



# The Benefits and Applications of *Lactobacillus plantarum* in Food and Health: A Narrative Review

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(Received 10 Dec 2023; accepted 18 Mar 2024)

## Abstract

*Lactobacillus plantarum* is a type of gram-positive lactic acid bacteria. This bacterium is considered a safe probiotic and, many applications and benefits including prolonging food shelf-life, enhancing antioxidant activity, improving food flavor characteristics and antimicrobial activities in the food industry, and application as a potential starter for dairy products have been attributed to it. Various studies have also emphasized its health-giving properties. As a result, the features and wide application of this bacterium, as well as the safety of *L. plantarum* and its strains, have made it a popular probiotic in the food and medical industries. Thus, in the present study keywords including *L. plantarum* and *Lactiplantibacillus plantarum* along with application, benefits, food, health, anti-oxidant, anti-diabetic, anti-obesity, anti-inflammatory, antiviral, and anti-depression were searched in databases of PubMed, Scopus, Web of Science, Science direct and Google Scholar with no time restriction. Then, important features, benefits, and uses of *L. plantarum* were categorized and discussed. The ability of *L. plantarum* on the food such as prolonging food shelf-life, enhancing antioxidant activity, improving food flavor characteristics and antimicrobial activities in the food industry, and as a potential starter for dairy products is effective. In addition, several studies have emphasized of *L. plantarum* health-giving properties.

**Keywords:** *Lactobacillus plantarum*; Benefits; Application; Health; Human; Food

## Introduction

A probiotic bacterium should be safe for the consumer in addition to having basic and beneficial health properties. A particular strain that is of interest due to its many applications is *Lactobacillus plantarum* (1). *L. plantarum* belongs to the lactic acid bacteria, which are a broad group of Gram-positive bacteria living in several ecological spectrums, including meats, traditional foods, fermented foods, plants, and the digestive tract of mammals (2-3). It is useful for maintaining the

integrity of the intestinal wall (4), supporting the immune system (5), and interacting with genes (6). *L. plantarum* can colonize different environments by facilitating metabolic flexibility through maintaining diverse functional genomes (7-9). Some of the distinct proven health benefits conferred by consuming food products containing *L. plantarum* include the reduction of gastrointestinal infection, a decrease in the risk of inflammatory bowel disease, and stimulating effects on the im-



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immune system. Additionally, this bacterium can prevent the growth of food pathogens and enhances product shelf life in bio-processed food through its natural inhibitory ability (10-12). Furthermore, this strain is capable of further developing nutritional quality and flavor characteristics as well as reducing undesirable compounds, enhancing antimicrobial and antioxidant activities, and extending food shelf life (13-14).

In summary, *L. plantarum* is a lactic acid-producing bacteria that is also able to produce antibacterial bioactive compounds and exopolysaccharides (EPS), exhibiting antagonistic potential against enteric foodborne pathogens activities (10). A variety of immunomodulating properties such as anticancer, anti-allergic, antiviral activities and etc. have also been attributed to *L. plantarum* which is known as a safe probiotic bacterium (7). However, unlike various properties, few reports have focused on discussing all aspects of the benefits and applications of *L. plantarum* in different fields and, comprehensive review articles on explaining positive effects of *L. plantarum* in food, industry and health are limited.

Therefore, the present study discusses benefits and applications of *L. plantarum* in different fields with emphasis on therapeutic properties and health applications.

### Benefits of *L. plantarum*

#### Antioxidant properties

Several studies have linked reactive oxygen species (ROS) to cell damage in the human body and to chronic diseases, including cancer. *L. plantarum* strains have antioxidant properties and with their residence in the intestines play an important role in protecting against free radicals (12). For example, *L. plantarum* NJAU-01 showed total antioxidant capacity (T-AOC) and antioxidant enzyme

activity of superoxide dismutase (SOD), glutathione peroxidase (GSH-Px), and catalase (CAT) at  $10^9$  CFU/mL. Also, the potential of *L. plantarum* NJAU-01 to reduce oxidative stress by increasing oxidation-resistance enzymes and inhibiting lipid oxidation has been proven (11, 13).

