

Role of Psychobiotics in Irritable Bowel Syndrome & Inflammatory Bowel Disease Patients: A Microbial Mechanism

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ABSTRACT

Background: Probiotics are live microorganisms which, when taken in sufficient quantities, have positive effects on health. The gut microbes are important in maintaining the balanced and healthy gut bacteria and are also known as “friendly” or “good” bacteria. Dysbiosis (imbalance in the good bacteria) in the gastrointestinal microbial composition is identified as a major contributor to chronic inflammatory conditions. Inflammatory Bowel Disease (IBD) and irritable bowel syndrome (IBS) are prevalent gastrointestinal disorders characterized by chronic inflammation and dysregulation of gut function, respectively.

Purpose: To study and analyse the gut microbiome mechanism that plays a crucial role in maintaining the integrity of gut. This review is a comprehensive analysis of current research on the therapeutic potential of probiotics in managing IBD and IBS.

Summary and Future Findings: This review highlights the mechanism of the gut microbiome that plays a central role in the pathogenesis of both conditions, thus paving the way for microbiome-based therapies such as probiotics. The use of Psychobiotics (Probiotics that help in maintaining good gut health and mental health) should be a practicing approach in dealing with the gut related diseases.

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Objectives

- To explore the gut brain connection and their mechanisms.
- To study the psychobiotics communication for maintaining the gut flora.
- To study and analyze the mechanism of psychobiotics in maintain gut health of IBD/ IBS patients and in improving the mental health disorders.

Introduction

Probiotics are live microorganisms that provide essential health benefits to the host health when taken in adequate amounts. Microbes work on many different aspects of health. The probiotics not only help in improving the gut health but also impact the behavioral and psychological function of the body and such probiotics are called as Psychobiotics.

Irritable Bowel Syndrome (IBS) and Inflammatory Bowel Disease (IBD) being the most common, chronic yet unidentified gut health diseases affect the gut microbiome along with which they also affect the patient’s mental health aspects. According to the recent researches the gut microflora is disturbed in this disease which is known as dysbiosis. The use of psychobiotics helps to improve the symptoms in IBS/IBD patients through positive alterations in gut brain axis [1].

The Gut Brain Connection and Their Mechanisms

“The microbiome and gut are communicating with the brain, and conversely the brain is communicating with the gut and the microbiome.” The two organs are linked through biochemical signaling between the nervous system in the digestive tract, called the enteric nervous system, and the central nervous system, which includes the brain. The longest nerve in the body that is vagus nerve acts as a primary information connection between the gut and the brain. The gut has been called a “second brain” because it produces many of the same neurotransmitters as the brain does, like serotonin, dopamine, and gamma-aminobutyric acid, all of which play a key role in regulating mood [2].

According to the recent researchers the bidirectional correlation has been identified which is known as BGM (BRAIN- GUT- MICROBIOME). This bidirectional correlation between gut and brain comprise of – ENS, CNS, and endocrine system along with metabolic, neural and immune mediators. The gut brain axis role is multidisciplinary which integrates with the intestinal functions such as cognitive and emotional cores of the brain with peripheral gut functions like, intestine permeability, enteric reflex, enter-endocrine signaling, enteric reflex, etc. This bidirectional relationship is a great way where the two organs (gut and brain) communicate through each other [2].

According to research conducted by the gut brain axis also performs the role in several physiological processes of our body such as insulin secretion, fat and bone metabolism, glucose regulation as well as small functions such as satiety, food

intake [3]. The various intestinal activities and homeostasis of the intestinal microbiota are well managed by probiotic microorganisms whereas the gut brain axis is regulated by calcitonin gene-related peptide (CGRP).

The Psychobiotics Communication for Maintaining the Gut Flora

Psychobiotics are defined as probiotics that confer mental health benefits to the host when ingested in a particular quantity through interaction with commensal gut bacteria. The sound and beneficial composition of the gut microbiota functions in 2 ways eubiosis state and dysbiosis state. They perform variety of functions such as secretion of gamma-aminobutyric acid (GABA), serotonin, or dopamine, the reduction of cortisol synthesis and the synthesis of short-chain fatty acids, which are key to the proper functioning of the intestinal epithelium. Whereas in dysbiosis, the microbiome produces pro-inflammatory cytokines, the secretion of bacterial toxins, and the removal of harmful metabolites from the diet. In this working the probiotics are essential in improving their functioning and maintaining the gut integrity. Psychobiotics are bacterial species that can alter brain function by influencing immune function, hormonal signaling or modulating neurotransmitter levels and availability [4].

