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REVIEW PAPER

Health promoting benefits of postbiotics produced by lactic acid bacteria: Exopolysaccharide

Yekta Gezginç[1]*, Tuğba Karabekmez Erdem[2], Hazel Dilşad Tatar[1], Sermet Ayman[1], Eda Ganiyusufoğlu[3], K. Sinan Dayısoylu[1]*

[1]Department of Food Engineering, Faculty of Engineering and Architecture, University of Kahramanmaraş Sütçü İmam, Dulkadiroğlu 46100, Kahramanmaraş, Türkiye.
[2]Department of Food Proccessing, Vocational School of Technical Sciences, University of Kahramanmaraş Sütcü Imam, Dulkadiroğlu 46100, Kahramanmaraş, Türkiye.
[3]Department of Nutrition and Dietetics, Faculty of Health Sciences, University of Kahramanmaraş Sütcü Imam, Dulkadiroğlu 46100, Kahramanmaraş, Türkiye.

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Corresponding Author
Tel.: +90 344 280 2089
E-mail: yekgan@ksu.edu.tr

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Abstract

Exopolysaccharides are high molecular weight polymers of repeated sugar units with diverse chemical structure and unique properties and produced by microorganisms. Lactic acid bacteria are important exopolysaccharide producers. Lactic acid bacteria derived exopolysaccharides, one of the postbiotics, are known to have technological properties such as stabilizing, thickening, emulsifing and also biological activities. Lactic acid bacteria can synthesis exopolysaccharides with large structural variability and this diversity brings these polymers to possess several bioactivities. Bioactivities such as immunomodulatory, antiinflammatory, antitumor and antimutagenicity, antioxidant, antibacterial and antiviral, cholesterol-lowering, antihypertensive activity and gastro-protective activity bring these biopolymers commercial value in the global market and potential to be used in biomedical and pharmaceutical applications. Therefore, to evaluate the availability of these natural exopolysaccharides for new applications extensive understanding of the structure-function relationships will be required. In this review, it is presented a comprehensive overview for the most recent reports on the health benefits of postbiotic lactic acid bacterial exopolysaccharides.

Introduction

Exopolysaccharides (EPSs) are high molecular weight and long chain polymers composed of branched, repeating units of sugars or sugar derivatives. They are surrounding the envelope of most bacteria and are mainly involved in cell adhesion and protection (Sanlibaba & Çakmak, 2016; Taylan et al., 2019; Noroozi et al., 2021). EPS has been widely produced by lactic acid bacteria (LAB). The most noticeable EPS producing LABs are *Lactobacillus, Leuconostoc, Weissella, Lactococcus, Streptococcus, Pediococcus* and *Bifidobacterium* spp. Microbial EPS can be divided into two groups according to their chemical composition: homopolysaccharides (HoPs) which contain a single type of monosaccharides; cellulose, dextran, pullulan, levan, curdlan, etc. and heteropolysaccharides (HePs) which comprise repeating units of different monosaccharides, gellan, galactan, xanthan, kefiran etc. (Laws et al., 2001; Ruas-Madiedo & De Los Reyes-Gavilán, 2005; Chaisuwan et al., 2020; Kavitake et al., 2020).

EPSs can be used in a variety of industrial fields, including biomedical, wastewater treatment, cosmetic, textile, food, and pharmaceutical applications, and are responsible for physicochemical modifications. EPSs mostly serve as stabilizing, thickening, emulsifing agents

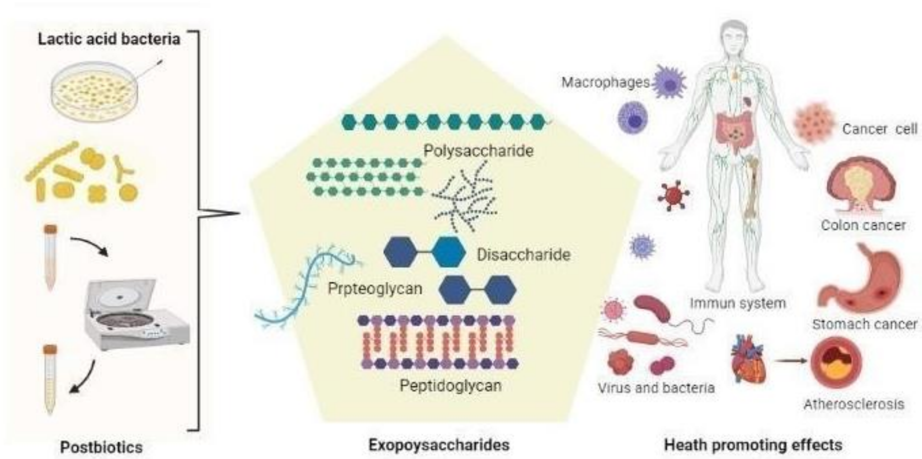

Figure 1. The representation of the health promoting effects of exopolysaccharides, a postbiotic produced by lactic acid bacteria.

and particularly in food industry, it contributes to unique important qualities such as the advanced viscosity and rheology, sensory quality, extended shelf-life, etc. Beside these physicochemical properties, it has been already shown that LAB produced EPSs have numerous physiological functions and potential health benefits (Figure 1). EPS bioactivities are influenced by different factors such as molecular weight, constituent sugars, conformation, glycosidic linkage, and degree of branching (Kumar et al., 2020; Rana & Upadhyay, 2020). The molecule binding and penetration may be related to the size or molecular weight. Lower weight average molecular weight EPS may have stronger binding ability to cell receptors and may penetrate more easily into a cell with better bioactivities than larger weight average molecular weight EPS (Li & Shah, 2016).

The bioactivities of EPS were similarly altered by monosaccharides in their structure. Immunomodulatory activities were observed in EPS fractions isolated from *Lactobacillus reuteri* Mh-001. The antiinflammatory properties of these EPS were regulated by the monosaccharide percentages. For macrophages, the EPS fraction with the highest quantity of galactose had the best antiinflammatory efficacy (Chen et al., 2019). The sugar compositions could be linked to receptor recognition on the immune cell surface (Ren et al., 2016). Sulfate groups (number and position) are also the most important parameters regulating the bioactivities of sulfated EPS. Besides, biological, physical, chemical and biomolecular modifications were reported which can be used to improve the biological activities of microbial EPS (Korcz et al., 2018; Chaisuwan et al., 2020; Schilling et al., 2020).

EPS produced by LAB, including probiotic LAB, has been chosen for a variety of applications due to their biological activity *in vitro* and *in vivo*. Probiotics are living microorganisms that, when ingested in sufficient quantities, have a beneficial effect on the host. Probiotics must be able to grow and persist in the human intestine in order to provide health benefits. The current definition of a probiotic requires that it be alive; thus, it does not apply to dead bacterial cells or cell components. However, recently it is stated that the positive effects of probiotics on health are not only caused by microorganisms but also by the metabolites they produce (Thantsha et al., 2012; Perricone et al., 2014). So, the term 'postbiotic' was invented to describe the health benefits of probiotics that go beyond their inherent viability, adding a new aspect to the probiotic concept (Abbasi et al., 2021). 'Postbiotic' refers to inactivated microbial cells (dead cells), cell fractions; peptidoglycans, polysaccharides, cell surface proteins, teichoic acids or short-chain fatty acids (SCFAs), enzymes, bacteriocins, and organic acids which are also called 'cell-free supernatant (CFS)' made by live cells through the fermentation process. EPSs are also naturally made by live probiotic cells. They can have a variety of physiological health-promoting effects on the consumer if consumed in sufficient quantities (Teame et al., 2020).

