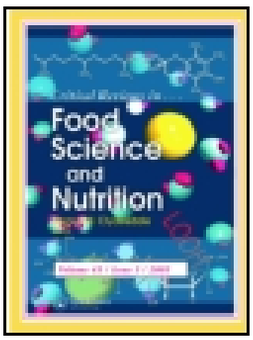

Critical Reviews in Food Science and Nutrition

ISSN: 1040-8398 (Print) 1549-7852 (Online) Journal homepage: https://www.tandfonline.com/loi/bfsn20

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To cite this article: Karim Naghmouchi, Yanath Belguesmia, Farida Bendali, Giuseppe Spano, Bruce S. Seal & Djamel Drider (2019): *Lactobacillus fermentum*: a bacterial species with potential for food preservation and biomedical applications, Critical Reviews in Food Science and Nutrition, DOI: 10.1080/10408398.2019.1688250

To link to this article: https://doi.org/10.1080/10408398.2019.1688250

Published online: 15 Nov 2019.

CRITICAL REVIEWS IN FOOD SCIENCE AND NUTRITION
https://doi.org/10.1080/10408398.2019.1688250

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REVIEW

Lactobacillus fermentum: a bacterial species with potential for food preservation and biomedical applications

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ABSTRACT

Lactic acid-producing bacteria are the most commonly used probiotics that play an important role in protecting the host against harmful microorganisms, strengthening the host immune system, improving feed digestibility, and reducing metabolic disorders. *Lactobacillus fermentum* (*Lb. fermentum*) is a Gram-positive bacterium belonging to *Lactobacillus* genus, and many reportedly to enhance the immunologic response as well as prevent community-acquired gastrointestinal and upper respiratory infections. Additionally, *Lb. fermentum* strains produce diverse and potent antimicrobial peptides, which can be applied as food preservative agents or as alternatives to antibiotics. Further functions attributed to probiotic *Lb. fermentum* strains are their abilities to decrease the level of blood stream cholesterol (as cholesterol-lowering agents) and to potentially help prevent alcoholic liver disease and colorectal cancer among humans. Finally, *Lb. fermentum* is a key microorganism in sourdough technology, contributing to flavor, texture, or health-promoting dough ingredients, and has recently been used to develop new foods stuffs such as fortified and functional foods with beneficial attributes for human health. Development of such new foodstuffs are currently taking important proportions of the food industry market. Furthermore, an increasing awareness of the consumers prompts the food-makers to implement alternative environmental friendly solutions in the production processes and/or suitable biological alternative to limit the use of antibiotics in feed and food. Here, we give an account on the application of *Lb. fermentum* strains in the biomedical and food preservation fields, with a focus on probiotic features such as bacteriocin production. We also summarize the use of *Lb. fermentum* as cell factories with the aim to improve the efficacy and health value of functional food.

KEYWORDS

Alcoholic liver disease; cholesterol-lowering agents; colorectal cancer; fermenticin; food preservation; lactic acid bacteria; medical application; probiotic

Introduction

Lactic acid bacteria (LAB) are in the phylum *Firmicutes*, class bacilli, order *Lactobacillales* that play important roles during food production, nutritional supplementation, agriculture, and human-animal medicine (Bintsis 2018). LAB constitute a diverse group of Gram-positive bacteria, devoid of catalase activity and producing lactic acid as the main end-product of carbohydrates fermentation. The LAB group is composed of genera including *Aerococcus*, *Carnobacterium*, *Enterococcus*, *Lactobacillus*, *Lactococcus*, *Leuconostoc*, *Oenococcus*, *Pediococcus*, *Streptococcus*, *Tetragenococcus*, *Vagococcus*, and *Weissella* (Cholakov et al. 2017). LAB are present in different ecological niches, and many studies have established differences at their genetic and physiological levels (Ait Seddik et al. 2017). With more than 240 species (http://www.bacterio.net/lactobacillus.html), *Lactobacillus* is certainly the most studied genus in the LAB group. *Lb. fermentum* lactic acid bacterium is an obligatory species widely distributed in nature, often isolated from fermenting plant materials (Nielsen et al. 2007), dairy products (Coton, Berthier, and Coton 2008), bread (Russo et al. 2014), naturally fermented sausages (Kaban and Kaya 2008), breast milk (Martín et al. 2003), and saliva (Dal Bello and Hertel 2006; Sonomoto and Yokota 2011). The beneficial effects of *Lb. fermentum* has resulted in the development of different probiotic preparations as listed in Table 1. *Lb. fermentum* antagonistic properties and particularly production of antimicrobial peptides (called fermenticins) are presented as potential means for medical application and food preservation processes (Fuochi, Volti, and Furneri 2017). Remarkably, there are several strains from LAB especially *Lactobacillus*, *Bifidobacteria*, and *Enterococcus* with probiotic characteristics (Franz et al. 2003; Vaughan et al. 2005). Within *Lactobacillus*, *Lb. fermentum* is not as well-studied relative to other species of the genus. For example, investigators have proposed using *Lb. fermentum* for treatment and prevention of gastrointestinal disorders,

