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Lactic acid bacteria and immune system regulation and impact on related diseases

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Abstract. Lactobacillus is a common food-grade microorganism with good bioactivity, which has been maturely used in the food industry. The significant role of Lactobacilli in immunomodulation has gradually become a research hotspot, and their significant impact on immune diseases through the modulation of the immune system gives them great potential to become materials for the treatment of immune diseases. This paper describes the interaction between Lactobacilli and the immune system, and the effect of immunomodulation of Lactobacilli on immune diseases, with a view to providing a theoretical basis for helping Lactobacilli to become a therapeutic agent for immune diseases.

Keywords: lactic acid bacteria, immune system regulation, immune diseases, health

1. Introduction

Lactic acid bacteria is a general term for a group of bacteria that metabolise carbohydrates to produce large amounts of lactic acid. Their cellular morphology is diverse, lactic acid bacteria are usually Gram-positive, have complex nutritional requirements, mostly do not form spores, are contact enzyme-negative, cytochrome-positive, and are anaerobic or partially anaerobic. They usually include Lactococcus spp, Lactobacillus spp, Bifidobacterium spp and so on. Numerous studies have shown that lactobacilli have a variety of beneficial effects on the human body, such as regulating intestinal flora [1], antitumour effects [2], immunomodulatory effects [3], etc. Since immune diseases, allergic diseases, infectious diseases or cancer can be prevented and cured through the regulation of the immune system [4], the regulation of the immune system by lactobacilli has become a hot research object in the field in recent years. In this paper, we review the interaction between lactic acid bacteria

and immune system and the effect of lactic acid bacteria on related immune diseases, in order to provide a theoretical basis for the application of lactic acid bacteria in immune diseases.

2. Interaction between lactic acid bacteria and human immune system

2.1. Classification and common species of lactic acid bacteria

Lactobacillus is a recognised food-grade microorganism. As a microorganism with a long history, Lactobacilli are widely distributed in nature with a rich diversity of species, and about 80 genera and about 700 species of Lactobacilli have been identified [5].Bacteriologically, they can be classified taxonomically into the following genera: Aerococcus, Heterococcus, Saccharomyces, Enterococcus, Lactobacillus, Lactococcus, Coccidioides, Streptococcus, Tetracoccus, Staphylococcus, and Bifidobacterium [6]. Among these lactic acid bacteria that have been identified, a large portion of them is an integral part of the human intestinal tract, and many experts at home and abroad have proved that lactic acid bacteria in the intestinal tract are inextricably linked to human health.

Morphologically, they are mainly divided into two categories: spherical and rod-shaped , common spherical lactic acid bacteria are mainly Streptococcus spp., Streptococcus spp. and Streptococcus spp. and Streptococcus spp. and Lactobacillus spp. are common rod-shaped lactic acid bacteria [7]. Some of the genera of Lactobacillus are often used in the processing of dairy products and pickled vegetables [8].

In terms of biochemical mechanisms, they can be classified into homo-lactic fermentation and hetero-lactic fermentation [9]. Lactic acid bacteria can break down sugars into lactic acid during fermentation, and if the fermentation product is only lactic acid it is called orthotropic lactic acid fermentation, such as Streptococcus lactis, Lactobacillus casei and Streptococcus lactis. If there are other products (acetic acid, ethanol, CO2, H2) in addition to lactic acid, it is called heterogeneous lactic acid fermentation, such as Lactobacillus, Streptococcus lactis[10].

2.2. Regulatory effect of lactobacilli on human immune system

Immunomodulation is usually reflected in the regulation of specific immunity and non-specific immunity, while specific immunity is generally divided into humoral immunity and cellular immunity.

