A novel approach to *Lactiplantibacillus plantarum*: From probiotic properties to the omics insights

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ABSTRACT

Lactiplantibacillus plantarum (previously known as *Lactobacillus plantarum*) strains are one of the lactic acid bacteria (LAB) commonly used in fermentation and their probiotic and functional properties along with their health-promoting roles come to the fore. Food-derived *L. plantarum* strains have shown good resistance and adhesion in the gastrointestinal tract (GI) and excellent antioxidant and antimicrobial properties. Furthermore, many strains of *L. plantarum* can produce bacteriocins with interesting antimicrobial activity. This probiotic properties of *L. plantarum* and existing in different niches give a great potential to have beneficial effects on health. It is also has been shown that *L. plantarum* can regulate the intestinal microbiota composition in a good way. Recently, omics approaches such as metabolomics, secretomics, proteomics, transcriptomics and genomics try to understand the roles and mechanisms of *L. plantarum* that are related to its functional characteristics. This review provides an overview of the probiotic properties, including the specific interactions between microbiota and host, and omics insights of *L. plantarum*.

1. Introduction

Fermentation is a quite old food processing method that has been used for many years as a method to extend the shelf-life of foods, as well as improves the sensory properties and nutritional value of nourishments and plays a significant role in improving food safety (Malo and Urquhart, 2016). Lactic acid fermentation is one of the most common types of fermentation and is mainly used in dairy fermented products, fermented meat and fish, fermented vegetables, and fermented cereals (Mathur et al., 2020). Lactic acid bacteria (LAB) are a group of Gram-positive bacteria including several genera such as *Lactobacillus*, *Streptococcus, Lactococcus*, *Pediococcus* and *Enterococcus* which have the ability to tolerate low pH, high salt concentrations and heat treatments (Dillon, 2014). Therefore, the probiotic and bio-preservation potential of LAB is one of the most popular topics off-lately.

Lactiplantibacillus plantarum (formerly known as *Lactobacillus plantarum*) is a versatile microorganism that can be found in a wide range of ecological niches from the human gastrointestinal (GI) tract to different fermented foods (Zheng et al., 2020). Commercially, *L. plantarum* is used as a starter culture for a variety of food fermentations and as a probiotic culture (Zheng et al., 2020). It has been reported that *L. plantarum* strains have many functional properties in the food industry (Fig. 1), such as improving the nutritional quality, flavour properties, antioxidant activities, antimicrobial activities, and the shelf-life of foods as well as reducing undesirable compounds (Yilmaz et al., 2022). *L. plantarum* has a Qualified Presumption of Safety (QPS) from the European Food Safety Authorities (EFSA). Also, *L. plantarum* is listed as "generally recognized as safe" (GRAS) status by the United States Food and Drug Administration (US FDA) (Hazards et al., 2017). Because many LAB species are accepted as QPS and GRAS, the bacteriocins produced by these strains are also considered safe (Abdulhussain, Razavi, 2020).

On the other hand, the excellent antioxidant (Jeong et al., 2021; Tang et al., 2018; Tian et al., 2022) and antimicrobial (Y. Liu et al., 2022; D.-M. Liu et al., 2022; Rajoka et al., 2020; Surve et al., 2022) properties of *L. plantarum* together with its tolerance to acidic pH (Nath et al., 2020; Tang et al., 2018), its GI resistance (Y. Liu et al., 2022; D.-M. Liu et al., 2022; Rajoka et al., 2020; Surve et al., 2022), and its adhesion capacity to intestinal mucosa (Y. Liu et al., 2022; D.-M. Liu et al., 2022; Metrouh et al., 2022; Surve et al., 2022) have also made this LAB can have beneficial effects on the host health. Furthermore, previous studies have reported that several strains of *L. plantarum* can modify the composition of the intestinal microbiota (Hang et al., 2022; Hussain et al., 2020; Wang et al., 2019). In fact, the relationship between *L. plantarum* strains and indigenous gut microbiome has been a trend scientific research topic (S. Huang et al., 2021; Y.-Y. Huang et al., 2021; Li et al., 2020).

Along with the functional properties of *L. plantarum* strains, advances have been seen in omics approaches including metabolomics, secretomics, proteomics, transcriptomics, and genomics with the aim of understand the roles and mechanisms behind these properties (including the specific interaction between microbiota and host) (Zhang et al., 2021). On the other hand, Lugli et al. (2022) stated a novel approach as "probiogenomics", which represents the probiotic identity card. A probiotic identity card is a combination of bacterial cell enumeration by flow cytometry and shotgun metagenomic sequencing. As an example, this approach revealed that a remarkable amount of commercial probiotic supplements including *L. plantarum* had inconsistencies in the formulation when compare with their statement (Lugli et al., 2022). Therefore, omics approaches are gaining importance because they help to understand the mechanisms behind the functional and probiotic properties of *L. plantarum*. It will be discussed the recent literature on the probiotic properties of *L. plantarum* (including the relationship between the gut microbiome and *L. plantarum*) as well as omics approaches of *L. plantarum* in this review.

2. Probiotic properties and roles of *Lactiplantibacillus plantarum*

L. plantarum is one of the most significant members of lactobacilli and it has been commonly used as a probiotic due to its outstanding probiotic qualities (good GI tolerance, adhesion, antioxidant, and antibacterial properties) (Table 1). Even though, earlier studies mostly have focused on isolating the probiotic strains of *L. plantarum* along with their bioactive metabolites, nowadays the roles of *L. plantarum* strains and their bacteriocins in the food industry as well as their adaptability to

environmental stress can be better-understood (S. Huang et al., 2021; Y.-Y. Huang et al., 2021; Y. Liu et al., 2022; D.-M. Liu et al., 2022; Patil et al., 2020). *L. plantarum* exists in different niches, however, the probiotic potential of strains isolated from fermented foods will be discussed in this section in the light of recent studies (Pan et al., 2021) since probiotic characteristics of *L. plantarum* strains isolated from these nourishments are one of the focuses of interest (Fig. 1).

2.1. Resistance to gastrointestinal conditions

An essential feature to consider a microorganism as a probiotic is to survive the harsh conditions of the human GI tract. Thus, a probiotic must initially withstand the low pH conditions of the stomach and subsequently tolerate exposure to bile acids and salts in the small intestine, among others. In this hostile environment, different strains of *L. plantarum* have been shown to be potential probiotics due to their pH and bile tolerance achieved through various strategies such as maintenance of intracellular pH homeostasis, rapid recycling of damaged proteins, and induction of several stress response pathways; and the induction of bile salt hydrolase and maintaining the proton motive force, respectively (Fidanza et al., 2021). In this lines, *L. plantarum* MA2 strain and B23 strain showed good tolerance and could survive at low pH (2.5–3) (Tang et al., 2018). In a similar way, Nath et al. (2020) demonstrated that *L. plantarum* GCC_19M1 displayed significant tolerance to low pH conditions. Specifically, this strain exhibited survival rates that ranged between 93.48 % and 96.97 % when exposed to simulated gastric juice (pH=3). Furthermore, *L. plantarum* GCC_19M1 was also found to be significantly tolerant to 0.3 % bile, 0.5 % pancreatin, and 5 % NaCl. Also, *L. plantarum* SJ14 shown good tolerance to acid and bile-like human GI tract conditions (Metrouh et al., 2022). Strains of *L. plantarum* isolated from pickles and kimchi (KACC11451 and Wikim0112, respectively) demonstrated excellent GI environment resistance (D.-M. Liu et al., 2022).

