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EPS-producing *Leuconostoc* as probiotics: biomedical potential and structure–function perspectives

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With the increasing prevalence of diseases associated with gut dysbiosis, such as gastrointestinal diseases, immunological disorders, metabolic and cardiovascular diseases, and cancer, there is a growing need for effective strategies to restore the gut microbiota and promote overall health. In this context, underexplored lactic acid bacteria, particularly those capable of producing exopolysaccharides (EPSs), are gaining attention due to the diverse and pleiotropic health benefits of their EPSs. This narrative review provides an overview of the health-promoting properties of *Leuconostoc* species and their associated EPSs, with particular emphasis on the structure–function relationships underlying EPS bioactivity. Furthermore, it examines the mechanisms through which EPS-producing *Leuconostoc* strains may influence gut and systemic health and discusses their potential as next-generation microbiome-based interventions. Notably, most available evidence is derived from *in vitro* and other preclinical models, while clinical studies directly validating the efficacy and health benefits of *Leuconostoc* EPSs in humans remain limited.

KEYWORDS
bacterial polysaccharides, exopolysaccharides, lactic acid bacteria, prebiotics, probiotics, synbiotics

1 Introduction

The role of the gut microbiota in intestinal homeostasis and disease has emerged as a major focus of biomedical research. The gut microbiota constitutes a dynamic microbial ecosystem that interacts extensively with the host and dietary substrates, contributing to the regulation of intestinal barrier function, immune responses, and microbial metabolic activity. Increasing evidence indicates that alterations in microbial community composition, specific taxa, and microbial metabolites are associated with the pathophysiology and clinical manifestations of several prevalent disorders, including irritable bowel syndrome (IBS) (Shaikh et al., 2023), colorectal cancer (CRC) (Wong and Jun, 2023), type 2 diabetes (T2D) (Slouha et al., 2023), breast cancer (Nandi et al., 2023) and Parkinson's disease (Li Z. et al., 2022). These observations have stimulated growing interest in strategies aimed at modulating the gut microbiota and its functional outputs to support intestinal and systemic health.

Among these bacteria are lactic acid bacteria (LAB), which constitute an important part of our gut microbiome. The probiotic properties of specified LAB are well established, particularly for strains formerly classified within the genus *Lactobacillus*, which is why these LAB

strains, together with strains of selected *Bifidobacterium* species, account for the majority of clinically studied probiotic strains/products (Dempsey and Corr, 2022; Dronkers et al., 2020). Probiotics are 'live microorganisms that, when administered in adequate amounts, confer a health benefit on the host' (Hill et al., 2014). It should be emphasized that not all strains belonging to a genus, or even to a species, are established as probiotics. Binda et al. (2020) state that at least one appropriately conducted human clinical trial demonstrating a health benefit is required for a candidate microorganism to qualify as a probiotic, with rare exceptions in which evidence may support a broader taxonomic group. In addition, probiotic strains must be adequately characterized; they must be safe for the intended application and remain viable in the product at an efficacious dose for the entire duration of its shelf life. Selected LAB strains not only have a long history of safe use as probiotics but also exhibit several health-promoting properties. Primary metabolites such as lactic acid (LA) and short-chain fatty acids (SCFAs) have been shown to regulate gut health by lowering the pH and preventing the growth of pathogens (Sun and O'Riordan, 2013). At the same time, LA and SCFAs promote the growth of beneficial microbes and also regulate the immune system and metabolic genes, affecting overall health (Iraporda et al., 2015; Mirzaei et al., 2022). Despite all these confirmed attributes, clinical studies seem inconclusive about the manner of probiotic supplementation and its efficacy regarding specific health outcomes (National Institutes of Health, Office of Dietary Supplements, 2025; Das et al., 2022; Estevinho et al., 2024; McFarland et al., 2018; Merenstein et al., 2024).

Strains belonging to the *Leuconostoc* genus are less investigated when it comes to their probiotic potential. *Leuconostoc* strains can be found in the environment, fermented food and dairy products, posing a minor but detectable member of the gut microbiota. In fact, they are the most commonly used heterofermentative dairy LAB, next to *Lactococcus*, *Streptococcus* and lactobacilli. While *Leuconostoc* has long been applied in food fermentation, its biomedical potential remains relatively understudied compared to better-characterized LAB genera within the lactobacilli and other widely studied genera such as *Bifidobacterium*. *Leuconostoc* bacteria can produce high amounts of lactic acid, which is known for its anti-inflammatory and antimicrobial effects. Some strains were also found to be producing short-chain fatty acids (SCFAs), which are linked to systemic health regulation via local and distal immunomodulation, anticancer and antimicrobial properties. This implicates their beneficial impact on the whole gut microbiome composition and metabolome, as well as beneficially regulating the host metabolism. While existing LAB-EPS reviews have increasingly addressed structure–activity relationships, they remain organized around broad taxonomic or functional categories rather than genus-specific mechanistic insights, limiting their utility for targeted probiotic development. Focusing on *Leuconostoc* allows examining how its distinctive EPS structures may mediate host–microbiome interactions through prebiotic activity, immune modulation, and metabolite signaling. A prebiotic is defined as "a substrate that is selectively utilized by host microorganisms conferring a health benefit" (Gibson et al., 2017).

Though the production of EPS is a key characteristic of this genus, this feature has been mainly exploited in the dairy industry due to its viscosity, which adds to the creamy texture of the milk matrix. However, more and more light is shed on other aspects of EPS that show the great role it may play in promoting health. Given its great potential, more focus is now put on characterizing the biological activity of uninvestigated EPS. Moreover, there is still a gap in knowledge between the structural characteristics and various biological activities.

For this aim, this narrative review briefly introduces the probiotic properties observed in *Leuconostoc* bacteria, followed by a thorough overview of the structural diversity and therapeutic potential of *Leuconostoc*-EPS. In this review, we propose that strain-specific structural features of *Leuconostoc*-derived EPS, including glycosidic linkage patterns, monosaccharide composition, and molecular weight, are important determinants of how these polymers interact with the host and its microbiota. Within the current definition of a synbiotic, as a mixture comprising live microorganisms and substrate(s) selectively utilized by host microorganisms that confers a health benefit on the host, which distinguishes between complementary and synergistic formulations (Swanson et al., 2020), we propose that combining *Leuconostoc* strains with their own or heterologous EPS may represent a complementary synbiotic approach. In this case, the bacterial strain and EPS would contribute through different mechanisms, such as supporting bacterial survival, influencing the gut microbiota, or directly affecting host responses.

A literature search was conducted using PubMed and SciSpace to identify studies relevant to *Leuconostoc*-derived exopolysaccharides (EPSs), with searches combining terms related to *Leuconostoc*, exopolysaccharides, lactic acid bacteria, probiotics, prebiotics, gut microbiota, immunomodulation, antioxidant activity, and structure–function relationships. Given the relatively recent and limited body of research specifically addressing *Leuconostoc* EPSs, particular emphasis was placed on studies published within the past decade, while earlier studies were considered where relevant to foundational concepts or mechanisms. References were selected based on their relevance to the scope of the review and the availability of experimental evidence.