The main functions of probiotics include

- protecting the integrity of the intestinal barrier.
- reducing the synthesis of pro-inflammatory cytokines.
- producing neuroactive compounds (e.g., GABA).
- modulating neurotrophic factors (e.g., brain-derived neurotrophic factors, or BDNFs), and influencing the synthesis of neurotransmitters.
- psychobiotics are also used to reduce stress, reduce depressive symptoms, alleviate anxiety disorders, improve cognitive function, and reduce stress-related gastrointestinal complaints, among others.

How Microbes Affect the Psychophysiological Markers of Depression and Anxiety

Firstly, by affecting the hypothalamic-pituitary-adrenal (HPA) axis stress response and reducing systemic inflammation.

Second, by a direct effect on the immune system.

By the secretion of molecules such as neurotransmitters, proteins, and short fatty acids chains [5].

How Probiotics Influence the Gut Brain Axis and Their Mechanism of In Maintaining the Gut -Brain Health of Ibd/Ibs Patients

Irritable bowel syndrome (IBS) is the most common functional gastrointestinal disorder in the Western World. It is a multifactorial condition involving genetics, physiological and psychological responses to stress, diet, age, geographical origin, infections, and use of antibiotics. IBS symptoms are related to gastrointestinal (GI) dysmotility, hypersensitivity, immune activation and changes in composition and function of gut bacteria (the microbiota) and the gut mucosal barrier [1].

In their study related to gut brain axis in 2015, explained that, the dysbiosis in the microbiota and subsequent dysfunction in the GBA determines changes in intestinal motility and secretion contributing to visceral hypersensitivity and cellular alterations of the entero-endocrine system and immune system [6,7]. The pathogenesis of visceral hypersensitivity that is presented in IBS is regarded a consequence of dysbiosis in terms of dysregulation of the GBA. IBS is also related to psychiatric disturbances such as depression and anxiety.

Inflammatory Bowel Disease is also a gut dysbiosis diseases which have pathologically similar condition but comprise of two diagnostically distinct disorders: Crohn's disease (CD) and ulcerative colitis (UC), both manifesting as chronic and relapsing inflammatory disorders. In Chron's disease inflammation. In Crohn's disease, inflammation affects the entire gastrointestinal tract, whereas in ulcerative colitis, the inflammatory reaction is confined to the rectum and colon [8].

According to the recent researches conducted by there is increasing incidence in the developing countries, its specific etiopathogenetic mechanism at the basis of IBD remains to be fully elucidated, although there is consensus on the involvement of an exaggerated immune response induced by different triggering stimuli deriving from the gut microbiota, pathogenetic microorganisms, or from the environment in a genetically susceptible host [9-11]. The enteric microbiota is considered a fundamental player in the development of IBD, influencing both the acute phase and the more latent inflammation-induced neuronal dysfunction. Indeed, the correlation between gut dysbiosis, i.e., changes in intestinal microbial composition, and IBD etiopathogenesis has been consistently shown both in preclinical and clinical studies.

Several other ongoing researches stated that, in addition to intestinal symptoms, besides gastrointestinal symptoms, patients with IBD also experience extra-gastrointestinal stress-related issues, including major depression and generalized anxiety, which can affect treatment outcomes and decrease the likelihood of achieving remission. In their prospective studies concluded that IBD patients suffering from psychiatric disorders are at higher risk of requiring surgery and of incurring functional gut disorders [12].

While studying about the microbes in the small intestines in their study identified that, the microbiota is dominated by 4 predominant bacterial phylae of which the most abundant are the Gram-positive Firmicutes (among them more than 180 species of Lactobacillus), and Actinobacteria (among others the Bifidobacteriae), the Gram-negative Bacteroides (B. Fragilis as the most important) and Proteobacteria (E. coli, salmonella, yersinia, shigella, vibrio, haemophilus, etc.). The microbiota also includes vast numbers of viruses, protozoa, archae and fungi [13,14].