Fermented foods can contain probiotic LAB and LAB-derived EPSs with prebiotic attributes which may promote beneficial bacteria to colonize in the gut (Zhou et al., 2019). The production of biofilm by microorganisms induces colonization and ensures population maintenance in the difficult environment of the human gastrointestinal tract (GIT). It has been demonstrated that attaching probiotic LAB to epithelial cells in the GIT prevents pathogenic organism colonization, stimulates the host immune system, and protects epithelial cells from toxic substances (Jurášková et al., 2022). Furthermore, LAB-derived EPS can avoid infectious illnesses by reducing or inhibiting pathogenic bacteria from forming biofilms.

Prebiotics, paraprobiotics and postbiotics have a number of therapeutic properties, including immunomodulatory, antiinflammatory, antigastrointestinal, antiadhesion, antibiofilm, antiviral, antihypertensive, hypocholesterolemic, antiproliferative, antioxidant, and etc. (Teame et al., 2020; Abbasi et al., 2021) (Table 1) (Figure 2).

This article reviews current scientific findings on the beneficial effects of LAB produced EPS as postbiotics, with an emphasis on their health-promoting properties.

Table 1. Biological activities of EPS producing lactic acid bacteria species

LAB Species	Polysaccharide	Biological Acivity	Reference
Lactobacillus plantarum ZDY2013	Sulfated EPS	Antioxidant	Zhang et al., 2016
Lactobacillus plantarum L-14	EPS	Antiinflammatory	Kwon et al., 2020
Lactobacillus plantarum RJF4	EPS	Antioxidant, cholesterol lowering, antiproliferative	Dilna et al., 2015
Lactobacillus plantarum RJF4	EPS	Antiproliferative, antioxidant	Dilna et al., 2015
Lactobacillus plantarum LRCC5310	EPS	Antiviral	Kim et al., 2018
Lactobacillus plantarum SKT109	EPS	Antioxidant	Wang et al., 2018
Lactobacillus plantarum, *Lactobacillus casei*	EPS	Antitumor	Deepak et al., 2016a
Lactobacillus casei 01	EPS	Antiproliferative	Liu et al., 2011
Lactobacillus kefiranofaciens DN1	HePS (Man, Ara, Glc, Gal, Rha)	Antibacterial	Jeong et al., 2017
Lactobacillus kefiranofaciens DN1	EPS	Antibacterial	Jeong et al., 2017
Lactobacillus kefiranofaciens	Kefiran	Cholesterol lowering	Maeda et al., 2004
Lactobacillus kefiranofaciens	Kefiran	Antiinflammatory	Furuno & Nakanishi, 2012
Lactobacillus reuteri Mh-001	EPS fraction containing a high amount of galactose	Immunomodulatory	Chen et al., 2019
Lactobacillus reuteri DSM17938, *Lactobacillus reuteri* L26	EPS	Antigastrointestinal	Kšonžeková et al., 2016
Lactobacillus delbureckii	EPS	Antibacterial	Adebayo-Tayo & Fashogbon, 2020
Lactobacillus delbrueckii subsp. *bulgaricus*	HePS (Gal and Glc)	Antioxidant	Tang et al., 2017
Lactobacillus sanfranciscensis	EPS	Antioxidant	Zhang et al., 2019
Lactobacillus acidophilus	EPS	Antioxidant	Deepak et al., 2016b
Lactobacillus helveticus MB2-1	Cell-bound HePS (Glc, Man, Gal, Rha, Ara)	Anticancer	Li et al., 2015
Streptococcus thermophilus ASCC 1275	Sulfated EPS	Antiinflammatory	Li & Shah, 2016
Streptococcus thermophilus AR333	Polysaccharide	Immunoregulatory	Ren et al., 2016
Streptococcus mutans MTCC 497	EPS	Antiinflammatory	Buddana et al., 2015
Weissella confusa	Dextran	Antifungal	Adesulu-Dahunsi et al., 2018
Weisella confusa	HePS (Gal, Man, Glc, Fru, Rha, Ara, Xyl, Rib)	Antioxidant, immunomodulatory	Adebayo-Tayo et al., 2018
Weissella cibaria 27 (W27)	EPS	Antibacterial	Yu et al., 2018
Leuconostoc mesenteroides S81	HoPS	Antiinflammatory	Taylan et al., 2019
Leuconostoc pseudomesenteroides YB-2	Dextran	Antibacterial	Ye et al., 2019
Pediococcus acidilactici NCDC *252*	EPS	Antioxidant, anticancer	Kumar et al., 2020

Immunomodulatory activities

An immunomodulatory effect of LAB may be attributed to postbiotics; such as exopolysaccharides. EPS have good immunomodulatory and immune-protective functions. Immune stimulating activities of EPS have been already studied both *in vitro* and *in vivo.* Immunomodulator mechanisms may be interconnected to gut microbiota. Most EPS can enhance the diversity and balance of microorganisms in the gut by promoting the growth of the intestinal microbiota. Several EPS derived from LAB, such as *Lactobacillus plantarum*, *Pediococcus pentosaceus, Weissella cibaria,* and *Weissella confusa*, showed prebiotic characteristics and could encourage the growth of a probiotic strain, *Bifidobacterium bifidum* DSM 20456, *in vitro* (Chaisuwan et al., 2020). It was reported that EPS molecules can prevent gastrointestinal tract cancers, inhibit infections, and immunodeficiency induced diseases, such as inflammatory bowel diseases. Two patterns have been proposed to explain EPSs' immunomodulatory capability. Firstly, acidic HePs with phosphate in their composition are good stimulators of the immune response. Secondly, to strengthen the first lines of defense, the mucosal immune system is triggered by increasing host immunoglobulin A (IgA) secretion (Saadat et al., 2019).

Levan (S81), a HoP from *Leuconostoc mesenteroides* S81, had a strong immunomodulatory role, induced the antiinflammatory cytokine IL-4, and had a strong antioxidant capacity with a half maximal effective concentration (EC_{50}) value of 1.7 mg mL^{-1} as determined by an *in vitro* hydroxyl radical scavenging activity test (Taylan et al., 2019).

Macrophages are known as a major factor in the inflammatory response. And one of the cytokines produced stimulating agents, nitric oxide (NO), is associated with macrophage immunological capabilities. Ren et al. (2016) found that high concentration of EPS333 (≥500 µg/mL) which is gained from *Streptococcus thermophilus* AR333, could promote the NO production in macrophages RAW 264.7. It was suggested that *Streptococcus thermophilus* AR333 could be a potential source of immunoregulatory polysaccharide and could be a potential immunostimulant in dairy products.

