Applied Microbiology and Biotechnology (2018) 102:9949–9958
https://doi.org/10.1007/s00253-018-9403-9

MINI-REVIEW

Immunobiosis and probiosis: antimicrobial activity of lactic acid bacteria with a focus on their antiviral and antifungal properties

Mattia Pia Arena[1] · Vittorio Capozzi[1] · Pasquale Russo[1] · Djamel Drider[2] · Giuseppe Spano[1] · Daniela Fiocco[3]

Received: 28 August 2018 / Revised: 18 September 2018 / Accepted: 18 September 2018 / Published online: 2 October 2018

Abstract

Lactic acid bacteria (LAB), a heterogeneous group of bacteria that produce lactic acid as the main product of carbohydrate degradation, play an important role in the production and protection of fermented foods. Moreover, beside the technological use of these microorganisms added to control and steer food fermentations, their beneficial healthy properties are largely overt. Thus, numerous LAB strains have obtained the probiotic status, which entails the ability to maintain and promote a good health of consumers. In particular, increasing consideration is being focused on probiotic microorganisms that can improve the human immune response against dangerous viral and fungal enemies. For such beneficial microbes, the term "immunobiotics" has been coined. Together with an indirect host-mediated adverse effect against undesirable microorganisms, also a direct antagonistic activity of several LAB strains has been largely demonstrated. The purpose of this review is to provide a fullest possible overview of the antiviral and antifungal activities ascribed to probiotic LAB. The interest in this research field is substantiated by a large number of studies exploring the potential application of these beneficial microorganisms both as biopreservatives and immune-enhancers, aiming to reduce and/or eliminate the use of chemical agents to prevent the development of pathogenic, infectious, and/or degrading causes.

Keywords Probiosis · Lactic acid bacteria · Antiviral · Antifungal

Multifunctional features of lactic acid bacteria

The term lactic acid bacteria (LAB) embraces a vast number of bacterial species among which many strains have been proved to have multifunctional features including high fermentative capacity and/or important beneficial skills for humans. Within LAB, there are several phylogenetically different species belonging to the *Bacilli*, *Clostridia*, and *Mollicutes* classes (Garrity and Holt 2001). Within *Bacilli* class, six bacteria families, i.e. *Aerococcaceae*, *Carnobacteriaceae*, *Enterobacteriaceae*, *Lactobacillaceae*, *Leuconostocaceae*, and *Streptococcaceae*, encompass the LAB genera mainly associated with food such as *Lactococcus*, *Enterococcus*, *Streptococcus*, *Leuconostoc*, *Weissella*, *Oenococcus*, *Pediococcus*, *Tetragenococcus*, and *Carnobacterium* (Franz, and Holzapfel 2011).

LAB share the characteristic to be Gram-positive, usually non-motile and non-spore forming, catalase-negative, aerotolerant organisms, forming lactic acid as the main fermentative product through carbohydrates degradative metabolism (Axelsson 2004). The ability to ferment sugar, the increase of the acidity, and the production of several secondary metabolites are the main reason why LAB, since ancient times, have been used as a sort of starter cultures in order to improve the preservation, flavor, and texture of fermented food and feed products (Kleerebezem et al. 2017; Petruzzi et al. 2017; Kumar et al. 2017; Jeon et al. 2015). Furthermore, LAB are also exploited to increase the nutritional value of fermented foods, e.g., in yogurt, profiting by their ability to produce essential substances such as folate and riboflavin (Da Silva et al. 2016).

Several LAB strains, most of them belonging to *Lactobacillus* genus, have been shown to perform human and animal health-promoting activities, such as modulation of immune response, prevention of cancer, reduction of

✉ Giuseppe Spano
giuseppe.spano@unifg.it

[1] Dipartimento di Scienze Agraria, degli Alimenti e dell'Ambiente, Università degli Studi di Foggia, 71122 Foggia, Italy

[2] Université de Lille-ICV-Institut Charles Viollette, EA7394. F-59000 Lille, France

[3] Department of Clinical and Experimental Medicine, University of Foggia, Foggia, Italy

chronic bowel inflammations and cholesterol levels, improvement of the intestinal barrier, inhibition of pathogenic organisms, beneficial interactions with the endogenous intestinal microbiota (Mombelli and Gismondo 2000; Pothuraju and Sharma 2018; Vijayaram and Kannan 2018). The claim by which these microorganisms are commonly known is the term "probiotics" defined as "live microorganisms which when administered in adequate amount confer a health benefit on the host" (FAO/WHO 2001).

In order to absolve to probiotic features, beneficial microorganisms need to tolerate the harsh conditions of the oro-gastro-intestinal environment, adhere on the intestinal mucosa and colonize the gut tract, and produce helpful bioactive molecules (Arena et al. 2017; Al-Tawaha and Meng 2018). The criteria by which microorganisms can be claimed probiotics are listed in Table 1, although they do not need to possess all cited properties but only some specific features, according to the aim to be reached.

In this review, we tread the current state of the art on the antiviral and antifungal ability of lactic acid bacteria that hold probiotic skills.

Probiosis and immunobiosis

Probiotic LAB have been introduced widely in human and animal feed in increasing manner in the past last decades due to their positive impact on the prevention of some diseases and the maintaining of a well state of health. There is an active molecular dialog between the commensal microorganisms and the host mucosal immune system (Galdeano et al. 2007). In humans, probiotics can interact with the gut-associated lymphoid tissue (GALT) and modulate the immune response to injury and pathogenic organisms. Peyer's patches, i.e. lymphoid follicles located in the submucosa layer of the ileum and intestinal mucosa layer, are involved in the intestinal immune defense recognizing antigens and pathogenic microorganisms through specialized cells called microfold cells (M cells). Peyer's patches hold macrophages, dendritic cells, B lymphocytes, and T lymphocytes that actively contrast the possible enemies (Bonnardel et al. 2015; Diener 2016). The intestinal IgA cells are mainly produced in the Peyer's patches and their principal role is to protect the digestive tract which constitutes a border line between the external and the internal environments. They continually select what is useful for the organism, such as food nutrients, and what is harmful, such as pathogenic microorganisms and viruses (Laissue et al. 1993). Probiotic bacteria, such as strains of *Lactobacillus casei* and *Bifidobacterium breve*, have been recently reported to enhance the levels of specific IgA contributing to improve the mucosal resistance against *Candida* infections (Mendonça et al. 2012).

Table 1 Principal criteria by which microorganisms can be claimed as probiotics

Probiotic features
1. Survival through the oro-gastrointestinal tract, in order to reach the intestinal compartment
2. Adhesion to intestinal epithelial surface, in order to explicit the beneficial effects
3. Safety for human use
4. Tolerance to technological processing, in order to survive in the matrix used as carrier for the consumer
5. Production of helpful metabolic compounds, such as vitamins and short fatty acids
6. Modulation of immune response, acting on the expression of genes involved in the pro- and/or anti-inflammation processes
7. Antimicrobial activity, inhibiting pathogens adhesion and/or growth
8. Enhancement of intestinal barrier function
9. Co-aggregation probiotic-probiotic and/or probiotic-pathogens

Several studies tried to outline the mechanisms through which probiotic bacteria can have an influence in the stimulation of immune system. Plausibly, the cell wall of probiotics seems to promote the macrophages activation and the augmentation of IgA-producing cells in the gut *lamina propria*. Probiotic cells may be able to bind M cells and/or to direct the macromolecular antigen uptake to Peyer's patches (Majamaa et al. 1995; Isolauri 1999). Thus, specific components of the probiotic cell are essential for the immune modulation and, earlier, for adhesion ability to intestinal mucosa, which is indispensable in order to create an intimate contact between bacteria and the intestine (Santarmaki et al. 2017). There are many evidences that probiotic bacteria producing vitamins could provide anti-inflammatory effects that could be considered as adjunct IBD treatments to decrease some of the unwanted side effects caused by primary treatments (de Moreno de LeBlanc et al. 2018).