#### EPS production

EPS is one of the crucial bioactive compounds produced by *L. plantarum*. *L. plantarum* produces exopolysaccharides consisting of galactose, glucose, and mannose (14). They are secreted extracellularly and have antibacterial, anti-biofilm, antioxidant, anti-tumor, and immune-stimulating activities (Fig. 1). Different strains of *L. plantarum* can produce heteropolysaccharides, homopolysaccharides, as well as exopolysaccharides resistant to harsh conditions such as acid and bile (15). For example, the exopolysaccharides of *L. plantarum* strains include *L. plantarum* YW32 EPS composed of different sugar monomers such as mannose, galactose, fructose, and glucose, while the exopolysaccharide of *L. plantarum* NTU 102 contains fructose, galactose, arabinose, glucose, mannose, and different polarity of maltose. Three monomers, mannose, glucose, and galactose, have been found in EPS generated by *L. plantarum* KF5 (11). The constant component observed in the exopolysaccharide of *L. plantarum* NTMI05 and *L. plantarum* NTMI20 is galactose. Approximately 90-96% of the composition of EPS produced by *L. plantarum* is carbohydrates. Although, the presence of other components in the composition of EPS such as sulfate groups, proteins, nucleic acids, and uronic acid is also possible, even at low levels (15). Several applications of EPS are demonstrated in Fig. 1.

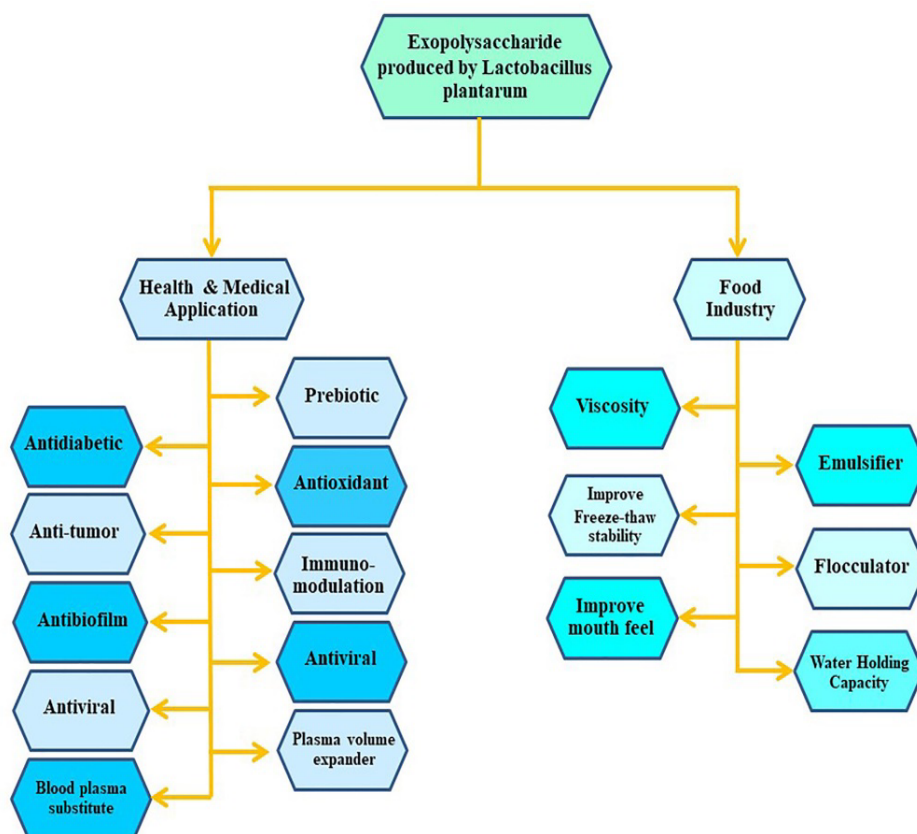


Fig. 1: Summary of the functions of *L. plantarum* exopolysaccharides (15, 16)

### Bacteriocin production

Bacteriocins produced by *L. plantarum* are known as plantaricin. This group of antibacterial peptides does not indicate toxicity against eukaryotic cells while, has a wide range of antimicrobial activity against many pathogenic bacteria. Plantaricins strongly control Gram-positive, Gram-negative and fungal cells by connecting to the membrane lipid layers. They are more effective on Gram-positive bacteria such as *Staphylococcus aureus*, *Bacillus cereus* and *Listeria monocytogenes*, but they also have an effect on Gram-negative bacteria such as *Pseudomonas* and *Escherichia coli* species. The use of the bacteriocins generated by *L. plantarum* in food products contributes to the organoleptic properties of the products and plays a main role in the natural biological preservation (17).

### Applications of *L. plantarum*

#### Food applications of *L. plantarum*

The consumption of probiotic products such as fermented drinks, and probiotic cheese and yogurts has increased in recent years. The most common probiotic used in the production of probiotic products is the bacterium *L. plantarum* (18-19).