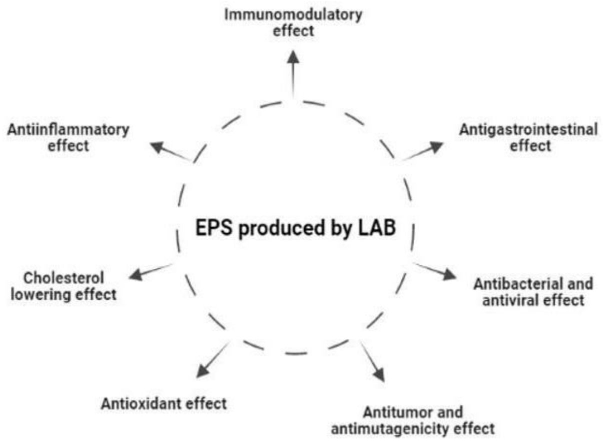

Figure. 2. Biological activities of exopolysaccharides produced by lactic acid bacteria.

EPS can also act as a substrate for other organisms in complex ecosystems (Zannini et al., 2016). In this context, Salazar et al. (2008) stated that intestinal *Bifidobacteria* can produce EPS, which can act as a fermentable substrate for microorganisms in the human gut. They also reported that it promotes alterations in SCFA profiles and changes in relationships between intestinal microbial populations.

The immunomodulating effects and immune-protective functions of EPS that have been reported in both *in vitro* and *in vivo* studies are frequently related to EPS derivatives from various strains of Lactobacilli including *Lb. casei*, *Lb. johnsonii* JCM 2012, *Lb. salivarius* Ls33, *Lb. rhamnosus* CRL1505, *Lb. plantarum* ATCC 14917, *Lb. buchneri* and *Lb. kefiri* (Teame et al., 2020; Rajoka et al., 2020).

Antiinflammatory effects

Inflammation is a complex process initiated by immune system as a response to defend the body from negative stimulation caused by pathogens, toxins, injuries etc. Various cells, metabolic pathways and molecular mediators are activated/induced in inflammation. Upon stimulation, immune cells (e.g. macrophages and mast cells) release inflammatory mediators (e.g. cytokines) that trigger a response from immune system. Cytokines play a key role in inflammation. Pro-inflammatory cytokines (e.g. interleukin-1 (IL-1α, IL-1β), IL-6, tumor necrosis factor (TNF), interferon gamma (IFNγ)) are synthesized and secreted from immune cells and promote inflammation. Antiinflammatory cytokines (e.g. IL-4, IL-10, IL-13) on the other hand inhibit the synthesis of proinflammatory cytokines and suppress the inflammation. Pro-inflammatory cytokines and antiinflammatory components are in a dynamic balance. Besides these proteins, cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS) are also major players in inflammatory reactions, they are rapidly expressed under inflammatory conditions (Dinarello, 2000; Minghetti, 2004; Opal & DePalo, 2000; Venkatesha et al., 2017). Through inflammation, healing process is initiated. Excessive inflammatory responses, on the other hand, can harm host tissues and pose serious risks. Antiinflammatory agents are the compounds used for controlling the inflammation process through altering the metabolic pathways activated in inflammation. Natural products have been constantly investigated for their antiinflammatory activities and LAB EPSs, as a postbiotic, has been the subject of these studies recently (Kwon et al., 2020; Öner et al., 2016; Venkatesha et al., 2017). Antiinflammatory activity of a substance can be tested via different approaches and there are studies reporting LAB EPS's antiinflammatory properties determined by various tests.

Li and Shah (2016) investigated the antiinflammatory activity of EPS derived from *Streptococcus thermophilus* ASCC 1275 via measuring proinflammatory/antiinflammatory cytokine secretion ratios (IL-1β/IL-10, IL-6/IL-10, and TNF-α/IL-10) in RAW 264.7 macrophages stimulated by inflammation initiator lipopolysaccharide (LPS). They found that EPS treatment reduced the pro-/antiinflammatory cytokine secretion ratios of IL-1β/IL-10, IL6/IL-10, and TNF-α/IL-10 in a dose-dependent manner, indicating that EPS had good antiinflammatory activity on LPS stimulated RAW 264.7 macrophages by lowering the pro/antiinflammatory cytokine secretion ratios. They also reported that EPS decreased inflammation inducer NO and reactive oxygen species production in LPS stimulated RAW 264.7 macrophages. In another study, LPS induced RAW 264.7 cells precultured with EPS obtained from *Lactobacillus plantarum* L-14 and proinflammatory cytokine (IL-6, TNF-α, and IL-1β) production in RAW 264.7 cells were analyzed. It was found that IL-6, TNF-α, and IL-1β levels and expression of COX-2 and iNOS genes were suppressed in EPS treated RAW 264.7 cells. It was stated that EPS could be used in natural products in regulating inflammatory reaction (Kwon et al., 2020).

Buddana et al. (2015) determined the antiinflammatory activity of native and sulfated *Streptococcus mutans* MTCC 497 EPS via inhibition of albumin denaturation technique. Compounds that limit protein denaturation or promote protein stability are thought to be antiinflammatory since protein denaturation is linked to inflammation. In this work, the antiinflammatory effect of EPS was evaluated against heat-mediated protein denaturation and compared to diclofinac sodium, a common antiinflammatory medicine. Researchers reported that at 100 µg/ml concentration, native and sulfated EPS showed antiinflammatory activity of 37% and 45%, respectively. While at 400 µg/mL concentration diclofinac sodium showed complete inhibition, sulfated EPS showed 82% antiinflammatory activity at 500 µg/mL concentration with the half maximal inhibitory concentration (IC_{50}) value of 111.55 µg/mL.

Prado et al., (2016) studied the antiinflammatory activity of kefir polysaccharide extract (ExPP) via hyaluronidase enzyme assay by which the inhibitory activity of ExPP on hyaluronidase enzyme was determined. The enzyme hyaluronidase hydrolyzes hyaluronic acid, which causes extracellular matrix breakdown, which promotes inflammation. Researchers reported that lyophilized (L) ExPP showed 63% antiinflammatory activity compared to dimethyl sulfoxide (DMSO). ExPP (L) inhibited the enzyme with a minimal activity of 2.08 mg/mL and a maximum activity of 2.57 mg/mL, IC_{50} value of lyophilized ExPP was 2.31 mg/mL. They stated that compared with a commercial product (ethanolic extract of propolis), ExPP demonstrated superior action and it have the potential to be used as an antiinflammatory compound. In another kefir related study, kefiran produced by *Lactobacillus kefiranofaciens* was investigated for its antiinflammatory activity on antigen stimulated bone marrow-derived mast cells. Mast cells play a key role in the inflammatory process. Upon stimulation, mast cells degranulate or release compounds that induce inflammation. Researchers found that kefiran treatment significantly inhibited antigen-induced degranulation by suppressing β-hexosaminidase secretion, an indicator of degranulation, completely at 3 mg/mL concentration. Also kefiran suppressed TNF-α, an important inflammatory cytokine, secretion in mast cells completely at 3 mg/mL concentration. Findings of the study indicated the antiinflammatory effect for kefiran in a dose-dependent manner (Furuno & Nakanishi, 2012).