2 Selection of *Leuconostoc* probiotic candidates based on resistance to gastrointestinal and industrial processing stressors

More and more studies explore the probiotic potential of *Leuconostoc* strains, while previous studies were more focused on industrial applications, e.g., as starter cultures in food fermentation. One of the reasons is that this genus shows a large diversity regarding stress resistance, as opposed to other generally more robust LAB genera (D'Angelo et al., 2017; Schifano et al., 2021). The selection of *Leuconostoc* strains with probiotic potential requires consideration of both gastrointestinal survival and technological robustness. Candidate strains should tolerate the major stresses encountered during gastrointestinal transit, including exposure to oral enzymes, low gastric pH, bile salts, and intestinal conditions, while also exhibiting sufficient adhesion to intestinal epithelial cells to support persistence in the gastrointestinal tract. At the same time, strain viability should be maintained during industrial processing and storage, including fermentation, harvesting, freeze-drying, and exposure to temperature, pH, oxidative, and osmotic stresses.

However, stress resistance has been assessed with the absence of EPS production, which is significantly linked to improving pH and

bile salt resistance (Alp and Aslim, 2010; Fedorová et al., 2018). Apart from helping in resisting stress, it also improves another crucial feature for effective probiotics – adhesion to the gut epithelium (Luan et al., 2022). However, EPS not only improves resistance and persistence of its producing strain in the gut but also bears several health-promoting features for the host. As gastrointestinal-associated stress resistance is a crucial feature for a probiotic candidate, many health-promoting attributes linked to *Leuconostoc* seem not to have been further exploited in this matter.

New solutions to improve delivery and effective colonization of the probiotic have renewed interest in adhesive properties and biofilm-based probiotics (Yermagambetova et al., 2024; Adegbolagun et al., 2023; Visan and Cristescu, 2023). Several LAB exhibit adhesive properties and produce exopolysaccharides (EPSs), which surround the bacterial cell and protect against stress conditions. For this reason, it is essential to identify new probiotic candidates, develop optimized encapsulation strategies, and incorporate synergistic bioactive compounds, including LAB-derived metabolites, prebiotics and postbiotics, the latter being defined as preparations of inanimate microorganisms and/or their components that confer a health benefit on the host (Abouelela and Helmy, 2024; Jan et al., 2024; Parhi et al., 2024; Khursheed et al., 2022). This shifts the focus to less investigated LAB species and their naturally produced bioactive compounds, that could enhance the weak points for probiotic delivery, survival and efficacy.

3 Safety assessment of potential probiotic *Leuconostoc* strains

In addition to the ability of potential probiotic strains to withstand gastrointestinal and industrial processing stresses, safety is a crucial criterion in their selection. Although opportunistic infections involving *Leuconostoc pseudomesenteroides* have been reported, primarily in immunocompromised patients, these cases appear to be uncommon (Ghobrial et al., 2023). At the same time, *Leuconostoc* species have a history of use in food fermentation. However, neither probiotic status nor safety should be inferred solely from genus-level affiliation. The term "probiotic" should be applied to specific, sufficiently characterized microorganisms for which safety for the intended use and a health benefit have been demonstrated in accordance with established criteria (Binda et al., 2020). Safety assessment should be grounded in accurate species-level identification and should account for genus- and species-specific risk factors, followed by evaluation at the strain level. Phenotypic screening of candidate strains should use standardized analytical methods, including testing for antimicrobial susceptibility and resistance to relevant antibiotics, hemolytic activity, biogenic amine production, and D-lactate production. Whole-genome sequencing (WGS) should complement phenotypic testing by verifying whether known genetic determinants linked to the observed antimicrobial resistance are present, with emphasis on acquired antimicrobial resistance genes, and when applicable, by assessing genes that encode recognized virulence factors. Although a long history of food use can support the safety of a microorganism, it is not, on its own, sufficient evidence. In addition, depending on the intended use and source of the microorganism, development of biomedical or next-generation probiotics should address relevant legal and ethical requirements, including compliance with the Nagoya Protocol where applicable (Johansen, 2017), and appropriate informed consent when microorganisms are isolated from human subjects or human-derived samples. Therefore, safety assessment remains relevant at the strain level, particularly when evaluating *Leuconostoc* isolates for potential probiotic applications.

4 Health implications of *Leuconostoc* bacteria

Selection of probiotic strains should also consider their biological characteristics, including host-associated functional properties and antipathogenic activity. *Leuconostoc* bacteria are naturally found in the environment and play a vital role in the spontaneous fermentation of foods such as vegetables and dairy products. Due to their regular and natural presence in fermented foods, they also represent a minor but consistent component of the human gut microbiome. While traditionally exploited in the dairy industry for their fermentative properties, recent studies have increasingly focused on the potential probiotic and health-promoting effects of selected *Leuconostoc* strains, due to the production of several beneficial metabolites (Figure 1). However, only a few *Leuconostoc* strains, including *Leu. mesenteroides* NTM048 and VITA-PB2, have so far been evaluated in randomized human clinical trials demonstrating strain-specific health effects (Mo et al., 2025).

Regarding immunostimulatory activity, several *Leu. mesenteroides* strains have shown immunomodulatory properties *in vitro* and *in vivo*. Most studies focus on *Leu. mesenteroides* NTM048, demonstrating its immunostimulatory and thus gut homeostasis-promoting properties. Matsuzaki *et al.* found that this strain induces Immunoglobulin A (IgA) *in vitro* and *in vivo* in mice, where fecal and serum IgA levels were raised upon supplementation with NTM048, showing that this strain potently promotes the intestinal and systemic immune response (Matsuzaki et al., 2014). The authors emphasize the high production of EPS, which is also known for its IgA-stimulating activity. Another study, conducted as a randomized, double-blind, placebo-controlled trial, provides evidence for the immune-boosting effect on $CD8^+CD28^+$ T cells, which are known to protect against viral infections and suppress tumor cells (Kuroda et al., 2018). CD4(+) T-cell stimulating activity has also been reported for this strain (Matsuzaki et al., 2016). In yet another study, NTM048 supplementation in a psoriasis mouse model reduced disease symptoms and interleukin-17 (IL-17) levels. The authors suggest that this effect is derived from changes in the intestinal microbiota and thus produced metabolites, such as deoxycholic acid (Ogawa et al., 2021).

Interestingly, the immunomodulatory properties of *Leu. mesenteroides* WHH1141 were also shown to have an impact on metabolic health (Gao et al., 2023). Upon supplementation in ovalbumin-induced food allergy in mice, it promoted weight loss and restored gut homeostasis. It also improved food allergy symptoms and regulated IL-4, IL-5 and IL-13 cytokine expression. In a randomized human clinical trial, VITA-PB2 supplementation reduced blood ethanol and acetaldehyde levels, increased aldehyde dehydrogenase (ALDH) and glutathione peroxidase (GPx) activity, reduced reactive oxygen species (ROS), and improved subjective hangover symptoms, particularly thirst (Mo et al., 2025). Another study shows that supplementation with *Leu. mesenteroides* EH-1 reduced abdominal fat in mice fed a high-fat diet and modulated metabolic pathways affecting fat metabolism. This

