International Journal of Immunology
2024, Vol. 12, No. 1, 2024, pp. 10-18
https://doi.org/10.11648/j.iji.20241201.12

Review Article

The Science Underlying the Probiotic Strain Bifidobacterium in Beneficial Effects on Immunological and Gastrointestinal Health

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Abstract

Probiotics have demonstrated a lot of promise in improving gut health in humans. Despite the encouraging data, nothing is known about the therapeutic effectiveness of many of the probiotics on the market, and it's sometimes unclear how they work. Humans have long used Bifidobacterium, a well-known, multifunctional probiotic, to treat gastrointestinal, immunological, and infectious disorders. It is also therapeutically useful. This review provides a theoretical framework for comprehending the mechanisms of action of Bifidobacterium and highlights the functional advantages from the most pertinent animal and clinical trials. The genus Bifidobacterium belongs to the Actinobacteria phylum. = Firmicutes, Bacteroidetes, and Actinobacteria constitute the most abundant phyla in the human intestinal microbiota, Firmicutes and Bacteroidetes being predominant in adults, and Actinobacteria in breast-fed infants, where bifidobacteria can reach levels higher than 90% of the total bacterial population. They are among the first microbial colonizers of the intestines of newborns, and play key roles in the development of their physiology, including maturation of the immune system and use of dietary components. Indeed, some nutrients, such as human milk oligosaccharides, are important drivers of bifidobacterial development. Some Bifidobacterium strains are considered probiotic microorganisms because of their beneficial effects, and they have been included as bioactive ingredients in functional foods, mainly dairy products, as well as in food supplements and pharma products, alone, or together with, other microbes or microbial substrates. Well-documented scientific evidence of their activities is currently available for bifidobacteria containing preparations in some intestinal and extraintestinal pathologies. In particular, it regulates luminal metabolism, maintains gut microbiota stability, and eventually promotes a precisely calibrated homeostatic equilibrium in the host-microbiome relationship. An ideal probiotic selection would benefit from clinical proof of the multifunctional activities' efficacy and mechanism of action.

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Received: 26 January 2024; **Accepted:** 4 February 2024; **Published:** 21 February 2024

Keywords

Probiotics, Bifidobacterium, Health Benefits, Clinical Efficacy, Gut Microbiota, Intestinal Health, Immunology, Immune Modulation, Immune Response

1. Introduction

The gut is a dynamic, complex ecosystem that has developed unique immune cells traits throughout time as a result of constant exposure to a variety of pathogenic agents and antigens [1]. Numerous intestinal immune cell types are crucial to the host's ability to fight off infections and control immunity to inhaled antigens and commensal microorganisms. However, intestinal commensal microorganisms with advantageous immunomodulatory qualities might influence immune cell functions and activities to a significant extent [2]. In fact, immunological homeostasis is maintained and both innate and adaptive immune responses are modulated by immune cells, commensal microbes, and nutrients interacting and responding to one another continuously in a stable environment [3]. The immune system operates better as a result of this contact. Owing to its unique cellular, molecular, and anatomical features, the gut is thought to be a crucial habitat for good bacteria to maintain their health-promoting properties. Every animal, including humans, comes into touch with a wide variety of distinct bacteria throughout their lifetimes in their intestines [4]. The bacteria that make up the gut microflora have been chosen by evolution based on their ability to thrive and multiply in the intestinal environment. The ability of host organisms to strengthen their immune systems through improved immunological responses to illnesses, such as inflammatory and infectious disorders [5, 6], is one advantage of this relationship. Regularly, specific changes in the gut microbial communities can support or impede changes to the host immune system and the subsequent onset of autoimmune disorders.

Probiotics are defined as "Live microorganisms which, when administered in adequate amounts, confer health benefits on the host" by the Food and Agriculture Organization and the World Health Organization [7, 8]. These days, probiotics constitute a significant category of beneficial bacteria that may be ingested or added to food, supplements, and the gut [9]. Probiotics can improve immune functioning by interacting with various immune cells and altering the makeup of intestinal microbiota when ingested [10-14]. Probiotics are consequently generally recognized to have immunomodulatory and health-promoting qualities [8, 15].