In another study, *L. plantarum* KU15149 was reported to have gastric and bile salt tolerance (Han et al., 2020). The high tolerance to low pH of *L. plantarum* was also shown by Gupta et al. (2021), who observed that up to 40 LAB strains (including 11 *L. plantarum* strains) survived in a simulated GI tract. However, it should be noted that of the 11 strains of *L. plantarum* examined, L/ M-2 and H/ M-3 strains were found to have a reduction in viable count at low pH (=3). This different tolerance to low pH levels could affect the probiotic potential of the different strains of *L. plantarum*. On the other hand, it should also be noted that the resistance that probiotic strains must present at low pH is fundamental, but it
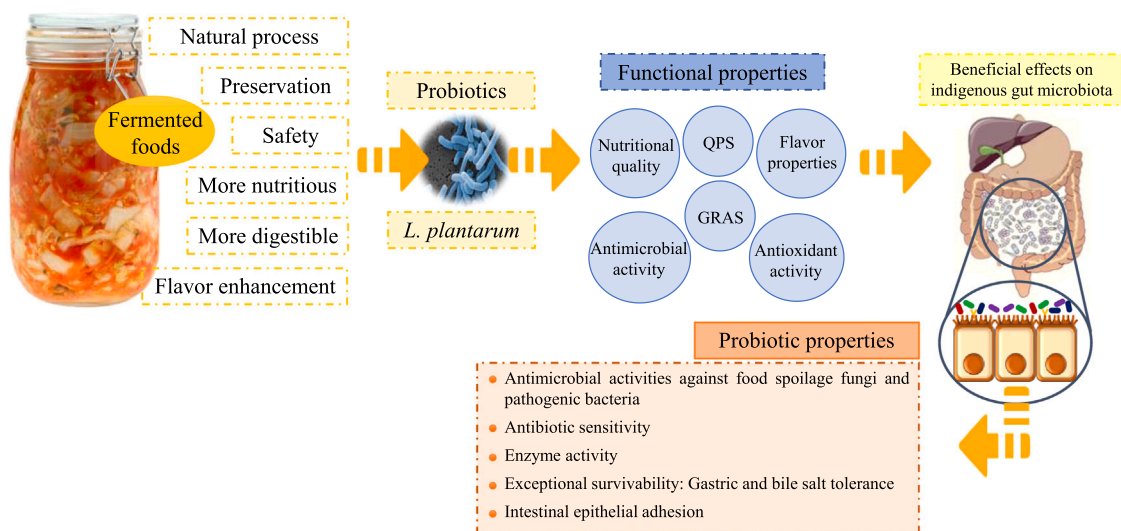

Fig. 1. Functional and probiotic properties of *Lactiplantibacillus plantarum* from fermented foods. (QPS: Qualified Presumption of Safety; GRAS: Generally Recognized as Safe).

Table 1

Probiotic and biological properties of selected *Lactiplantibacillus plantarum* strains isolated from fermented foods.

Fermented food	Isolated *L. plantarum* strains	Probiotic properties	Reference
Dhokla batter and jaggery (Indian fermented foods)	*L. plantarum* DKL3 and JGR2	1. Good tolerance to acid and bile 2. Good adherence to intestinal epithelial cells 3. Produced exopolysaccharides, folate and riboflavin 4. Had antimicrobial activities	Surve et al. (2022)
Chinese traditional naturally fermented Paocai	*L. plantarum* DMDL 9010	1. Good gastrointestinal tolerance and good adhesion 2. Antioxidant and antibacterial properties	D.-M. Liu et al. (2022)
Kimchi	*L. plantarum* LRCC5314	1. Very stable survival at low pH (=2.0) and in 0.2 % bile acid with 89.9 % adhesion to Caco-2 cells 2. Inhibited the activities of α-amylase and α-glucosidase - Decreased inflammatory cytokines levels	Yoon et al. (2022)
Kimchi	*L. plantarum* strains	1. *L. plantarum* LRCC5193 and LRCC5304 showed the high-stress tolerability 2. *L. plantarum* LRCC5193 had the best heat, acid and bile acid tolerance along with intestinal adhesion to the Caco-2 cells compared with other isolates	Lim et al. (2018)
Kimchi	*L. plantarum* strains	1. *L. plantarum* LB5 had the highest tolerance to low pH (=2.5), 0.3 % bile, and the heat treatment (up to 60 °C) as well as showed good adherence to the Caco-2 cells 2. *L. plantarum* LB5 exhibited antibacterial activity against common food-borne pathogenic bacteria 3. It has not been detected any antibiotic resistance in *L. plantarum* LB5	Sohn et al. (2020)
Theobroma cacao	*L. plantarum* Lp03, Lp289, and Lp291	1. All strains had good tolerance to heat and low pH 2. All strains exhibited antimicrobial activity and produced hydrogen peroxide	das Neves Selis et al. (2021)
Pickles and kimchi	Wikim0112 and KACC11451	1. Good intestinal epithelia adhesion (ratios of 60–62 %) 2. Inhibition of pathogens colonization 3. Excellent antioxidant capacity (more than 70 % activity similar to superoxide dismutase)	Jeong et al. (2021)
Algerian traditional cheese ("Jben")	SJ14	1. Good tolerance to acid and bile 2. Good adhesion to intestinal cells 3. Antimicrobial capacity against pathogenic and opportunistic bacteria and antifungal properties	Metrouh et al. (2022)

does not mean that acid pH-tolerant strains always show probiotic properties.

2.2. Adhesion capacity to intestinal mucosa and/ or to extracellular matrix components

Adherence to the mucosal film of the epithelial cells or adherence to the components of the extracellular matrix of the intestinal tract are desired characteristics in a probiotic microorganism because they will favor the colonization and persistence of the probiotic in the host (Fidanza et al., 2021). Moreover, the adhesion of beneficial bacteria in the intestinal tract also contributes to the inhibition of pathogens colonization and improves mucosal healing (Jeong et al., 2021). In this context, various works have focused on studying the adherence capacity of *L. plantarum*. An example was the study carried by Surve et al. (2022), where the cell adhesion assay on human intestinal epithelial cells revealed that the extent of adhesion to HT-29 intestinal epithelial cells of *L. plantarum* DKL3 and JGR2 was similar to that of the probiotic strain *Lacticaseibacillus rhamnosus* GG. Thus, both *L. plantarum* strains showed adherence extents of 82.8 % and 79.6 %, respectively. In a similar way, Y. Liu et al. (2022), D.-M. Liu et al. (2022) demonstrated through the analysis of self-coagulation that *L. plantarum* DMDL 9010 strain had good adhesion to the intestinal epithelium, which could be related to the presence of genes that encode different proteins attributed to adhesion to different extracellular matrices and intestinal mucus. For their part, Jeong et al. (2021) observed intestinal epithelia adhesion ratios of approximately 60–62 % (evaluated using Caco-2 cells) in *L. plantarum* strains KACC11451 and Wikim0112, with KACC11451 standing out for presenting the highest percentages. Tang et al. (2018) also found differences adherence to Caco-2 cells in vitro between two different strains of *L. Plantarum* (MA2 and B23), highlighting B23 for presenting the best extents. *L. plantarum* KU15149 was considered as a potential probiotic despite having a lower ability to adhere to HT-29 cells than that shown by the probiotic *Lacticaseibacillus rhamnosus* GG, since KU15149 was considered equally sufficient to exert its benefits on the host (Han et al., 2020). Recently, Metrouh et al. (2022) investigated the probiotic potentials of a new *L. plantarum* strain (SJ14) in vitro. This strain has

exhibited good adhesion to intestinal cells. Moreover, an isolated of *L. plantarum* N-1 were examined by Tian et al. (2022) with the same promising results in terms of good Caco-2 cell adhesion.

2.3. Antioxidant activity

Oxidative stress refers to a condition in which the existing balance between antioxidants and prooxidants in the cell is altered, which leads to DNA hydroxylation, protein denaturation, lipid peroxidation and even cell apoptosis. In this way, oxidation exerts detrimental effects on the cell and therefore on living organisms. In this field of damage to health, some probiotics have been displayed to have antioxidant activity, reducing oxidation and therefore the damage caused by oxidation reactions. Probiotics can act as antioxidant agents through different mechanisms, among which are the metal ion chelating ability, antioxidant enzymes system, antioxidant metabolites, mediation of antioxidant signaling pathways, regulation of enzymes that produce reactive oxygen species (ROS) and also through the modulation of the intestinal microbiota (Wang et al., 2017).