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Table 1. List of commercially available *Lactobacillus fermentum* probiotic strains.

Product name capsule and powder	Industry manufacturing *Lb. fermentum* probiotic product	Sources/Strains	References
FloraFIT® Probiotics	Danisco USA, Inc	*Lb. fermentum* SBS-1	Morovic (2017a, 2017b)
Pro-Bio PCC	Phamanex, LLC.	*Lb. fermentum* PCC®	West et al. (2011)
BioOne™ *Lb. fermentum* ME-3®	SpectrumceuticalsPty Ltd., Australia	*Lb. fermentum* ME-3	Mikelsaar and Zilmer (2009)
Life-SpaceProbiotic	Lifespace communities, inc.	*Lb. fermentum* CECT5716	Lara-Villoslada et al. (2009)
HEREDITUM® Probiotic	BIOSEARCH S.A. Granada (Spain)	*Lb. fermentum* LC40 (CECT5716)	Popova, Mitev, and Nikolov (2016)
LACTEOL	Lacteol Laboratory, France	Mixture of *Lb. fermentum* and *Lb. delbrueckii*	Salazar-Lindo et al. (2007)
Lactobacillus fermentum probiotic powder	AMBIO Co., Ltd., Korea	*Lb. fermentum*	Cox et al. (2010)
Lactobacillus fermentum Powder mixed with inulin	Wuhan Healthdream Biological Technology Co. Ltd., China	*Lb. fermentum*	Strompfová, Lauková, and Cilik (2013)

attenuation of colorectal cancer (CRC) risk, and prevention of alcoholic liver disease (Barone et al. 2016; So, Wan, and El-Nezami 2017; Liu et al. 2019). Also, Owusu-Kwarteng et al. (2015) reported on the potential of *Lb. fermentum* as a technological starter for fermented food products, and as a food preservative agent. For instance, *Lb. fermentum* is a key microorganism in sourdough technology, contributing to flavor, texture, or health-promoting dough ingredients (De Vuyst et al. 2009). Recently, Weckx et al. (2010) using a meta-transcriptomic approach, revealed that mature wheat sourdoughs represent a stabilized ecosystem with *Lb. plantarum* and *Lb. fermentum* as the dominating LAB species. Prevalence of both species was also found in sourdoughs from different origins such as rye, spelt, and African amylaceous fermented foods. Genes involved in probiotic and nutritional functions, including riboflavin synthesis, were identified opening new perspectives in the field of the functional foods based on cereals matrix (Turpin, Humblot, and Guyot 2011; Russo et al. 2014). In Figure 1, the main functions and beneficial affects attributed to this species are reported.

The present review summarizes some of the important benefits from utilizing *Lb. fermentum* as a species relative to the medical sector and as probiotic with multifunctional applications in food preservation, such as the fermenticin producing strains.

Safety assessment and beneficial attributes of *Lb. fermentum*

The use of LAB strains as potential probiotics and medical applications has spread out worldwide. The health-promoting effects of probiotic bacteria are well supported by convincing clinical trials and studies completed in animal models. These health-promoting effects include anti-infective properties (Isolauri et al. 1991), anti-inflammatory activities (Peran et al. 2006; Rodríguez-Nogales et al. 2017), immunomodulatory activity (Martín et al. 2003) or prevention of allergic diseases (Furrie 2005). Risks and adverse effects associated with probiotics use remains rare and often has not been assessed in randomized controlled trials (Hempel et al. 2011; Zawistowska-Rojek and Tyski 2018). Different investigators, have nevertheless, reported bacteriemia, endocarditis, ulcerative colitis, and other associated risks especially in immunocompromised patients upon probiotics uptake (Franko et al. 2013; Meini et al. 2015; Haghighat and Crum-Cianflone 2016). Theoretical risks exist and include systemic infections, deleterious metabolic activities, and excessive immune stimulation in susceptible individuals, and potential gene transfer (Doron and Snydman 2015). Notwithstanding these sporadic cases, probiotics are considered as safe supported by their long history of applications. The most widely used species belonging to *Lactobacillus* genera include *Lb. rhamnosus*, *Lb. acidophilus*, *Lb. coryneformis*, *Lb. paracasei*, *Lb. plantarum*, and *Lb. jensenii* (Suárez-García et al. 2012; Franko et al. 2013; Datta et al. 2017; Ait Seddik et al. 2017; Rossi, Amadoro, and Colavita 2019).