The common dysbiotic finding in IBS is an increase in Streptococcus spp. (countered by a reduction in Lactobacillus spp) and a reduced abundance of Bacteroidetes, i.e. an overall reduction in beneficial bacteria and an increase in pathogenic species. An increase in the non-butyrate and mucin-degrading Clostridiace group may also play a significant role as well as a decrease in the probiotic Bifidobacterium, a known aid of the mucosal barrier. However, findings are not uniform and observations are conflicting [15,16].

The common findings observed a decrease in probiotic species such as Lactobacillus and Bifidobacterium and an increase in pathogenic species which is highly responsible for the gut dysbiosis.

Based on the research carried out by, IBS is a stress-sensitive disorder and the treatment of IBS should also focus on managing stress and stress-induced responses [2]. Over the last decade the characterization of the gut-brain-axis has progressed tremendously and current evidence now points toward multiple

mechanisms being involved in the microbiota to brain signalling, including endocrine and Neurocrine pathways and that the brain can alter the composition of the microbiota and mental behaviour via the autonomic nervous system.

In Inflammatory Bowel Diseases also the bacterial species are considered to play a beneficial role against IBD, such as *Lactobacillus*, and *Faecalibacterium* within Firmicutes, and *Bifidobacterium* within Actinobacteria [17].

How Probiotics Helps in Maintaining the Eubiosis Condition

Probiotics enhances the anti-inflammatory cytokines, suppress pro inflammatory pathways and inhibit apoptosis activity. Also, after the introduction of the *Lactobacilli* into the duodenum, gastric vagal nerve activity showed an increase within minutes. Aguilera, in his study on Gut Microbes in 2015, stated that Visceral pain secondary to the increase in inflammatory cells during dysbiosis following antibiotics can be reverted by administration of *Lactobacillus* and lactic acid producing bacteria [18].

During a 4-week intervention trial conducted by, with non-depressed individuals, probiotics were associated with reduced rumination and aggressive thoughts [19]. Study on probiotics formulations concluded that, administration of a probiotic formulation containing *Lactobacillus* and *Bifidobacteria* reduced psychological stress in humans [20]. It was suggested that the administration of *Bifidobacteria* resulted in increased tryptophan levels giving probiotics an antidepressant potential by influencing tryptophan metabolism.

Summary and Future Findings

Functional gastrointestinal disorders such as IBS/IBD are associated with many other health complications that affect the quality of life to a greater extent. There is a research-based correlation between the severity of the symptoms and the presence of stress factors which in turn affect the microbiome functioning leading to increased emotional instability as per the researchers the gut microbiota composition of an IBS patient is similar to that of depressive patient.

Probiotics class known as psychobiotics helps in improving the gut health and mental health parameters of an individual. The strains of probiotics that are beneficial in alleviating the symptoms of IBS/IBD get disturbed due to psychological disorders which comes secondary with the IBS/IBD patients.

Therefore, the gut brain connection, microbiota composition, properly planned treatment with beneficial probiotic supplementation can decrease stress markers and reduce intestinal complaints intensified by stress, may have additional benefits and increase the effectiveness of therapy.

The communicative relationship between the two organs includes a variety of components such as hormones, immunity, neurology, metabolism that act as a functional change in the working of the microbiota. The relationship is maintained by normal ecological balance of the microbiota.

Though their mechanism of work is not that clear but according to the ongoing researches the discovery and modulation in the gut brain axis can affect the bodily functions in a positive or negative manner and also opens up the direction for further research where the microbiota will not only help in regulating the gut health but this second brain is also influencing other

mechanism of the body that helps to decrease the symptoms of many other diseases also.

Psychobiotics are the new class of probiotics which possess anti-inflammatory, anxiolytic, antidepressant properties along with the changes in emotional, hormonal, neural status of the patient. The gut microbes do play a crucial role in one health and they are highly disturbed even with the little inflammation or other psychological.

The recent researches concludes that the HPA axis (Hypothalamic-Pituitary Axis) involvement regulate the immune system, maintains the gut integrity, and permits the interaction between fermentation products with the host such as SCFAs (Short Chain Fatty Acids) and neuroactive compounds with their psychobiotics effects.

A wide array of microbe mechanisms by which psychobiotics microorganisms exert their psychobiotics potential is beneficial in alleviating the symptoms of many gastrointestinal as well as psychological diseases.

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