Numerous studies have shown that lactobacilli promote specific immunity by activating immune cells and increasing antibody production, which in turn improves human immunity. In terms of increasing the production of antibodies in the body, some scholars have found that Bifidobacterium bifidum can stimulate the production of sIgA (antibody) in infants when studying the regulation of the infant's immune system, and it has been proved that oral administration of Bifidobacterium bifidum has a significant effect on the immune function of infants whose body weights are obviously lower than normal, and it can significantly increase the level of IgA (antibody) in the body of the infants [11]. It has also been reported that the administration of Bifidobacterium bifidum to infants for a period of time resulted in a significant increase in sIgA levels in the infants, which favoured the enhancement of immune cell activity and immunoglobulins in the infants [12]. It has also been shown that when Lactobacillus acidophilus was allowed to be administered for a period of time to an animal model of mice infected with human rotavirus, the level of sIgA expression in the intestinal tract of the animal model was substantially increased. In addition, regarding the study on the stimulation of

immune cells in the body by lactobacilli, some scholars colonised Bifidobacterium lactis strain BB-12 in single association with a sterile animal model, inducing the transcription of NF-k into the active subunit of ReIA as well as the activation of sex-protein kinase P38 in the intestinal epithelial cells of the animal model, and increasing the gene expression of IL-6, which suggests that this strain stimulates the signaling to enhance the pro-inflammatory factors[13]. Miettinen [14] and others found that Lactobacillus rhamnosus GG was also able to induce the production of NF-KB in human macrophages to regulate cellular immunity and promote human immunity.

In addition to promoting specific immune regulation, Lactobacillus has a role in regulating non-specific regulation of the body. Currently, it is found that Lactobacillus bulgaricus (belonging to the Lactobacillus family) and Lactobacillus casei (belonging to the Lactobacillus family) have the function of activating macrophages and stimulating the body to produce immune response, and at the same time, they can enhance the activity of T-cells, macrophages, as well as NK-cells, regulate the immune system of the body, and improve the immune vitality of the body [15]. Some studies have shown that increasing the dose of Lactobacillus rhamnosus (belonging to the Lactobacillus family) Lcr35 can stimulate the secretion of anti-inflammatory factors, such as TNF-α, IL-1β, IL-12, and so on, and can balance the inflammatory response and maintain the immune microenvironmental homeostasis by stimulating the production of small quantities of anti-inflammatory cytokines, such as IL-10 [16]. In another study on Lactobacillus plantarum (belonging to the Lactobacillus family) NR74, it was found that it could also inhibit the production of some pro-inflammatory factors to achieve immunomodulation, in a similar way to Lactobacillus rhamnosus in regulating the immune system [17].

In summary, the regulation of specific immunity by Lactobacillus is mainly divided into the regulation of humoral immunity and cellular immunity, through the activation of immune cells, increase the production of antibodies in the body, increase the immune response and other ways to enhance the expression of specific immunity in the body, which significantly enhances the immunity of the body. And lactobacilli modulate non-specific immunity mainly by inhibiting the production of pro-inflammatory factors and reducing the inflammatory response. In addition, lactobacilli also play an important role in the construction and repair of the body's immune system during the development process, and it produces an immune response to specific antibodies in the intestinal tract and other regions, so lactobacilli play an important beneficial effect on the host by regulating the immune system of the body in many ways and from many angles.

3. Application of Lactobacilli to Immune System Diseases

3.1. Autoimmune diseases

Autoimmune diseases (AIDs) usually refers to, in some specific circumstances, the body's own immune tolerance is damaged, the body's immune system to produce a strong, continuous immune response to their own cells, resulting in cellular and tissue damage and clinical symptoms [18]. In recent years, some scholars have revised the criteria on AIDs, according to the criteria in this example part of the current more popular AIDs are mainly acquired immunodeficiency syndrome (HIV), inflammatory bowel disease (IBD) and so on [19].