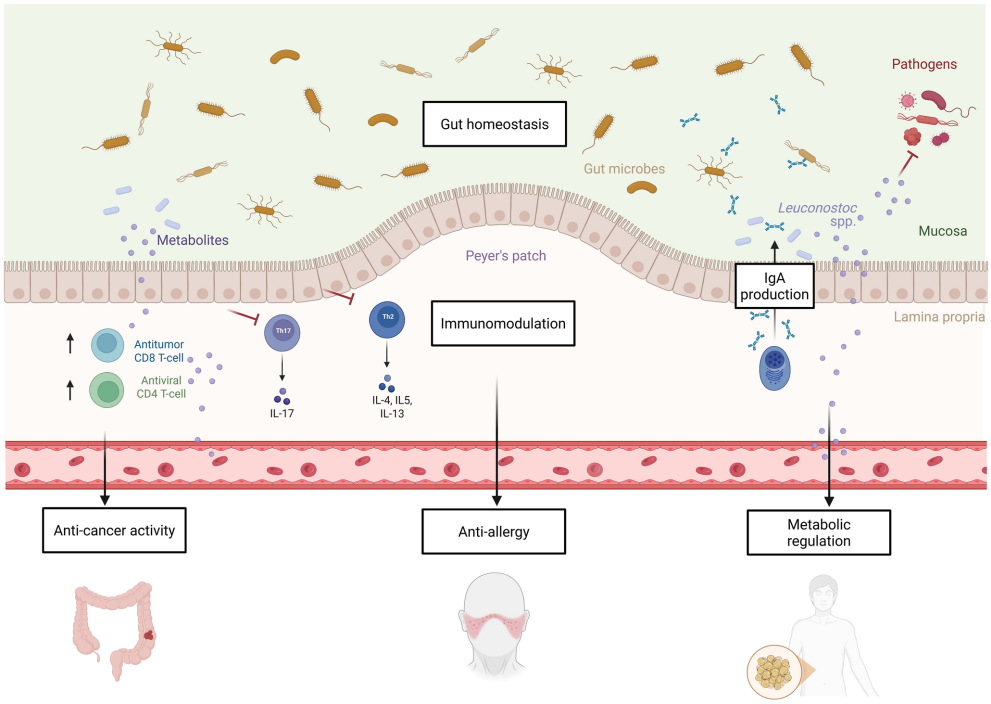

FIGURE 1
The effect of *Leuconostoc* spp. on the host organism. *Leuconostoc* spp. contribute to gut homeostasis through dual modulation of the gut microbiota: Promoting the growth of beneficial commensals while impeding the colonization of pathogenic species. This genus also produces beneficial metabolites with downstream effects on immune function and host metabolism. At the immune level, particular *Leuconostoc* strains have been shown to enhance T-cell activity with antitumor properties, reduce pro-inflammatory cytokine production, and increase IgA secretion — Collectively contributing to observed anticancer and anti-allergy effects. Metabolic effects include the regulation of adipose tissue metabolism and body weight.

effect is attributed to the high amounts of butyric acid produced by this bacterium, which interacts with free fatty acid receptor 2 (Ffar2) (Pham et al., 2022). Similarly, *Leuconostoc citreum* strain isolated from whole crop rice samples has been shown to modulate key pathways involved in adipogenesis and lipogenesis *in vitro*, underscoring its potential as an anti-obesity agent (Han et al., 2023). Interestingly, *Leu. mesenteroides* strain isolated from traditional dairy products in Iran also interferes with immunologic and metabolic pathways involved in colon cancer development, as demonstrated in *in vitro* studies (Zununi Vahed et al., 2017).

Remarkably, *Leuconostoc* bacteria also exhibit antimicrobial and antibiofilm properties. Recent *in vitro* and *in vivo* studies using the *Caenorhabditis elegans* model show that certain *Leuconostoc* strains can protect against pathogenic infections and age-related biomarkers, and exhibit immune and metabolic regulation (Schifano et al., 2021). *Leu. mesenteroides* LVBH107 was shown *in vitro* to inhibit biofilm formation by *Porphyromonas gingivalis*, a common oral pathogen causing periodontitis (Luan et al., 2022). Moreover, *in vitro*, postbiotics derived from *Leu. mesenteroides* J.27 were shown to be effective against pathogens like *Vibrio parahaemolyticus*, *Pseudomonas aeruginosa*, *and Escherichia coli* (Toushik et al., 2022). In yet another study, 5 *Leuconostoc* strains significantly inhibited the growth of *E. coli* and *Listeria monocytogenes,* both *in vitro* and in food matrix (Thangavel and Subramaniyam, 2019).

Overall, these results show that the investigated *Leuconostoc* strains potently modulate the immune system, improve metabolism or combat pathogens effectively. However, other *Leuconostoc* species besides *Leu. mesenteroides* remain underinvestigated. Moreover, studies exploring pleiotropic health effects of a particular strain could also be of interest to explore which *Leuconostoc* strains may have stronger probiotic potential in promoting overall health.

5 Exopolysaccharides from *Leuconostoc*

EPSs are high-molecular-weight polymers synthesized and secreted by microorganisms into their surrounding environment, where they may remain loosely attached to the bacterial cell surface (Wang W. et al., 2023). The structural diversity of these polymers is influenced by factors such as the microbial strain, fermentation conditions, and available substrates (Netrusov et al., 2023). This diversity manifests in variations in monosaccharide composition, charge, and the type of linkages between monomeric units.

The monosaccharides that constitute EPSs include sugars such as glucose, galactose, rhamnose, mannose, fructose, arabinose, and xylose, as well as sugar derivatives like N-acetylgalactosamine and N-acetylglucosamine. These monomers are synthesized by specific enzymes, including glucansucrases and fructansucrases, which catalyze the conversion of sucrose into glucose and fructose, respectively, linking them via glycosidic bonds (Yu et al., 2022).

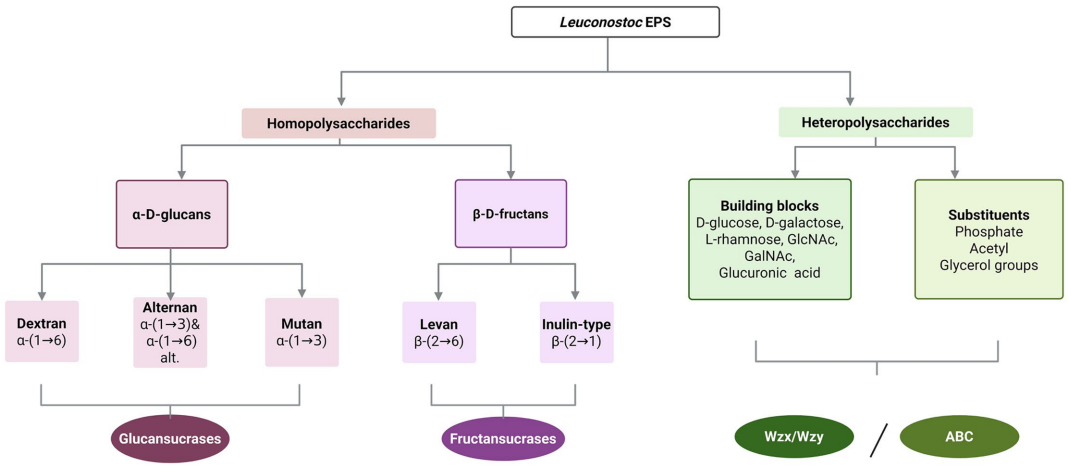

FIGURE 2
Exopolysaccharides produced by *Leuconostoc* spp. *Leuconostoc* species produce two main classes of exopolysaccharides: Homopolysaccharides and heteropolysaccharides. Homopolysaccharides are further divided into α-D-glucans – Encompassing dextran, alternan, and mutan, all synthesized by glucansucrases – and β-D-fructans, which include levan and inulin-type fructans, produced by fructansucrases. Heteropolysaccharides, by contrast, are structurally defined by their specific building blocks and substituents, and are biosynthesized through either the Wzx/Wzy-dependent or ABC-dependent pathway.