Due to the importance acquired by oxidation processes, many studies have been carried out in which the antioxidant capacity of *L. plantarum* has been evaluated with promising results. For instance, Y. Liu et al. (2022), D.-M. Liu et al. (2022) demonstrated that *L. plantarum* DMDL 9010 showed an excellent antioxidant capacity through the superoxide anion (O_2^-) scavenging activity method, and 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay, with the supernatants showing a higher antioxidant capacity than bacterial precipitates. Contrarily, Tian et al. (2022) observed that the extracts obtained from cell-free *L. plantarum* N-1 had a lower antioxidant capacity (determined by the DPPH assay and reducing power) than the extracts containing the bacteria cells, evidencing the presence of antioxidant compounds in intact cells of *L. plantarum* N-1. Despite this difference, both extracts showed a good antioxidant capacity, superior to other probiotic strains (Tian et al., 2022). For their part, Jeong et al. (2021), displayed that *L. plantarum* Wikim0112 and KACC11451 showed more than 70 % activity similar to superoxide dismutase (SOD), in addition to having a remarkable antioxidant capacity through the DPPH and 2,2′-azino-bis

(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) assays, highlighting Wikim0112 strain for showing the highest activities. Also, *L. plantarum* KU15149 had a high abundance of antioxidants, as measured by DPPH assay and β-carotene bleaching inhibition (Han et al., 2020).

Tang et al. (2018) determined that *L. plantarum* MA2 had a high antioxidant capacity through the cellular antioxidant activity (CAA) test, highlighting the antioxidant capacity of cell-free extract of the logarithmic phase compared to cell-free extract of the stationary phase and fermentation supernatant of the logarithmic phase. In addition, these authors determined that the antioxidant capacity of cell-free extract was due to the presence of intracellular antioxidant enzymes (such as catalase, feruloyl esterase, glutathione peroxidase, glutathione reductase, glutathione transferase, NADH oxidase, NADH peroxidase, and SOD) and non-enzymatic substances. Moreover, Tang et al. (2018) related extracellular metabolites such as polysaccharides, proteins, and pyruvate with the antioxidant capacity exerted by the fermentation supernatant of the logarithmic phase.

2.4. Bacteriocin production

Bacteriocins are peptides or proteins synthesized by the ribosomes of certain bacteria which have antibacterial activity against foodborne pathogens and food spoilage bacteria (W. Wang et al., 2018; Y. Wang et al., 2018; J. Wang et al., 2018; Zeng et al., 2014). In this way, bacteriocins can exert various benefits both in food and in the hosts since they can increase shelf-life and protect against unwanted colonization, respectively. Many strains of *L. plantarum* have been shown to be capable of producing bacteriocins, giving this microorganism probiotic properties (Yilmaz et al., 2022). Concretely, *L. plantarum* generates a bacteriocin normally referred to as plantaricin, which frequently belongs to class I (lantibiotic) and class II (non-lantibiotic) bacteriocins. Although, most plantaricins pertain to class II, since they are non-lantibiotic (Choi et al., 2021). An example of plantaricin belonging to group II is that produced by *L. plantarum* LPL-1 (named as Plantaricin LPL-1). This bacteriocin is a novel class IIa bacteriocin and is a promising bio-preservative in the food industry (W. Wang et al., 2018; Y. Wang et al., 2018; J. Wang et al., 2018). Y. Liu et al. (2022), D.-M. Liu et al. (2022), also detected that DMDL 9010 strain was characterized by generating a plantaricin that acted as an antimicrobial agent.

The bio-preservation potential of 220 LAB containing different strains of *L. plantarum* isolated from Brazilian artisanal cheeses was investigated also in terms of bacteriocin production (Margalho et al., 2021). There was a significant variation amongst isolates of the same species of *L. plantarum* indicating that the source of isolation affects their probiotic properties. Considering its capacity to produce a bacteriocin-like antimicrobial agent, *L. plantarum* 1QB77 was chosen among the other strains and during cheese production. On the other hand, Zeng et al. (2014), studied 21 *L. plantarum* strains. Thus, they observed that 10 strains out of 21 have been reported to have the ability to produce bacteriocins. Surve et al. (2022) also determined the potential of *L. plantarum* DKL3 and JGR2 to produce various types of bacteriocins. Specifically, they observed that both strains had genes related to plantaricin, while only JGR2 had genes related to lactococin.

The production of bacteriocins with antimicrobial activity against Gram-negative bacteria is presented as a very prominent feature since this property is relatively unusual in LAB (Metrouh et al., 2022). In this context, it should be noted that it has been reported that many *L. plantarum* strains have been shown to produce bacteriocins that are effective against Gram-negative bacteria. Concretely, KLDS1.0391, ZJ5, not specified, TN635, B23, and AA135 strains were producers of the bacteriocins Plantaricin MG, Plantaricin ZJ5, bacteriocins ST28MS and ST26MS, bacteriocin BacTN635, bacteriocin Lac-B23, and Plantaricin AA135, respectively, which have antimicrobial effect against several Gram-negative bacteria (Abo-Amer, 2007; Gong et al., 2010; Smaoui et al., 2010; Song et al., 2014; Todorov and Dicks, 2005; Zhang et al., 2018).

Given that bacteriocins produced from certain *L. plantarum* strains have been claimed to have antimicrobial activities against foodborne spoilage and pathogens bacteria (W. Wang et al., 2018; Y. Wang et al., 2018; J. Wang et al., 2018; Zeng et al., 2014) this microorganism may have probiotic potential and deserve further studies to be able to increase their use in the food industry.

2.5. Antimicrobial activity

Probiotics are characterized by inhibiting the growth, development, and colonization of pathogenic microorganisms. This inhibition can be achieved through different means which mainly include competition for nutrients and adhesion space, induction of environmental changes harmful to pathogens, the generation of antimicrobial substances (including the aforementioned bacteriocins) and modulation of their immune responses (Fidanza et al., 2021). The antimicrobial properties are one of the most distinctive features of probiotics and they give the ability to modify the host's gut microbiota. However, this subsection will exclusively address the antimicrobial power of *L. plantarum* and not its modulation on the intestinal microbiota since this probiotic property will be attend in depth in the following subsection.

Much research has observed that during the fermentative metabolism of *L. plantarum*, it produces several antimicrobial compounds (apart from bacteriocins) that may include organic acids such as lactic, citric, isobutyric, and acetic acids, ethanol, diacetyl, and H_2O_2 (Y. Liu et al., 2022; D.-M. Liu et al., 2022; Markkinen et al., 2022). Furthermore, *L. plantarum* can also produce exopolysaccharides with natural antifungal activity (Rajoka et al., 2020). The cell-free supernatants of *L. plantarum* WiKim0112 and KACC11451 showed the ability to inhibit six food-borne pathogens (namely *Escherichia coli* O157:H7 ATCC 35150, *Listeria monocytogenes* ATCC 15313, *Salmonella choleraesuis* KCCM40763, *Shigella boydii* KCCM41649, *Staphylococcus aureus* ATCC25923, and *Yersinia enterocolitica* KCCM41657) (Jeong et al., 2021). Similarly, Surve et al. (2022) found that *L. plantarum* DKL3 and JGR2 inhibited the growth of *Escherichia coli* MTCC 728, *Escherichia faecalis* ATCC 14506, *Listeria monocytogenes* ATCC 19115, and *Pseudomonas aeruginosa* ATCC 27853, this inhibition being greater in the case of *Pseudomonas aeruginosa* ATCC 27853. The antimicrobial effect of both strains of *L. plantarum* was attributed not only to the presence of bacteriocins, but it was also related to the formation of organic acids that lead to a drop in the pH of the medium, which can alter the development of pathogens (Surve et al., 2022). For its part, *L. plantarum* DMDL 9010 had effective antibacterial components including various organic acids against 4 different pathogens (Y. Liu et al., 2022; D.-M. Liu et al., 2022). Organic acids, especially lactic acid, were also responsible for the antimicrobial capacity exhibited by various strains of *L. plantarum* (namely, Lp03, Lp289, and Lp291). These three strains significantly inhibited the growth of pathogens *Neisseria gonorrhoeaes* and *Gardnerella vaginalis* after 24 h of coincubation (das Neves Selis et al., 2021).

The antibacterial capacity against pathogenic and opportunistic bacteria (both Gram negative and positive) as well as the antifungal capacity against 8 fungi was determined in *L. plantarum* SJ14 by Metrouh et al. (2022). They observed that *L. plantarum* SJ14 displayed a broad spectrum of activity against *Enterobacter cloacae*, *Escherichia coli*, *Klebsiella pneumoniae*, and *Salmonella typhi*, including extended-spectrum beta-lactamase-producing *Enterobacteriaceae* (ESBL). The antimicrobial activity of *L. plantarum* SJ14 was not related to the decrease in pH carried out during its metabolism, since the antagonistic effect against the aforementioned pathogenic bacteria was tested at pH 7. Additionally, Metrouh et al. (2022) demonstrated that the antimicrobial activity of *L. plantarum SJ14* was not affected by different thermal treatments (60–100 ºC for 30 min). Similarly, the antimicrobial activity of this strain was stable in a very wide pH range (2–10), with acid conditions (pH 2–6) being optimal for this functional trait.

