Integrative Food, Nutrition and Metabolism

Review Article ISSN: 2056-8339

Why do we need *Lactobacilli*?

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Abstract

Probiotics are used as health adjuncts to provide a wide variety of health benefits. Probiotics mainly include *Lactobacilli* and *bifidobacteria*. Probiotics are beneficial bacteria that are traditionally used to treat various gastrointestinal diseases. Some studies in adults show a reduction of symptoms associated with irritable bowel syndrome. Newer areas of research include systemic immune responses (including atopic eczema) that accompany food–related allergies in children. *Lactobacilli* confer many positive health benefits on humans. Lactic acid bacteria help to improve digestion and absorption, can prevent, or treat diarrheal disease and constipation, can prevent diarrhoea induced by rotavirus, and normalize intestinal flora, acts as adjuvant for vaccines, has the ability to prevent allergic reactions, has the ability to prevent liver disease induced by alcohol intake and can prevent colon cancer, help to maintain stable total and LDL cholesterol over the year. *Lactobacilli* also helped to consistently maintain lower levels of total IgE and showed a significant decrease in gamma-glutamyl transferase (GGT). *Lactobacillus* has the potential to increase the gut IgA immune response and thereby to promote the gut immunological barrier. Thus, the increasing antibiotic resistance of pathogenic bacteria (particularly in hospitals) motivates current interest in probiotics, and the rise of consumers demand for natural substitutes of drugs. Thus, the objective of this review is to highlight the significance of probiotics like *Lactobacilli* to overall human health.

Definition of Probiotics

A professional panel appointed by the WHO and the Food and Agriculture Organization of the United Nations in 2001 defined Probiotics as 'live microorganisms which, when administered in adequate amounts, confer a health benefit on the host.' Lactic acid bacteria are sometimes termed probiotics and are used as health adjuncts to provide a wide variety of health benefits [1]. These bacteria mainly include *Lactobacilli* and *Bifidobacteria*.

Characteristics of *Lactobacilli* Species

Lactobacilli Species are aerotolerant, anaerobic, gram-positive bacilli, non-spore-forming- bacilli. *Lactobacilli* cells are straight and uniform with rounded ends, and they may form chains. Some may appear as coccobacilli.

Lactobacilli Species and Its Significance:

The intestinal microenvironment is composite. It contains typical microflora and immune cells associated with mucosal surfaces. The indigenous microflora of the digestive tract consists of autochthonous microorganisms, which mostly stay, in the host and the transient one. These microorganisms play a role in the development and maintenance of the activity of the immune system associated to the gut-associated-lymphoid tissue (GALT); that includes IgA, CD4, CD8 T cells and intraepithelial lymphocyte (IEL) activation. The gut flora can be modified by the ingestion of certain non-pathogenic microorganisms called "probiotics" [2]. A group of these bacteria is the lactic acid bacteria (LAB), which can influence the intestinal microenvironment and produce beneficial effects in the host. Dietary consumption of certain strains of lactic acid bacteria (LAB) which act as probiotics enhances immunity [3-6]. Solis et al. through their study indicated that lactic bacteria such as *Lactobacillus bulgaricus* used in food processing could induce a transient production of interferon in healthy subjects [3]. Therapy with *Lactobacillus GG* lead to a significant increase in nonspecific humoral response during the acute phase of the infection, as revealed by the number of IgG, IgA, and IgM Ig-secreting cell. Thus, indicating that *Lactobacillus* GG helps in the recovery from rotavirus diarrhoea by enhancing the local immune defense. This study also recognized specific IgA response to rotavirus, thus making it relevant in protection against reinfections [4]. Kishi et. al. performed a study to evaluate if the oral administration of *Lactobacillus brevis* subsp. coagulans in human subjects modifies immunological responses and whether live and heat-treated preparations produced a different response. It was observed that oral administration of live *Lactobacillus brevis* subsp. coagulans significantly increased interferon alpha production in a dose-dependent manner. *Lactobacillus brevis* subsp. coagulans intake was shown to be most beneficial in subjects with initially low levels of interferon alpha production. The study also indicated that the heat-treated *Lactobacillus brevis* subsp. coagulans did not elicit a response similar to that of the live bacteria [5]. Lactic acid bacteria found in food can exert beneficial effects (probiotic) by transiently colonizing the intestine. Factors that seem to be important for transforming the host's immune reactivity include survival of these Lactic acid bacteria during intestinal transit or adhesion to epithelium or both. Since *Lactobacillus acidophilus* strain La1 were shown to be adherent to enterocytes *in vitro,* Schiffrin et. al. postulated that contact with immune cells might occur *in vivo.* In this study, volunteers were given a fermented product containing *Lactobacillus acidophilus* and Lymphocyte subsets and leukocyte phagocytic activity in blood were studied. Lymphocyte subsets did not indicate any modifications. However, there was an enhancement of the phagocytosis of *Escherichia*

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Key words: *Lactobacilli; probiotics; significance*

Received: February 01, 2022; **Accepted:** February 11, 2022; **Published:** February 15, 2022

coli ssp. Bacterial adhesion to enterocytes and/ or fecal colonization, have seen to be valuable selection criteria for immunomodulation. Thus, indicating that the ingestion of specific lactic acid bacteria strains can enhance the anti-infective mechanisms of defense [6].