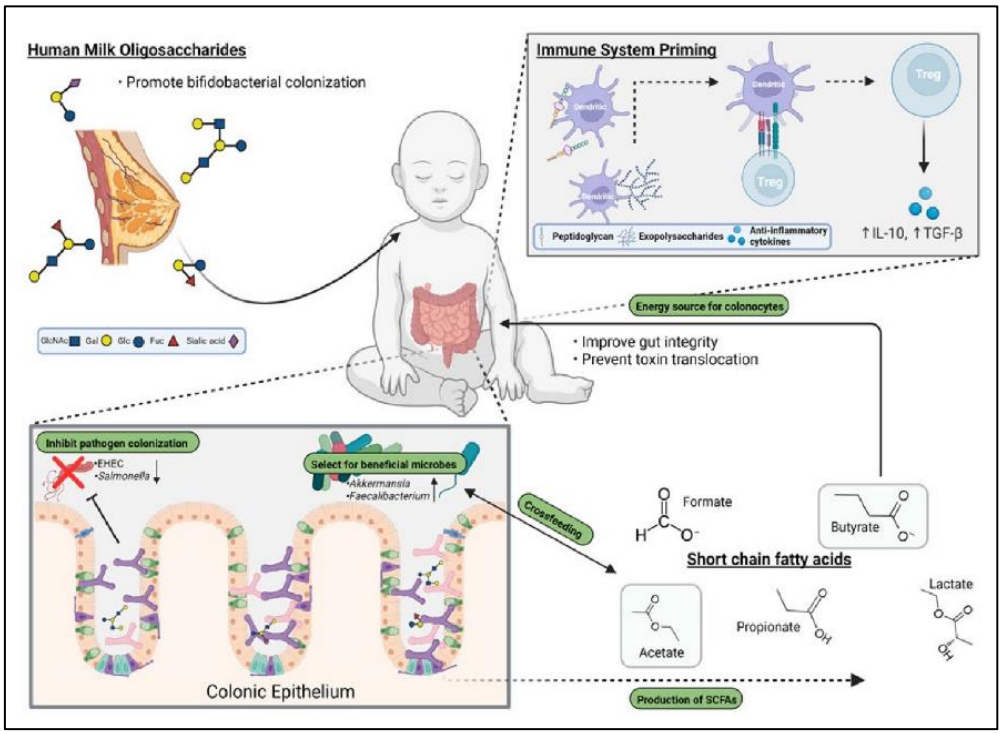

Figure 1. *Influence of bifidobacteria on promoting a healthy gut microbiota and factors that affect their colonization [38].*

In fact, these microbes have a great deal of dependability when it comes to delaying the beginning of certain illnesses [16, 17]. As a result, taking probiotics might offer more affordable options for managing illnesses [18-21]. Probiotics are recognized to have many health benefits, but it's important to comprehend the processes underlying how they interact with immune cells to promote immunomodulatory effects [22]. Additionally, it's critical to identify new and developing probiotic strains with comparable qualities [9, 23-25].

Remarkably, the bulk of studies that are now accessible concentrate on the metabolic aspects of probiotics, with comparatively little study being done on their immunomodulatory effects. Only a portion of the processes underlying the interaction between probiotics and host immune cells have been explained in the literature. In order to better understand how immune cells and probiotics interact to improve immune function, the current study attempts to compile and summarize the most important scientific findings that have been published to far. Thus, a summary of current understanding on the immunomodulatory capabilities of probiotic bacteria in enhancing the human immune system is given.