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Inflammatory bowel disease is now a more prevalent contemporary health problem. Numerous studies have shown that the development of IBD is related to the disturbance of its intestinal flora, whereas Lactobacilli can improve the intestinal flora and enhance the capacity of the intestinal immune system in different ways, which can help to complement the treatment of IBD.Paturi [20] et al. have demonstrated that two strains of Lactobacillus acidophilus LAFTI L10 and Lactobacillus paracaseus LAFTI L26 are able to enhance the immune response in the whole body, especially in the intestinal tract response with the secretion of anti-inflammatory factors IL-10 and IFNγ. Similarly, another study conducted a controlled experiment in an animal model and found that Lactobacillus paracasei ST11 inhibited the expression of IL-1β and other expressions in the intestinal mucosa, reducing the probability of developing colitis in an animal model, which is conducive to the improvement of the anti-inflammatory capacity of the intestinal immune system [21]. In addition, there are also scholars in the study on the effect of Lactobacillus Royce strain (belonging to the Lactobacillus family) DSM17938 on necrotising colitis in preterm infants with low birth weights found that the probability of suffering from necrotising colitis was significantly reduced in the experimental this that received the intervention of this bacterium, which suggests that this bacterium is beneficial to preterm infants with abnormal birth weights in lowering the chances of developing inflammation of the intestinal tract [22].

In summary, this chapter focuses on the analysis of the regulatory role of lactobacilli for inflammatory bowel disease, combined with domestic and international literature found that lactobacilli are densely distributed in the intestinal system of the human body, and have a significant role in the regulation of the immune system in this region, a number of animal models and specific population experiments have been confirmed that lactobacilli are mainly through the enhancement of the intestinal immune system response, the promotion of anti-inflammatory factor secretion and inhibition of pro-inflammatory factor secretion and other Lactobacilli maintain the homeostasis of the intestinal immune environment and reduce the production of inflammatory diseases. In addition, the inflammation produced by other prevalent autoimmune diseases can also be alleviated by the role of lactobacilli in regulating the immune system. Therefore, maintaining the number of lactic acid bacteria in the body is an important way to keep the body immune.

3.2. Allergic diseases

Allergic diseases are usually understood as conditions caused by an over-response of the body's immune system, with excessive immune function leading to damage to the body's cells and tissues. According to the available data, the main cause of allergic diseases is the decrease in the number of regulatory T-cells due to the limited number of flora, which subsequently causes an imbalance between the Th1 and Th2 immune responses, thus contributing to the development of allergic diseases [23].

A number of studies have discussed the preventive and therapeutic role of lactobacilli in allergic diseases.Isolauri [24] et al. found that infants with probable atopic eczema who were fed hydrolysed whey containing lactobacilli suffered from atopic dermatitis to a significantly lesser extent than those who were not fed hydrolysed whey containing lactobacilli, suggesting that lactobacilli have a significant preventive and curative effect. The anti-allergic mechanism of lactobacilli has also been demonstrated in animal models, Andreas[25] and other scholars evaluated the potential of Lactococcus

lactis and Lactobacillus plantarum against allergic diseases in a mouse model and found that the two Lactobacillus strains induced high levels of IL-12 and IFN-γ in splenocyte cell cultures of naïve mice, and concluded that these Lactobacillus strains in conjunction with allergens may be a good candidate for type I allergy for the potential development of mucosal vaccination. In addition, in the prevention of food allergy, lactic acid bacteria also play a role in alleviating the disease that produces food allergy.Guo [26] et al. in their study evaluated the in vivo allergenicity of fermented milk beverage (FMB) prepared from compounds of four Lactobacillus strains with the ability to hydrolyse allergenic milk proteins, confirming that FMB modulates the T helper cells in vivo in a mouse model, as compared to skimmed milk beverage (SM) Th1/Th2 and Th17/T regulatory cell immune homeostasis, as well as enriched the abundance of the common immunomodulatory symbiotic bacteria Trichoderma sp. within their gut microbiota, suggesting that the milk beverage treated with Lactobacillus is a hypoallergenic beverage that also contributes to the immunity of the body's intestinal system.

In summary, the anti-allergic mechanism of lactobacilli is mainly to regulate the balance of Th1 and Th2 immune responses in the body and hydrolyse allergenic precursors in the target, and some studies have been conducted on their role as intestinal mucosa in the regulation of allergic diseases. However, the anti-allergic mechanism of lactic acid bacteria is not yet very precise, and the research focuses on some specific lactic acid bacteria, but it can be assumed that most of the lactic acid bacteria have some anti-allergic effect, which is waiting to be investigated.