Some LAB, such as *Lactobacillus rhamnosus* and *Lactobacillus reuteri*, have been demonstrated to raise the level of IgA-specific antigen-secreting cells to rotavirus and reduce the shedding of rotavirus (Majamaa et al. 1995). Albeit the underlying mechanisms are not well elucidated, the adhesion ability of the aforementioned probiotic species would seem to be the key for the reduction of diarrhea caused by rotavirus (Shornikova et al. 1997; Tuomola et al. 1999), accompanied by the capability to stimulate antibodies against rotavirus (O'Halloran et al. 1998).

In parallel to adhesion, co-aggregation is a suitable feature preferable associate to a probiotic strain. Co-aggregation is the ability of microorganisms to adhere to each other, such as probiotic-probiotic and/or probiotic-pathogen. The co-aggregation properties of probiotic bacteria isolated from food products, such as some strains of *Lactobacillus acidophilus*, *Lactobacillus plantarum*, *L. rhamnosus*, *Lactobacillus*

paracasei, and *L. reuteri*, were demonstrated to be specific and time-dependent against *Escherichia coli* and the oral pathogen *Streptococcus mutans*, underlying the possible anticaries properties of probiotic (Twetman et al. 2009; Prabhurajeshwar and Chandrakanth 2017).

Thanks to the intimate contact occurring upon co-aggregation, probiotics can inhibit the harmful microorganisms by producing antimicrobial molecules in very close proximity of them. The antimicrobial substances mainly produced by LAB can be classified into low and high molecular mass compounds (i.e., with a molecular mass < 1000 Da and > 1000 Da, respectively) (Šušković et al. 2010). The first group, also named non-bacteriocin group, includes organic acids (such as lactic, acetic, phenyllactic, 4-hydroxyphenyllactic, benzoic acids) (Sjögren et al. 2003; Valerio et al. 2004; Niku-Paavola et al. 1999), hydrogen peroxide, diacetyl, acetaldehyde, acetoin, and carbon dioxide. In the undissociated form, organic acids can diffuse across the cell membrane exploiting the chemical gradient caused by the different pH between the cytosol (alkaline) and the external environment (acidic). Once inside the bacteria cell, they can interfere with metabolic functions and dissipate the membrane potential (Tejero-Sariñena et al. 2012; Lorca and de Valdez 2009). Hydrogen peroxide, instead, is able to alter the redox potential of bacterial cell and to damage the protein structures due to its oxidizing effect (Pridmore et al. 2008; Reid 2008). Diacetyl, acetaldehyde, and acetoin, produced through heterofermentative metabolisms, play a role in the enhancement of shelf life of some foods as they can control the growth of spoilage microorganisms (Jyoti et al. 2003; Lanciotti et al. 2003). Carbon dioxide is responsible for the inhibition of enzymatic decarboxylations and the dysfunction of membrane permeability in fungi.

The second group of antimicrobial compounds produced by LAB, i.e., high molecular mass substances, includes proteinaceous molecules referred to as bacteriocins (Sidooski et al. 2018). The bacteriocins produced by LAB are classified based on their molecular weight, heat sensitivity, mechanism of action, and spectrum of activity (review by Šušković et al. 2010; López-Cuellar et al. 2016; Collins et al. 2017). Regardless of the type of bacteriocins (e.g., heat-stable or heat-labile, single or two-peptide bacteriocin, linear or circular structure), these molecules have received considerable attention due to their potential application in food industry as biopreservatives. Besides, the bacteriocin biosynthetic ability is a desirable probiotic feature, as their antibacterial spectrum can embrace spoilage organisms and foodborne pathogens (Chen and Hoover 2003). For LAB bacteriocins, four classes have been proposed: (i) lantibiotic bacteriocins, (ii) non-lantibiotic bacteriocins, (iii) bacteriolysins, and (iv) lipid- or carbohydrate-required bacteriocins (Šušković et al. 2010). The mode of action of bacteriocins can vary from the modulation of enzyme activity, inhibition of outgrowth of spores, destabilization of cell membrane, or formation of pores, which can occur through binding lipids, dissipating proton motive force, thus altering the chemical membrane potential (Chen and Hoover 2003; Héchard and Sahl 2002; Venema et al. 1995; Cotter et al. 2005).

Biopreservative activity of probiotic LAB: from bacteriocins to organic acids through an in situ fermentation approach

In the food fermentation field, those cultures of microorganisms, properly selected and added to raw material in order to accelerate and steer the fermentation process, are named starter cultures. Many LAB are commonly used as microbial starters in several fermented foods based on matrices such as vegetables, meat, cereals, and milk (Sandine and Thunell 2018; Russo et al. 2016). In these products, the starter microorganisms, besides contributing to transform the raw material into a more palatable product, synthesize several metabolites, such as lactic acid, acetic acid, hydrogen peroxide, diacetyl, bacteriocins, which act as natural preserving agents. Thus, a greater acidifying capacity and/or the ability to produce larger amounts of bacteriocins are among the criteria by which the starter bacteria are selected.

Bacteriocin-producing starter cultures may not only contribute to food safety, by inhibiting foodborne pathogen microorganisms, but also prevent the growth of undesirable autochthonous bacteria that produce off-flavor. Some LAB cultures can be particularly capable to produce antimicrobial compounds but may be unable to satisfactorily carry out the desired fermentation of that particular food product. These cultures could be added during or after the fermentation process only for increasing the shelf life of the food product. These bacteriocin-producing adjunct cultures need to be also opportunely selected in order to not interfere with the performances of starter cultures and negatively affect the fermentation process (Bravo et al. 2009; Silva et al. 2018; O'Sullivan et al. 2003). Bacteriocins-producing LAB can be also added to non-fermented products, with the aim to protect them during their shelf life. In these cases, the used cultures are named bacteriocin-producing protective bacteria and they are added as food ingredient in food manufacturing (Woraprayote et al. 2016). Many studies have been carried out to improve the biopreservative action of microbes during the conservation process of the food product. Thus, numerous researches aimed to develop immobilization or microencapsulation methods for bacteriocin-producing bacteria or purified bacteriocins, directly into the food matrix, or on its surface, or in the food packaging (Champagne and Fustier 2007; Woraprayote et al. 2016; Woraprayote et al. 2018; Malhotra et al. 2015).

Bacteriocins used in combination with other methods of preservation, such as chemical additives (e.g., EDTA, sodium lactate, and potassium diacetate), heating, and high-pressure treatments, have been shown to improve the biopreservative action (Egan et al. 2016). To date, nisin (Nisaplin, Danisco; licensed as a food preservative (E234)) and pediocin PA1 (MicrogardTM, ALTA 2431, Quest) are the only bacteriocins commercialized as food preservatives (Simha et al. 2012; Favaro et al. 2015). However, the screening and characterization of numerous other bacteriocins produced by LAB could expand the industrial application of these compounds in the near future (Sánchez-Hidalgo et al. 2011; Suda et al. 2012).

Nisin, produced principally by *Lactococcus lactis* but also by *Streptococcus* strains (O'Connor et al. 2015), is mainly active against Gram-positive bacteria, e.g., *Listeria* and *Staphylococcus* genera, and the spore forming bacteria, e.g., *Bacillus* and *Clostridium* genera (Chen and Hoover 2003). Pediocin is produced by *Pediococcus* spp. and is highly active against *L. monocytogenes* and *S. aureus* pathogens, and also against *Pseudomonas* genera and *E. coli* species (Garsa et al. 2014).