Interestingly, *Lb. fermentum* is included in the list of taxonomic units proposed by the European Food Safety Authority (EFSA 2007) for the qualified presumption of safety (QPS) status (Lara-Villoslada et al. 2009). The main representative of this group is *Lb. fermentum* CECT-5716 a probiotic strain isolated from breast milk and selected for its safety, functionality (EFSA 2007), anti-infectious, and immunomodulatory properties (Żarłok 2016). Moreover, Gil-Campos et al. (2012) and Maldonado et al. (2012) established the safety and tolerance of an infant formula supplemented with *Lb. fermentum* strains among infants and suggested the use of such a formula for prevention of community-acquired infection and upper respiratory tract infections. Also, this species has been proposed as an efficient mean to treat infectious mastitis during lactation (Arroyo et al. 2010).

Recently, Jayashree et al. (2018) established the potency of *Lb. fermentum* MTCC 8711 to prevent the adhesion of methicillin-resistant *Staphylococcus aureus* (MRSA) to human colon adenocarcinoma cells, Caco-2. Another research group reported the capability of *Lb. fermentum* TCUESC-01 to tolerate conditions mimicking the human stomach and intestine along with its ability to undergo autoaggregation. These attributes accompanied by its susceptibility to antibiotics may increase its application as a potential probiotic strain (Melo et al. 2017). Interestingly, encapsulation of *Lb. fermentum* NCIMB 5221 in poly-L-lysine-alginate was reported as an effective oral delivery system (Tomaro-Duchesneau et al. 2012). This encapsulation permitted the bacterium to survive simulated gastrointestinal conditions and a 2.5 log gain in viability versus free cells (non-capsulated cells) with, respectively, $5.50 \times 10^6 \pm 1.00 \times 10^5$ and $1.10 \times 10^4 \pm 1.00 \times 10^3$ CFU/mL. Another relevant application of fresh or lyophilized cultures containing (10^7 to 10^9 CFU) of *Lb. fermentum*

