evidence supports the interrelated roles of genetic, environmental, microbial and immunological factors[7][8]. IBD is thought to result from an aberrant and continuing inflammatory response to commensal microbes in a genetically susceptible host[7]. Alterations in the intestinal epithelial and mucosal barrier are known to support bacterial translocation resulting in dysfunctional intestinal inflammatory cascade[9][10][11], leading to pathologic proliferation of inflammatory mediators. There is an increasing level of evidence highlighting the key role of intestinal microbiota in driving inflammatory response during disease development and progression[12][13][14]. The microbial imbalance in the colon, also known as gut

dysbiosis, is associated with dysregulated immune responses that further disturbs the colonic health. Thus, IBD encompasses a distinct tripartite pathophysiological circuit involving altered colonic mucosal barrier, dysregulated immune response and gut microbial dysbiosis as hallmarks of this complex pathology[1].

3. Combining prebiotic and probiotic functionalities to break the inflammatory cycle in IBD

Given the complexity of the involvement of multiple factors in the onset, progression, and pathogenesis of IBD, preventive and therapeutic approaches that hinder or break the inflammatory circuit by resolving one or more of the pathophysiological inflammatory components are needed. In this view, probiotic and prebiotic dietary fibres (DF) that regulate immune parameters by influencing gut microbiota and colonic barrier functions are important in the context of IBD[15]. The use of synbiotic formulations that capture the synergy of probiotic and prebiotic functioning is considered a pragmatic approach to resolving the gut inflammatory cycle[15][16][17][18].

Mechanistic research evidence indicates augmented efficacy of synergistic synbiotic combinations in modulating gut inflammation. An in-vivo study utilising a synbiotic combination of whole-plant dietary fibre and spore probiotic have been confirmed to protect mice against chemically induced IBD, with synergistic effect being more profound than that observed for either probiotic or prebiotic alone[19]. Preconditioning of mice with synbiotic (sugarcane-derived complex whole-plant prebiotic DF and probiotic *Bacillus coagulans* spores) – supplemented diet proved significantly effective in repressing the onset and severity of Dextran-Sulfate-Sodium (DSS)-induced colitis in mice model of IBD. The synbiotic pre-supplementation resulted in a substantial prophylactic and anti-inflammatory effect, reducing disease severity, colonic damage, and inflammatory mediators while modulating the metabolite and short-chain fatty acids (SCFA) profiles of DSS-induced gut damage.

The synergistic synbiotic combination of whole-plant prebiotic sugarcane fibre and *B. coagulans* spores was also demonstrated to impart therapeutic effect by reducing established gut inflammation in a genetically mutant mice model of IBD[20]. While prebiotic and probiotic supplemented diet were effective in alleviating some inflammatory parameters, synergistic synbiotic was most efficacious in modulating local and systemic cytokine profiles, reduce colonic epithelial damage and ameliorating severity of diseases symptoms. Furthermore, synbiotic combination was confirmed to confer site-specific modulations in gut microbiota diversity and boosted SCFA levels along the entire colon length. This study also highlights the importance of fermentation of prebiotic fibre and concomitant production of SCFAs at uniform rate to nourish the whole colon (proximal and distal)[20][21][22].

The benefits from prebiotic dietary fibre are largely dependent on the presence and/or abundance of fibre-digesting gut bacteria to produce anti-inflammatory SCFAs with immune regulating properties[23][24]. However, dysbiosis in IBD with characteristic depletion of fibre-degrading-SCFA-producing bacterial members and concurrent reduced levels of SCFAs is commonly reported. Thus, lack of fibre-digesting gut members in IBD limits the health outcomes through consumption of fibre-rich diet during inflammatory dysbiotic state. Similarly, probiotic administration alone without a fibre substrate would also be unreliable to affect health outcomes.

Thus, co-administration of probiotic bacteria that can synergistically metabolise the administered prebiotic DF as synbiotic and consequently improve the probiotic activity to produce beneficial metabolites and influence the microbiota is imperative in positively modulating the microbial environment to induce immune homeostasis.

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