EPSs are classified into two main groups: homopolysaccharides (HoPSs) and heteropolysaccharides (HePSs), as shown in Figure 2. HoPSs are composed of repetitive units of a single monosaccharide, categorized as α-D-glucans or β-D-glucans based on their structure. *Leuconostoc* species produce various HoPSs, including α-D-glucans like dextran, mutan, and alternan, and β-D-fructans such as levan and inulin-type polymers. These polymers differ not only in their monosaccharide composition but also in the type of glycosidic linkages. Dextran primarily contains α-(1 → 6) linkages with occasional branching, alternan has alternating α-(1 → 3) and α-(1 → 6) bonds, and mutan has predominantly α-(1 → 3) linkages (Abarquero et al., 2022). Among β-D-fructans, levan has β-(2 → 6) linkages, while inulin-type polymers consist of β-(2 → 1) linkages. These HoPSs are synthesized by specific enzymes, such as glucansucrases for glucans and fructansucrases for fructans, using sucrose as the primary substrate (Meng et al., 2016).

While it was long believed that *Leuconostoc* exclusively produce HoPSs, an increasing number of recent studies show that many *Leuconostoc* strains also synthesize HePSs (Zeidan et al., 2017). However, these HePSs remain poorly characterized and require further investigation (Poulsen et al., 2020). HePSs are composed of 3–8 repeated subunits of monosaccharides, such as D-glucose, D-galactose, and L-rhamnose, along with monosaccharide derivatives like N-acetylglucosamine and N-acetylgalactosamine, glucuronic acid, or substituted monosaccharides containing functional groups such as phosphate, acetyl, or glycerol. Unlike HoPSs, HePSs are synthesized through the Wzx/Wzy-dependent and ABC transporter-dependent pathways and do not rely on sucrose as a substrate (Schmid et al., 2015). A detailed overview of the LAB-EPS biosynthesis pathways is provided in the review by Jurášková et al. (2022).

The EPSs produced by different *Leuconostoc* strains exhibit significant variability in their monosaccharide composition, the ratio of these units, and the nature of the glycosidic linkages and charge characteristics. The structural variability within this genus highlights the significant potential of *Leuconostoc*-derived EPSs, emphasizing the importance of further exploration (Table 1).

6 Functional activity of *Leuconostoc*-EPS

Certain bacterial EPSs exert a range of health-promoting effects (Figure 3) that depend both on the producing species and on detailed structural features of the polysaccharide. In recent years, considerable attention has turned to the biomedical potential of EPSs from LAB (Rahbar Saadat et al., 2019; Liang et al., 2024; Sharma et al., 2024; Jurášková et al., 2022). Within this group, *Leuconostoc* strains are prolific EPS producers, but even among *Leuconostoc*-derived polymers, biological activities can differ dramatically depending on the specific EPS structure.

6.1 Prebiotic activity and gut microbiota regulation

Due to their complex carbohydrate structures, EPSs can be metabolized by commensal gut bacteria capable of fermenting indigestible fibers. As fermentable substrates, these EPSs support the production of SCFAs, which play a key role in maintaining gut health and metabolic balance.

Via cross-feeding, certain *Leuconostoc*-EPSs help modulate the composition of the gut microbiota, favoring health-promoting bacteria while also enhancing SCFA production. α-glucan and dextran from *Leuconostoc*-EPSs have been shown to support the growth of selected beneficial gut bacteria, particularly members of the phylum *Bacteroidetes*, under specific experimental conditions (Kim et al., 2022; Miyamoto et al., 2023; Bisson et al., 2023). For *Leu. mesenteroides* strain B3, the extracted lowly branched dextran not only improved the growth of three probiotic bifidobacteria but was also shown to improve their stress tolerance to oxygen (Bisson et al., 2023). Dextran from *Leu. mesenteroides* SPCL742 investigated in an *in vitro* human fecal fermentation model supported the growth of *Bacteroides* spp. and beneficial bacteria such as *Bifidobacterium* spp., while purified *Leu. mesenteroides*α-glucan produced by *Leu. mesenteroides* NTM048 was shown to influence gut bacterial composition and confer

TABLE 1 Exopolysaccharides (EPSs) from *Leuconostoc*.

Species/strain	Source	EPS	Preparation form	Molecular weight	Structure	Biological application	Refs
Leuconostoc mesenteroides RSG7	Pepino	Dextran	Purified EPS (isolated dextran fraction)	5.47×10^6 Da	α-(1 → 6) glycosidic linkages as backbone and α-(1 → 2), α-(1 → 3), α-(1 → 4), and α-(1 → 6) glycosidic linkages as side chains, honeycomb-like porous structure	Significant promotion for *S. thermophilus*, *B. animalis* ATCC27673, and *B. longum* LTBL16 ➔ prebiotic activity *in vitro* (bacterial growth/ fermentation assay)	Wang B. et al. (2023)
Leuconostoc pseudomesenteroides DRP-5	Homemade wine	Dextran	Purified EPS (isolated dextran fraction)	6.23×10^6 Da	Linear glucan with α-(1 → 6)-linked glucosidic bonds	Antioxidant activity *in vitro* (chemical radical-scavenging assay)	Du et al. (2018)
Leuconostoc pseudomesenteroides YF32	Soy bean paste	Dextran	Purified EPS (isolated dextran fraction)	5.54×10^6 Da	Linear backbone composed of consecutive α-(1 → 6)-linked d-glucopyranose units	n.d.	Yang et al. (2018)
Leuconostoc pseudomesenteroides JF17	Juçara fruit	Dextran	Purified EPS (isolated dextran fraction)	n.d.	α-(1 → 6) unbranched glycosidic chain, porous structure	Antioxidant activity *in vitro* (chemical radical-scavenging assay)	Farinazzo et al. (2020)
Leuconostoc mesenteroides NTM048	Green peas	Dextran	Purified EPS (isolated dextran fraction)	n.d.	Linear, α-(1 → 6)-linked glucose with occasional α(1 → 3) branches, glucose polymers 94% and fructose polymers 6%	Vaccine adjuvant in an *in vivo* mouse model + *in vitro* immune cell assay	Matsuzaki et al. (2017, 2021)
Leuconostoc mesenteroides CM9, CM30 and SM34	Sheep and camel milk	Dextran	Crude EPS	$1–4 \times 10^8$ Da	α-(1,6) linkages, partially branched in the O-3 position	Immunomodulation *in vitro* (macrophage/immune cell line)	Zarour et al. (2017)
Leuconostoc citreum NM105	Manchurian sauerkraut	Dextran	Purified EPS (isolated dextran fraction)	1.01×10^8 Da	Sheet-like smooth glittering and highly branched surface, α-(1 → 6) linkages in the main chain and α-(1 → 2) linkages in branch point	n.d.	Yang et al. (2015)

(Continued)

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TABLE 1 (Continued)