Overall, the antifungal activity of LAB appears to be correlated to metabolic products that can also act in synergy. The chemical nature and the produced amount of these compounds are species- and strain-dependent (Crowley et al. 2013) and include organic acids (hydrocinnamic acid, DL-phenyllactic acid, DL-hydroxyphenyllactic acid, polyporic acid, azelaic acid, 2-hydroxybenzoic acid, 4-hydroxybenzoic acid, p-coumaric acid, vanillic acid, caffeic acid, succinic acid, 2-pyrrolidone-5-carboxylic acid), fatty acids (decanoic acid, 3-hydroxydecanoic acid, (S)-(-)-2–hydroxyisocaproic acid, coriolic acid, ricinoleic acid), cyclopeptides [cyclo(L-Pro-L-Pro), cyclo(L-Leu-L-Pro), cyclo(L-Tyr-L-Pro), cyclo(L-Met-L-Pro), cyclo(Phe-Pro), cyclo(Phe-OH-Pro), cyclo(L-Phe-L-Pro), cyclo(L-Phe-trans-4-OH-L-Pro), cyclo(L-His-L-Pro), and cyclo(Leu-Leu)], reuterin, hydrogen peroxide, and volatile compounds such as diacetyl (Leyva Salas et al. 2017).

In the overview to focus on the antifungal and antiviral activity of LAB, an example of the use of bacteria to prevent and/or decelerate the fungal growth in food could be that of cereal-based fermented products. Cereals and their derivative products are sensitive to the contamination by spoilage filamentous fungi, and this is a critical problem both from an economic point of view, due to the loss of raw material, and from a safety concern, due to the potential production of mycotoxins into food matrix (Pitt and Hocking 2009; Oliveira et al. 2014). LAB can have antagonistic activity against filamentous fungi, and, although the real mechanisms by which they contrast the fungal development are still unclear, it seems associated to cytoplasmic acidification and failure of proton motive forces (Reis et al. 2012; Russo et al. 2017). Among organic acids, phenyllactic acid (PLA) seems to be the most antifungal compound produced by LAB (Lavermicocca et al. 2000; Ström et al. 2002; Cortés-Zavaleta et al. 2014). Consequently, the addition of LAB cultures, or their cell free supernatants, showing antifungal activity, has been proposed for several food industry applications, including dairy and cereal-based productions, malting process, and fruits and vegetables storage (Axel et al. 2015; Oliveira et al. 2015; Cheong et al. 2014; Crowley et al. 2012; Russo et al. 2017). In malting wheat grains, treatments with strains of *Lactobacillus sakei*, *Pediococcus acidilactici*, and *Pediococcus pentosaceus* have been shown to reduce the production of *Fusarium* mycotoxins and the development of *F. culmorum* and *F. poae*. That reduction was linked to probable mechanisms of binding of mycotoxins b and/or their detoxification by LAB (Juodeikiene et al. 2018). In fact, it seems plausible that LAB could detain enzymes able to destabilize the mycotoxin structure making them less active. This feature has been already reported for other microorganisms, including *Eubacterium*, which are able to produce specific enzymes (e.g., deepoxidase) that catalyze the oxidation of the toxic epoxy ring of some mycotoxins in a strain-specific manner (Karlovsky 1999; Garvey et al. 2008; Juodeikiene et al. 2012; Mccormick 2013; Hathout and Aly 2014).

Recently, Miezkin et al. (2017) found a synergist effect of acetic, lactic, 2-pyrrolidone-5-carboxylic, (S)-(-)-2–hydroxyisocaproic, and 2-hydroxybenzoic acids produced by *Lactobacillus harbinensis* strains against several fungi. Moreover, the production of diacetyl together with 2,3-pentadione, acetic acid, and butanoic acid was suggested as the key antifungal capability of *L. paracasei* strain (Aunsbjerg et al. 2015).

In Fig. 1, a schematic representation of probiosis, immunobiosis, and biopreservative activity of LAB is reported.

Probiosis and antiviral activity

In recent years, the problem of antibiotic resistance has troubled both the scientific community and consumers. Antibiotic resistance of pathogenic bacteria is the mechanism through which bacteria become resistant to the antibiotic used in the medical treatments of the diseases. The overuse of those medications, as well as a lack of new drug development by the pharmaceutical industry, determined the worldwide emergence of resistant bacteria (Ventola 2015). Consequently, many efforts have been made in order to find antibiotic bio-alternatives, such as phages, bacteriocins, essential oils, metals, minerals, organic acids, or enhancement of modulation of human immune response (Lazarus et al. 2018; Ouwehand et al. 2016). In this regard, probiotics have been found to

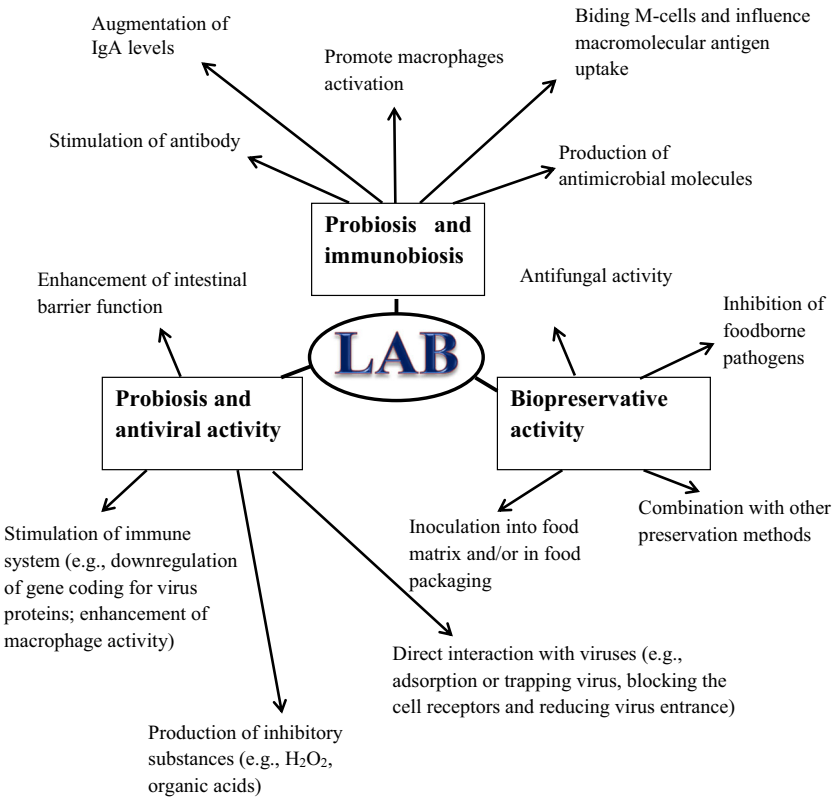

Fig. 1 Schematic representation of probiosis, immunobiosis, and biopreservative activity of lactic acid bacteria (LAB)

reduce the risk of certain infectious disease directly acting against the etiologic agent of the disease or indirectly modulating the host's immune response and modifying the gut microflora in order to prevent pathogen colonization (Cavera et al. 2015).

The multiple actions of probiotic in the oro-gastrointestinal tract include the production of metabolites that modify the acid and redox environment and disadvantage the pathogenic colonization, the enhancement of intestinal barrier function and mucin production, and the competition for nutrients and adhesion sites against pathogens. Moreover, the production of antimicrobial compounds that directly intervene to reduce the growth of enemies and the stimulation of immune system response are two main mechanisms able to contrast the onset of infections and diseases (Arqués et al. 2015; Arena et al. 2016, 2014; Yahfoufi et al. 2018). The consumption of probiotic microorganisms, such as *Lactobacillus johnsonii* and *B. lactis*, has been related to increased phagocytosis of pathogens, such as *E. coli* (Schiffrin et al. 1994). Other probiotic bacteria have been shown to activate the lymphoid cells of the gut-associated lymphoid tissue through bacterial cell envelope constituents, such as peptidoglycan, and thanks to the intimated contact that is established when the probiotic cell adheres to the intestinal monolayer surface (Ranadheera et al. 2014). However, probiotics could also modulate immune response by acting on the permeability of the intestine to eventual antigens and enemies, including viruses, and by producing antimicrobial metabolites (Seo et al. 2010).