2. Growth and Development of Bifidobacteria During Infancy

Adult feces include bifidobacteria, although they make up a very minor percentage of the bacterial population overall. But in the first year of life, they are abundant in the feces and are among the forerunners of the bacterial succession that takes place in the baby's large intestine as the gut microbiota starts to form. After three to four months, bifidobacteria do in fact dominate the gut microbial populations quantitatively [26, 27]. There is likely an enrichment of Bifidobacterial members in the gut of nursing babies due to the diversity of Human milk oligosaccharides (HMOs) are found in significant amounts in human colostrum and milk. Some of them are resistant to the baby's digestion and go to the big colon, where gut bacteria may feed on them. HMOs have a variety of structural features and are primarily made up of a lactose core connected to units (n = 0 to 15) of either lacto-N-biose (type I) or N-acetyl-lactosamine (type II) monosaccharides (glucose, galactose, N-acetylglucosamine, fucose, or sialic acid) [28]. Among the most well-known gut bacteria that may use HMOs are bifidobacteria.

Glycosyl hydrolases, which break certain bonds inside HMO molecules, are found in a number of species. The most well-characterized are those produced by B. bifidum, B. longum subsp. infantis, and B. breve. According to genomic evidence, bifidobacteria could have specific adaption features that account for this ecological specialty. For instance, B. longum subsp. infantis ATCC15697's genome study revealed that it is an archetypal human milk-consuming bacteria due to the presence of genes in its genome that encode enzymes involved in the breakdown of HMOs [29].

Lacto-N-biosidase activity, which enables an effective degradation of HMOs, is anticipated to be present in B. bifidum [30]. The most prevalent species among newborns breastfed are these two species, which are adapted for HMO [31, 32]. Therefore, the reason for these species' prevalence in breastfed infants is their capacity to exploit otherwise indigestible carbohydrates. While B. bifidum strains are more varied and some of them are unable to consume fucosylated or sialylated HMOs, the latter species appear to have a similar HMO usage pattern [33]. Similar to B. bifidum, the HMO usage profile of B. breve varies depending on the strain; however, certain strains of B. breve utilize HMOs that have sialic acid or fucosyl residues attached to them. In any event, the fact that B. breve is able to use these milk oligosaccharides helps to explain why it is so prevalent in breastfed infants' feces [34]. The finding that other bacterial communities eventually stabilize colonize the gut provides additional evidence for the presence of a crucial bifidobacteria-gut microbiota-host cross talk [35]. This is consistent with the theory that the establishment, stability, and development of the gut microbiota are shaped by strong bacterial correlations [36].

3. Beneficial Effects of Bifidobacterium in Intestinal Immunity

3.1. Bifidobacteria for Prevention and Management of Disease

The scientific and medical communities are become increasingly aware of the conditions linked to gastrointestinal and immunological illnesses, such as systemic lupus erythematosus, obesity, metabolic syndrome, irritable bowel syndrome, and inflammatory bowel disease [37]. It's interesting to note that changes in the commensal gut microbiota may also be linked to some conditions that worsen and exhibit extraintestinally, such psoriasis, rheumatoid arthritis, or mental disorders [38].

Accordingly, it has been suggested that the application of bacteriotherapy, mostly in the form of probiotic administration, frequently as an adjunct to medical therapies, may be beneficial for the restoration of a healthy state within the context of all these illnesses. One of the major genera of commensal bacteria found in the human GIT is Bifidobacterium, and several studies have linked its presence to health benefits [41]. Every species of Bifidobacterium seems to have a distinct immunological impact on the host; B. bifidum stands out for its capacity to increase the T-regulatory response, which may be important given its application in long-term inflammatory conditions [42]. In this sense, utilizing a dendritic cell/naive T-cell paradigm, supplementing the gut microbiota from a cohort of patients with systemic lupus erythematosus with a B. bifidum strain largely restored the aberrant immunological response typical of lupus [43]. In

recent years, a number of reviews have examined the potential benefits of bifidobacteria on human health [44-46].