Species/strain	Source	EPS	Preparation form	Molecular weight	Structure	Biological application	Refs
Leuconostoc mesenteroides S81	Fermented sourdough	Levan	Purified EPS (isolated levan fraction)	n.d.	β-(2 → 6)-linked fructan, spheroidal and compact structure	Antioxidant, immunomodulation *in vitro* (chemical radical-scavenging assay + macrophage cell line)	Taylan et al. (2019)
Leuconostoc mesenteroides	Sauerkraut	Dextran	Purified EPS (isolated dextran fraction)	8.79×10^7 Da	Linear with α-(1 → 6) linkages	n.d.	Du et al. (2017)
Leuconostoc mesenteroides KIBGE-IB22	Fermented cabbage	Dextran & levan	Crude EPS (mixed dextran & levan)	$1.5–2.0 \times 10^7$ Da	Small pores, linear glucose chain in α-(1 → 6), with occasional α-(1 → 3) glycosidic bond branches	n.d.	Siddiqui et al. (2014)
Leuconostoc lactis L2	Hami melon	Dextran	Purified EPS (isolated dextran fraction)	3.7×10^6 Da	Linear polymer composed of α-(1 → 6)-linked D-pyranose residue, compact, branched and tubular	n.d.	Zhao et al. (2019)
Leuconostoc mesenteroides P35	French goat cheese	Dextran	Purified EPS (isolated dextran fraction)	$6.7–9.9 \times 10^6$ Da	Branched dextran with a backbone consisting of α-D-Glc*p* (1 → 6) with side chains bound to O-3 positions of 1,3,6-linked α-D-Glc*p*	n.d.	Azari-Anpar et al. (2023)
Leuconostoc mesenteroides HDE−8	Homemade longan fermentation broth	Glucan	Purified EPS (isolated glucan fraction)	1.7×10^6 Da	D − glucose linked by α − (1 → 4) and α − (1 → 6) bonds, irregular sheet−like structure	n.d.	Yang et al. (2024)
Leuconostoc citreum BH10	Birch sap	Dextran	Purified EPS (isolated dextran fraction)	6.34×10^6 Da	Glucose with 90.45% α-(1,6) linkages and 9.55% α-(1,3) branch linkages	n.d.	Ge et al. (2024)

(Continued)

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TABLE 1 (Continued)

Species/strain	Source	EPS	Preparation form	Molecular weight	Structure	Biological application	Refs
Leuconostoc mesenteroides SN-8	Dajiang	Dextran	Purified EPS (isolated dextran fraction)	1.46×10^5 Da	Mainly composed of glucan and also contained certain mannose residues that were found to be connected by α-1,6 glycosidic bonds	Scavenge free radical and anti-cancer activity *in vitro* (chemical radical-scavenging assay + cancer cell line)	Wu et al. (2021)
Leuconostoc mesenteroides subsp. *mesenteroides* LM187	Sichuan paocai	Heteropolysaccharide	Purified EPS (heteropolysaccharide)	7.757×10^5 Da	Mainly composed of glucose. Contained both α-type and β-type glycosidic bonds. Contained arabinose, galactose, and rhamnose, but less uronic acid. EPS displayed a large number of scattered, fluffy, porous cellular network flake structures.	Good acid resistance, bile salt resistance, cholesterol-lowering properties and anti-oxidant activity *in vitro* (simulated gastric/bile digestion assay + chemical radical-scavenging assay)	Zhang et al. (2021)
Leuconostoc mesenteroides 201,607 (LM)	Fermented food	Heteropolysaccharide	Purified EPS (heteropolysaccharide)	n.d.	Glucose (57.1%), rhamnose (29.53%), and galactose (13.36%)	Immunomodulation *in vitro* (macrophage cell line)	Vijayalakshmi et al. (2024)
Leuconostoc citreum N21	Dried milk cake	Dextran	Purified EPS (isolated dextran fraction)	6.07×10^6 Da	Composed of D-glucopyranose units in a linear chain with consecutive α (1 → 6) linkages. No branching was found in the structure of the EPS	n.d.	Yang et al. (2019)
Leuconostoc mesenteroides subsp. *cremoris*	Dairy products	n.d.	Crude EPS	1.71×10^4 Da	Mannose as a major component	Antibacterial and immunostimulator properties and are nontoxic with medicinal importance *in vitro* (antimicrobial MIC/disc-diffusion assay)	Mahdi et al. (2019)

(Continued)

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TABLE 1 (Continued)

Species/strain	Source	EPS	Preparation form	Molecular weight	Structure	Biological application	Refs
Leuconostoc pseudomesenteroides R2	Cabbage	Dextran	Purified EPS (isolated dextran fraction)	n.d.	Linear dextran α polysaccharides (1 → 6)	n.d.	Paulo et al. (2012)
Leuconostoc mesenteroides RM45, RM47, RM48, RM49, and RM70,	Spanish grape must and wine	Glucan	Isolated glucan fraction	n.d.	n.d.	n.d.	Montersino et al. (2008)
Leuconostoc mesenteroides RM43, RM44, RM50, RM51, RM52, RM53, RM54, RM55, RM60, and RM61		Fructan	Isolated fructan (levan) fraction	n.d.	n.d.	n.d.	

beneficial metabolic effects *in vivo* in mice (Kim et al., 2022; Miyamoto et al., 2023).

These findings suggest that certain *Leuconostoc*-derived EPSs may have prebiotic potential. Evidence demonstrating selective utilization and associated health benefits is always required to establish their prebiotic activity. Another study showed that purified dextran derived from *Leu. pseudomesenteroides* XG5 stimulated the growth of lactobacilli and *Bifidobacterium,* as well as SCFA production (Pan et al., 2020). It also showed a general shift in the *Firmicutes*/*Bacteroidetes* ratio (in accordance with the current bacterial taxonomy: *Bacillota*/*Bacteroidota* ratio), increasing the relative abundance of *Firmicutes* (current taxonomy: *Bacillota*) in male C57BL/6 J mice. The same was observed in non-obese diabetic (NOD) mice, where purified dextran derived from this particular strain not only altered the gut microbiota composition, but also increased SCFA levels (Pan et al., 2021). LM742 dextran isolated from *Leu. mesenteroides* SPCL742 also increased the concentration of SCFAs and pantothenate (Kim et al., 2022). Pantothenate, again, is known to support the growth of lactobacilli, *Prevotella* and *Actinobacteria* (current taxonomy: *Actinomycetota*) (Yao et al., 2018; Carrothers et al., 2015).

These results also show that specific EPS supplementation can activate a chain of beneficial gut microbiota regulation relevant for gut homeostasis.

Though these studies do not provide deeper insights into the structure–function relationship in the context of EPS activity, other studies provide possible explanations. One of them is that high amounts of 1 → 4 branches within EPS and longer chain length usually exhibit higher viscosity, which may protect the producing bacteria better from external stressors (Zhang et al., 2024). This allows *Leuconostoc* strains to reach the gut safely, which could promote the growth of SCFA-producing bacteria due to the high lactic acid production, which serves as a substrate. Other studies found that mainly α-(1 → 2) branches, (1 → 3), (1 → 6), and (3 → 6) glycosidic bonds in EPS produced by *Leuconostoc* are collectively responsible for modulating the gut microbiota, with the degree of branching and linkage type influencing the selectivity of fermentation by beneficial bacteria (Yoshida et al., 2026; Jurášková et al., 2025; Kim et al., 2022; Miyamoto et al., 2023; Gu et al., 2024).