LAB can exert antiviral capabilities by three main mechanisms: (i) the direct interaction with viruses, (ii) the production of antiviral inhibitory substances, or/and (iii) the stimulation of immune system. The direct interaction is probably the most common process by which probiotic bacteria are able to inactive viruses. It occurs through adsorption or trapping the virus and is strictly a strain-dependent mechanism (Al Kassaa et al. 2014). Strains of *L. paracasei*, *L. rhamnosus*, *L. plantarum*, and *L. reuteri* have been studied for their ability to trap vesicular stomatitis virus (VSV) (Botić et al. 2007), while *Enterococcus faecium* and *Lactobacillus gasseri* strains have been reported to directly inactive influenza viruses and herpes simplex type 2 (HSV-2), respectively (Al Kassaa et al. 2015; Wang et al. 2013). Frequently, many probiotics can attach to cell surfaces, thereby affecting the first stages of the viral infection by blocking the virus binding to the cell receptors and reducing its entrance into the cell (Bermudez-Brito et al. 2012; Varyukhina et al. 2012).

Moreover, antiviral activity by probiotic can occur also through the stimulation of host's immune system. A strain of *Bifidobacterium adolescentis* has been proved to decrease HPV16 mRNA transcript and protein levels demonstrating antiviral capability (Cha et al. 2012). As the HPV oncogene mRNA and protein overexpression are

correlated to carcinogenesis process of the cervical cancer (Woodman et al. 2001), the downregulation exerted by *B. adolescentis* highlights the potential application of that strain in the prevention of HPV-associated cervical cancer (Cha et al. 2012; Li et al. 2010).

The production of inhibitory substances can also contrast viruses and their activities. For example, hydrogen peroxide produced by LAB is able to attenuate human immunodeficiency virus (Conti et al. 2009), while lactic acid, the main product of the LAB metabolism, reduce the pH values and make the environment unfavorable for viruses, such as human lymphotropic virus and herpes simplex virus (Martin et al. 1985, 2010; Tuyama et al. 2006). Other bacterial molecules, such as non-protein cell wall component, could contrast viral replication (Mastromarino et al. 2011). Several LAB bacteriocins have been investigated for their ability to reduce coliphage HSA viral progeny (Humaira et al. 2006) or to affect intracellular viral multiplication and late stages of replication of herpes simplex virus (HSV-1 and HSV-2) (Wachsman et al. 1999, 2003; Todorov et al. 2005). The antiviral effect of bacteriocins during viral multiplication seems to depend on their ability to avoid the aggregation of viral particles by blocking the receptors sites on host cells (Wachsman et al. 2003). Numerous studies on antiviral activity against viral respiratory infections brought to light that the oral administration of probiotic LAB, such as strains of *L. plantarum*, *Lactobacillus casei*, and *Lactobacillus fermentum*, decreased influenza virus effects (Maeda et al. 2009; Boge et al. 2009; Olivares et al. 2007). Moreover, a strain of *L. rhamnosus*, in combination with *B. animalis* subsp. *lactis* biotype, has been proved to ameliorate the incidence of respiratory virus infections (RVI) (Rautava et al. 2009). The ability to beneficially modulate the IFN-c and IL secretion in order to contrast respiratory syncytial virus was correlated to the assumption of *L. rhamnosus* (Chiba et al. 2013; Salva et al. 2011). *L. plantarum* was investigated for its antiviral and protective effects against influenza virus, associated to a beneficial modulation of innate immunity of dendritic and macrophage cells and cytokines production pattern. The strains were able to modulate the levels of cytokines IL-12 and IFN-c in bronchoalveolar lavage fluids, and to reduce the degree of inflammation upon infection with influenza virus (Park et al. 2013).

The most known and studied antiviral activity by LAB is that against enteric viruses that are commonly associated with diarrhea and gastroenteritis in humans (Maragkoudakis et al. 2010). *L. casei* and *L. rhamnosus* stains could reduce the symptoms of acute infectious diarrhea in infants and children (Agarwal and Bhasin 2002; Szajewska and Mrukowicz 2001). The production of NO^{-} and H_2O_2 by strains of *E. faecium*, *L. fermentum*, *Lactobacillus pentosus*, and *L. plantarum* could account for their antiviral activity (Al Kassaa et al. 2014).

The research focused on sexually transmitted viruses (STV) that are relatively more recent and various inhibitory activities have been found against widespread viruses such as human papilloma (HPV) and human immunodeficiency virus (HIV) (Weiss et al. 2004). Some authors have shown that the probiotic activity against these kinds of virus possibly involves the suppression of oncogene proteins (Cha et al. 2012) and/or the stimulation of macrophages activity (Khania et al. 2012).

Several studies proposed an antiviral mechanism based on probiotic metabolites that can alter the production of viral proteins. In detail, Olaya Galán et al. (2016) suggested that four metabolites produced by probiotic bacteria were able to reduce the quantity of the intracellular NSP4 protein, which is produced by rotavirus during the infection. The consumption of probiotics has been associated also to an amelioration of the incidence of viral respiratory infection such as those caused by rhinovirus. The ingestion of *Bifidobacterium animalis* subspecies *lactis* has been shown to have an effect on the baseline state of innate immunity in the nose and on the subsequent response of the human host to rhinovirus infection in a clinical trial of volunteers. *B. animalis* subspecies *lactis* seems to manifest its anti-rhinovirus activity by modulating the inflammatory host response, e.g., CXCL8 nasal response, and by decreasing the shedding of virus in the nasal secretion (Turner et al. 2017).

Several compounds produced by probiotic microorganisms have been associated with antiviral activity. For example, cells from two *L. plantarum* strains, as well as their derivatives, were found to antagonize the enterovirus Coxsackievirus B4 (CV-B4), which can infect different human tissues and provoke abnormal function or destruction of various organs and cells (Arena et al. 2018). The inhibitory effect by *L. plantarum* against CV-B4 was associated to a direct interaction probiotic-pathogen, although the antiviral mode of action needs to be further elucidated. Similarly, other authors described antiviral effect by *L. reuteri* against enteroviruses Coxsackievirus A and Enterovirus 71, achieved through a direct physical interaction between bacterial and viral particles, which hinders the virus entry into host cells (Ang et al. 2016). Moreover, another study showed that a *B. adolescentis* strain was active against Coxsackievirus B3 (CV-B3) by inhibiting its intracellular replication and acting on host IFN-mediated antiviral response (Kim et al. 2014).

Probiotics could be also a suitable alternative or co-treatment of urogenital infections with the aim to reduce antibiotic use and avoid the increasing development of resistance. In women, in most of the studies, probiotic intervention was supplied via vaginal route although also the oral via seems to be effective. In the vaginal mucosa environment, probiotic colonization determines a pH reduction and, then, an inhibition of bacterial vaginosis, urinary tract infections, vulvovaginal candidiasis, and human papillomavirus (HPV) (Hanson et al. 2016). The use of probiotic *L. rhamnosus* GG has been demonstrated to be efficient in the prevention of

mucosal infections by the fungal pathogen *Candida albicans*, probably due to a reduction of its adhesion, invasion, and hyphal extension in vaginal and oral sites (Mailänder-Sánchez et al. 2017).

Conclusion

LAB represent a remarkable resource in the fight against fungi and viruses and key allies allowing the potential reduction of fungicidal and virucidal chemical agents. Such microorganisms are able both to act directly against pathogens and through the production of metabolites that interfere with fungi and virus activity. Although the detailed mechanisms by which LAB contrast microbial enemies are not well elucidated, many steps forward have been made in the last decades and many others are still being done, as nowadays, the attention of consumers and scientists is oriented toward an increasing use of bio-renewable and non-chemical approaches in both food manufacture and medical treatments.