EPS, as one of these postbiotics, were reported to show antiinflammatory effect in the studies mentioned above. Naturally it cannot be argued that all types of LAB EPSs have this effect because different strains can produce EPSs in different structures. However, studies show that LAB EPSs can act as an antiinflammatory agent. Therefore, with the extensive pharmaceutical studies, LAB EPS may be exploited for the development of antiinflammatory drugs as an alternative to synthetic compounds.

Antitumor and antimutagenicity

One of the postbiotics generated by LAB, exopolysaccharide (EPS), can act as ligands for host cells and protect the host by aggregating with pathogens in the intestine (CastroBravo et al., 2018). Furthermore, it has been found that EPS has anticancer properties as well as oxidative stress protection (Saadat et al., 2019; Li et al., 2013).

Microbial EPSs produced from biological, safe sources such as LAB, accepted an alternative to chemotherapy due to its side effcts. Due to their bioactive qualities, LAB have a wide variety of medical applications and have low cytotoxicity and adverse effects, providing them a good substitute for synthetic anticancer drugs (Farag et al., 2020).

The invention and introduction of potential antitumor drugs with low immune system side effects has become a critical goal in many immunopharmacology studies. EPSs derived from safe natural sources, such as LAB, typically have low cytotoxicity and side effects and may be a viable alternative to synthetic antitumor agents (Ismail & Nampoothiri, 2013).

Liu et al. (2011) and Wang et al. (2014) demonstrated the antiproliferative effect of *L. casei* 01 EPS on the HT-29 cell line, as well as the anticancer activity of EPS from *L. plantarum* 70810 on HepG-2, BGC-823, and mainly HT-29 malignant cell. EPSs from *Lactobacillus casei*, *Lactobacillus plantarum*, and *Lactobacillus acidophilus* have exhibited antitumor effects against a variety of cell lines in a dose-dependent manner (Deepak et al., 2016a; 2016b).

Under both normoxic and hypoxic conditions, the effect of EPS from *Lactobacillus acidophilus* on messenger RNA (mRNA) expression of several genes was investigated using quantitative real-time (RT)-PCR. The hazardous concentration was calculated as 5 mg/mL. EPS has been found to suppress the expression of genes involved in tumor angiogenesis and survival. In two colon cancer cell lines, EPS was also observed to cause cytotoxicity (Deepak et al., 2016b).

Dilna et al., (2015) reported that EPS from *Lb. plantarum* RJF4 had a specific antiproliferative effect to cancer cells and inhibited them. According to the cell viability test results, EPS showed toxic effect to MiaPaCa2-pancreatic cancer cell line in dose dependent manner and remained nontoxic to normal cell line (L6 and L929 fibroblast cells).

Antioxidant activity

Biological systems are exposed to oxidative stress with high levels of reactive oxygen species and free radicals. The presence of oxidative stress is associated with various diseases such as cancer, liver cirrhosis, and fatty liver (Dilna et al., 2015). EPSs from LAB have been discovered to contribute in the elimination of free radicals, so acting as natural strong antioxidants. They have also been found to be harmless, suggesting that they could be used as a replacement for synthetic antioxidants due to their toxicity (Saadat et al., 2019). The ability of LAB-derived EPSs to perform good antioxidant activity has been widely investigated by *in vitro* and *in vivo* studies.

EPS, composed of glucose and mannose, was purified from *Lb. plantarum* RJF4 EPS increased 32% total antioxidant capacity, 23.63% 1,1-Diphenyl-2-picrylhydrazyl (DPPH) radical scavenging ability and 50% reduction potential (compared to the ascorbic acid, as a standard) (Dilna et al., 2015).

In DPPH radical-scavenging, reducing power (RP), and ferric reducing antioxidant power (FRAP) assays, EPS from *Lactobacillus acidophilus* showed excellent antioxidative activity on colon cancer cell lines *in vitro*. In all of these assays, increasing the concentration of EPS improved the antioxidative capabilities of the EPS (Deepak et al., 2016b). Similarly EPS from *Lactobacillus plantarum* SKT109 showed superior DPPH-scavenging activity toward hydroxyl (68.52%) radicals at a dose of 5 mg/mL (Wang et al., 2018).

In vitro tests revealed that EPS from *Pediococcus acidilactici* NCDC 252 had antioxidant and profileration reduction potential on HCT116 (colon cancer cells) in a dose-dependent manner. EPS had a total antioxidant potential of 11.9 %, and it inhibited HCT116 cell by 67.1-87.3% at 10 and 100 g/mL, respectively. After *in vivo* experiments, it was indicated that EPS could be employed therapeutically as an antioxidant and anticancer agent (Kumar et al., 2020).

The antioxidant potential of EPSs generated by *Lactobacillus sanfranciscensis*, which was isolated from a Chinese traditional sourdough, was analyzed via free radical ($ABTS^{•+}$) scavenging activity. The scavenging activity rate of polysaccharides were reported to 10.42%, while the EPS concentration was 0.0625 mg/mL. So, certain antioxidant activity even at low EPS concentrations was determined (Zhang et al., 2019).

Antibacterial and antiviral activity

EPS has the ability to have an antagonistic effect on pathogenic bacteria. Exopolysaccharides could actively communicate with Gram-negative and Gram-positive bacteria based on the permeability of their cell membranes, affecting the respiratory chain, cell division machinery, and eventually cell death (Hasheminya & Dehghannya, 2020). Antibiotic use, as is well known, reduces the antagonistic activity of normal microbial flora against pathogenic microorganisms. Probiotic EPSs are used to supplement the treatment of human diseases (Angelin & Kavitha, 2020).

The antilisterial activity of probiotics *Lactobacillus acidophilus* LA5, *Lactobacillus casei* 431, and *Lactobacillus salivarius* was studied *in vitro* and in food concepts. All *Lactobacillus spp.* postbiotics retained more than 50% of their residual antimicrobial activity, implying that *Lb. salivarius* CFS can be used as an effective food additive for controlling *Listeria monocytogenes* (Moradi et al., 2019).

The EPS producing *Lactobacillus kefiranofaciens* DN1 isolated from kefir was investigated for its antibacterial activity against *L. monocytogenes* and *Salmonella enteritidis*. It was discovered that EPS DN1 had bactericidal effects on several pathogens at concentrations of at least 1%. Therefore, the EPS produced by *Lactobacillus kefiranofaciens* DN1 could be used in the food industry to assure food safety or developed as an alternative treatment for foodborne infections (Jeong et al., 2017).

The antibacterial activity of EPS produced by *Lactobacillus delbureckii* against pathogens was researched. It was revealed that EPSs had antibacterial activity with the highest susceptibility against the test pathogens *Bacillus subtilis* and *Staphylococcus aureus* (Adebayo-Tayo & Fashogbon, 2020).

The LAB *Weissella cibaria* 27 (W27) isolated from kimchi was used as an EPS producer to understand the effects of sucrose for improving its EPS productivity. The results showed certain antibacterial activity against *E. coli* BL21, *B. subtilis* and *S. aureus* with or without the addition of sucrose. The inhibition zones for *B. cereus* and *E. coli* increased by the addition of sucrose, however the inhibition zone for *S. aureus* decreased (Yu et al., 2018).