*L. plantarum* is easily cultured and grows well, and because it is a safe probiotic it is of great interest in the food industry (10). *L. plantarum* is usually found in the digestive system and fermented foods and is commonly used in the food industry as a starter, bio-preservative, and producer of useful metabolites (9). It is used in the health sector due to its anti-cancer, antioxidant, antimicrobial and anti-inflammatory properties. The bacterium's anti-proliferative, anti-diabetic, and anti-obesity properties are widely applied in the field of medicine (1, 11). Various applications of *L. plantarum* are given in Fig. 2.

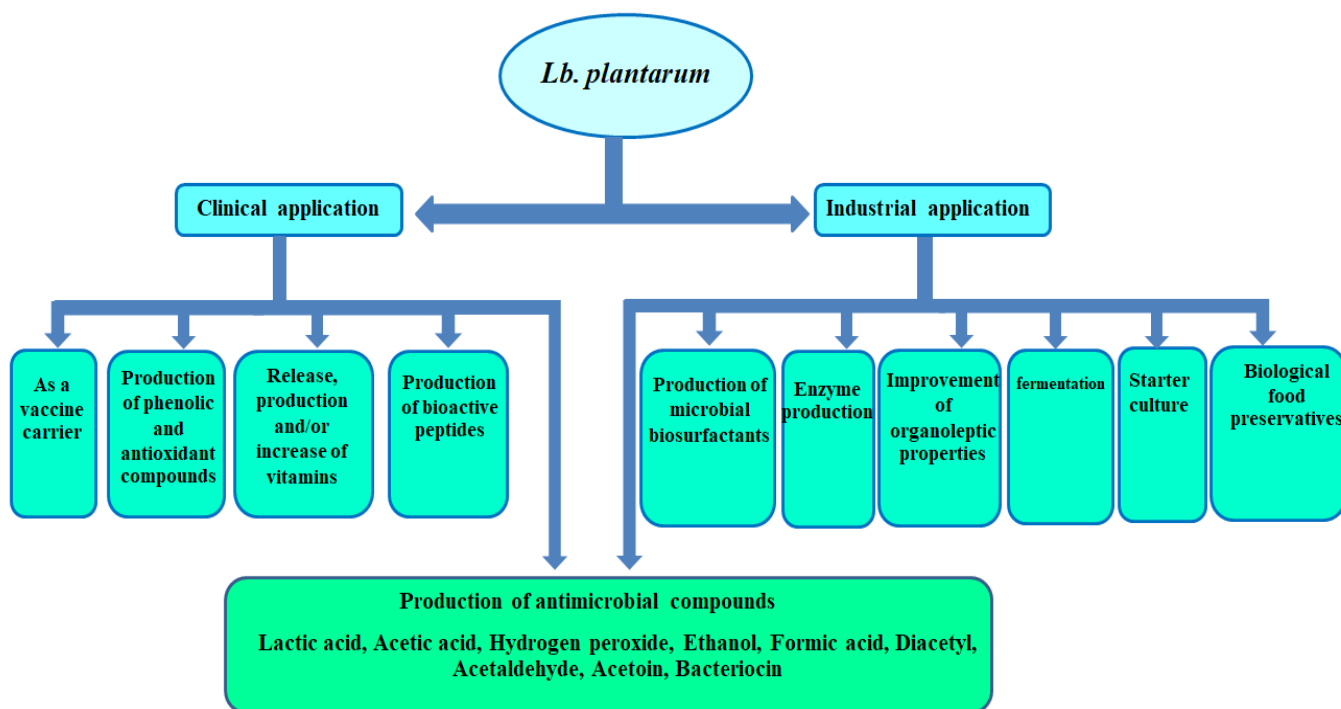


Fig. 2: Summary of *L. plantarum* applications (15)

### Industrial applications of *L. plantarum*

Industrial applications of *L. plantarum* include the extensive production of different enzymes, i.e.,  $\alpha$ -amylase (hydrolysis of starch), microbial esterase (production of a wide selection of phenolic alcohols, short chain fatty acids), microbial lipases (triacylglycerol acylhydrolases) (food processing, organic synthesis, formulation detergents, and oil production),  $\alpha$ -glucosidase (sugar hydrolysis),  $\beta$ -glucosidase (hydrolysis of feryl-alkyl-glucosides, such as diglucosides and oligoglucosides), Phosphoketolase-2 (energy metabolism), enolase (glycolysis, formation of phosphoenol pyruvate from 2-phosphoglycerate), lactate dehydrogenase (reduction of pyruvate to lactate, fermentation of hemolactate), improvement of aroma, taste, and texture in fermented foods/products (by the production of diacetyl organic acid and flavor (LA, acetic acid), production of bio-surfactants (BSs), production of bio-preservative compounds

(to help preserve food products, fermentation), and acting as a starter culture and a food bio-preservative (9, 11, 20) (Fig. 2). In addition, *L. plantarum* has greatly contributed to medicine, without side effects, through various applications in the pharmaceutical industry, including the production of bioactive peptides, i.e., antimicrobial cyclic dipeptides (CDPs), the release, production, and/or the enhancement of vitamins (folate, riboflavin, and vitamin B12) (1). The industrial uses of some *L. plantarum* strains are given in Table 1.