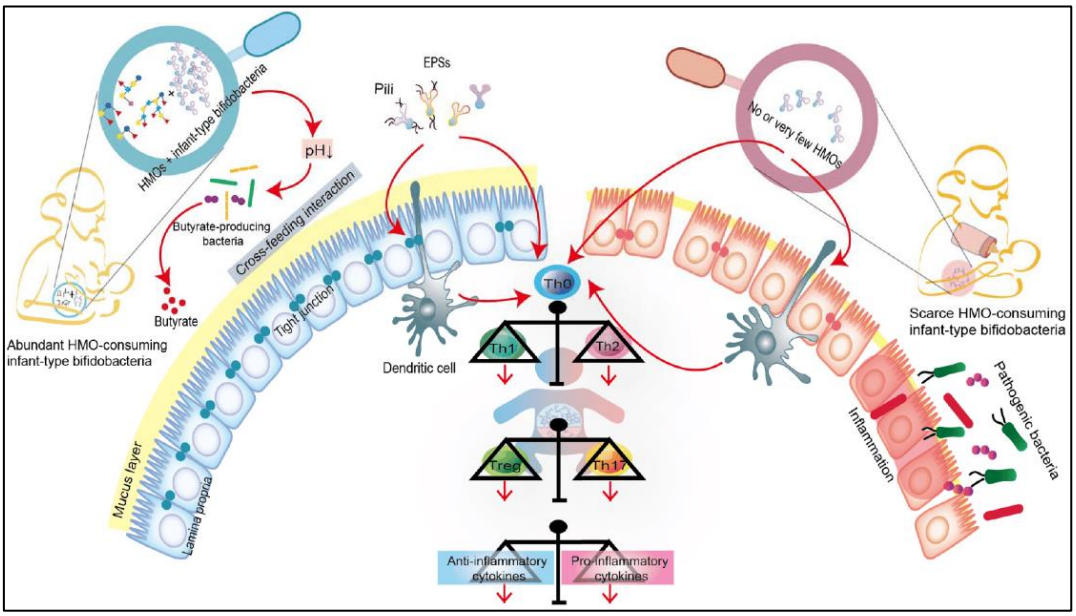

Figure 2. *Co-evolution of intestinal infant-type bifidobacteria and HMOs-mediated immune system imprinting early in life [40].*

3.2. Role of Bifidobacteria for Antibiotic-Associated Diarrhea and Other Intestinal Disorders

Because probiotics can stimulate the production of mucin, which limits the pathogen's adhesion to the gut surface, produce short-chain fatty acids and other antimicrobial substances that may reduce the density of H. pylori, and protect against human pathogens through host receptor competition and immune modulation, they can be used as an adjuvant therapy for the eradication of H. pylori [47]. Conversely, other scientists concur that probiotic treatment does not alleviate symptoms because it lowers H. pylori levels, based on further meta-analyses [48]. According to several published studies, administering a pretreatment with yogurt that included combinations of lactobacilli and bifidobacteria enhanced the removal of H. pylori [49, 50]. After 10 days of treatment of the commercial mix of probiotic VSL#3, which comprises many of the previously described probiotic bifidobacteria, a recent research found that 32.5% of adults had eradicated H. pylori [51].