Funding information This research was supported by the Apulian Region in the framework of Project "Biotecnologie degli alimenti per l'innovazione e la competitività delle principali filiere regionali: estensione della conservabilità e aspetti funzionali (BiotecA)". Vittorio Capozzi was supported by Fondo di Sviluppo e Coesione 2007-2013—APQ Ricerca Regione Puglia "Programma regionale a sostegno della specializzazione intelligente e della sostenibilità sociale ed ambientale—FutureInResearch".

Compliance with ethical standards

This article does not contain any studies with human participants or animals performed by any of the authors.

Conflict of interest The authors declare that they have no competing interests.

References

Agarwal KN, Bhasin SK (2002) Feasibility studies to control acute diarrhea in children by feeding fermented milk preparations Actimel and Indian Dahi. Eur J Clin Nutr 56:S56–S59

Al Kassaa I, Hober D, Hamze M, Chihib NE, Drider D (2014) Antiviral potential of lactic acid bacteria and their bacteriocins. Probiotics Antimicrob Proteins 6:177–185

Al Kassaa I, Hober D, Hamze M, Caloone D, Dewilde A, Chihib NE, Drider D (2015) Vaginal *Lactobacillus gasseri* CMUL57 can inhibit herpes simplex type 2 but not Coxsackievirus B4E2. Arch Microbiol 197:657–664

Al-Tawaha R, Meng C (2018) Potential benefits of *Lactobacillus plantarum* as probiotic and its advantages in human health and industrial applications: a review. Adv Environ Biol 12:16–27

Ang LYE, Too HKI, Tan EL, Chow TKV, Shek PCL, Tham E, Alonso S (2016) Antiviral activity of *Lactobacillus reuteri* Protectis against *Coxsackievirus* A and *Enterovirus* 71 infection in human skeletal muscle and colon cell lines. Virol J 13:111–123

Arena MP, Capozzi V, Spano G, Fiocco D (2017) The potential of lactic acid bacteria to colonize biotic and abiotic surfaces and the investigation of their interactions and mechanisms. Appl Microbiol Biotechnol 101:2641–2657

Arena MP, Elmastour F, Sane F, Drider D, Fiocco D, Spano G, Hober D (2018) Inhibition of *coxsackievirus* B4 by *Lactobacillus plantarum*. Microbiol Res 210:59–64

Arena MP, Silvain A, Normanno G, Grieco F, Drider D, Spano G, Fiocco D (2016) Use of Lactobacillus plantarum strains as a bio-control strategy against food-borne pathogenic microorganisms. Front Microbiol 7:464–474

Arena MP, Russo P, Capozzi V, López P, Fiocco D, Spano G (2014) Probiotic abilities of riboflavin-overproducing *Lactobacillus* strains: a novel promising application of probiotics. Appl Microbiol Biotechnol 98(17):7569–7581

Arqués JL, Rodríguez E, Langa S, Landete JM, Medina M (2015) Antimicrobial activity of lactic acid bacteria in dairy products and gut: effect on pathogens. Biomed Res Int 2015:1–10

Aunsbjerg SD, Honoré AH, Marcussen J, Ebrahimi P, Vogensen FK, Benfeldt C, Skov T, Knøchel S (2015) Contribution of volatiles to the antifungal effect of *Lactobacillus paracasei* in defined medium and yogurt. Int J Food Microbiol 194:46–53

Axel C, Röcker B, Brosnan B, Zannini E, Furey A, Coffey A, Arendt EK (2015) Application of *Lactobacillus amylovorus* DSM19280 in gluten-free sourdough bread to improve the microbial shelf life. Food Microbiol 47:36–44

Axelsson L (2004) Lactic acid bacteria: classification and physiology. In: Salminen S, von Wright A, Ouwehand A (eds) Lactic acid bacteria. Marcel Dekker, New York, pp 1–66

Bermudez-Brito M, Plaza-Dıaz J, Munoz-Quezada S, Gomez-Llorente C, Gil A (2012) Probiotic mechanisms of action. Ann Nutr Metab 61:160–174

Boge T, Remigy M, Vaudaine S, Tanguy J, Bourdet-Sicard R, van der Werf S (2009) A probiotic fermented dairy drink improves antibody response to influenza vaccination in the elderly in two randomised controlled trials. Vaccine 27:5677–5684

Bonnardel J, Da Silva C, Henri S, Tamoutounour S, Chasson L, Montañana-Sanchis F, Gorvel JP, Lelouard H (2015) Innate and adaptive immune functions of Peyer's patch monocyte-derived cells. Cell Rep 11: 770–784. doi:https://doi.org/10.1016/j.celrep.2015.03.067

Botić T, Danø T, Weingartl H, Cencič A (2007) A novel eukaryotic cell culture model to study antiviral activity of potential probiotic bacteria. Int J Food Microbiol 115:227–234

Bravo D, Rodríguez E, Medina M (2009) Nisin and lacticin coproduction by *Lactococcus lactis* strains isolated from raw ewes' milk. J Dairy Sci 92:4805–4811

Cavera VL, Arthur TD, Kashtanov D, Chikindas ML (2015) Bacteriocins and their position in the next wave of conventional antibiotics. Int J Antimicrob Agents 46:494–501

Cha MK, Lee DK, An HM, Lee SW, Shin SH, Kwon JH, Kim KJ, Ha NJ (2012) Antiviral activity of *Bifidobacterium adolescentis* SPM1005-A on human papillomavirus type 16. BMC Med 10:72–77

Champagne CP, Fustier P (2007) Microencapsulation for the improved delivery of bioactive compounds into foods. Curr Opin Biotechnol 18:184–190

Chen H, Hoover DG (2003) Bacteriocins and their food applications. Compr Rev Food Sci Food Saf 2:82–100

Cheong EYL, Sandhu A, Jayabalan J, Kieu Le TT, Nhiep NT, My Ho HT, Zwielehner J, Bansal N, Turner MS (2014) Isolation of lactic acid bacteria with antifungal activity against the common cheese spoilage mould *Penicillium commune* and their potential as biopreservatives in cheese. Food Control 46:91–97

Chiba E, Tomosada Y, Guadalupe MVP, Salva S (2013) Immunobiotic *Lactobacillus rhamnosus* improves resistance of infant mice against respiratory syncytial virus infection. Int Immunopharmacol 17:373–382

Collins FW, O'Connor PM, O'Sullivan O, Gómez-Sala B, Rea MC, Hill C, Ross RP (2017) Bacteriocin gene-trait matching across the complete *Lactobacillus* pan-genome. Sci Rep 7:3481–3494

Conti C, Malacrino C, Mastromarino P (2009) Inhibition of herpes simplex virus type 2 by vaginal lactobacilli. J Physiol Pharmacol 6:19–26

Cortés-Zavaleta O, López-Malo A, Hernández-Mendoza A, García HS (2014) Antifungal activity of lactobacilli and its relationship with 3-phenyllactic acid production. Int J Food Microbiol 173:30–35

Cotter PD, Hill C, Ross RP (2005) Bacteriocins: developing innate immunity for food. Nat Rev Microbiol 3:777–788

Crowley S, Mahony J, van Sinderen D (2012) Broad-spectrum antifungal-producing lactic acid bacteria and their application in fruit models. Folia Microbiol 58:291–299

Crowley S, Mahony J, van Sinderen D (2013) Current perspectives on antifungal lactic acid bacteria as natural bio-preservatives. Trends Food Sci Technol 33:93–109