### Health applications of *L. plantarum*

Consumption of *L. plantarum* strains ameliorate some diseases especially acute and chronic infections, inflammatory syndrome, cardiovascular diseases, metabolic disease, as well as cancer (33). Important benefits and applications of *L. plantarum* in health and diseases are shown in Table 2.

**Table 1:** The potential industrial applications of some *L. plantarum* strains

| <i>Applications</i>                    | <i>Species/Strain</i>  | <i>Example products</i>   | <i>References</i> |
|--|--|---|-------------------|
| Production of microbial biosurfactants | <i>L. plantarum</i> ATCC8014                                 | The biosurfactant was characterized to be a mixture of carbohydrate, protein and lipid known as glycolipoprotein.                 | (21)              |
|  | <i>L. plantarum</i> 60FHE                                    | Mixture of glycoproteins  | (22)              |
|  | <i>L. plantarum</i> (PTCC1896)                               | Microbial biosurfactants (BSs)  | (1)               |
| Enzyme production                      | <i>L. plantarum</i> MGL-8                                    | Glycolipoprotein (BSF)  | (8)               |
|  | <i>L. plantarum</i> FNCC 260 and FNCC 343                    | Aminobutyric Acid (GABA)  | (8)               |
|  | <i>L. plantarum</i> DM5                                      | Glucansucrase/ viscosifier and stabilizer   | (23)              |
|  | <i>L. plantarum</i> MTCC1407                                 | $\alpha$ -Amylase (or 1,4- $\alpha$ -D-glucan glucanohydrolase)   | (1)               |
|  | <i>L. plantarum</i> (AMZ5)                                   |   |                   |
|  | <i>L. plantarum</i> S21                                      |   |                   |
|  | <i>L. plantarum</i> WCFS1                                    | Esterase  |                   |
|  | <i>L. plantarum</i> MTCC4451                                 | Lipase  |                   |
|  | <i>L. plantarum</i> MF32                                     |   |                   |
|  | <i>L. plantarum</i> LL441                                    | $\alpha$ -Glucosidase   |                   |
|  | <i>L. plantarum</i> (LP1, LP2, LP3, LP5, LP6, LP7, and LP11) | $\beta$ -Glucosidase  |                   |
| Improvement of organoleptic properties | <i>L. plantarum</i> LM3                                      | Enolase   |                   |
|  | <i>L. plantarum</i> (NCIM 2084)                              | Lactate Dehydrogenase (LDH)   |                   |
|  | <i>L. plantarum</i> WiKim0067                                | Sensory of vegetable sponge beverage fermented  | (24)              |
|  | <i>L. plantarum</i> ATCC 8014                                | Fermented foods in Nigeria  | (25)              |
| Fermentation                           | <i>L. plantarum</i> SD1S6L2                                  |   |                   |
|  | <i>L. plantarum</i> P-8                                      | Improved the stability and volatile flavour compounds of fermented milk.  | (26)              |
|  | <i>L. plantarum</i> strains WiKim83 and WiKim87              | In various fermented foods  | (27)              |
|  | <i>L. plantarum</i> QZ227                                    | Wheat fermented silage  | (25)              |
|  | <i>L. plantarum</i> IMAU80106, IMAU10216, and IMAU70095      | Fermentation properties and subsequent changes in Yogurt  | (28)              |
| Starter culture                        | <i>L. plantarum</i> P-8                                      | Fermented milk  | (26)              |
|  | <i>L. plantarum</i> LA0445                                   | Starter culture for Cucumber fermentations  | (29)              |
|  | <i>L. plantarum</i> Lb9                                      | Starter culture in caper berry fermentation   | (30)              |
|  | <i>L. plantarum</i> SK15                                     | Starter culture for prevention of biogenic amine accumulation in fermented beverage containing <i>Hericium erinaceus</i> mushroom | (16)              |
| Biological food preservatives          | <i>L. plantarum</i> 106 and 107                              | As a bio-control strategy against food-borne pathogenic microorganisms  | (16)              |
|  | <i>L. plantarum</i> FFNL739 and FFNL1810                     | Improve safety of wheyless Domiati-like cheese  | (31)              |
|  | <i>L. plantarum</i> YML007                                   | Application as a food preservative  | (24)              |
|  | <i>L. plantarum</i> TK9                                      | Food-related bio-preservative   | (32)              |