Likewise, *Lactobacillus rhamnosus* isolated from human breastmilk demonstrated strong antibacterial activity against pathogenic *E. coli* and *Salmonella typhimurium in vitro*. HePs from *Lactobacillus gasseri* inhibited *L. monocytogenes* MTCC 657 more effectively. With an initial population of 9 log CFU/mL, EPS-C70 from camel milk exhibited 2 to 3 log reduction against tested food-borne pathogens, with the highest inhibition observed against *S. aureus* and *E. coli* (Alsaadi et al., 2020).

The antiviral effect of *L. plantarum* LRCC5310 isolated from the Korean traditional fermented food kimchi was investigated both *in vitro* and *in vivo*. EPS extracted from *L. plantarum* LRCC5310 were also stated to be effective in the control of rotavirus infection, which is a leading cause of violent diarrhea in newborns and young children worldwide. *L. plantarum* LRCC5310 EPS could help protect the intestinal mucosal barrier from viral shedding and other damages caused by virus infection adjuvant. Moreover, *L. plantarum* LRCC5310 EPS exhibits potent antirotavirus activity *in vitro*, especially against extracellular rotaviruses (Kim et al., 2018).

Cholesterol lowering properties

Excessive cholesterol and high blood pressure could be counted among the risk factors for cardiovascular diseases. High blood pressure levels have been linked to cardiovascular illness, particularly atherosclerosis, and as a result, the incidence of cerebral infarction, cerebral thrombosis, and cardiopathy is on the rise. Furthermore, existing mitigating or curing approaches are limited in intravenous feeding and cannot fundamentally heal diseases, therefore the need for a safe, effective, and side-effect-free cholesterol-lowering agent like EPS is urgent (Chien et al., 2010; Glass & Witztum, 2001).

EPS generated by LAB have been actually able to control cholesterol levels due to the adsorption ability of polymers to this molecule (Ruas-Madiedo, 2014). A growing number of studies have found that LAB-produced EPS has a hypocholesterolemic effect.

By inhibiting cholesterol absorption, EPS as a postbiotic drug can improve lipid metabolism. In a preclinical animal model, consumption of kefiran by *Lactobacillus kefiranofaciens* delayed the development of atherosclerosis (Khalil et al., 2018; Uchida et al., 2010). Kefiran also reduced blood pressure and stabilized blood glucose levels in rats fed a high cholesterol diet. As a result, EPSs like kefiran have the potential to prevent cardiovascular diseases (Maeda et al., 2004).

Dilna et al., (2015), reported antioxidant activity, α-amylase inhibition, cholesterol lowering, and antiproliferative activities of EPS produced by Lactobacillus *plantarum* RJF4. The variation in health-promotion benefits of EPS depends on species, strain, and EPS type (Ryan et al., 2015). Another research by London et al. (2014) found that dietary intervention with EPS producing probiotics causes lipid metabolism to be modulated in a mouse model of atherosclerosis by lowering blood cholesterol and triglyceride levels. It could lead to positive changes in lipid metabolism.

Gastro-protective activity

Helicobacter pylori infections and long-term use of nonsteroidal antiinflammatory drugs can cause toxic effects on gastric epithelial cells which can lead to gastric ulcers. *Streptococcus thermophilus* CRL1190 and its EPS have been suggested to possess gastroprotective activity. *S. thermophilus* CRL1190 was reported to inhibit the adhesion of *H. pylori* to stomach gastric mucosa, modulate the inflammatory response in gastric epithelial cell line AGS and prevent the gastritis development (Marcial et al., 2017; Rodríguez et al., 2009; Saadat et al., 2019).

Polysaccharides from *L. reuteri* DSM17938 and *L. reuteri* L26 BiocenolTM were determined for their health benefits as an immune protective agent on intestinal porcine epithelial cell line-1 (IPEC-1) cells against haemolytic enterotoxigenic *E. coli* (ETEC) bacteria. They subsequently decreased ETEC-induced gene expression for the proinflammatory cytokines (IL-1, IL-6), which suggesting to role as a prophylactic effect to gastrointestinal infections (Kšonžeková et al., 2016).

Conclusion

Microorganisms are assumed to be protected by EPS from bacteriophages, antibiotics, physical stressors, and toxic compounds. Considering the probiotics, the EPS produced by these microorganisms could also operate as a physical barrier to prevent the toxin from interacting with eukaryotic cells, either by blocking toxin receptors on the cell surface or by serving as toxin-scavengers. LAB group comprises probiotic members also members producing postbiotics with health benefit properties such as EPS. Anticancer, antioxidant, antimicrobial, antiinflammatory, and immunomodulatory activities of LAB EPS have been studied. Studies show that LAB species can synthesis structurally diverse EPSs having different chemical substituents, linkages, and functional groups that brings these compounds the ability to possess biological activities in varying degrees. Information about EPS genetics, biological differences, biosynthetic pathways, metabolic models are used in metabolic engineering studies to modify EPS production and EPS composition. However, studies continue on the basic principles for the production of different EPSs from LAB via metabolic engineering and researches on this subject will probably multiply by diversifying. With aforementioned bioactivities LAB EPSs have the potential to be used in a number of fields including drug delivery, medicine, food, and agriculture and future studies may result in obtaining ready to consume LAB EPSs with outstanding biological activities and EPSs may appear constantly in certain product formulations in the fields of medicine and food.

References

Abbasi, A., Rad, A. H., Ghasempour, Z., Sabahi, S., Kafil, H. S., Hasannezhad, P., Saadat, Y. R., & Shahbazi, N. (2021). The biological activities of postbiotics in gastrointestinal disorders. *Critical Reviews in Food Science and Nutrition*, 1-22. https://doi.org/10.1080/10408398.2021.1895061

Adebayo-Tayo, B., & Fashogbon, R. (2020). In vitro antioxidant, antibacterial, in vivo immunomodulatory, antitumor and hematological potential of exopolysaccharide produced by wild type and mutant *Lactobacillus delbureckii* subsp.*bulgaricus*. *Heliyon*, *6*(2), 1-10. https://doi.org/10.1016/j.heliyon.2020.e03268

Adebayo-Tayo, B., Ishola, R., & Oyewunmi, T. (2018). Characterization, antioxidant and immunomodulatory potential on exopolysaccharide produced by wild type and mutant Weissella confusa strains. *Biotechnology Reports*, *19*, e00271. https://doi.org/10.1016/j.btre.2018.e00271

Adesulu-Dahunsi, A. T., Sanni, A. I., Jeyaram, K., Ojediran, J. O., Ogunsakin, A. O., & Banwo, K. (2018). Extracellular polysaccharide from Weissella confusa OF126: Production, optimization, and characterization. *International Journal of Biological Macromolecules*, *111*, 514-525. https://doi.org/10.1016/j.ijbiomac.2018.01.060

Alsaadi, L. G., Baker, B. A. A., Kadhem, B. M., Mahdi, L. H., & Mater, H. N. (2020). Exopolysaccharide as antiviral, antimicrobial and as immunostimulants: A review. *Plant Archives*, *20*(2), 5859-5875. eISSN: 2581-6063.