6.2 Antimicrobial and antibiofilm properties

Individual EPSs not only promote the proliferation of beneficial bacteria within the gut microbiota but have also been shown to significantly reduce the abundance of pathogenic species, contributing to the overall stability and resilience of the microbial ecosystem. This is particularly significant, given that the human microbiota constitutes a critical component of the host's first line of defense against enteric pathogen colonization, primarily through mechanisms of competitive exclusion that hinder pathogen adhesion to epithelial surfaces and subsequent invasion. Additionally, specific EPSs have antibiofilm properties, disrupting the biofilm matrix and inhibiting the adherence of pathogens to biotic and abiotic surfaces.

Among the various microbial products, certain EPSs produced by *Leuconostoc* species have demonstrated notable antimicrobial activity against several pathogenic bacteria, but also antiviral activity against Human Adenovirus Type 5 (Vijayalakshmi et al., 2024; Biliavska et al., 2019, 5). For instance, partially purified EPS derived from *Leu. mesenteroides* 201607 was shown to inhibit the growth of several common pathogens like *Salmonella enterica*, *Staphylococcus aureus* and *E. coli*

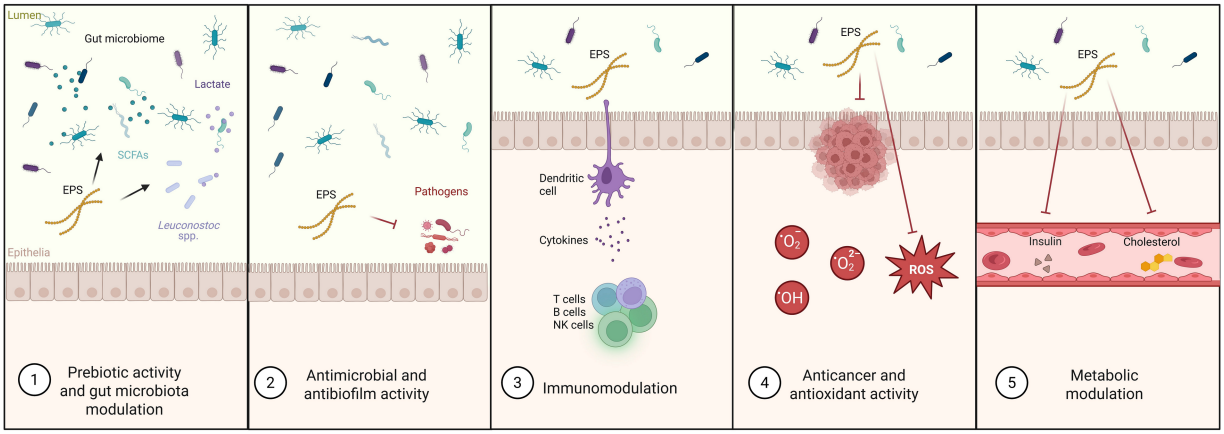

FIGURE 3
Bioactivity of *Leuconostoc*-EPSs (exopolysaccharides). Certain *Leuconostoc*-EPSs exert pleiotropic effects across multiple host and microbial axes. At the microbiota level, they function as prebiotics by serving as substrates for beneficial gut residents, promote the survival/persistence of *Leuconostoc* spp., and stimulate lactate production, which is subsequently converted to short-chain fatty acids (SCFAs) by commensal bacteria. Beyond microbiota modulation, particular *Leuconostoc*-EPSs display direct antimicrobial and antibiofilm activity, as well as immunomodulatory effects via cytokine regulation and immune cell activation. Additional bioactivities may include anticancer and antioxidant properties, and metabolic regulation through the modulation of glucose and lipid metabolism.

(Vijayalakshmi et al., 2024). Another EPS, also purified from the species *Leu. mesenteroides* (strain B3), decreased the growth of the same gastric pathogens and of others, such as *Enterococcus faecium* and *Lis. monocytogenes* and inhibited biofilm formation by *Lis. monocytogenes* (Bisson et al., 2023). Antibiofilm activity of purified EPS from *Leu. citreum* BH10 was also found to be effective against *S. aureus* biofilm (Ge et al., 2023). Moreover, both crude and purified EPS from *Leu. mesenteroides* subsp. *cremoris* were found to be effective against multidrug-resistant *Burkholderia cepacia* strains (Mahdi et al., 2019). Interestingly, that study also showed that this effect was stronger for purified EPS than crude.

There are several proposed mechanisms of EPS that could be responsible for its antibacterial, antiviral and antibiofilm activity. Regarding the first, several studies suggest that specific EPSs could disrupt the structure of the bacterial cell wall or cell membrane and that they could also impede cell division by affecting the respiratory chain or DNA degradation (Hasheminya and Dehghannya, 2020; Wu et al., 2010; Abdalla et al., 2021). It is also speculated that particular EPSs interact with bacterial cell wall components that are necessary for cell communication and biofilm formation (Spanò et al., 2016). Regarding antiviral activity, certain EPSs could affect viral infectivity at several stages, including the adsorption and penetration stage, but also in the stage of reproduction (Yang et al., 2017). Additionally, the immunostimulatory activity of EPS may also play a role in its antiviral activity.

When it comes to the responsible structural components, previous studies on LAB-EPS proposed (1 → 4) bonds and thus high viscosity to play a key role in antibacterial activity, as these functional groups can donate more lone pair electrons, strengthen hydrogen bonding between EPS molecules, and give the EPS high viscosity and other physical properties (Zhang et al., 2024). However, the main features of purified EPS_B3 dextran mixture from a *Leu. mesenteroides* strain with antibacterial and antibiofilm activity described by Bisson et al. (2023) are high molecular weight and a low branching degree. Differences in individual EPS structures and properties could therefore contribute to their different activities against specific pathogens.

6.3 Immunomodulatory effects

Exopolysaccharides (EPSs) produced by *Leuconostoc* species are increasingly recognized for their potential immunomodulatory properties. Certain EPSs can interact with the host immune system, influencing responses such as cytokine production and immune cell activation, thereby contributing to the regulation of immune-related conditions.

For instance, purified EPS derived from *Leu. pseudomesenteroides* XG5 was found to reduce interleukin (IL)-21 and enhance the population of T regulatory (T_{reg}) cells in NOD mice, through the modulation of the gut microbiota (Pan et al., 2021). This resulted in the delayed onset of immune diabetes. In another study, the *in vitro* effect of purified EPS from *Leu. mesenteroides* NTM048 on Peyer's patch cells and splenocytes showed an increase in antigen-specific IgA and modulation of T helper cell type (Th) 1 and 2 (Matsuzaki et al., 2015). EPS from the same strain was also shown to induce IL-6, IL-10 and IL-12 and expression of retinoic acid-related genes in bone marrow-derived dendritic cells (DCs) (Matsuzaki et al., 2018). Moreover, partially purified EPS from *Leu. mesenteroides* 201607 decreased proinflammatory cytokines and increased anti-inflammatory cytokines in murine macrophage RAW264.7 cells (Vijayalakshmi et al., 2024). These findings suggest that specific EPSs not only reinforce gut mucosal immunity but also promote broader systemic immune responses.