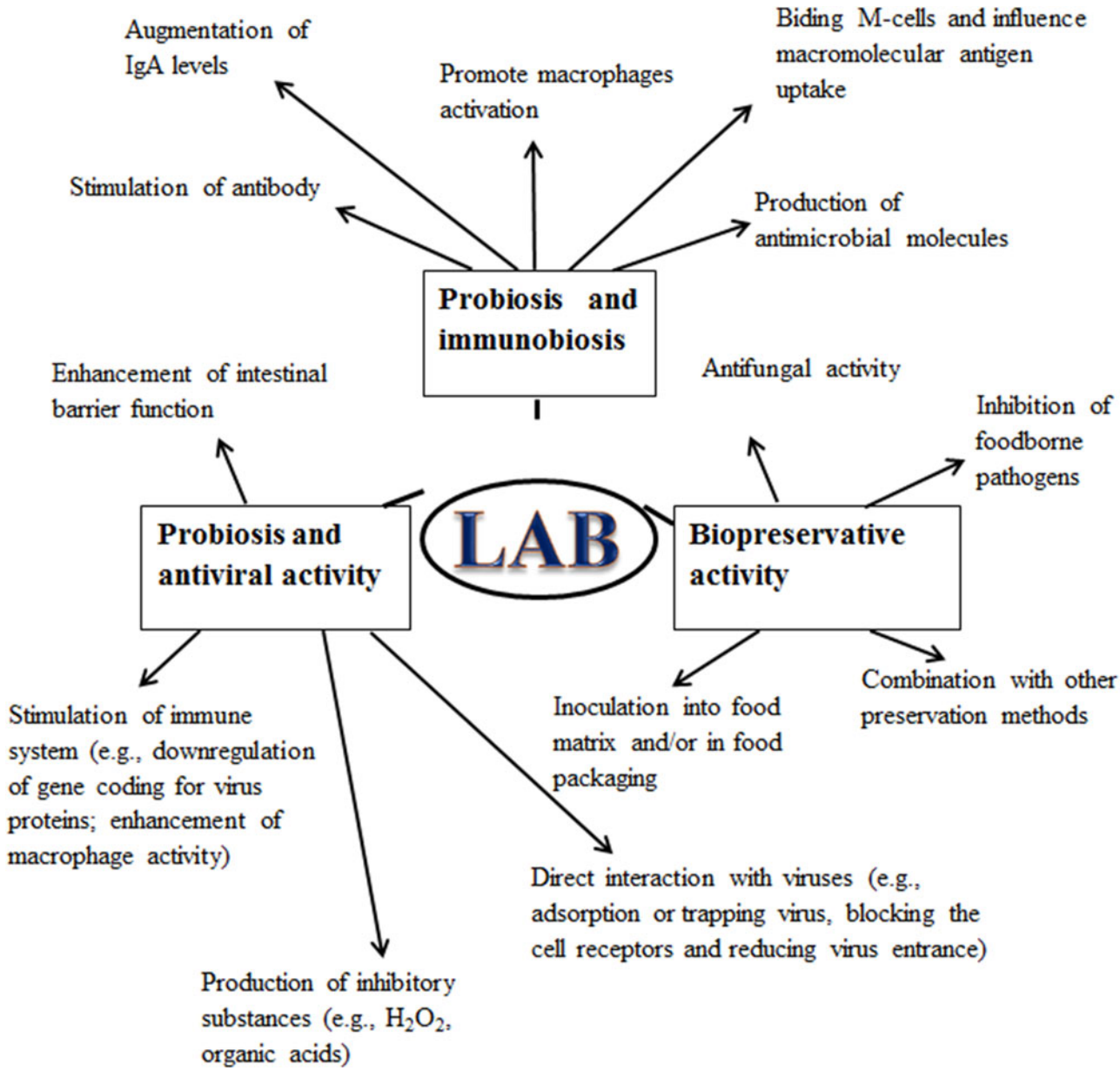

Figure 1. Schematic representation of probiosis, immunobiosis, and biopreservative activity of Lactic Acid Bacteria (LAB).

CCM-7421 was in healthy dogs and for those suffering from gastrointestinal disorders during 4-days to 14-days treatment (Strompfová, Kubašová, and Lauková 2017), arguing for a positive impact on the health of these animals.

Lactobacillus fermentum as probiotic for health applications

Alcoholic liver disease (ALD) prevention

Alcoholism is a devastating disease, with its pathogenesis characterized by progressive accumulation of lipids in the liver, inflammation, steatohepatitis, and in some individuals, the final stages include fibrosis and cirrhosis (Barone et al. 2016). Probiotics have received increasing attention in the past few years due to their well-documented gastrointestinal health-promoting claims. Byoung-Kook et al. (2017) studied the effect of *Lb. fermentum* LA-12 for the prevention of alcoholic steatohepatitis in a rat model, via the gut-liver axis. Four-week administration of *Lb. fermentum* LA-12 restored the intestinal barrier function and reduced alcohol-induced inflammatory mediators, indicating a potential claim of this strain, in attenuating leaky gut and liver damage, or preventing the progression of alcoholic steatohepatitis (ASH). Barone et al. (2016) reported in mice that *Lb. fermentum*, reduced considerably ethanol-induced tissue damage and can be used as probiotic with therapeutic potential for alcoholic liver disease. According to Sharma et al. (2014), which led a study on ageing mice, *Lb. fermentum* could be utilized to protect the liver for preventing endotoxemia by improving the intestinal barrier function or by enhancing the antioxidant activity of glutathione peroxidase and glutathione reductase. However, no clinical study has been conducted with humans. So, the beneficial effects of probiotic strains of *Lb. fermentum* on diseases related to

alcohol over-consumption remain to be established among human patients.