**Table 2:** Important benefits and applications of *L. plantarum* strains in health and disease

| <i>Name of strain</i>                      | <i>Application</i>                             | <i>Disease</i>                    | <i>Benefits</i>   | <i>References</i> |
|--|--|-----------------------------------|---|-------------------|
| <i>L. plantarum</i> Lp62                   | Immune-modulating                              | Inflammatory diseases             | Preventing the adhesion of pathogens to the epithelial cells  | (34)              |
| <b>L. plantarum</b> IS-10506               | Immunomodulation                               | Immature intestinal immune system | Stimulation of TGF- $\beta$ 1   | (35)              |
| <b>L. plantarum</b> YIT0132                | Immunomodulation with anti-allergic effects    | Atopic dermatitis                 | Reduced symptoms with immunomodulatory effect via attenuation of IgE  | (36)              |
| <i>L. plantarum</i> X1                     | Anti-diabetic activity                         | Type 2 diabetes mellitus          | $\alpha$ -Glucosidase inhibitory activity ameliorates type 2 diabetes   | (37, 38)          |
| <i>L. plantarum</i> MG4229, MG4296, MG5025 |  |                                   |   |                   |
| <i>L. plantarum</i> LMT1-48                | Anti-obesity activity                          | Obesity                           | Weight loss by regulating adipogenesis  | (39-41)           |
| <i>L. plantarum</i> 22A-3                  | Anti-allergic activity                         | Allergy                           | TGF- $\beta$ secretion in passive cutaneous anaphylaxis of mice   | (42)              |
| <i>L. plantarum</i> IIA-1A5                | Anti-Cancer activity                           | Cancer                            | Inhibitory properties against WiDr human colon cancer cell lines through preventing the proliferation                 | (43-45)           |
| <i>L. acidophilus</i> IIA-2B4              |  |                                   |   |                   |
| <i>L. plantarum</i> UM55                   |  |                                   |   |                   |
| <i>L. plantarum</i> YIT013                 |  |                                   |   |                   |
| <i>L. plantarum</i> 299v                   | Anti-IBS                                       | IBS disease                       | Normalization of digestive functions in patients with IBS   | (46-48)           |
| <i>L. plantarum</i> LP01                   |  |                                   |   |                   |
| <i>L. plantarum</i> DP189                  | Anti-depression activity                       | Mental stress conditions          | Production of neurotransmitters affecting the brain-gut axis such as $\gamma$ -aminobutyric acid (GABA) and serotonin | (31-50)           |
| <b>L. plantarum</b> PS128                  | Antioxidative and anti-inflammatory activities | Exercise-induced inflammation     | Oxidative stress and inflammation alleviation   | (33)              |
| <i>L. plantarum</i> HY7714                 | Anti-photoaging effects                        | Skin aging                        | Improves skin hydration and anti-photoaging effects   | (51)              |
| <i>L. plantarum</i> 299v                   | Anti-cardiovascular disease                    | Cardiovascular disease            | Reduces cardiovascular disease risk in smokers; decreases in systolic blood pressure, leptin and fibrinogen           | (52)              |

TGF- $\beta$ : Transforming Growth Factor- $\beta$

### *Health-conferring and immune-modulating properties*

Since *L. plantarum* has the ability to enhance the mucosal immune response without negatively affecting immune homeostasis, it can be a suitable carrier for antigens delivery. *L. plantarum* can also increase antigen immunogenicity and provide an immune defense against harmful antigens. In addition, its use as a mucosal vaccine

carrier has been proven as *L. plantarum* can modify the immune tolerance of an immune response (54). Keeping the balance of the microbiota of the gastrointestinal tract improves general health of society (19, 53). The regular consumption of *L. plantarum* maintains and also progresses the beneficial intestinal microflora balance in the host organism, eliminates potential food toxins, protects against intestinal infections, lowers blood