2.6. Indigenous gut modulation

The whole gut microbiome comprises the communities of bacterial, viral, archaeal, fungal, and protozoal communities that live within the GI tract and establish a beneficial association with the host. Specifically, the gut microbiota enables the fermentation of otherwise inaccessible dietary food source, while supplying a source of vitamins and permitting the metabolism of xenobiotics (Lavelle and Hill, 2019). Moreover, intestinal microorganisms execute an essential part in the metabolic homeostasis, immune education, and neurological responses in the human body (Arun et al., 2021; de Almada et al., 2015).

In view of these facts, the gut microbiome occupies an important place in the maintenance of host health and the pathogenesis of a large number of sicknesses (Pham et al., 2021). Therefore, the exact balance of the different species that constitute the intestinal microbiome, also known as eubiosis, is crucial to prevent infectious and non-infectious diseases and impede the disturbance of the microbial community equilibrium, name as dysbiosis (Al-Rashidi, 2022). However, the composition and/ or the activity of the gut microbiota is affected by many factors (including the birth mode, gender, host genetics, immune system and health or disease state of the host, geographical location, socio-economic factors, diet, the employ of therapeutic medicines, etc.) since the intestinal microbiota define an open microbial ecosystem (Surono et al., 2022; Veiga et al., 2014). In fact, the gut microbiome are constantly exposed to transient exogenous microorganisms transmitted by food (Veiga et al., 2014). On this matter, probiotics have the ability to adjust the composition of the intestinal microbiota and correct abnormal responses of the immune system (Zhang et al., 2019), thus exerting different beneficial effects on the host (Fig. 2).

Taking into account the above, the use of probiotics could represent a therapeutic strategy to modulate the gut microbiota and improve human diseases (Ng et al., 2009; Wang et al., 2022). In this sense, there are several research where a clear regulation of the intestinal microbiota by different strains of *L. plantarum* is observed (Table 2). For instance, Hang et al. (2022) reported that *L. plantarum* ZJ316 exerted a modulating effect of the microbiota in an in vitro intestinal model. Specifically, these authors observed that ZJ316 strain increased the growth of *Veillonella*, which could improve the immunity of the human respiratory and digestive system (Djais et al., 2019). At the same time, *L. plantarum* ZJ316 had a positive impact on the portion of *Bifidobacterium* and *Lactobacillus*, which are identified as beneficial microbiota for the host. On the other hand, it was observed that *L. plantarum* ZJ316 reduced the presence of *Blautia*, that was related to intestinal inflammation in obese children (Hang et al., 2022). At the same time, ZJ316 strain lessened the *Enterobacteriaceae* family that includes commensal organisms and primary and opportunistic pathogens which could easily reproduce in inflamed intestines, contributing to the microbial imbalance (Sassone-Corsi et al., 2016). For their part, Canaviri-Paz et al. (2021) observed that the consumption of a quinoa-based beverage fermented with *L. plantarum* P31891 (at a probiotic dose of 2.5×10^{14} CFU/day) during 14 days favoured the increase of the probiotic *Lactobacillaceae* family in the intestine of healthy people. However, despite favouring the amount of *Lactobacillus* spp., the intake of *L. plantarum* ZJ316 did not alter the indigenous microecology of the intestine of the patients, thus maintaining the correct balance of the gut microbiome, and therefore guaranteeing its probiotic effect.

Wang et al. (2019) observed that the administration of *L. plantarum* PFM 105 in weaning pigs modulated the intestinal microbiota of the piglets. Specifically, this strain increased the intestinal amount of symbiotic and beneficial microorganisms, including bacteria from *Bifidobacteriaceae* and *Prevotellaceae* families. In addition, *L. plantarum* PFM 105 could improve the metabolic capacity of the gut microbiota, since this microorganism incremented the expression of genes implicated to the biosynthesis and metabolism of glycans, and in the metabolisms of cofactors and vitamins. Furthermore, this influence in the microbiota resulted in a considerable improvement in the development of small intestinal villi of the piglets and in a decrease in diarrhoea, ameliorating clinical performance and decreasing the mortality of the animals. In the same line, W. Wang et al. (2018), Y. Wang et al. (2018) and J. Wang et al. (2018) identified that the administration of *L. plantarum* ZLP001 for 30 days to weaned pigs modified the intestinal microbiota of the animals. Specifically, this strain reduced the abundance of certain bacterial species correlated with the expression of proinflammatory cytokines. Simultaneously, *L. plantarum* ZLP001 increased the abundance of beneficial probiotic bacteria belonging to the *Lactobacillaceae* family and decreased the cell density of detrimental *Clostridium* sensu stricto 1. In addition, *L. plantarum* ZLP001 had the ability to modulate the expression of butyrate-producing enteric microbiota related to the expression of host defence peptides (HDP), being able to improve the innate immune response.

On the other hand, it has been observed that *L. plantarum* regulate the intestinal microbiota in obese mice, attenuating the effects of this disease. Specifically, Hussain et al. (2020) observed that oral administration of *L. plantarum* LB818 (1×10^9 CFU/mL) in obese-induced mice
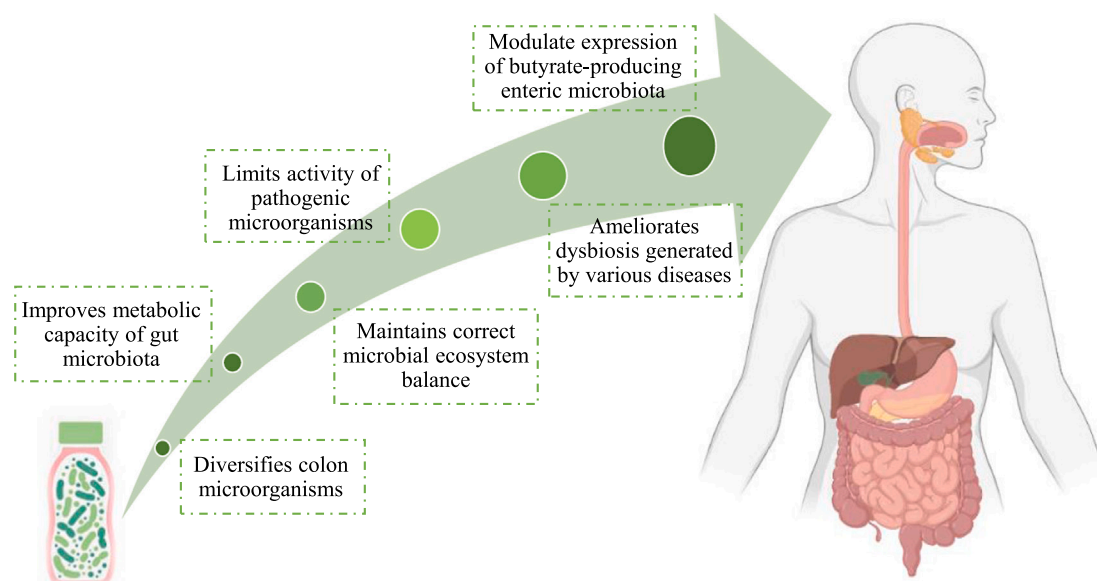

Fig. 2. Effects caused in the gut microbiota after the administration of certain probiotics.

Table 2

Effect of different *Lactiplantibacillus plantarum* strains on the intestinal microbiota.