This suggests that probiotics may be an effective means of disease prevention.

At the beginning of the present century, the Russian scientist Metchnikoff proposed that the consumption of fermented milk was useful in maintaining good health [1]. Since that time, the works of numerous researchers have confirmed the nutritional advantages of fermented milk as a source of calcium, as well as the effects of its various ingredients. These studies have also indicated the probiotic action of lactic acid bacteria to improve digestion and absorption, reduce diarrhoea and constipation, and normalize intestinal flora [7,8]. Some species of lactic acid bacteria have several potential nutritional or health benefits. Some of these benefits include control of intestinal infections, enhanced nutritional value of foodstuff, better digestion of lactose, control of serum cholesterol levels and control of some types of cancer. As indicated by Gilliland et al. some of these potential benefits may have been due to the growth and action of the bacteria during the manufacturing process of cultured foods. It is also suggested that the ingestion of foods containing lactic acid bacteria, could give rise to positive health benefits due to the development and action of certain Lactic Acid bacteria in the intestinal tract [7]. In another review, article B. R. Goldin has indicated that *Lactobacillus GG* can serve as an adjuvant for vaccines, can prevent or treat diarrheal disease, can prevent diarrhea induced by rotavirus, has the ability to prevent allergic reactions due to milk, has the ability to prevent liver disease induced by alcohol intake and can prevent colon cancer [8].

Fermented milk has also been reported to provide other beneficial effects such as the lowering of serum cholesterol levels [9]. Although there are controversies about the potential beneficial effects of milk and fermented milk products on lipoprotein levels. Agerbaek et. al. in their study showed that daily intake of moderate amounts (200 ml/ day) of fermented milk product, significantly reduced total cholesterol after 6 weeks. Since the HDL-cholesterol and triglyceride remained unchanged, the drop in total cholesterol was credited to a fall in LDL-cholesterol by 10% [9].

Studies indicate that fermented milk and the lactic acid bacteria in it act on the immune mechanism *in vivo* and increase the body's resistance to infection, cancer and allergy [10]. The prolonged intake of yogurt has been linked with 'better health'. Trapp CL et al. have previously indicated that normal adults consuming 450 g of yogurt daily for 4 months showed an increase in the production of gamma-interferon by five-fold [10]. In this study conducted by Trapp CL et al. both the senior adults (age 55-70) and the young adults (age 20-40) showed a decrease in allergic symptoms due to the consumption of yogurt. This study also showed that the seniors who did not consume yogurt had an increase in both total and LDL cholesterol. In case of the seniors who consumed yogurt, both total and LDL cholesterol remained stable over the year. A significant decrease in gamma-glutamyl transferase (GGT) was also observed in seniors consuming yogurt. In addition, seniors consuming yogurt consistently had lower levels of total IgE throughout the year [10].

The intestine is a significant site for host-microbe interactions since it is heavily colonized with bacteria. Most research mainly focuses on intestinal pathogens that cause localized and systemic infections, however most intestinal microflora are not harmful, but, instead, are beneficial to the host [11]. The list of helpful functions attributed to intestinal bacteria continues to grow. Some of the advantages of beneficial bacteria include nutrient processing [12], regulation of intestinal angiogenesis [13], and development of gut-associated lymphoid tissues (GALT) [14], induction of oral tolerance [15], mucosal immunity [16], and diversification of the preimmune Ab repertoire [17]. Some studies also indicate that the lack of proper interactions between bacteria and the human host causes allergies and Crohn's disease in developed countries is [18,19].

Treatment with careless antibiotic decreases or abolishes the critical intestinal probiotic flora, prompts local mucosal starvation, and makes the patients susceptible to opportunistic infections and microbial intestinal translocation. Studies have been conducted on more than 1000 isolates of human-specific lactobacilli. Some strains, especially those of *plantarum* type, have confirmed effective in colonizing the colonic mucosa, defeating the potentially pathogenic flora, and may have other probiotic effects as well. A very new enteral formula has been designed based on probiotic bacteria and fiber and aimed at colonizing the intestinal mucosa with a local probiotic effect and fermentation of fiber [20]. The intestinal microflora helps in antigenic exclusion [20]. The resident microflora prevents adherence of antigens to the intestinal mucosa by different mechanisms, such as by increasing production of specific antibody secreting cells and mucus, by competing for nutrients and adhesion sites and by producing antimicrobial agents [20]. Morishita et al. in their study mono-or decontaminated germ-free chickens were with various species of facultative anaerobes and obligate anaerobes that were isolated from chickens, humans, pigs, and fermentation products, and their sera were studied for agglutinins against these organisms. Based on this study, little or no detectable agglutinins were observed against *Lactobacillus easel* and *Lactobacillus plantarum* from fermentation products [21,22].