Angelin, J., & Kavitha, M. (2020). Exopolysaccharides from probiotic bacteria and their health potential. *International Journal of Biological Macromolecules*, *162*, 853-865. https://doi.org/10.1016/j.ijbiomac.2020.06.190

Buddana, S. K., Venkata Naga Varanasi, Y., & Reddy Shetty, P. (2015). Fibrinolytic, antiinflammatory and antimicrobial properties of α-(1-3)-glucans produced from *Streptococcus mutans* (MTCC 497). *Carbohydrate Polymers*, *15*, 152–159. https://doi.org/10.1016/j.carbpol.2014.08.083

Castro-Bravo, N., Wells, J. M., Margolles, A., & Ruas-Madiedo, P. (2018). Interactions of surface exopolysaccharides from Bifidobacterium and Lactobacillus within the intestinal environment. *Front in Microbiology*, *9*, 2426, 1-15. https://doi.org/10.3389/fmicb.2018.02426

Chaisuwan, W., Jantanasakulwong, K., Wangtueai, S., Phimolsiripol, Y., Chaiyaso, T., Techapun, C., Phongthai, S., You, S., Regenstein, J. M., & Seesuriyachan, P. (2020). Microbial exopolysaccharides for immune enhancement: Fermentation, modifications and bioactivities, *Food Bioscience, 35*, 1-17. https://doi.org/10.1016/j.fbio.2020.100564

Chen, Y. C., Wu, Y. J., & Hu, C. Y. (2019). Monosaccharide composition influence and immunomodulatory effects of probiotic exopolysaccharides. *International Journal of Biological Macromolecules*, *133*, 575-582. https://doi.org/10.1016/j.ijbiomac.2019.04.109

Chien, Y. L., Wu, L. Y., Lee, T. C., & Hwang, L. S. (2010). Cholesterol-lowering effect of phytosterol-containing lactic-fermented milk powder in hamsters. *Food Chemistry*, *119*(3), 1121-1126. https://doi.org/10.1016/j.foodchem.2009.08.023

Deepak, V., Ram Kumar Pandian, S., Sivasubramaniam, S. D., Nellaiah, H., & Sundar, K. (2016a). Optimization of anticancer exopolysaccharide production from probiotic *Lactobacillus acidophilus* by response surface methodology. *Preparative Biochemistry* 396 *and Biotechnology*, *46*(3), 288–297. https://doi.org/10.1080/10826068.2015.1031386

Deepak, V., Ramachandran, S., Balahmar, R. M., Pandian, S. R. K., Sivasubramaniam, S. D., Nellaiah, H., & Sundar, K. (2016b). In vitro evaluation of anticancer properties of exopolysaccharides from *Lactobacillus acidophilus* in colon cancer cell lines. *In Vitro Cellular &Developmental Biology-Animal*, *52*(2),163-173. https://doi.org/10.1007/s11626-015-9970-3

Dilna, S. V., Surya, H., Aswathy, R. G., Varsha, K. K., Sakthikumar, D. N., Pandey, A., & Nampoothiri, K. M. (2015). Characterization of an exopolysaccharide with potential 404 health-benefit properties from a probiotic *Lactobacillus plantarum* RJF4. *LWT-Food Science and Technology*, *64*, 1179-1186. https://doi.org/10.1016/j.lwt.2015.07.040

Dinarello, C. A. (2000). Proinflammatory cytokines. *Chest*, *118*(2), 503–508. https://doi.org/10.1378/chest.118.2.503

Farag, M. M., Moghannem, S. A., Shehabeldine, A. M., & Azab, M. S. (2020). Antitumor effect of exopolysaccharide produced by *Bacillus mycoides*. *Microbial pathogenesis*, *140*, 1-10. https://doi.org/10.1016/j.micpath.2019.103947

Furuno, T., & Nakanishi, M. (2012). Kefiran suppresses antigen-induced mast cell activation. *Biological and Pharmaceutical Bulletin*, *35*(2), 178–183. https://doi.org/10.1248/bpb.35.178

Glass, C. K. & Witztum, J. L. (2001). Atherosclerosis: the road ahead. *Cell*, *104*(4), 503-516. https://doi.org/10.1016/s0092-8674(01)00238-0

Hasheminya, S. M., & Dehghannya, J. (2020). Novel ultrasound-assisted extraction of kefiran biomaterial, a prebiotic exopolysaccharide, and investigation of its physicochemical, antioxidant and antimicrobial properties. *Materials Chemistry and Physics*, *243*, 1-8. https://doi.org/ 10.1016/j.matchemphys.2020.122645

Ismail, B., & Nampoothiri, K. M. (2013). Exposition of antitumour activity of a chemically characterized exopolysaccharide from a probiotic *Lactobacillus plantarum* MTCC 9510. *Biologia*, *68*(6), 1041–1047. https://doi.org/10.2478/s11756-013-0275-2

Jurášková, D., Ribeiro, S. C., & Silva, C. C. (2022). Exopolysaccharides produced by lactic acid bacteria: From biosynthesis to health-promoting properties, *Foods*, *11*(2), 156. https://doi.org/10.3390/foods11020156

Jeong, D., Kim, D. H., Kang, I. B., Kim, H., Song, K. Y., Kim, H. S., & Seo, K. H. (2017). Characterization and antibacterial activity of a novel exopolysaccharide produced by Lactobacillus kefiranofaciens DN1 isolated from kefir. *Food Control*, *78*, 436-442. https://doi.org/10.1016/j.foodcont.2017.02.033

Kavitake, D., Kalahasti, K. K., Devi, P. B., Ravi, R., & Shetty, P. H. (2020). Galactan exopolysaccharide based flavour emulsions and their application in improving the texture and sensorial properties of muffin. *Bioactive Carbohydrates and Dietary Fibre*, *24*, 1-8. https://doi.org/10.1016/j.bcdf.2020.100248

Khalil, E. S., Abd Manap, M. Y., Mustafa, S., Alhelli, A. M., & Shokryazdan, P. (2018). Probiotic properties of exopolysaccharide-producing lactobacillus strains ısolated from Tempoyak. *Molecules*, *23*(2), *398*, 1-20. https://doi.org/10.3390/molecules23020398

Kim, K., Lee, G., Thanh, H. D., Kim, J. H., Konkit, M., Yoon, S., Park, M., Yang, S., Park, E., & Kim, W. (2018). Exopolysaccharide from *Lactobacillus plantarum* LRCC5310 offers protection against rotavirus-induced diarrhea and regulates inflammatory response. *Journal of Dairy Science*, *101*(7), 5702-5712. https://doi.org/10.3168/jds.2017-14151

Korcz, E., Kerényi, Z., & Varga, L. (2018). Dietary fibers, prebiotics, and exopolysaccharides produced by lactic acid bacteria: potential health benefits with special regard to cholesterol-lowering effects. *Food & Function*, *9*(6), 3057-3068. https://doi.org/10.1039/c8fo00118a

Kšonžeková, P., Bystrický, P., Vlčková, S., Pätoprstý, V., Pulzová, L., Mudroňová, D., Kubašková, T., Csank, T., & Tkáčiková, Ľ. (2016). Exopolysaccharides of *Lactobacillus reuteri*: Their influence on adherence of *E. coli* to epithelial cells and inflammatory response. *Carbohydrate Polymers*, *141*, 10-19. https://doi.org/10.1016/j.carbpol.2015.12.037