Interestingly, a study comparing EPS produced by *Leu. mesenteroides* NTM048 with an enzymatically synthesized variant showed that the latter had a larger impact on the immune system, specifically in terms of mucosal and systemic antibody production to ovalbumin both *in vitro* and *in vivo* in mice (Matsuzaki et al., 2021). Moreover, enzymatically synthesized levan, originally produced by this strain, contributes to this immunomodulatory effect but cannot replicate the same level of mucosal IgA stimulation on its own (Ishida et al., 2016). Thus, it seems that several components of HoPSs contribute synergistically to the observed immunomodulatory effects.

The main mechanism by which specific EPSs appear to modulate the immune system is by interacting with toll-like receptors (TLRs), which can either suppress or stimulate the production of proinflammatory cytokines. This effect was observed for β-(2,1)-fructans and β-(2,6)-type

fructans, which exhibited different effects depending on the type of TLRs (Akkerman et al., 2024; Oerlemans et al., 2021). When it comes to immunostimulation, there also seems to be an impact of the molecular weight of levan-type β-(2,6)-fructans, as higher molecular weight contributed to greater TLR stimulation (Akkerman et al., 2024). The same study also suggests that the length of the molecule matters, as longer molecules may have a reduced ability to bind to the ligand binding site, which could, in turn, lead to lower immune stimulation. Longer chain length of β2 → 1-fructans was also shown to be less potent in modulating the cytokine response (Vogt et al., 2013). Though β-(2,6)-fructans are also able to inhibit certain types of TLRs, such as TLR5, there is no established relationship between their molecular weight and inhibitory effect. When it comes to *Leuconostoc*-EPSs, studies elucidating the particular underlying pathway of immunomodulation are scarce. However, regarding the structural characteristics of immunomodulatory NTM048 EPS, its size ranges from 10 to 40 kDa and is mainly composed of glucose and fructose, which could be responsible for its immunomodulatory activity (Matsuzaki et al., 2015; Oerlemans et al., 2021). Moreover, in a study investigating the immunoactive compounds of *Leu. mesenteroides* NTM048 EPS, it seemed that larger EPS fragments or whole glucans are essential for immune receptor recognition, rather than smaller fragments containing mainly glycan linkages (Inuki et al., 2022).

These studies suggest that by modulating inflammatory pathways, specific EPSs might enhance the effectiveness of pathogen-related immune response, as well as mitigate chronic inflammatory disorders. Though there seems to be a relationship between immunomodulating activity and the molecular weight and type of EPS, more studies are still required to explore the immunomodulating activity of particular EPS compounds produced by other less-investigated *Leuconostoc* strains.

6.4 Antioxidant and anticancer properties

Certain EPSs from *Leuconostoc* exhibit antioxidant potential by scavenging reactive oxygen species (ROS) and reducing oxidative stress. This activity is attributed to the presence of functional groups, such as hydroxyl groups, in the EPS structure. Antioxidant activity has been linked to the prevention of chronic diseases, including cardiovascular disease and neurodegenerative disorders, as well as suppressing tumor growth.

Antioxidant activity was found for several different *Leuconostoc* strains. For instance, the high molecular weight dextran produced by *Leu. mesenteroides* SN-8, and purified, with α- (1 → 6) glycosidic linkages, showed a scavenging rate of 32% for hydroxyl radicals and 40% for 1,1-diphenyl-2-picrylhydrazyl (DPPH) (Li et al., 2020). *Leu. mesenteroides* 201,607-EPS, partially purified, also exhibited levels of 52.43% and 44.58% for DPPH and 2,2-azino-*bis*-3-ethylbenzothiazoline-6-sulphonic acid (ABTS), respectively (Vijayalakshmi et al., 2024). Purified *Leu. pseudomesenteroides* DRP-5 dextran showed increasing scavenging activity with elevated concentrations for hydroxyl radicals superoxide anion radicals, ABTS radicals, Fe^{2+} and Fe^{3+} (Du et al., 2018). A highly branched EPS produced by *Leu. citreum* B-2 and purified could scavenge up to 98.39% for hydroxyl radicals at a concentration of 15 mg/mL, while it also removed high amounts of ABTS and DPPH, in a concentration-dependent fashion (Li et al., 2020). The same trend was observed for purified *Leu. mesenteroides* LM187-EPS, where around 50% of DPPH was scavenged with a concentration of 5 mg/mL, while hydroxyl radical scavenging activity was up to 71% (Zhang et al., 2021). The authors explain the higher scavenging activity of EPS against hydroxyl radicals through the inhibition of their formation, primarily by chelating Fe^{2+} or Cu^{+} ions, potent pro-oxidants that play key roles in catalytic oxidation reactions. The antioxidant activity of *Leuconostoc*-produced specific EPSs is mainly related to their functional groups rather than to a specific glycosidic bond. These EPSs are mainly dextrans with an α-(1 → 6)-linked glucopyranose backbone, and their antioxidant activity has been associated with hydroxyl and carboxyl groups (Wu et al., 2021; Liu et al., 2024). In *Leu. citreum* 1.2461, purified EPS (EPS-1) protected cells from oxidative damage, with higher hydroxyl group content linked to greater ABTS scavenging activity (Li Y. et al., 2022). The monosaccharide composition, particularly the presence of glucuronic acid, may also contribute to the antioxidant activity of *Leu. mesenteroides* EPS, as suggested for the EPS isolated from *Leu. mesenteroides*-induced soybean protein isolate gel (Yang et al., 2021).

Emerging research also suggests that certain *Leuconostoc* EPSs may have a potent antitumor activity *in vitro*, which may be primarily attributed to their antioxidant activity. For instance, isolated dextran from *Leu. mesenteroides* B-1149 inhibited the growth of cervical cancer (HeLa) and colon cancer (HT29) cell lines by 25% and 40%, respectively, while increasing the growth of murine macrophage J774A.1 cells, suggesting preliminary selectivity toward cancer cells and low cytotoxicity toward the tested non-cancerous cells (Shukla and Iliev, 2014). In another study, purified EPS-8-2 extracted from *Leu. mesenteroides* displayed significant *in vitro* antioxidant activity and inhibitory potential on the growth of HepG2 tumor cells by promoting apoptosis and induced cell cycle arrest in G1 and G2 phases (Wu et al., 2021). However, the study evaluated only HepG2 cells and did not assess cytotoxicity toward normal cells or cancer-cell selectivity. Anticancer activity and preliminary cancer-cell selectivity was reported for purified EPSs from *Leu. citreum* S3 and *Leuconostoc holzaapfelii* S8 against Caco-2 colorectal cancer cells, with lower cytotoxicity observed toward normal fetal lung fibroblasts (MRC-5) (Khider et al., 2022). As current evidence is based solely on *in vitro* studies, further research is needed to validate the potential antitumor activity of EPS through complementary *in vitro* and preclinical studies, with particular emphasis on establishing cancer-cell selectivity, elucidating the underlying mechanisms of action, and evaluating antitumor efficacy *in vivo*.

6.5 Metabolic and cardiovascular health

Several studies have reported that particular *Leuconostoc* EPSs reduce cholesterol levels and balance glucose levels *in vitro* and in animal models. If confirmed in clinical trials, these effects may contribute to the prevention of cardiovascular disease and metabolic diseases such as type 2 diabetes.