Various authors have investigated the appearance of serum immunoglobulins in axenic animals after inoculation of their digestive tracts with different bacterial strains [21,22]. Balish et. al. through their study indicated that when *L. acidophilus* was administered to germfree rats, *L. acidophilus* multiplied readily in the gastrointestinal tract and caused only minimal alterations in the serum proteins [21]. The inability of *L. acidophilus* to induce significant alterations in serum proteins partly explains why bacteria such as *L. acidophilus* are able to persist in very large numbers in the intestinal tract. An interesting observation from this study was also that *L. acidophilus* was the only microorganism found viable in the internal organs 4 weeks after oral challenge. The survival of *L. acidophilus* in tissues was another sign of this tolerance [21].

Malin *et. al.* in their study investigated the effect of oral bacteriotherapy with human *Lactobacillus casei* strain GG (10(10) colony-forming units twice daily for 10 days) in Crohn's disease and in juvenile chronic arthritis. Both these diseases are chronic inflammatory diseases associated with impaired mucosal barrier function. During oral bacteriotherapy, the gut immune response was indirectly assessed in 14 children with Crohn's disease, 9 children with juvenile chronic arthritis, and in 7 controls. The results indicated that the immunostimulatory effect of *Lactobacillus GG* was specific for Crohn's disease, irrespective of its activity: the mean number of specific antibody secreting cells in the IgA class to beta-lactoglobulin and to casein increased significantly. The results obtained by Malin *et. al.* indicate that orally administered *Lactobacillus* GG has the potential to increase the gut IgA immune response and thereby to promote the gut immunological barrier. Consequently, *Lactobacillus* GG could provide an adjunct nutritional therapy for Crohn's disease [23].

Oral administration of *Lactobacillus* sp. enhanced the antibody production to influenza vaccine applied subcutaneously [24] Pouwels *et. al.* has confirmed that different *Lactobacillus* species show huge variations in adjuvanticity. It was also observed that *L. casei* and *L. plantarum* were more effective than other *Lactobacillus* species to evoke a humoral response or a delayed-type hypersensitivity (DTH) reaction. These studies by Pouwels et. al. also suggest that the generation of an effective vaccine carrier based on genetically engineered *Lactobacillus* is feasible since high levels of antigen can be produced with vectors containing efficient transcription and translation regulatory elements. Pouwels *et. al.* has indicated that a low but significant immune response is obtained after subcutaneous priming followed by oral immunization with *Lactobacillus* that intracellularly synthesize the HA-beta glucuronidase fusion protein [24].

Thus, Pouwels et. al. through their study have shown that *Lactobacilli* are not only functional as antigen carriers, but in addition, they can enhance immune responses based on their intrinsic adjuvant activity. This long-lasting effect of activation is of great importance for the application of *Lactobacilli* in vaccine development. Oral immunization may be rendered more effective after preactivation with orally-administered 'adjuvant-*Lactobacillus*. This makes *Lactobacillus* a unique adjuvant since most adjuvants presently available are effective only when applied systemically (parenterally) [24]. In conclusion, data from this study suggests that the generation of *Lactobacillus*-based live vectors as vaccines, instead of pathogen-derived live vaccines, seems now within reach for model antigens [24].

Oral administration of *Lactobacillus casei* enhanced anti-salmonella IgA level and inhibited the growth of Salmonella [25]. Majamaa *et. al.* through their study compared different lactic acid bacteria for their effect on the immune response to rotavirus in children with acute rotavirus gastroenteritis.

Lactobacillus casei therapy was associated with an enhancement of IgA specific antibody-secreting cells (sASC) to rotavirus and serum IgA antibody level at convalescent stage. Thus, this study indicated that certain strains of lactic acid bacteria, particularly *Lactobacillus casei*, promote serum and intestinal immune responses to rotavirus, and thus may be important in establishing immunity against rotavirus reinfections [26].

Conclusion

Lactobacilli are a type of beneficial bacteria called Probiotics, which confer many positive health benefits on humans. Dietary consumption of certain strains of lactic acid bacteria (LAB) which act as probiotics enhances immunity. Lactic acid bacteria help to improve digestion and absorption, can prevent or treat diarrheal disease and constipation, can prevent diarrhoea induced by rotavirus, and normalize intestinal flora, acts as adjuvant for vaccines, has the ability to prevent allergic reactions due to milk, has the ability to prevent liver disease induced by alcohol intake and can prevent colon cancer. Consumption of yogurt helped to maintain stable total and LDL cholesterol over the year. Seniors consuming yogurt consistently had lower levels of total IgE and showed a significant decrease in gamma-glutamyl transferase (GGT). *Lactobacillus* GG has the potential to increase the gut IgA immune response and thereby to promote the gut immunological barrier. *Lactobacilli* act as antigen carriers and can enhance immune responses based on their intrinsic adjuvant activity. *Lactobacillus casei*, is important in establishing immunity against rotavirus reinfections.

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