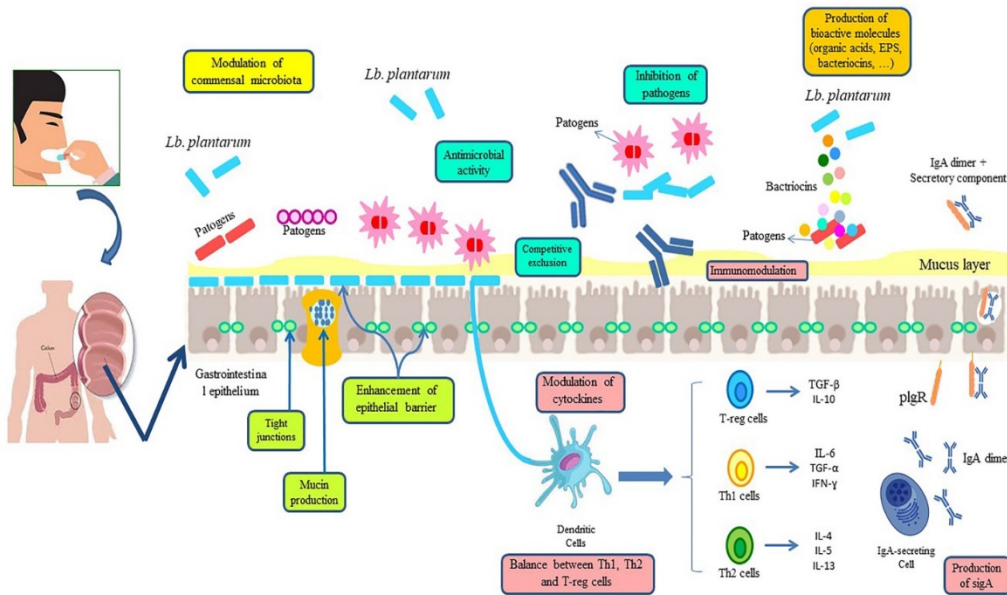
cholesterol, prevents digestive disorders including irritable bowel syndrome, ulcerative colitis, and diarrheal diseases, such as diarrhea caused by antibiotics and *Clostridium difficile*. Moreover, several *L. plantarum* beneficial properties include anti-cancer, anticoagulant, antiviral, and modulator. In addition, stimulation of antibody production by *L. plantarum* strains has been proved in previous articles (53-54).

**Anti-allergic activity**

The Probiotic action in the intestinal lumen is mediated by two distinct pathways: first, by transfer of antigens to the lumen and second, by capturing antigens with Dendritic cells (DCs) through long-range receptors within the lumen. They recruit, process, and present T helper cell 0 (Th0) cells that can be transformed into Th1, Th2, and Regulatory T cells (Treg). Treg is induced to generate various cytokines such as Interleukin 10 (IL-10) and Transforming Growth Factor- $\beta$  (TGF- $\beta$ ), which are used to regulate the stimulation of Th1 and Th2 immune cells (55). Regarding allergic diseases, Treg inhibits Th2 stimulation, which leads to the production of

immunoglobulin E (IgE), mast cells, and eosinophil degranulation. TGF- $\beta$  can also increase mucosal protection by inducing plasma cells to produce IgA. Moreover, probiotics modulate the immune system by activating the Toll-like receptor (TLR), signaling non-immune or immune cells (56, 57). Of note, TLR activation in DCs induces the development of Treg cells, produced under the epithelium of the intestinal tract and circulate systemically in different parts of the human body, such as the lungs, skin, and intestine. It is worth mentioning that Treg cells, along with other regulatory cells, restrain the production of IgE through B cells and Th2 cell responses (Fig. 3).

Some researches stated that oral administration of *L. plantarum* restored intestinal flora in peanut-allergen-sensitized mice and reduced allergic symptoms including diarrhea, the abundance of serum-specific IgE, and the production of histamine (58). Also, they demonstrated a suppression in interleukin-10 and a rise in interferon- $\gamma$  by *L. plantarum* administration (58). Therefore, *L. plantarum* most likely exhibits anti-allergic activities through modulation of gut flora.



**Fig. 3:** Some functional cases of *L. plantarum*. In general, the mechanisms by which *L. plantarum* strains exert their health benefits are 1. Modulation of the normal microbiota (yellow details); 2. Elimination or inhibition of pathogenic agents (blue details). 3. Increasing intestinal epithelial barrier with increased mucin production and formation of tight junctions (green details). 4. Modulation of the immune system (pink description) and 5. production of bioactive molecules (orange description) (15)

### **Anti-diabetic activity**

Anti-diabetic activity is one of the abilities of *L. plantarum*. For example, *L. plantarum* X1 has a potential antidiabetic capability by inhibiting  $\alpha$ -glucosidase activity in vitro, and its oral administration improves hyperglycemia, hormone levels, insulin resistance, glucose tolerance, and lipid metabolism. *L. plantarum* X1 can also partially increase antioxidant capacity and improve cytokine secretion and pancreatic damage in type 2 diabetic mice. In addition, *L. plantarum* X1 is capable of significantly restoring acetic acid levels and increasing butyric acid levels in the feces of diabetic rats. In addition, type 2 diabetic mice receiving *L. plantarum* X1 exhibited an increase in the *Bacteroidetes* abundance and a decrease in the *Firmicutes* ratio. These observations indicate that *L. plantarum* X1 has the potential to improve type 2 diabetes (38). In another study, *L. plantarum* MG4229, MG4296, and MG5025 strains showed strong  $\alpha$ -glucosidase and  $\alpha$ -amylase inhibitory activity, radical inhibition, and antioxidant activities. Therefore, it can be said that these strains have hypoglycemic and antioxidant activity. Probiotics can potentially prevent and control diabetes (43).