L. plantarum strain	Main effects on gut microbiota	Reference
ZJ316	1. Increase *Veillonella*, *Bifidobacterium*, and *Lactobacillus* genus 2. Reduced the presence of *Enterobacteriaceae* family	Hang et al. (2022)
P31891	1. Increase *Lactobacillaceae* family 2. Does not alter the indigenous microecology	Canaviri-Paz et al. (2021)
PFM 105	1. Increase *Prevotellaceae* and *Bifidobacteriaceae* families 2. Increases the expression of genes involved in the biosynthesis and metabolism of glycans 3. Favours the metabolisms of cofactors and vitamins	Wang et al. (2019)
ZLP001	1. Reduces bacterial species correlated with proinflammatory cytokines 2. Increases *Lactobacillaceae* family 3. Reduces the cell density of detrimental *Clostridium* sensu stricto 1 4. Modulates the expression of butyrate-producing enteric microbiota	J. Wang et al. (2018)
LB818	1. Restores the microbial gut eubiosis in obese patients 2. Promotes the presence of *Bacteroidetes*, *Akkermansia*, *Bifidobacterium*, and *Lactobacillus* 3. Maintains an adequate equilibrium between *Bacteroidetes*: *Firmicute* ratio	Hussain et al. (2020)
HAC01	1. Increases the relative abundance of *Lachnospiraceae* family 2. Influences the regulation of gene expression associated to lipid metabolism in the in the mesenteric adipose tissue	Park et al. (2017)
Dad-13	1. Increases of butyric acid-producing bacteria 2. Inhibits *Enterobacteriaceae* growth	Kamil et al. (2022)
Sgs 14	1. Reverses the dysbiosis generated by virulent strains of *Listeria monocytogenes*	Dushku et al. (2020)
HNU082	1. Improves the growth of *Bifidobacterium*, *Lactobacillus*, *Akkermansia* and *Faecalibacterium* Increases metabolic short-chain fatty acids	Shao et al. (2017)

HNU082	1. Increases the gut microbiota diversity
	2. Reduces structural differences in gut microbiota
	3. Enlarges the growth of *Bidobacterium pseudolongum* and *Bacteroides ovatu.*
	  1. Reduces proinflammatory microorganism
	  1. Increases metabolic short-chain fatty acids
		Wu et al. (2022)

Y15	1. Enlarges short-chain fatty acids-producing bacteria 1. Returns the original structurer of microbiota	Y. Liu et al. (2022)

restored their intestinal microbiota favouring the presence of essential bacteria, enclosing *Akkermansia*, *Bacteroidetes*, *Bifidobacterium* and *Lactobacillus*. Moreover, the administration of this strain maintained an adequate equilibrium between *Bacteroidetes*: *Firmicute* ratio, providing an appropriate intestinal balance. Likewise, Park et al. (2017) found that administration of the *L. plantarum* HAC01 strain favourably modulated the gut microbiota in an obese murine model. Specifically, oral administration of the strain HAC01 (1×10^9 CFU/animal) for 8 weeks influenced specific bacterial families such as *Lachnospiraceae* and *Ruminococcaceae*. This regulation could be linked to positive effects in obese mice, since after the supply of *L. plantarum* HAC01 the relative abundance of *Lachnospiraceae* increased, which ameliorates the dysbiosis generated by obesity. Moreover, these same authors conclude that *L. plantarum* HAC01 influenced the regulation of gene expression associated to lipid metabolism in the mesenteric adipose tissue.

L. plantarum has also been shown to affect the microbiota of malnourished patients. Specifically, Kamil et al. (2022) observed that the intake of *L. plantarum* Dad-13 ($1 \times 10^{8-9}$ CFU/g) for 50 days achieved the modulation of butyric acid-producing bacteria, increasing its presence in undernourished infants. This modulation was associated with beneficial effects, since it favoured the growth of the *Firmicutes* phylum, that includes various butyric acid-producing bacteria, such as *Faecalibacterium prausnitzii*, which has been postulated as a probiotic due to its anti-inflammatory properties and its immunomodulatory effect (Fluitman et al., 2017; Leylabadlo et al., 2020). Additionally, *L. plantarum* Dad-13 inhibited the growth of the potency pathogenic family *Enterobacteriaceae*. This inhibition of pathogens was also demonstrated by Dushku et al. (2020), who observed that the administration of *L. plantarum* Sgs14 to *Cornu aspersum* snails decreased the presence of the *Listeria monocytogenes* and reversed the dysbiosis generated by virulent strains of this harmful bacteria.

The effect of *L. plantarum* on the gut microbiota was also investigated in hyperlipidemic diets. In this line, Shao et al. (2017) studied the influence of *L. plantarum* HNU082 intake (1×10^8 CFU/mL during 28 days) on the gut microbiome in rats. Specifically, they observed that the inclusion of this strain improved the host hyperlipidemia index, since this microorganism promoted the degradation of triglycerides, total cholesterol and high-density lipoprotein cholesterol, while avoiding the microbial disorder generated by hyperlipidemia. This improvement was related to the fact that the consumption of *L. plantarum* promoted the growth of certain bacteria (such as *Akkermansia*, *Bifidobacterium*, *Faecalibacterium* and *Lactobacillus*) that are involved in the pyruvate, butanoate, propanoate, and glycerolipid metabolism pathways, and in the biosynthesis of peptidoglycans, carotenoids, and fatty acids. On the other hand, the change in the microbiome produced by *L. plantarum* HNU082 increased metabolic short-chain fatty acids, which are also common intestinal anti-inflammatory elements and potential biomarkers of hyperlipidaemia prevention. Additionally, Shao et al. (2017) observed that the stable presence of *L. plantarum* HNU082 in the intestine was closely connected to the plentiful active carbohydrate enzymes and phosphotransferase system in the genome, which supported the strain to colonize and improve an advantage in rivalry for intestinal nutrition, again favouring host health.

For their part, Wu et al. (2022) investigating the influence of *L. plantarum* HNU082 on dysbiosis produced in a mouse model with induced ulcerative colitis. They discovered that the intake of this bacterial strain (1×10^9 CFU/mL during 7 days) significantly increased the diversity of the intestinal microbiota, while reducing its structural differences. Specifically, *L. plantarum* HNU082 decreased the proinflammatory microorganisms related to colitis (such as *Helicobacter hepaticus*) and increased the presence of other probiotic bacteria (*Bacteroides ovatu* and *Bidobacterium pseudolongum*), which are associated to the reduction of the colon inflammation, with the reduction of obesity and diabetes, and with the synthesis of short-chain fatty acids. Additionally, this study showed that *L. plantarum* HNU082 is capable of activating two microbial metabolic pathways that produce short-chain

fatty acids, thus inhibiting intestinal inflammation (Wang et al., 2020) and regulating the physiological activity of the host, suggesting the ability of *L. plantarum* HNU082 to repair the intestinal mechanical barrier (Wu et al., 2022). Moreover, this repairing effect could be enhanced by the increase in mRNA expression of mucin-2 mRNA and by the decrease in mRNA expression of intercellular cell adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1), and certain proinflammatory cytokines caused by *L. plantarum* HNU082. Similarly, Chen et al. (2017) identified that *L. plantarum* LP-Only administration attenuated intestinal inflammation through regulation of the microbiota in interleukin-10 knockout mice, demonstrating the efficacy of this strain for the treatment of colitis.

It has also been observed that the employ of *L. plantarum* can influence several parameters modified by diabetes. Specifically, Y. Liu et al. (2022), D.-M. Liu et al. (2022) observed that the administration of *L. plantarum* Y15 (3×10^8 CFU/mL for 6 weeks) improved biochemical indices of fasting blood glucose (FBG), insulin, glycosylated haemoglobin (HbA1c), and index of insulin resistance (HOMA-IR) in diabetic rats type 2. Simultaneously, the use of this strain reduced the proinflammatory cytokines interleukin-6 (IL-6), interleukin-8 (IL-8), and tumour necrosis factor-alpha (TNF-α). In addition, the administration of *L. plantarum* Y15 remodelled the structure of the intestinal microbiota and reduced the levels of lipopolysaccharides as a consequence of the increase in short-chain fatty acids. Administration of *L. plantarum* Y15 in diabetic rats also upregulated the expressions of genes related to the inflammation and insulin signalling pathway, suggesting that this microorganism may serve as a potential probiotic for the improvement of type 2 diabetes.