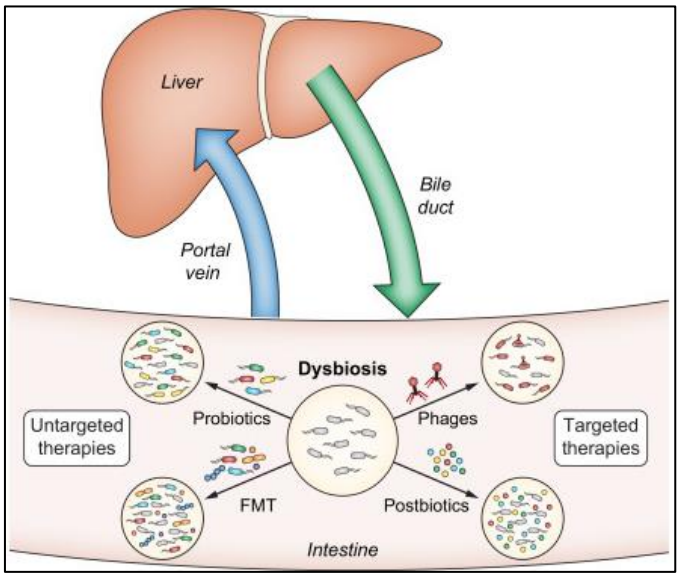

Figure 3. *Microbiome-centered therapies for patients with liver disease [54].*

3.3. Significance of Bifidobacteria in Liver Disease

Because probiotics, such as bifidobacteria, have a positive effect on altering the makeup of the intestinal microbiota, which can affect the beginning of liver disease, they have become a part of innovative treatment methods in hepatology [52]. The role that gut microbiota plays in the etiology of cirrhosis and other liver problems is the reason behind the growing interest in the use of probiotics in the prevention and treatment of liver disease. Probiotics cannot, however, be used in liver therapies with a fair assurance of efficacy because the scientific data in this area is still debatable [53].

3.4. The Science of Bifidobacteria in Inflammatory Bowel Disease (IBD)

In addition, the use of Bifidobacterium strains has been effective in reducing the symptoms of IBS. Bowel inflammations As a number of taxonomic and functional alterations, as well as imbalances in the host-microbiota cross-talk, have been reported, there is mounting evidence of the pathogenic role of the host microbiota in inflammatory bowel disease (IBD) [55]. This might be interpreted as a reciprocal interaction between modified bacterial community characteristics, functions, or metabolites and modified immune function (mucosal barrier, innate bacterial killing, or immunological control) [56]. IBD may develop or worsen as a result of a dysregulated immune response to commensal gut bacteria, in which there seems to be a deficiency in local tolerance mechanisms towards commensal microorganisms [57]. Research on the microbiota associated with the mucosa of the feces and the gut has shown quantitative and qualitative alterations in composition and function linked to IBD, with a shift towards an inflammatory microbiome [58]. Reduced compositional complexity is seen, along with the disappearance of typical anaerobic bacteria [59], a brief instability in composition during clinical remission [60], and a dysbiosis toward certain microorganisms, with both an over- and underrepresentation of particular species [61]. Ulcerative colitis (UC) has been linked to an overabundance of Desulfovibrio species, which may produce sulfides and hence have pathogenic potential [62]. Furthermore, it has been observed that there is a rise in microbial genes related to the metabolism of sulfur-containing amino acids such cysteine and sulfate transport systems [63].