Kumar, R., Bansal, P., Singh, J., & Dhanda, S. (2020). Purification, partial structural characterization and health benefits of exopolysaccharides from potential probiotic *Pediococcus acidilactici* NCDC 252. *Process Biochemistry*, *99*, 79-86. https://doi.org/10.1016/j.procbio.2020.08.028

Kwon, M., Lee, J., Park, S., Kwon, O. H., Seo, J., & Roh, S. (2020). Exopolysaccharide isolated from *Lactobacillus plantarum* l-14 has anti-inflammatory effects via the tolllike receptor 4 pathway in lps-induced raw 264.7 cells. *International Journal of Molecular Sciences*, *21*(23), 1–18. https://doi.org/10.3390/ijms21239283

Laws, A., Gu, Y., & Marshall, V. (2001). Biosynthesis, characterisation, and design of bacterial exopolysaccharides from lactic acid bacteria. *Biotechnology Advances*, *19*(8), 597-625. https://doi.org/10.1016/s0734-9750(01)00084-2

Li, J. Y., Jin, M. M., Meng, J., Gao, S. M., & Lu, R. R. (2013). Exopolysaccharide from *Lactobacillus plantarum* LP6: Antioxidation and the effect on oxidative stress. *Carbohydrate Polymers*, 98, 1147–1152. https://doi.org/10.1016/j.carbpol.2013.07.027

Li, S., & Shah, N. P. (2016). Characterization, anti-Inflammatory and antiproliferative activities of natural and sulfonated exopolysaccharides from *Streptococcus thermophilus* ASCC 1275. *Journal of Food Science*, *81*(5), M1167–M1176. https://doi.org/10.1111/1750-3841.13276

Li, W., Xia, X., Tang, W., Ji, J., Rui, X., Chen, X., Jiang, M., Zhou, J., Zhang, Q., & Dong, M. (2015). Structural characterization and anticancer activity of cell-bound exopolysaccharide from Lactobacillus helveticus MB2-1. *Journal of Agricultural and Food Chemistry*, *63*(13), 3454-3463. https://doi.org/10.1021/acs.jafc.5b01086

Liu, C. T., Chu, F. J., Chou, C. C., & Yu, R. C. (2011). Antiproliferative and anticytotoxic effects of cell fractions and exopolysaccharides from *Lactobacillus casei* 01. *Mutation Research/Genetic Toxicology and Environmental Mutagenesis*, *721*(2), 157–162. https://doi.org/10.1016/j.mrgentox.2011.01.005

London, L. E. E., Kumar, A. H. S., Wall, R., Casey, P. G., O'Sullivan, O., Shanahan, F., Hill, C., Cotter, P. D., Fitzgerald, G. F., Ross, P. R., Caplice, N. M., & Stanton, C. (2014). Exopolysaccharide-producing probiotic Lactobacilli reduce serum cholesterol and modify enteric microbiota in ApoE-deficient mice. *The Journal of Nutrition*, *144*(12), 1956-1962. https://doi.org/10.3945/jn.114.191627

Maeda, H., Zhu X., Omura, K., Suzuki, S., & Kitamura, S. (2004). Effects of an exopolysaccharide (kefiran) on lipids, blood pressure, blood glucose and constipation. *Biofactors*, *22*, 197–200. https://doi.org/10.1002/biof.5520220141

Marcial, G., Villena, J., Faller, G., Hensel, A., & de Valdéz, G. F. (2017). Exopolysaccharide producing *Streptococcus thermophilus* CRL1190 reduces the inflammatory response caused by *Helicobacter pylori*. *Beneficial Microbes*, *8*(3), 451-461. https://doi.org/10.3920/BM2016.0186

Minghetti, L. (2004). Cyclooxygenase-2 (COX-2) in inflammatory and degenerative brain diseases. *Journal of Neuropathology and Experimental Neurology*, *63*(9), 901–910. https://doi.org/10.1093/jnen/63.9.901

Moradi, M., Mardani, K., & Tajik, H. (2019). Characterization and application of postbiotics of Lactobacillus spp. on *Listeria monocytogenes* in vitro and in food models. *LWT-Food Science and Technology*, *111*, 457-464. https://doi.org/10.1016/j.lwt.2019.05.072

Noroozi, E., Tebianian, M., Taghizadeh, M., Dadar, M., & Mojgani, N. (2021). Anticarcinogenic potential of probiotic, postbiotic metabolites and paraprobiotics on human cancer cells. In N. Mojgani & M. Dadar (Eds.), *Probiotic Bacteria and Postbiotic Metabolites: Role in Animal and Human Health* (pp. 166). Springer.

Opal, S. M., & DePalo, V. A. (2000). Anti-inflammatory cytokines. *Chest*, *117*(4), 1162–1172. https://doi.org/10.1378/chest.117.4.1162

Öner, E. T., Hernández, L., & Combie, J. (2016). Review of Levan polysaccharide: From a century of past experiences to future prospects. *Biotechnology Advances*, *34*(5), 827–844. https://doi.org/10.1016/j.biotechadv.2016.05.002

Perricone, M., Bevilacqua, A., Corbo, M. R., & Sinigaglia, M. (2014). Technological characterization and probiotic traits of yeasts isolated from Altamura sourdough to select promising microorganisms as functional starter cultures for cereal-based products. *Food Microbiology*, *38*, 26-35. https://doi.org/10.1016/j.fm.2013.08.006

Prado, M. R. M., Boller, C., Zibetti, R. G. M., de Souza, D., Pedroso, L. L., & Soccol, C. R. (2016). Anti-inflammatory and angiogenic activity of polysaccharide extract obtained from Tibetan kefir. *Microvascular Research*, *108*, 29–33. https://doi.org/10.1016/j.mvr.2016.07.004

Rana, S., & Upadhyay, L. S. B. (2020). Microbial exopolysaccharides: Synthesis pathways, types and their commercial applications. *International Journal of Biological Macromolecules*, *15*(157), 577-583. https://doi.org/10.1016/j.ijbiomac.2020.04.084

Rajoka, M. S. R., Wu, Y., Mehwish, H. M., Bansal, M., & Zhao, L. (2020). Lactobacillus exopolysaccharides: New perspectives on engineering strategies, physiochemical functions, and immunomodulatory effects on host health. *Trends in Food Science & Technology*, *103*, 36-48. https://doi.org/10.1016/j.tifs.2020.06.003

Ren, W., Xia, Y., Wang, G., Zhang, H., Zhu, S., & Ai, L. (2016). Bioactive exopolysaccharides from a *S. thermophilus* strain: Screening, purification and characterization. *International Journal of Biological Macromolecules*, *86*, 402-407. https://doi.org/10.1016/j.ijbiomac.2016.01.085

Rodríguez, C., Medici, M., Rodríguez, A. V., Mozzi, F., & de Valdez, G. F. (2009). Prevention of chronic gastritis by fermented milks made with exopolysaccharide-producing *Streptococcus thermophilus* strains. *Journal of Dairy Science*, *92*(6), 2423-2434. https://doi.org/10.3168/jds.2008-1724

Ruas-Madiedo, P., & De Los Reyes-Gavilán, C. G. (2005). Invited review: Methods for the screening, isolation, and characterization of exopolysaccharides produced by lactic acid bacteria. *Journal of Dairy Science*, *88*(3), 843-856. https://doi.org/10.3168/jds.S0022-0302(05)72750-8

Ruas-Madiedo, P. (2014). Food oligosaccharides: Production, analysis and bioactivity; Biosynthesis and bioactivity of exopolysaccharides produced by probiotic bacteria. In F.L. Moreno & M.L. Sanz (Eds.), *Food oligosaccharides production, analysis and bioactivity* (pp. 118-133). John Wiley & Sons, West Sussex.