2.7. Omics approaches to understand the roles of Lactiplantibacillus plantarum including metabolomics, transcriptomics, and proteomics

Recent breakthroughs in advanced 'Omics' approaches including metabolomics, secretomics, proteomics, transcriptomics, and genomics coupled with chemometrics tools (mathematical and statistical tools) have led to comprehensive and deeper understanding of mechanisms of action behind the functionality and specific interaction between probiotics and host (Fig. 3). These approaches have successfully answered to the variation in the phenotype of different microorganisms with respect to their genetic information. Thus, these have been quite useful tools to bridge the gap between genetic information and the metabolites of the particular cell. Among these, transcriptomics and proteomics

enables the quantification of mRNA and proteins, respectively, at a specific physiological condition (Manzoni et al., 2018), while metabolomics mainly deals with the study of biological molecules known as metabolites (<1500 Da) (Wishart, 2008). Thus, it is noteworthy that all these approaches are totally different from the traditional methods of characterization and one single approach is never sufficient to characterize the organism, considering its complex and unique nature. Most of the LAB species have been commonly and widely used as health promoting bacteria in foods. However, it has only been recent that advancements in the techniques and approaches have deciphered the mechanisms explaining the beneficial impact of these bacteria on the host (Heena Sharma et al., 2021; H. Sharma et al., 2021). To date, several researchers have integrated the utilisation of various 'omics' approaches to understand the functional role of LAB, including *L. plantarum* (Huang et al., 2017; O'Donnell et al., 2020; Zhang et al., 2021).

2.8. Metabolomics approach to comprehend the role of Lactiplantibacillus plantarum

Metabolomics mainly includes the study of biological molecules of size less than 1500 Da, thus, deals with all such metabolites present in a given organism. Highly sophisticated instruments are generally used for this purpose including liquid chromatography-mass spectrometry (LC-MS), gas-chromatography coupled with mass spectrometry (GC-MS), and nuclear magnetic resonance (NMR). To date, LAB have been used widely for the production of fermented foods and thus, metabolomics have proven a quite useful tool to characterize the fermented foods and understand the technological aspects (Adebo et al., 2019; Gao et al., 2021; Heena Sharma et al., 2021; H. Sharma et al., 2021; Sharma and Ramanathan, 2021). However, each organism behaves owing to its genetic make-up, which in turn influences the generation of metabolic end-products and protein analysis. Earlier study conducted by Faijes et al. (2007) deals with reliable extraction methodology for the metabolites of *L. plantarum*. They deduced that extraction methodology significantly influences the obtention of intracellular metabolites and cold methanol and boiling ethanol were the best solvents for metabolites extraction from this organism. A group of researchers have explored the adhesion ability of *L. plantarum* ATCC 14917 by subjecting it to alkali and acid stress employing a metabolomic approach and demonstrated that alkali stress resulted in decreased amino acid metabolism while few components involved in energy metabolism were higher in acidic group
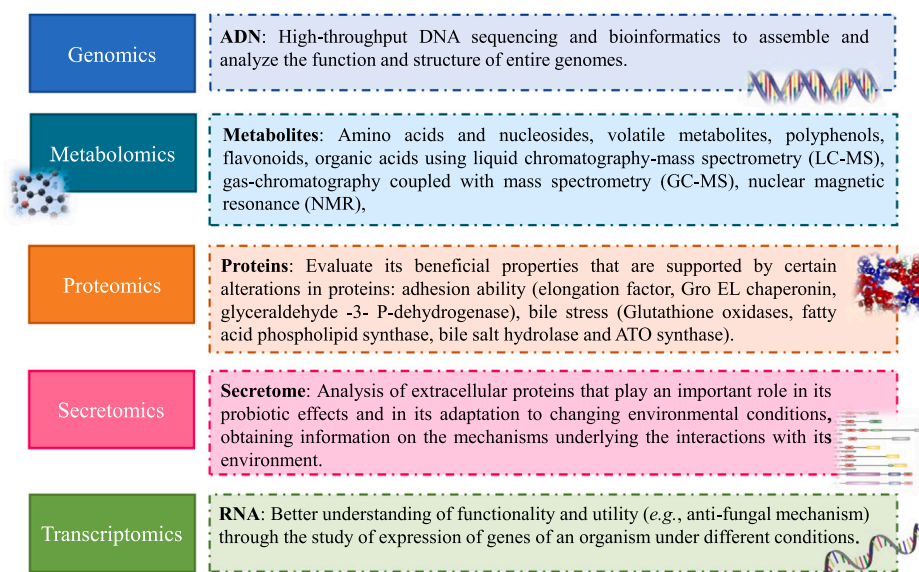
Genomics	**ADN**: High-throughput DNA sequencing and bioinformatics to assemble and analyze the function and structure of entire genomes.
Metabolomics	**Metabolites**: Amino acids and nucleosides, volatile metabolites, polyphenols, flavonoids, organic acids using liquid chromatography-mass spectrometry (LC-MS), gas-chromatography coupled with mass spectrometry (GC-MS), nuclear magnetic resonance (NMR),
Proteomics	**Proteins**: Evaluate its beneficial properties that are supported by certain alterations in proteins: adhesion ability (elongation factor, Gro EL chaperonin, glyceraldehyde -3- P-dehydrogenase), bile stress (Glutathione oxidases, fatty acid phospholipid synthase, bile salt hydrolase and ATO synthase).
Secretomics	**Secretome**: Analysis of extracellular proteins that play an important role in its probiotic effects and in its adaptation to changing environmental conditions, obtaining information on the mechanisms underlying the interactions with its environment.
Transcriptomics	**RNA**: Better understanding of functionality and utility (*e.g.*, anti-fungal mechanism) through the study of expression of genes of an organism under different conditions.

Fig. 3. Understanding probiotic functional properties using omics approach.

(W. Wang et al., 2018; Y. Wang et al., 2018; J. Wang et al., 2018). The antimicrobial capacity of *L. plantarum* has also been demonstrated through the use of metabolomics. For example, (Zhang et al., 2021) determined through metabolomic analysis that the presence of *L. plantarum* CCFM8724 in *Streptococcus mutans-Candida albicans* mixed-species biofilms inhibited the formation of carbohydrates related to biofilm formation, while increasing the concentration of sugar alcohols such as xylitol or sorbitol. Thus, the conjunction of these facts could be related to the inhibition of the growth of Streptococcus mutans and therefore with the antimicrobial capacity of *L. plantarum*.

Apart from the characterization of *L. plantarum*, the utilisation of metabolomic techniques in diverse food groups have also been studied extensively (Table 3). One of the studies involving the use of this organism in fermented sea buckthorn juice deciphered the metabolites (a total of 46 different compounds) responsible for flavour development and other beneficial effects (Markkinen et al., 2022). For this, the authors employed NMR spectroscopy and subsequently evaluated the data obtained through Principal Component Analysis (PCA) and Orthogonal Principal Least Squares Discrimination (OPLS-DA). Thus, Markkinen

et al. (2022) observed that metabolites such as L-malic acid, amino acids and nucleosides were held responsible for fermentation in early stages while, longer fermentation time favoured the formation of bioactive compounds including antimicrobial compounds such as acetic, lactic, and 3-phenyllactic acids (3-PLA). In addition, Zhao et al. (2021) used *L. plantarum* dy-1 in fermentation of aqueous barley extracts in order to reveal the functional properties of the product and better understanding of fermentation process occurring in barley extract. In this case, a total of 124 substances were identified by ultra-high performance liquid chromatography tandem with high resolution mass spectrometry (UPLC-HRMS) in combination with a multivariate analysis that used a PCA and a Partial Least Squares Discrimination Analysis (PLS-DA). Among the compounds determined during fermentation, metabolites such as 3-PLA, indole-3-lactic acid, and cafestol were found, which could explain the functionality of the fermentation carried out by *L. plantarum* dy-1 due to the antifungal features revelled by 3-PLA and also due to the beneficial properties against metabolic diseases and the anti-carcinogenic, anti-inflammatory and antioxidant activity shown by indole-3-lactic acid (Galligan, 2018) and cafestol (Cavin et al., 2002; Lee

Table 3
Possible functional properties of *Lactiplantibacillus plantarum* revealed using omics approach.