Da Silva FFP, Biscola V, LeBlanc JG, de Melo Franco BDG (2016) Effect of indigenous lactic acid bacteria isolated from goat milk and cheeses on folate and riboflavin content of fermented goat milk. LWT-Food Sci Technol 71:155–161

de Moreno de LeBlanc A, Levit R, de Giori GS, LeBlanc JG (2018) Vitamin producing lactic acid bacteria as complementary treatments for intestinal inflammation. Antiinflamm Antiallergy Agents Med Chem 17:50–56

Diener M (2016) Roadblock for antigens – take a detour via M cells. Acta Physiol 216:13–14. https://doi.org/10.1111/apha.12595

Egan K, Field D, Rea MC, Ross RP, Hill C, Cotter PD (2016) Bacteriocins: novel solutions to age old spore-related problems? Front Microbiol 7: 461–482. https://doi.org/10.3389/fmicb.2016.00461

Galdeano CM, De Leblanc ADM, Vinderola G, Bonet MB, Perdigon G (2007) Proposed model: mechanisms of immunomodulation induced by probiotic bacteria. Clinical Vaccine Immunol 14:485–492

Garrity GM, Holt JG (2001) The road map to the manual. In: Bergey's manual® of systematic bacteriology. Springer, New York, pp 119–166

Garsa AK, Kumariya R, Kumar A, Lather P, Kapila S, Sood S (2014) Industrial cheese whey utilization for enhanced production of purified pediocin PA-1. LWT Food Sci Technol 59:656–665. https://doi.org/10.1016/j.lwt.2014.07.008

Garvey GS, McCormick SP, Rayment I (2008) Structural and functional characterization of the TRI101 trichothecene 3-O-acetyltransferase from *Fusarium* sporotrichioides and *Fusarium graminearum*: kinetic insights to combating *Fusarium* head blight. J Biol Chem 283: 1660–1669

Favaro L, Penna ALB, Todorov SD (2015) Bacteriocinogenic LAB from cheeses–application in biopreservation? Trends Food Sci Technol 41:37–48. https://doi.org/10.1016/j.tifs.2014.09.001

FAO/WHO (2001) Health and nutrition properties of probiotics in food including powder milk with live lactic acid bacteria. Retrieved from http://www.who.int/foodsafety/ publications/fs_management/probiotics/en/index.html

Franz CM, Holzapfel WH (2011) The importance of understanding the stress physiology of lactic acid bacteria. In: Stress responses of lactic acid bacteria. Springer, Boston, MA, pp 3–20

Hanson L, VandeVusse L, Jermé M, Abad CL, Safdar N (2016) Probiotics for treatment and prevention of urogenital infections in women: a systematic review. J Midwifery Women's health 61:339–355

Héchard Y, Sahl HG (2002) Mode of action of modified and unmodified bacteriocins from Gram-positive bacteria. Biochimie 84:545–557

Hathout AS, Ali SE (2014) Biological detoxification of mycotoxins: a review. Annals Microbiol 64(3):905–919

Humaira Q, Sadia S, Ahmed S, Ajaz Rasool S (2006) Coliphage hsa as a model for antiviral studies/spectrum by some indigenous bacteriocin like inhibitory substances (BLIS). Pak J Pharma Sci 19:182–187

Isolauri E (1999) Immune e!Ects of probiotics. In: Hanson LA, Yolken RH, Probiotics, other nutritional factors and intestinal microyora, Vevey/Lippincott-Raven Publishers, Philadelphia, pp 229–241

Jeon SH, Kim NH, Shim MB, Jeon YW, Ahn JH, Lee SH, Hwang IG, Rhee MS (2015) Microbiological diversity and prevalence of spoilage and pathogenic bacteria in commercial fermented alcoholic beverages (beer, fruit wine, refined rice wine, and yakju). J Food Prot 78:812–818

Juodeikiene G, Bartkiene E, Cernauskas D, Cizeikiene D, Zadeike D, Lele V, Bartkevics V (2018) Antifungal activity of lactic acid bacteria and their application for Fusarium mycotoxin reduction in malting wheat grains. LWT-Food Sci Technol 89:307–314

Jyoti B, Suresh AK, Venkatesh K (2003) Diacetyl production and growth of *Lactobacillus rhamnosus* on multiple substrates. World J Microbiol Biotechnol 19:509–515

Khania S, Motamedifara M, Golmoghaddam H, Hosseinic HM, Hashemizadeha Z (2012) *In vitro* study of the effect of a probiotic bacterium *Lactobacillus rhamnosus* against herpes simplex virus type 1. Braz J Infect Dis 16:129–135

Karlovsky P (1999) Biological detoxification of fungal toxins and its use in plant breeding, feed and food production. Nat Toxins 7:1–23

Kim MJ, Lee DK, Park JE, Park IH, Seo JG, Ha NJ (2014) Antiviral activity of *Bifidobacterium adolescentis* SPM1605 against *coxsackievirus* B3. Biotechnol Biotechnol Equip 28: 681–688

Kleerebezem M, Kuipers OP, Smid EJ (2017) Editorial: lactic acid bacteria-a continuing journey in science and application. FEMS Microbiol Rev 1. 41(Supp_1):S1-S2. doi: https://doi.org/10.1093/femsre/fux036

Kumar P, Chatli MK, Verma AK, Mehta N, Malav OP, Kumar D, Sharma N (2017) Quality, functionality, and shelf life of fermented meat and meat products: a review. Critical Rev Food Sci Nutrition 57:2844–2856

Laissue JA, Chappuis BB, MuKller C, Reubi JC, Gebbers J-O (1993) The intestinal immune system and its relation to disease. Digestive Dis 11:298–312

Lanciotti R, Patrignani F, Bagnolini F, Guerzoni ME, Gardini F (2003) Evaluation of diacetyl antimicrobial activity against *Escherichia coli*, *Listeria monocytogenes* and *Staphylococcus aureus*. Food Microbiol 20:537–543

Lavermicocca P, Valerio F, Evidente A, Lazzaroni S, Corsetti A, Gobbetti M (2000) Purification and characterization of novel antifungal compounds from the sourdough *Lactobacillus plantarum* strain 21B. Appl Environ Microbiol 66:4084–4090

Lazarus RP, John J, Shanmugasundaram E, Rajan AK, Thiagarajan S, Giri S, Babji S, Sarkar R, Kaliappan PS, Venugopal S, Praharaj I, Raman U, Paranjpe M, Grassly NC, Parker EPK, Parashar UD, Tate JE, Fleming JA, Steele AD, Muliyil J, Abraham AM, Kang G (2018) The effect of probiotics and zinc supplementation on the immune response to oral rotavirus vaccine: a randomized, factorial design, placebo-controlled study among Indian infants. Vaccine 36: 273–279

Li GL, Jiang W, Xia Q, Chen SH, Ge XR, Gui SQ, Xu CJ (2010) HPV E6 downregulation and apoptosis induction of human cervical cancer cells by a novel lipid-soluble extract (PE) from *Pinellia pedatisecta* Schott *in vitro*. J Ethnopharmacol 132:56–64

Lorca GL, de Valdez GF (2009) *Lactobacillus* stress responses. In: *Lactobacillus* molecular biology: from genomics to probiotics, Å Ljungh, T Wadström (Eds.), Caister Academic Press, Norfolk, UK, pp. 115–138

López-Cuellar MDR, Rodríguez-Hernández AI, Chavarría-Hernández N (2016) LAB bacteriocin applications in the last decade. Biotechnol Biotechnol Equipment 30:1039–1050

Maeda N, Nakamura R, Hirose Y, Murosaki S, Yamamoto Y, Kase T, Yoshikai Y (2009) Oral administration of heat-killed *Lactobacillus plantarum* L-137 enhances protection against influenza virus infection by stimulation of type I interferon production in mice. Int Immunopharmacol 9:1122–1125

Malhotra B, Keshwani A, Kharkwal H (2015) Antimicrobial food packaging: potential and pitfalls. Frontiers Microbiol 6:611–619