Ryan, P., Ross, R., Fitzgerald, G., Caplice, N., & Stanton, C. (2015). Sugar-coated:exopolysaccharide producing lactic acid bacteria for food and human health applications. *Food &Function*, *6*, 679–693. https://doi.org/10.1039/C4fo00529e

Saadat, Y. R., Khosroushahi, A. Y., & Gargari, B. P. A. (2019). A comprehensive review of anticancer, immunomodulatory and health beneficial effects of the lactic acid bacteria exopolysaccharides, *Carbohydrate Polymers*, *217*, 79-89. https://doi.org/10.1016/j.carbpol.2019.04.025

Salazar, N., Gueimonde, M., Hernández-Barranco, A. M., Ruas-Madiedo, P., & de los ReyesGavilán, C. G. (2008). Exopolysaccharides produced by intestinal Bifidobacterium strains act as fermentable substrates for human intestinal bacteria. *Applied and Environmental Microbiology*, *74*(15), 4737–4745. https://doi.org/ 10.1128/AEM.00325-08

Sanlibaba, P., & Çakmak, G. A. (2016). Exopolysaccharides production by lactic acid bacteria. *Applied Microbiology*, *2*(2), 1-5. https://doi.org/10.4172/2471-9315.1000115

Schilling, C., Badri, A., Sieber, V., Koffas, M., & Schmid, J. (2020). Metabolic engineering for production of functional polysaccharides. *Current Opinion in Biotechnology*, *66*, 44-51. https://doi.org/10.1016/j.copbio.2020.06.010

Tang, W., Dong, M., Wang, W., Han, S., Rui, X., Chen, X., Jiang, M., Zhang, Q., Junjun, W., & Li, W. (2017). Structural characterization and antioxidant property of released exopolysaccharides from *Lactobacillus* delbrueckii ssp. *bulgaricus* SRFM-1. *Carbohydrate polymers*, *173*, 654-664. https://doi.org/10.1016/j.carbpol.2017.06.039

Taylan, O., Yilmaz, M. T., & Dertli, E. (2019). Partial characterization of a levan type exopolysaccharide (EPS) produced by *Leuconostoc mesenteroides* showing immunostimulatory and antioxidant activities. *International Journal of Biological Macromolecules*, *136*, 436-444. https://doi.org/10.1016/j.ijbiomac.2019.06.078

Teame, T., Wang, A., Xie, M., Zhang, Z., Yang, Y., Ding, Q., Gao, C., Olsen, R. E., Ran, C., & Zhigang, Z. (2020). Paraprobiotics and postbiotics of probiotic Lactobacilli, their positive effects on the host and action mechanisms: A review. *Frontiers in Nutrition*, *7*, 1-16. https://doi.org/10.3389/fnut.2020.570344

Thantsha, M. S., Mamvura, C. I., & Booyens, J. (2012). Probiotics–what they are, their benefits and challenges. In T. Brzozowski (Ed.). *New Advances in the Basic and Clinical Gastroenterology* (pp. 21-50). InTech: Croatia.

Uchida, M., Ishii, I., Inoue, C., Akisato, Y., Watanabe, K., Hosoyama, S., Toida, T., Ariyoshi, N., & Kitada, M. (2010). Kefiran reduces atherosclerosis in rabbits fed a high cholesterol diet. *Journal of Atherosclerosis and Thrombosis*, *17*, 980–988. https://doi.org/10.5551/jat.4812

Venkatesha, S. H., Acharya, B., & Moudgil, K. D. (2017). Natural Products as Source of AntiInflammatory Drugs. In J.M. Cavaillon & M. Singer (Eds.), *Inflammation - From Molecular and Cellular Mechanisms to the Clinic* (pp. 1661-1690). Wiley.

Wang, K., Li, W., Rui, X., Chen, X., Jiang, M., & Dong, M. (2014). Characterization of a novel exopolysaccharide with antitumor activity from *Lactobacillus plantarum* 70810. *International Journal of Biological Macromolecules*, *63*, 133–139. https://doi.org/10.1016/j.ijbiomac.2013.10.036

Wang, J., Fang, X., Wu, T., Min, W., & Yang, Z. (2018). Exopolysaccharide producing Lactobacillus plantarum SKT109 as adjunct culture in Cheddar cheese production. *LWT-Food Science and Technology*, *97*, 419-426. https://doi.org/10.1016/j.lwt.2018.07.011

Ye, G., Li, G., Wang, C., Ling, B., Yang, R., & Huang, S. (2019). Extraction and characterization of dextran from Leuconostoc pseudomesenteroides YB-2 isolated from mango juice. *Carbohydrate polymers*, *207*, 218-223. https://doi.org/10.1016/j.carbpol.2018.11.092

Yu, Y. J., Chen, Z., Chen, P. T., & Ng, I. S. (2018). Production, characterization and antibacterial activity of exopolysaccharide from a newly isolated *Weissella cibaria* under sucrose effect. *Journal of Bioscience and Bioengineering*, *126*(6), 769-777. https://doi.org/10.1016/j.biosc.2018.05.028

Zannini, E., Waters, D. M., Coffey, A., & Arendt, E. K. (2016). Production, properties, and industrial food application of lactic acid bacteria-derived exopolysaccharides. *Applied Microbiology and Biotechnology*,*100*(3),1121-1135.https://doi.org/10.007/s00253-015-7172-2

Zhang, G., Zhang, W., Sun, L., Sadiq, F. A., Yang, Y., Gao, J., & Sang, Y. (2019). Preparation screening, production optimization and characterization of exopolysaccharides produced by *Lactobacillus sanfranciscensis* Ls-1001 isolated from Chinese traditional sourdough. *International Journal of Biological macromolecules*, *139*, 1295-1303. https://doi.org/10.1016/j.ijbiomac.2019.08.077

Zhang, Z., Liu, Z., Tao, X., & Wei, H. (2016). Characterization and sulfated modification of an exopolysaccharide from *Lactobacillus plantarum* ZDY2013 and its biological activities. *Carbohydrate polymers*, *153*, 25-33. https://doi.org/10.1016/j.carbpol.2016.07.084

Zhou, Y., Cui, Y., & Qu, X. (2019). Exopolysaccharides of lactic acid bacteria: Structure, bioactivity and associations: A review. *Carbohydrate Polymers*, *207*, 317-332. https://doi.org/10.1016/j.carbpol.2018.11.093