For instance, an exopolysaccharide (LmEPS) produced by *Leu. mesenteroides* was purified and shown to improve glucose homeostasis and enhance glucagon-like peptide 1 (GLP-1) and insulin secretion, effects associated with increased gut microbial production of SCFAs and activation of SCFA receptors (Miyamoto et al., 2023). Thus, LmEPS may indirectly regulate host energy metabolism by promoting SCFA production, which can subsequently modulate host signaling pathways. These findings suggest that the prebiotic and metabolic effects of this EPS may act synergistically to support host metabolism. Interestingly, the glucose units of this EPS were mainly joined by α-1,6 linkages and branches formed via α-1,3 bonds, and previous studies drew a connection between hypoglycemic effects and (1 → 3), (1 → 4), and (1 → 6) glycosidic bonds of polysaccharides (Ji et al., 2024).

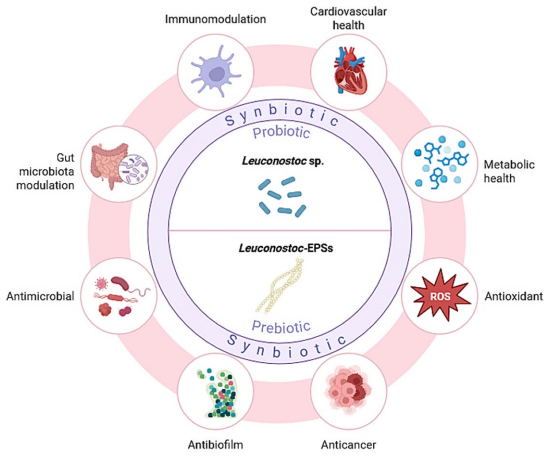

FIGURE 4
Proposed synbiotic rationale for *Leuconostoc* probiotics and their exopolysaccharides (EPSs). Schematic representation of the complementary bioactivities of *Leuconostoc* strains and their EPSs as potential probiotic and prebiotic components, respectively, highlighting their roles in immunomodulation, gut microbiota modulation, cardiovascular and metabolic health, antimicrobial and antibiofilm activity, anticancer potential, and antioxidant protection.

However, specific *Leuconostoc*-EPSs not only affect sugar metabolism but also fat metabolism. *In vitro* studies show that different *Leu. mesenteroides* strains releasing EPSs lower over 50% of cholesterol. This was shown for the released exopolysaccharide (rEPS)-producing strain *Leu. mesenteroides* LM187 and *Leu. mesenteroides* MKSR, which exhibited cholesterol-lowering rates of 53% and 59%, respectively (Zhang et al., 2021; Lee and Kim, 2019). One of the mechanisms by which EPSs are proposed to exert cholesterol-lowering activity involves their functional groups, such as carboxyl groups, which influence both their physicochemical properties and biological interactions (Zhang et al., 2024). These groups can bind bile acids in the intestine, preventing their reabsorption. Since bile acids are synthesized from cholesterol in the liver, their increased excretion prompts the liver to convert more cholesterol into bile acids, thereby lowering blood cholesterol levels. Additionally, the high viscosity of EPS can slow down intestinal absorption of cholesterol and dietary fats. Certain EPSs may also modulate the gut microbiota, promoting the growth of beneficial bacteria that convert cholesterol into coprostanol, which is more easily eliminated from the body (Kriaa et al., 2019). Stimulating SCFA production is another way in which cholesterol levels may be reduced (Nguyen et al., 2024).

7 Research gaps and future perspectives

Despite the growing body of evidence on *Leuconostoc*-EPS bioactivity, several critical research gaps remain. First, EPS from *Leuconostoc*, especially HePSs, remain poorly characterized in terms of both structure and bioactivity. Given the structural complexity and functional diversity of HePSs in other LAB genera (Ouarabi et al., 2025), systematic investigation of *Leuconostoc*-derived HePSs represents an important research gap. Second, other properties, such as molecular weight, are missing for many strains, which undermines cross-study comparisons and structure–activity extrapolations. Standardized reporting of molecular weight, branching degree, and glycosidic linkage composition should be adopted as a minimum dataset in future EPS characterization studies. Third, most bioactivity data are derived from *Leu. mesenteroides*, while the bioactive potential of *Leu. citreum*, *Leu. pseudomesenteroides*, and other *Leuconostoc* species and their EPSs remains largely unexplored. Fourth, although conflicting evidence exists regarding the relationships between EPS molecular weight, branching degree, sugar composition, and bioactivity, both high- and low-molecular-weight fractions, as well as homo- and heteropolysaccharides, have been reported to exhibit bioactivity. These relationships remain difficult to resolve because of substantial differences in EPS isolation and purification procedures, structural characterization, and bioactivity assays across studies. Moreover, no systematic structure–function studies have directly addressed these relationships in *Leuconostoc*-derived EPS. Standardized approaches are therefore needed to determine how specific structural features of *Leuconostoc* EPS contribute to their biological activity. Finally, the vast majority of current evidence is derived from *in vitro* experiments and animal models. Well-designed human clinical studies are therefore required to validate the therapeutic relevance of *Leuconostoc* strains and their EPSs and to support their development as evidence-based microbiome-targeted interventions. Given the broad biological activities reported for numerous *Leuconostoc* strains and *Leuconostoc*-derived EPSs (see Figure 4), future studies determining whether combining a *Leuconostoc* strain with its native or a heterologous EPS confers health benefits beyond those of the individual components would be of great value. Based on current evidence, such combinations would be most appropriately considered potential complementary synbiotics rather than synergistic synbiotics, unless selective utilization of the EPS by the co-administered strain and a concomitant health benefit are demonstrated (Swanson et al., 2020). Thus, the contributions of EPS to bacterial survival, gut microbiota modulation, and direct host bioactivity should be evaluated separately next to the probiotic characterization of the strain. Direct comparisons of native and heterologous strain-EPS pairings, alongside their individual components, could establish whether strain-EPS specificity provides an additional functional benefit. However, the future clinical translation of EPSs will critically depend on the development of robust standardization frameworks, enabling reproducible structural characterization, batch-to-batch consistency, and the establishment of quantitative bioactivity metrics necessary for their clinical evaluation.

8 Conclusion

Current studies highlight the significant potential of both *Leuconostoc* strains and their EPSs in addressing complex health conditions associated with gut microbiota dysregulation, immune imbalance, and metabolic disorders. Given that specific *Leuconostoc* strains exert distinct health-promoting effects and that certain EPSs exhibit beneficial bioactivity in isolation, the evidence reviewed here supports our proposal on the interesting potential of intentionally pairing a *Leuconostoc* strain with its own or an EPS from another species which may constitute a more targeted complementary synbiotic strategy than conventional probiotic formulations. However, to translate this potential into practice requires further validation in human studies, as most studies to date have been conducted *in vitro* or in animal models. Furthermore, EPS should be characterized more consistently across

studies, not only by type, but with respect to monosaccharide composition, molecular weight, and branching patterns. This way, clearer structure–function relationships can be established. Future research should also explore underexplored *Leuconostoc* strains and the biological activities of their EPSs, which may yield candidates with broad or highly targeted health benefits. A deeper understanding of these relationships will ultimately be essential for translating the structure-informed synbiotic perspective proposed here into rational, evidence-based interventions.

Author contributions

JK: Visualization, Conceptualization, Writing – review & editing, Writing – original draft. OK: Visualization, Writing – review & editing. MK: Funding acquisition, Writing – review & editing, Supervision.

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Conflict of interest

The author(s) declared that this work was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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