Applied omic technologies	Total number of identified compounds	Metabolites/ genes/ proteins identified	Functional properties revealed with omic approaches	Reference
Metabolomics				
NMR spectroscopy	46	Sugars, amino acids, organic acids, ketones, nucleosides and one alkaloid	1. Possible antimicrobial properties due to the presence of acetic, lactic, and 3-phenyllactic acid	Markkinen et al. (2022)
UPLC-HRMS	124	Amides, esters, amino acids, saccharides, nucleosides, and organic acids	1. Possible functional properties due to the presence of bioactive compounds such as phenyllactic acid, indole-3-lactic acid, and cafestol	Zhao et al. (2021)
HPLC-DAD and SPME-GC-MS	Not specified	Volatile compounds, polyphenols, and flavonoids	1. Antioxidant properties due to the release of hydroxycinnamic acids and catechins 2. Increase in the bioavailability of phenolic acids	Ferri et al. (2016)
Transcriptomics				
qRT-PCR	Not specified	223 DEG (111 upregulated and 112 downregulated)	1. Inhibits aflatoxin synthesis by *Aspergillus flavus* under the regulation of 223 genes of *Aspergillus flavus*. 1. Antifungal properties	Zhao et al. (2019)
qRT-PCR and microarray assay	9624	209 DEG (38 upregulated and 171 downregulated)	1. Altered genes related to global metabolic 2. Increased cellular stress 3. Promoted cell death 1. Antifungal properties	Crowley et al. (2013)
RNA-sequencing and qRT-PCR	Not specified	550 DEG (271 upregulated and 279 downregulated)	1. Hypocolesterolemic ability related to the increase on the expression of *Cyp7 a1* gene	Li et al. (2020).
High-throughput transcriptomic sequencing and qRT-PCR	> 2590	1051 DEG (513 upregulated and 538 downregulated)	1. *lp3014*, *lp284*, *pyrB*, *dhaT*, and *luxS* genes play an important role in biofilm formation 1. Ability to survive the GI tract through biofilm formation	Sun et al. (2020).
Proteomics				
2DE, MALDI-TOF-MS	129	Cytosolic fraction proteins	1. First proteomic map* (*No functional property decrypted)	Cohen et al. (2006)
2DE, capillary-LC-MS/ MS	29	Cell surface proteins	1. Postulated as proteins potentially involved in the probiotic action in the GI tract	Beck et al. (2009)
2DE, chip-LC-QTOF-MS	> 35	Cell wall proteins	1. Identification of proteins related to adhesiveness to the intestinal mucosa (elongation factor, Gro EL chaperonin, GroES co-chaperonin, and glyceraldehyde-3-phosphate-dehydrogenase)	Izquierdo et al. (2009)
2DE, chip-LC-QTOF-MS	Not specified	Whole cell proteins	1. Identification of 6 proteins linked to regulation of bile-related stress factors (including glutathione oxidases, fatty acid phospholipid synthase, bile salt hydrolase and ATP synthase) 1. Ability to survive in the small intestine	Hamon et al. (2011)
LC−MS/ MS	2063	506 DEP	1. Cold-adaptation mechanism mainly by down regulating DE proteins involved in carbohydrate metabolism and energy production, and fatty acid and amino acid biosynthesis	Liu et al. (2020).

NMR: Nuclear magnetic resonance; UPLC: Ultra-high performance liquid chromatography; HRMS: High resolution mass spectrometry; HPLC: High-performance liquid chromatograph; DAD: Photodiode array detector; SPME: Solid phase micro extraction; GS: Gas chromatography; MS: Mass spectrometry; CG: Gas chromatography; qRT-PCR: Real-time quantitative Reverse Transcription Polymerase Chain Reaction; DEG: Differentially expressed genes; 2DE: Two-dimensional electrophoresis gel; MALDI: Matrix-assisted laser desorption/ ionization; TOF: Time-of-flight; LC: Liquid chromatography; GI: Gastrointestinal; QTOF: quadrupole time-of-flight; DEP: Differential expressed proteins

et al., 2007; Shen et al., 2015), respectively.

Similar approach was earlier used by Ferri et al. (2016) in identifying the flavour and functional profile of sourdoughs (cereal-based fermented foods) wherein, various volatile metabolites, and polyphenols and flavonoids were identified utilising reverse phase high-performance liquid chromatography coupled to a photodiode array detector (HPLC-DAD) and solid phase micro extraction-gas chromatography coupled to a mass spectrometry (SPME-GS-MS), respectively. Moreover, the data obtained were treated using two-way Hierarchical Cluster Analysis (HCA) for the formation of heatmaps and the correlations between volatile compounds and antioxidants substances were visualized through correlation heatmaps. This metabolomic approach allowed to relate the antioxidant capacity of the doughs with the functional compounds released (for example, hydroxycinnamic acids, catechins and other flavonoids) by different strains of *L. plantarum* during fermentation. Thus, Ferry et al. evidenced an increase in the bioavailability of phenolic acids and their metabolites after the use of *L. plantarum*, which have *ex vivo* immunomodulatory effects (Nelson et al., 2016). For their part, Ming et al. (2018) also used a metabolomic analysis through GC-MS to increase knowledge about the grass carp fermentation process. These authors identified more than 80 distinct metabolites and displayed that the use of *L. plantarum* provided higher levels of organic acids (fumarate, 2-piperidinecarboxylic acid) and lower levels of amino acids (alanine, glycine, threonine, tryptophan, and lysine) with the progression of fermentation time after performing a multivariate assay through PCA and loadings analysis (LA).

2.9. Transcriptomics approach to comprehend the role of Lactiplantibacillus plantarum

Transcriptomics mainly involves the study of expression of genes of an organism under the influence of different conditions including oxidative stress, physiological conditions, fermentation process, etc. Thus, it provides a complete snapshot of a cells' total transcripts (Lowe et al., 2017). As previously detailed, it is a well-known fact that *L. plantarum* have diverse functional roles such as food preservative due to its antioxidant and antimicrobial nature, synthesize Vitamin- B groups, and have been widely used in a variety of foods (Goswami et al., 2017; Li et al., 2016; Liu et al., 2017). However, the mechanism behind the beneficial effects of this organism needs to be fully comprehended at the transcriptional level for better understanding of functionality and utility of *L. plantarum*. In fact, transcriptomics technologies such as real-time quantitative Reverse Transcription Polymerase Chain Reaction (qRT-PCR) and microarray assay have been proven quite useful techniques to understand the anti-fungal mechanism of *L. plantarum* (Table 3). It is believed to act against aflatoxin produced by *Aspergillus flavus* by upregulating the genes related to the organization and synthesis of polysaccharides in their cell wall (such as mannan endo-1, 6-alpha-mannosidase activity, endo-1,4-beta-xylanaseactivity, chitin and cellulose binding, and cell wall macromolecule catabolic process), while sixteen genes associated with aflatoxin biosynthesis (between them *aflB*, and *aflC*) are significantly downregulated (Zhao et al., 2019). Cell free supernatant of *L. plantarum* also showed effective results against two moulds associated commonly with food spoilage, *Aspergillus fumigatus* and *Rhizopus stolonifer* through qRT-PCR and microarray assay (Crowley et al., 2013). The study demonstrated a global shutdown of several genes (including *ERG24* and *ERG25* genes) involved in multiple cellular functions (carbohydrate, fatty acid, and amino acid metabolism, ergosterol biosynthesis pathway, etc.) to be responsible for the cell death and antifungal action, subsequently.