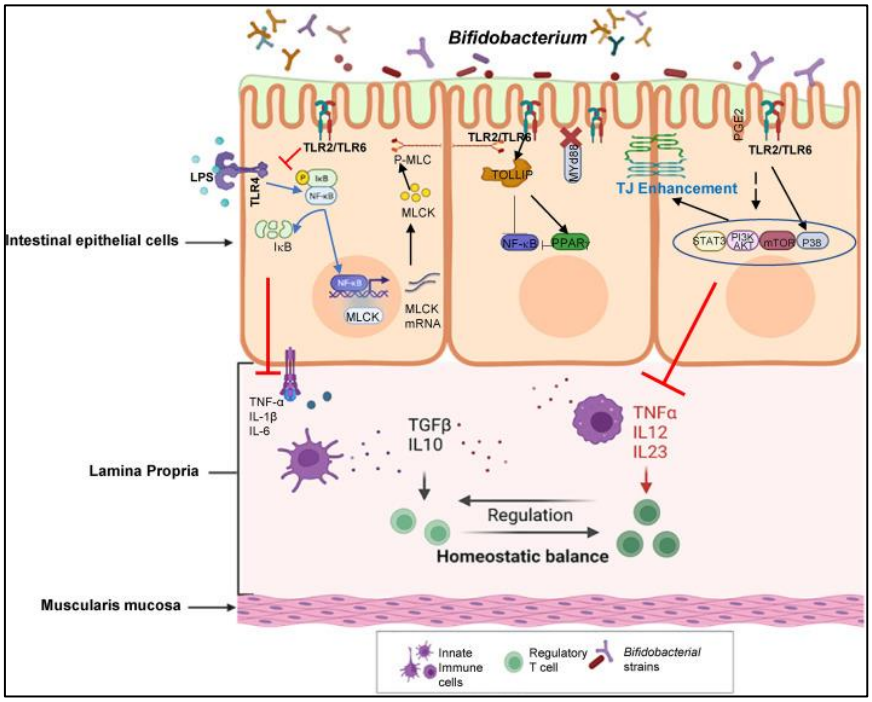

Figure 4. *Role of bifidobacteria in Intestinal Health [40].*

3.5. The Impact of Bifidobacteria in Functional Gastrointestinal Disorders (FGID)

When there is no obvious organic abnormalities present, a group of persistent or recurring symptoms that may be linked to the gastrointestinal tract are considered to be indicative of a functional gastrointestinal illness [64]. The physio-pathological function of microbiota in irritable bowel syndrome (IBS) is being supported by a growing body of

research, however many results' clinical significance is still up for debate [65]. Up to 20% of IBS cases, according to clinical research, are preceded by an intestinal infection that significantly modifies the host microbiota [66]. The precise mechanisms by which this alteration determines the persistency of IBS symptoms after the acute episode are not fully elucidated; a genetic susceptibility, an abnormal mucosal barrier integrity, variations in SCFA production, and an increase in mucosal entero-endocrine cells may contribute [67, 68]. A meta-analysis review showed that small intestinal bacterial overgrowth (SIBO) was present between 4% and up to 54% in IBS [69], suggesting that microbiota alterations may play a role in a subset of patients. However, the large differences between the studies, methodological problems, such as the lack of standardization, poor sensitivity and specificity of breath tests, as well as the questioned cut-off value of cultured duodenum/jejunum aspirates (> 105 CFU/mL), make the importance of SIBO in IBS unclear [70]. The importance of microbial changes in IBD is further supported by interventional studies that demonstrate the beneficial benefits of therapies targeted at the gut microbiota [71, 72]. In fact, a number of changes in the makeup of the microbiota have been reported; nevertheless, the variability of IBS and differences in methodology have led to inconsistent findings. However, new evidence suggests that dysbiosis occurs in a subgroup with IBS [73-75]. This subset exhibits alterations in the mucosa-associated microbiota, with a drop in Bifidobacterium and an increase in Bacteroides and Clostridium, and a loss in composition complexity.

3.6. The Function of Bifidobacteria Allergic Disease

Probiotic bifidobacteria have also been suggested as a means of preventing disorders other than the digestive tract, such allergies. Over the previous ten years, there has been a rise in the prevalence of food allergies, asthma, and atopic eczema. Numerous research have attempted to show how the gut microbiota affects allergy processes throughout the last ten years. It is thought that the relationship between microbes and the mucosal immune system may operate as a mediating factor for this effect. Accordingly, a number of investigations using in vivo research using animal models and human trials sought to show the advantageous effects of probiotics on the prevention and treatment of allergic illness [77]. Based on data from human trials and scientific research, the WAO released guidelines for the use of probiotics in the prevention of allergies. Probiotic use for eczema prevention may, nonetheless, be beneficial overall; however, further clinical trials are needed to expand the sample size and ensure the validity of the findings.

4. Conclusions

The term intestinal microbiota refers to the diverse range of bacteria that inhabit the human intestine. Human health is greatly impacted by this dynamic and intricate ecosystem of microorganisms. Disturbances in the makeup and functionality of the microbiota, or dysbiosis, have been linked to a variety of extra- and intestinal illnesses. Scientific interest in the species Bifidobacterium, which is present in the human gut microbiota, has been high. When intestinal microbiota dysbiosis occurs, there are frequently changes in the species composition or amount of intestinal bifidobacteria. In fact, variations in intestinal bifidobacteria have been linked to a number of illnesses, such as allergies, CRC, IBD, and IBS. This justifies the use of Bifidobacterium microorganisms as probiotics and explains why regulating the gut bifidobacteria population has frequently been seen as a target for dietary treatments. Depending on the strain and the ailment being studied, several strains have been evaluated as probiotics for various ailments, with varying outcomes. However, several strains of Bifidobacterium have demonstrated extremely encouraging outcomes, reducing symptoms of allergies, diarrhea, and irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD).

Conflicts of Interest

The authors declare no conflicts of interest.

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