### **Anti-Cancer activity**

Several studies were conducted on probiotics and showed that probiotics such as *L. plantarum* IIA-1A5 and *L. acidophilus* IIA-2B4 have inhibitory properties against WiDr human colon cancer cell lines (44). In addition, since aflatoxins have carcinogenic properties, exposure to aflatoxins through drinking and/or food can cause cancer. Previous studies have shown that the organic acids produced by *L. plantarum* UM55 can decrease the risk of cancer by removing aflatoxins (45). Furthermore, *Lactobacillus* has been proven to prevent the proliferation of various types of cancer cells. A study showed that *L. plantarum* YT013 may lead to apoptosis through the endogenous mitochondrial apoptosis pathway in addition to changing cancer cell morphology; in short, it may be considered a good candidate for anti-cancer treatments and prevention (46).

### **Anti-irritable bowel syndrome (IBS)**

The consumption of probiotics, especially *L. plantarum*, improves the function of the intestinal epithelial barrier and reduces the symptoms of IBS (47). Additionally, *L. plantarum* plays a main role in modulating visceral sensitivity, which is the main cause of abdominal pain in IBS patients. Also, it can modulate intestinal motility by directly acting on the intestinal nervous system or through epithelial cells (48). There is also growing evidence that suggests a direct relationship between changes in the gut microbiota and the development of IBS and its symptoms. Currently, the use of probiotics' therapeutic potential has been proposed to supplement or replace therapeutic strategies that are often insufficient. For example, *L. plantarum* 299V improved symptoms of pain and bloating in IBS. A study on *L. plantarum* LP01 in combination with *Bifidobacterium breve* BR 03 or *L. acidophilus* LA 02 to improve IBS symptoms showed that the combination of these strains led to a significant reduction in symptoms (39).

### **Anti-obesity activity**

According to previous studies, probiotics such as *Lactobacillus* strains exert some promising effects on weight loss by regulating adipogenesis (40). *L. plantarum* LMT1-48 reduces lipogenic SCD-1, HSL, PPAR $\gamma$ , and FAT/CD36 in the liver, resulting in the reduction of body weight and fat tissue. Consequently, it can be concluded that *L. plantarum* LMT1-48 has the potential to be a healthy food for obese people (57). A study stated that *L. plantarum* FRT4, in addition to reducing body weight, had a significant effect on reducing liver weight and fat weight compared to the control group (41). Liver metabolites and biochemical parameters showed significant changes in rats fed with bacteria. Other functions of *L. plantarum* LMT1-48 include changing the expression of key genes involved in intestinal barrier function and chronic inflammation and regulating the composition of the intestinal microbiota in intestinal dysbiosis (40- 41). In another study, researchers found that LP-KFY02 could prevent the increase



in weight indices caused by a high-fat diet. Their results showed that LP-KFY02 can effectively regulate the mRNA expression of lipoprotein lipase (LPL), peroxisome proliferator activator receptor  $\alpha$  (PPAR- $\alpha$ ), cholesterol 7 $\alpha$ -hydroxylase (CYP7A1), and carnitine palmitoyl transferase (31). *L. plantarum* can also decrease the levels of alkaline phosphatase (AKP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), triglyceride (TG), total cholesterol (TC), and low-density lipoprotein cholesterol (LDL-c) (31).