Mailänder-Sánchez D, Braunsdorf C, Grumaz C, Müller C, Lorenz S, Stevens P, Wagener J, Hebecker B, Hube B, Bracher F, Sohn K, Schaller M (2017) Antifungal defense of probiotic *Lactobacillus rhamnosus* GG is mediated by blocking adhesion and nutrient depletion. PLoS One 12:e0184438

Majamaa H, Isolauri E, Saxelin M, Vesikari T (1995) Lactic acid bacteria in the treatment of acute rotavirus gastroenteritis. J Pediatric Gastroenterol Nutrtion 20:333–338

Maragkoudakis PA, Chingwaru W, Gradisnik L, Tsakalidou E, Cencic A (2010) Lactic acid bacteria efficiently protect human and animal intestinal epithelial and immune cells from enteric virus infection. Int J Food Microbiol 141:S91–S97

Martin LS, McDougal JS, Loskoski SL (1985) Disinfection and inactivation of the human lymphotropic virus type III/lymphadenopathy-associated virus. J Infect Dis 152:400–403

Martin V, Maldonado A, Fernandez L, Rodriguez JM, Connor RI (2010) Inhibition of human immunodeficiency virus type 1 by lactic acid bacteria from human breastmilk. Breastfeed Med 5:153–158

Mastromarino P, Cacciotti F, Masci A, Mosca L (2011) Antiviral activity of *Lactobacillus brevis* towards herpes simplex virus type 2: role of cell wall associated components. Anaerobe 17:334–336

McCormick SP (2013) Microbial detoxification of mycotoxins. J Chemical Ecol 39(7):907–918

Mendonça FHBP, Santos SSFD, Faria IDSD, Gonçalves Silva CR, Jorge AOC, Leão MVP (2012) Effects of probiotic bacteria on *Candida* presence and IgA anti-Candida in the oral cavity of elderly. Brazilian Dental J 23:534–538

Mieszkin S, Hymery N, Debaets S, Coton E, Le Blay G, Valence F, Mounier J (2017) Action mechanisms involved in the bioprotective effect of Lactobacillus harbinensis K.V9.3.1.Np against *Yarrowia lipolytica* in fermented milk. Int J Food Microbiol 248:47–55

Mombelli B, Gismondo MR (2000) The use of probiotics in medical practice. Int J Antimicrob Agents 16:531–536

Niku-Paavola ML, Laitila A, Mattila-Sandholm T, Haikara A (1999) New types of antimicrobial compounds produced by *Lactobacillus plantarum*. J Appl Microbiol 86:29–35

O'Connor PM, Ross RP, Hill C, Cotter PD (2015) Antimicrobial antagonists against food pathogens: a bacteriocin perspective. Curr Opin Food Sci 2:51–57. https://doi.org/10.1016/j.cofs.2015.01.004

O'Halloran FM, Morrissey SD, Murphy L, Thornton G, Shanahan F, O'Sullivan GC, Collins JK (1998) Adhesion of potential probiotic bacteria to human epithelial cell lines. Int Dairy J 8:596

Olaya Galán NN, Ulloa Rubiano JC, Velez Reyes FA, Fernandez Duarte KP, Salas Cardenas SP, Gutierrez Fernandez MF (2016) In vitro antiviral activity of *Lactobacillus casei* and *Bifidobacterium adolescentis* against rotavirus infection monitored by NSP 4 protein production. J Appl Microbiol 120:1041–1051

Olivares M, Diaz-Ropero MP, Sierra S, Lara-Villoslada F, Fonolla J, Navas M, Rodriguez JM, Xaus J (2007) Oral intake of *Lactobacillus fermentum* CECT5716 enhances the effects of influenza vaccination. Nutrition 23:254–260

Oliveira PM, Zannini E, Arendt EK (2014) Cereal fungal infection, mycotoxins, and lactic acid bacteriamediated bioprotection: fromcrop farming to cereal products. J Food Microbiol 37:78–95

Oliveira PM, Brosnan B, Furey A, Coffey A, Zannini E, Arendt EK (2015) Lactic acid bacteria bioprotection applied to the malting process. Part I: strain characterization and identification of antifungal compounds. Food Control 51:433–443

O'Sullivan L, Ross RP, Hill C (2003) A lacticin 481-producing adjunct culture increases starter lysis while inhibiting nonstarter lactic acid bacteria proliferation during cheddar cheese ripening. J Appl Microbiol 95:1235–1241

Ouwehand AC, Forssten S, Hibberd AA, Lyra A, Stahl B (2016) Probiotic approach to prevent antibiotic resistance. Annals Med 48:246–255

Park MK, Vu NGO, Kwon YM, Lee YT, Yoo S, Cho YH, Hong SM, Hwang HS, Ko EJ, Jung YJ, Moon DW, Jeong EJ, Kim MC, Lee YN, Jang JH, Oh JS, Kim CH, Kang SM (2013) *Lactobacillus plantarum* DK119 as a probiotic confers protection against influenza virus by modulating innate immunity. PLoS One 8:e75368

Petruzzi L, Capozzi V, Berbegal C, Corbo MR, Bevilacqua A, Spano G, Sinigaglia M (2017) Microbial resources and enological significance: opportunities and benefits. Frontiers Microbiol 8: 995–1007

Pitt JI, Hocking AD (2009) Fungi and food spoilage. Springer, London, New York

Pothuraju R, Sharma RK (2018) Interplay of gut microbiota, probiotics in obesity: a review. Endocrine, metabolic & immune disorders-drug targets. Formerly Current Drug Targets-Immune Endocrine & Metabolic Disorders 18:212–220

Prabhurajeshwar C, Chandrakanth RK (2017) Probiotic potential of Lactobacilli with antagonistic activity against pathogenic strains: an in vitro validation for the production of inhibitory substances. Biom J 40:270–283

Pridmore RD, Pittet AC, Praplan F, Cavadini C (2008) Hydrogen peroxide production by *Lactobacillus johnsonii* NCC 533 and its role in anti-Salmonella activity. FEMS Microbiol Lett 283: 210–215

Ranadheera CS, Evans CA, Adams MC, Baines SK (2014) Effect of dairy probiotic combinations on in vitro gastrointestinal tolerance, intestinal epithelial cell adhesion and cytokine secretion. J Funct Foods 8: 18–25

Rautava S, Salminen S, Isolauri E (2009) Specific probiotics in reducing the risk of acute infections in infancy a randomised, double-blind, placebo-controlled study. Br J Nutr 101:1722–1726

Reid G (2008) Probiotic lactobacilli for urogenital health in women. J Clin Gastroenterol (Suppl 3, 42):234–236

Reis JA, Paula AT, Casarotti SN, Penna ALB (2012) Lactic acid bacteria antimicrobial compounds: characteristics and applications. Food Eng Rev 4:124–140

Russo P, Caggianiello G, Arena MP, Fiocco D, Capozzi V, Spano G (2016) Lactic acid bacteria of fermented fruits and vegetables, In: Paramithiotis S, Lactic acid fermentation of fruits and vegetables: Taylor & Francis

Russo P, Arena MP, Fiocco D, Capozzi V, Drider D, Spano G (2017) *Lactobacillus plantarum* with broad antifungal activity: a promising approach to increase safety and shelf-life of cereal-based products. Int J Food Microbiol 247:48–54

Salva S, Nun˜ez M, Villena J, Ramo'n A, Font G, Alvarez S (2011) Development of a fermented goats' milk containing *Lactobacillus rhamnosus*: *in vivo* study of health benefits J Sci Food Agric 91: 2355–2362

Leyva Salas M, Mounier J, Valence F, Coton M, Thierry A, Coton E (2017) Antifungal microbial agents for food biopreservation—a review. Microorganisms 5:37–90