Altered gene expression involving upregulation of 69 genes associated with biological and molecular functions and down regulation of 18 genes associated with biological and cellular processes was noticed upon the fermentation of medium with *L. plantarum* CGMCC 1.2437[T] for the improved production of γ-aminobutyric acid (GABA) utilizing high-throughput transcriptome sequencing for it (Zhuang et al., 2018). For

their part, the resistant ability of *L. plantarum* WCFS1 against wide variation of temperature, NaCl concentrations, pH values, amino acid levels, and oxygen availability in order to understand the fermentation characteristics and subsequent changes in transcriptome profile was evaluated by DNA microarray hybridizations (Bron et al., 2012). Moreover, the last research showed a way to correlate transcriptomic profiles with physiological characteristics of *L. plantarum* and therefore its possible functionality. Thus, it was observed that amino acid concentrations had no impact on the physiological characteristics of *L. plantarum* and practically no transcriptomic responses were observed for this fermentation variable. However, significant transcriptomic responses were observed for temperature, pH value, and NaCl and O_2 levels, as certain genes were upregulated, while others were downregulated (Bron et al., 2012). In addition to this, mechanism underlying the role of glycine betaine (GB) in *L. plantarum* ST-III as protective agent against salt stress was explored by Zhao et al. (2014) who reported that GB enhances the gene expression involved in carbohydrate metabolism which are positively correlated with salt resistance of *L. plantarum* ST-III. Further, *L. plantarum* utilises glucose or fructo-oligosaccharides as one of the carbon sources during fermentation (Chand et al., 2021) therefore, it becomes essential to know the mechanism of metabolism of such sugars. Transcriptomic study conducted by Chen et al. (2015) revealed that almost 363 genes participated in the metabolism of these sugars. Moreover, these authors discovered that the genes involved in fatty acid biosynthesis were repressed in cells grown on fructo-oligosaccharides. This modification resulted in an alteration of the fatty acid profile since their carbon chains were shortened. Consequently, Chen et al. (2015) concluded that the metabolism (transport and utilization) of the fructo-oligosaccharides favoured the increase in membrane fluidity of *L. plantarum* ST-III. Apart from this, subsequent studies also showed the capacity of *L. plantarum* for *de novo* folate synthesis. Thus, Liu et al. (2019) demonstrated the high yield of *de novo* folate production of the *L. plantarum* 4_3 in fermented soyabean, this being possible through the upregulation of p-aminobenzoic acid biosynthesis.

The use of transcriptomic techniques has been useful in studying the hypocholesterolemic ability of this microorganism (Table 3). Thus, Li et al. (2020) determined through RNA-sequencing and qRT-PCR that the intake of *L. plantarum* HT121 for 7 weeks is positively associated with lower triacylglycerols and higher glycocholic acid in hypercholsterolemic rats, since feeding the rats with this microorganism increased expression of *Cyp7 a1* gene (bile secretion-related gene).

The ability of *L. plantarum* J26 to withstand the harsh conditions of the GI tract, was demonstrated employing transcriptomic techniques by Sun et al. (2020). They showed that *L. plantarum* J26 stood out in terms of its biofilm formation potential when compared to 78 other LAB (isolated from a traditional fermented milk product in China). Specifically, after the use of high-throughput transcriptomic sequencing and qRT-PCR, Sun et al. (2020) found that genes such as *lp3014*, *lp284*, *pyrB*, *dhaT* and *luxS* play a fundamental role in biofilm formation. On the other hand, this same authors also detected the existence of more than 1000 differential genes with significantly regulated pathways including glycerine and pyrimidine metabolism and amino acid biosynthesis. Another group of researchers showed the potency of same strain *L. plantarum* J26 against oxidative stress in Caco-2 cells by up regulating 8-genes associated with inflammation and immune response and modulated the production of antioxidant enzymes.

2.10. Proteomics approach to comprehend the role of Lactiplantibacillus plantarum

Proteomics is the branch of 'omics' which mainly deals with study of complete set of proteins in a cell, tissue, or an organism. Proteins are the vital elements of the organism and thus, may serve as biomarkers for specific and unique properties or any disease manifestation. All the beneficial properties of *L. plantarum* are backed up by certain alterations in proteins and the underlying mechanisms are being explored by

proteomics approach (Table 3). First reference proteome map of the protein transition between logarithmic and stationary phase of *L. plantarum* growth was established by Cohen et al. (2006). Specifically, these authors investigated the cytosolic fraction proteome of *L. plantarum* WCFS1 by combining proteomic techniques for protein separation and subsequent identification (namely, two-dimensional gel electrophoresis (2DE) and matrix-assisted laser desorption/ ionization coupled with time-of-flight mass spectrometry (MALDI-TOF-MS), respectively). Thus, a total of 129 cytosolic proteins were identified. Also using proteomic techniques (i.e., 2DE and capillary liquid chromatography tandem mass spectrometry, LC-MS/ MS), Beck et al. (2009) identified a total of 29 different proteins associated with the cell surface of *L. plantarum* 299v, which were postulated as proteins potentially involved in the probiotic action of *L. plantarum* on the GI tract. Further, after few years a group of researchers was successful in reporting the reference proteomic database of *L. plantarum* CMCC-P0002. Concretely, Zhu et al. (2011) separated and identified a total of 423 whole-cell proteins and secretory proteins of *L. plantarum* CMCC-P0002 through the utilization of 2DE and matrix-assisted laser desorption/ ionization source and tandem time-of-flight mass spectrometry (MALDI-TOF/ TOF MS).

More specifically on the identification of cellular components involved in probiotic activities of *L. plantarum*, it is worth mentioning the pioneering study carried out by Izquierdo et al. (2009), where for the first time the adhesion ability was related to the presence of certain proteins in three different probiotic strains of *L. plantarum* (WHE 92, 299v, and CECT 4185). Thus, using 2DE, and chip-liquid chromatography-quadrupole time-of-flight-mass spectrometry (chip-LC-QTOF-MS), characteristic profiles of cell wall proteins related to the adhesion of the microorganism to the mucin were identified. Consequently, the proteins elongation factor, Gro EL chaperonin, GroES co-chaperonin, and glyceraldehyde-3-phosphate-dehydrogenase were linked with adhesion ability, because they were overexpressed in the cell wall of *L. plantarum* WEH 92 (strain with the highest adhesiveness). On the other hand, proteomics has also been a tool utilised to determine the stress response of *L. plantarum* against various agents (such as acids, and bile) with the aim of revealing functional properties as the resistance of the bacteria to passage through the stomach and its ability to survive in the small intestine (Hamon et al., 2011; Heunis et al., 2014). In this way, six proteins were identified (employing 2DE and chip-LC-QTOF-MS) in bile salt response of *L. plantarum* including glutathione oxidases, fatty acid phospholipid synthase, bile salt hydrolase and ATP synthase (Hamon et al., 2011). Each of these proteins actively participate in regulation of bile-related stress factors, thus also participating in the capacity of the bacteria to survive in the small intestine. Further, the molecular mechanism involved in the survivability of cold-tolerant *L. plantarum* was investigated to guarantee its functionality in refrigerated fermented foods. Thus, through proteomic techniques (namely, LC−MS/MS) it was observed that downregulation of pathways related to energy metabolism (carbohydrates, amino acids, and fatty acids) by 506 differentially expressed proteins resulted in the cold-tolerance ability of *L. plantarum* K25 (Liu et al., 2020).

Omics approaches including metabolomics, proteomics and transcriptomics have been used to unveil the mechanism behind the functional and probiotic properties of *L. plantarum* such as adhesion ability, response to acid and bile stress, and its' beneficial effect on health system. These approaches have provided the previously undocumented selective biomarkers for characterization and evaluating the efficacy of the particular strains. Obtained metabolites, genes and proteins through these approaches can further be investigated for the functional bioactivities and application.

3. Conclusions

L. plantarum is an appreciated functional microorganism due to both its recognized potential health benefits (including survivability in GI tract, adhesion ability, antioxidant capacity, antimicrobial activity, and modulation of the intestinal microbiota) and its ability to improve nutritional and sensory quality of certain foods, and its capacity to extend the shelf-life of fermented foods. These characteristics have made *L. plantarum* widely utilised as a probiotic culture in a broad variety of foodstuffs, some of its strains being promising cultures in the food industry in terms of enhancing novel and functional products.

Nonetheless, despite the recognized functional properties of different *L. plantarum* strains, there are currently many tasks to understand the role that this microorganism plays in the in the host health. Thus, further investigations are needed to characterize the molecular mechanisms by which *L. plantarum* exerts its probiotic effects. In this field, omics approaches are gaining importance because they enhance the understanding of the mechanisms behind the functional and probiotic properties of certain beneficial strains such as *L. plantarum*. Specifically, the use of metagenomics, transcriptomics, and proteomics allow the study of biological metabolites, the knowledge of gene expression, and the analysis of the complete set of proteins, respectively. These techniques have supported to better understand the mechanisms responsible for some functional properties of *L. plantarum* such as the mechanisms of adhesion to gastrointestinal tract, its ability to form biofilms, its antimicrobial and antifungal power, and its resistance to certain harsh conditions. However, there are still many points to be clarified, highlighting the importance of further research in the omics area to increase knowledge about how *L. plantarum* exerts its probiotic activity.

Conflicts of Interest

The authors declare no conflict of interest.

Data Availability

No data was used for the research described in the article.

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