### Anti-depression activity

*Psychobiotics* correspond to a novel class of probiotics, mainly *Lactobacillus* and *Bifidobacterium*, that have been shown to have mental health benefits, and can have a positive impact on mood and anxiety through the production of neurotransmitters affecting the brain-gut axis such as  $\gamma$ -aminobutyric acid (GABA) and serotonin (49). The microbiota-gut-brain (MGB) axis is involved in mood regulation and the treatment of depression, and this topic has recently attracted the attention of many researchers. According to some studies, depressive states are reduced by probiotics such as *L. plantarum* in patients with clinical depression (31, 49). The therapeutic potential of probiotics, especially *L. plantarum*, in the treatment of general depression cases, increases the hope of finding a new therapeutic approach for the treatment of Turkish depression. In a study, the antidepressant effect of *L. plantarum* DP189 was evaluated, and it improved the pathological changes in the hippocampus. The results proved that *L. plantarum* DP189 can prevent or decrease CORT-induced depression-like behaviors and hippocampal neuronal damage by lowering serum levels of IL-1 $\beta$  and TNF- $\alpha$ , reducing hippocampal mitogen-activated protein kinase 7 and c-Jun N-terminal kinase 2 levels, decreasing proapoptotic protein Bax immune content, and up-regulating the anti-apoptotic immunological content of Bcl-2 protein (50). Other effective strains in the treatment of depression include *L. plantarum* 286, which has antidepressant and antianxiety effects (49).

### Antiviral activity

Daily oral administration of *L. plantarum* L-137 (a strain selected based on pro-inflammatory characteristics in *in-vitro* study) increases survival and decreases virus titer in lungs of mice contaminated with influenza virus H1N1 through stimulating the type I interferon production (59). *L. plantarum* 299v was also found to stimulate specific systemic immune responses following oral administration. The noticed differences in the activation of toll-like receptor (TLR) 2-4 and CD14 antigens in the host has also been attributed to *L. plantarum*. Therefore, daily oral consumption of *L. plantarum* strains could lead to change in the generation of the pro-inflammatory cytokine IL-12 and the regulatory cytokine IL-10 through binding diverse dendritic cells to TLR (61). Non-steroidal anti-inflammatory drugs (NSAIDs), also called painkiller, are commonly used for their anti-inflammatory, antipyretic, and analgesic properties. However, these drugs have some side effects on the intestinal mucosal integrity and immunity, which can be modulated by *L. plantarum* since, these bacteria have immune-modulatory effects on pathogens or drug-induced mucosal stresses. Immune-modulatory properties of *L. plantarum* may also be effective on covid-19 infection. It is well known that upon infection with respiratory viruses like influenza and coronavirus (covid-19) related cytokines are triggered to induce a proper immune response, while, elevated levels of some circulating cytokines like Il-6 and hyperactivation of immune cells, can result in life-threatening systemic inflammatory syndromes and subsequent severity in cases of seasonal influenza infection and covid-19 (60). However, no study was obtained about the direct antiviral activity of *L. plantarum* on these diseases and further studies are needed to assess this approach.

### Risk assessment of *L. plantarum*

Applying probiotic strains in food products is increasing worldwide. On the other hand, these bacteria are sometimes unpredictable due to genetic and functional diversity in different human races. Thus, awareness of pathogenicity and safety level of probiotics is necessary, and must regu-

larly be checked by legal administrations (61). However, if a probiotic strain is consumed in excess, the balance of microbiota is disturbed and this imbalance may lead to allergy or autoimmune disease in the body (62). The consumption of probiotics can have a negative effect on the resident flora of the digestive tract and leave an empty ecological space after stopping the treatment. For example, if a particular strain of probiotic bacteria is in a baby's diet, it can cause problems, accordingly, some probiotic strains may not be suitable for certain ages (63). Since only a few studies have been done on manipulating the microbiota of people, it is not possible to make a definite judgment about it. However, some acquired genes for antibiotic resistance i.e., tet (M), tet (S), and erythromycin antibiotic resistance factor erm (B) have been found in *L. plantarum* (64). According to the evidence, the initial microbial composition of an infant's gut is important for the development of the gut microbiota and the developing immune system, and it should be noted that daily intake of a specific bacterial strain over a long period by an immature digestive tract may have adverse effects (60, 61). In one case, a bloodstream infection caused by *L. plantarum* was also reported in a person with endocarditis, which may be an example of the possible risk of probiotics in people with underlying diseases and immune system deficiencies (61, 62).

## Conclusion

*L. plantarum* is a probiotic bacterium with outstanding health-promoting properties and has been designated as a *generally recognized as safe* or GRAS probiotic. This bacterium is a versatile and useful probiotic with many different uses in the food industry, i.e., the ability to improve the properties and functional characteristics of fermented food. *L. plantarum* strains possess numerous probiotic properties shown promising results in experimental models of many diseases as well as human trials. However, further researches on the mechanisms related to the treatment of diseases is necessary. Increasing our knowledge

about the strain-specific diversity, probiotic properties, and health benefits of different *L. plantarum* isolates can be of great importance. Understanding the characteristics of *L. plantarum* strains facilitates the standardization of research applications and enables the easy use of specific strains for defined health applications.

## Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

## Acknowledgements

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

## Conflict of interest

The authors declare that they have no conflict of interest.

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