Sánchez-Hidalgo M, Montalbán-López M, Cebrián R, Valdivia E, Martínez-Bueno M, Maqueda M (2011) AS-48 bacteriocin: close to perfection. Cell Mol Life Sci 68:2845–2857. https://doi.org/10.1007/s00018-011-0724-4

Sandine WE, Thunell RK (2018) Types of starter cultures. In: Bacterial starter cultures for food, CRC Press, pp 127–144

Santarmaki V, Kourkoutas Y, Zoumpopoulou G, Mavrogonatou E, Kiourtzidis M, Chorianopoulos N, Tassou C, Tsakalidou E, Simopoulos C, Ypsilantis P (2017) Survival, intestinal mucosa adhesion, and immunomodulatory potential of *Lactobacillus plantarum* strains. Current Microbiol 74:1061–1067

Schiffrin EJ, Rochat F, Link-Amster H, Aeschlimann JM, Donnet-Hughes A (1994) Immunomodulation of human blood cells following the ingestion of lactic acid bacteria. J Dairy Sci 78:491–497

Shornikova AV, Casas IA, Isolauri E, Vesikari T (1997) *Lactobacillus reuteri* as a therapeutic agent in acute diarrhoea in young children. J Pediatric Gastroenterol Nutrition 24:399–404

Seo BJ, Mun MR, RK J, Kim CJ, Lee I, Chang YH, Park YH (2010) Bile tolerant *Lactobacillus reuteri* isolated from pig feces inhibits enteric bacterial pathogens and porcine rotavirus. Vet Res Commun 34: 323–333

Sidooski T, Brandelli A, Bertoli SL, Souza CKD, Carvalho LFD (2018) Physical and nutritional conditions for optimized production of bacteriocins by lactic acid bacteria–a review. Critical Rev Food Sci Nutrition, (just-accepted), 1–26

Silva CC, Silva SP, Ribeiro SC (2018) Application of bacteriocins and protective cultures in dairy food preservation. Frontiers Microbiol 9: 594–608

Sjögren J, Magnusson J, Broberg A, Schnürer J, Kenne L (2003) Antifungal 3-hydroxy fatty acids from *Lactobacillus plantarum* MiLAB. J Appl Microbiol 69:7554–7557

Ström K, Sjögren J, Broberg A, Schnürer J (2002) *Lactobacillus plantarum* MiLAB produces the antifungal cyclic dipeptides cyclo (L-Phe-L-Pro) and cyclo (L-Phetrans- 4-OH-L-Pro) and 3-phenyllactic acid. Appl Environ Microbiol 68:4322–4327

Suda S, Cotter PD, Hill C, Ross PR (2012) Lacticin 3147-biosynthesis, molecular analysis, immunity, bioengineering and applications. Curr Protein Pept Sci 13:193–204. https://doi.org/10.2174/138920312800785021

Šušković J, Kos B, Beganović J, Pavunc AL, Habjanič K, Matošić S (2010) Antimicrobial activity-the most important property of probiotic and starter lactic acid bacteria. Food Technol Biotechnol 48: 296–307

Szajewska H, Mrukowicz JZ (2001) Probiotics in the treatment and prevention of acute infectious diarrhea in infants and children: a systematic review of published randomized, double-blind, placebo-controlled trials. J Pediatr Gastroenterol Nutr 33:S17–S25

Tejero-Sariñena S, Barlow J, Costabile A, Gibson GR, Rowland I (2012) *In vitro* evaluation of the antimicrobial activity of a range of probiotics against pathogens: evidence for the effects of organic acids. Anaerobe 18:530–538

Todorov SD, Wachsman MB, Knoetze H, Meincken M, Dicks LMT (2005) An antibacterial and antiviral peptide produced by *Enterococcus mundtii* ST4V isolated from soya beans. Int J Antimicrob Agents 25:508–513

Tuomola EM, Ouwehand AC, Salminen SJ (1999) Human ileostomy glycoproteins as a model for small intestinal mucus to investigate adhesion of probiotics. Letters Appl Microbiol 28:159–163

Turner RB, Woodfolk JA, Borish L, Steinke JW, Patrie JT, Muehling LM, Lahtinen S, Lehtinen MJ (2017) Effect of probiotic on innate inflammatory response and viral shedding in experimental rhinovirus infection–a randomised controlled trial. Benefic Microbes 8:207–215

Tuyama AC, Cheshenko N, Carlucci MJ, Li JH, Goldberg CL, Waller DP, Anderson RA, Profy AT, Klotman ME, Keller MJ, Herold BC (2006) Acidform inactivates herpes simplex virus and prevents genital herpes in a mouse model: optimal candidate for microbicide combinations. J Infect Dis 194:795–803

Twetman L, Larsen U, Fiehn NE, Stecksén-Blicks C, Twetman S (2009) Coaggregation between probiotic bacteria and caries-associated strains: an *in vitro* study. Acta Odontol Scand 67:284–288

Valerio F, Lavemicocca P, Pascale M, Visconti A (2004) Production of phenyllactic acid by lactic acid bacteria: an approach to the selection of strains contributing to food quality and preservation. FEMS Microbiol Lett 23:289–295

Varyukhina S, Freitas M, Bardin S, Robillard E, Tavan E, Sapin C, Grill JP Trugnan G (2012) Glycanmodifying bacteria-derived soluble factors from *Bacteroides thetaiotaomicron* and *Lactobacillus casei* inhibit rotavirus infection in human intestinal cells. Microbes Infect 14:273–278

Venema K, Venema G, Kok J (1995) Lactococcal bacteriocins: mode of action and immunity. Trends Microbiol 3:299–304

Ventola CL (2015) The antibiotic resistance crisis: part 1: causes and threats. Pharm Ther 40:277

Vijayaram S, Kannan S (2018) Probiotics: the marvelous factor and health benefits. Biomed Biotechnol Res J 2:1–8

Wang Z, Chai W, Burwinkel M, Twardziok S, Wrede P, Palissa C, Esch B, Schmid MFG (2013) Inhibitory influence of *Enterococcus faecium* on the propagation of swine influenza a virus *in vitro*. PLoS One 8:e53043

Wachsman MB, Farias ME, Takeda E, Sesma F, De Ruiz Holgado AP, de Torres RA, Coto CE (1999) Antiviral activity of enterocin CRL against herpes virus. Int J Antimicrob Agents 12:293–299

Wachsman MB, Castilla V, De Ruiz Holgado AP, de Torres RA, Sesma F, Coto CE (2003) Enterocin CRL35 inhibits late stages of HSV-1 and HSV-2 replication in vitro. Antivir Res 58:17–24

Weiss L, Donkova-Petrini V, Caccavelli L, Balbo M, Carbonneil C, Levy Y (2004) Human immunodeficiency virus-driven expansion of CD4?CD25? regulatory T cells, which suppress HIV-specific CD4 T-cell responses in HIV-infected patients. Blood 104:3249–3256

Woodman CB, Collins S, Winter H, Bailey A, Ellis J, Prior P, Yates M, Rollason TP, Young LS (2001) Natural history of cervical human papillomavirus infection in young women: a longitudinal cohort study. Lancet 357:1831–1836

Woraprayote W, Malila Y, Sorapukdee S, Swetwiwathana A, Benjakul S, Visessanguan W (2016) Bacteriocins from lactic acid bacteria and their applications in meat and meat products. Meat Sci 120:118–132

Woraprayote W, Pumpuang L, Tosukhowong A, Zendo T, Sonomoto K, Benjakul S, Visessanguan W (2018) Antimicrobial biodegradable food packaging impregnated with Bacteriocin 7293 for control of pathogenic bacteria in pangasius fish fillets. LWT 89:427–433

Yahfoufi N, Mallet JF, Graham E, Matar C (2018) Role of probiotics and prebiotics in immunomodulation. Curr Opin Food Sci 20:82–91