3.3. Other immune-related diseases

In addition to modulating immune disorders, lactobacilli are important in maintaining the balance of the body's intestinal flora, and intake of lactobacilli helps to improve the intestinal microenvironment thereby inhibiting the growth of harmful microorganisms. Immunomodulation by lactobacilli to inhibit pathogenic bacterial infections has been reported for a long time. Lactobacillus casei can inhibit the adhesion of Escherichia coli to achieve the purpose of prevention and treatment of intestinal diseases [27], bifidobacteria and lactobacilli produce acid in the body to reduce the pH value in the body to inhibit the growth of abnormal bacteria, and promote the secretion of secretory sIgA to inhibit the damage caused by pathogenic bacteria to the host [28].Fukuda [29] and other scholars found that Bifidobacterium longum, which is a member of the Lactobacillus family, has an important effect on the immunomodulation of colonic bacteria. JCM1275T has anti-apoptotic and anti-inflammatory effects on colonic epithelial cells, which can help the body to resist pathogenic E.coli O157: H7, while the large amount of lactic acid it produces also helps to impede the entry of Shiga toxin from this strain of pathogenic E.coli into the intestinal bloodstream. In addition to inhibiting intestinal pathogenic bacteria to maintain microecological balance, lactobacilli also play an important role in the microecological balance of the female vagina. Lactobacilli in the vagina of healthy women act as the dominant strain to maintain the environmental pH by producing lactic acid, and produce bacteriocins and bioactive substances to directly or indirectly sterilise the bacteria in order to maintain the homeostasis of the vaginal immune environment [30].

It has also been reported that Lactobacillus has certain anti-tumour effects, Bifidobacterium has the role of producing lactic acid to promote apoptosis of spoilage cells, so Bifidobacterium promotes cellular immunity with anti-cancer effects, and oral intake of Bifidobacterium can help to curb the development of tumours [31]. There are other examples such as Lactobacillus bulgaricus has direct

anti-tumour effects; Lactobacillus casei can increase anti-LDL antibodies and lymphocytes, promoting host immunomodulation and preventing tumours; Streptococcus thermophilus produces bacteriocins, lactic acid and other substances that have anti-tumour activity [32].

4. Conclusions and discussions

Currently, with the deepening of immunological studies on lactic acid bacteria and the clinical pathology of lactic acid bacteria, more and more lactic acid bacteria are being used not only in the food industry, but also in healthcare applications are gradually expanding. Some of the more common lactic acid bacteria include Lactobacillus plantarum, Lactobacillus casei, Lactobacillus paracasei, Bifidobacterium bifidum, and Lactobacillus rhamnosus, etc. In addition to their single effect in vitro, these bacteria can also be combined with prebiotics to provide health benefits for the human body. At the same time, some of the lactic acid bacteria have also been proved to regulate the immune system and thus have a significant impact on immune diseases, generally through the activation of specific immune cells, promote the production of special antibodies, increase the expression of immune product factors, improve the immune system response to enhance the functional activity of the immune system, a large number of studies have proved that lactic acid bacteria modulate the immune system has been in the auto-immune diseases such as IBD, immunological diseases and other pathogenic bacterial infectious diseases. From the analysis of the existing data, most of the lactic acid bacteria have a regulatory effect on the immune system, waiting for further research to elucidate, but we also need to pay attention to the fact that there are great differences in the regulation of the immune system by different lactic acid bacteria, so the screening to obtain a good functional characteristics of lactic acid bacteria is of great practical significance, and more in-depth study of the mechanism of the immune regulatory effect of lactic acid bacteria is needed, not only in the development of better functional food to regulate immunity, but also to develop a better At the same time, more in-depth research is needed to study the immunomodulatory mechanism of lactic acid bacteria, not only to develop better functional food to regulate immunity, but also to apply the ability of lactic acid bacteria to regulate the immune system to clinical medicine, so as to help lactic acid bacteria become an indispensable material for the treatment of human immunological diseases.

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