Lactobacillus fermentum effect on gastrointestinal and upper respiratory tract infections

Probiotics are becoming increasingly popular as a nutrition supplement to reduce susceptibility to common infectious illnesses, such as upper respiratory tract (URT) and gastrointestinal (GI) illness. Investigators have reported that probiotic supplementation could be useful for enhancing immunity and reducing the duration of URT and GI illness among endurance athletes (Tiollier et al. 2007; Gleeson et al. 2011). Nevertheless, both studies present a lack of proper control studies using conventional formulations to compare the effects observed with *Lb. fermentum* probiotics. West et al. (2011) reported that *Lb. fermentum* (PCC®) can be a useful nutritional adjunct for healthy exercising males. Supplementation with the probiotic PCC® reportedly reduced the severity of self-reported symptoms and severity of gastrointestinal symptoms at higher training regimens among male athletes (West et al. 2011). The increased frequency of mild, low-grade symptoms of GI illness can reflect short-term adaptive responses in the GI tract with probiotic with use of PCC®. On the other hand, prophylactic administration of probiotic *Lb. fermentum* (PCC®) at a daily dose of 1.26×10^{10} as a freeze-dried powder in gelatin capsules resulted in a substantial reduction in the severity of respiratory illness among athletes (Cox et al. 2010). Affirmative conclusions remain difficult to establish in the case of concomitant uptake of traditional medications that could potentially interfere with the results expected from the use of a probiotic (Cox et al. 2010; West et al. 2011).

Other investigators reported that administration of a follow-on formula with *Lb. fermentum* CECT-5716 can be useful for the prevention of community-acquired gastrointestinal and upper respiratory infections among infants between 6 and 12 months old (Maldonado et al. 2012; Lopez-Huertas 2015). The experimental group showed 46% reduction in the incidence rate of gastrointestinal infections and 27% reduction in the incidence of upper respiratory tract infections at the end of the study period compared with the control group. *Lb. fermentum* CECT-5716 is also capable of fermenting a variety of carbohydrates in the intestine and producing short-chain fatty acids (SCFAs), which are an important source of energy for intestinal cells (Peran et al. 2006). SCFAs increase the absorption of water and salt in the intestine, participate actively in colon epithelial cell metabolism and reduce the pH value, thereby supporting the growth of healthy bacteria and inhibiting the growth of pathogenic microorganisms. Olivares et al. (2006) reported that *Lb. fermentum* CECT-5716 inhibited the adhesion of pathogens to the intestinal mucosa and caused elimination of some pathogens. Notably, *Lb. fermentum* also induced the production of mucin which is the initial barrier of the intestinal epithelium as protection against infections.

An in vivo study showed that *Lb. fermentum* 1.2029 significantly increased goblet cell density in the jejunum and the gene expression level of MUC2 mRNA in both the jejunum and ileum of broiler chickens (Cao et al. 2012). Remarkably, *Lb. fermentum* CECT-5716 was able to produce glutathione, a natural antioxidant, which reportedly protects the intestine from oxidative damage (Peran et al. 2006). *Lb. fermentum* Lee (LF-Lee) also had a potential functional activity and a preventive effect on constipation in mice. After LF-Lee treatment, the time to the first black stool defecation was only marginally longer than that in mice treated with bisacodyl with reportedly improved acid resistance, bile tolerance and improved hydrophobic properties (Qian et al. 2015). *Lb. fermentum* Lc40 (200 million CFU/day) was also shown to decrease the incidence of infantile gastrointestinal and respiratory infections in a 3 years follow-up study in infants (Maldonado-Lobón et al. 2015).

Lactobacillus fermentum as preventive agent in colorectal cancer (CRC)

Several probiotic formulations containing *Lb. fermentum*, typically those surviving in both gastrointestinal (Gardiner et al. 2002a) and genital environments (Gardiner et al. 2002b), and were found to reduce infection (Lopez-Huertas 2015) and overgrowth of harmful bacteria (Stotzer et al. 1996). *Lb. fermentum* has also been associated with beneficial properties by attenuating the risk of colorectal cancer (CRC) development (Kahouli et al. 2017; So, Wan, and El-Nezami 2017; Nazir et al. 2018). Kahouli et al. (2015) utilized an Apc Min/+ mouse model to demonstrate the use of probiotics as a preventive agent for colorectal cancer. It was suggested based on clinical and pre-clinical studies; this was often linked to the potency of short-chain fatty acids (SCFAs) in the gut. *Lb. fermentum* NCIMB-5221 showed resistance to simulated intestinal fluid (SIF) ($16.3 \pm 1.9\%$ minimum, 72 h, $p = .006$) and produced SCFAs in SIF at concentrations high enough to significantly inhibit Caco-2 proliferation ($74.73 \pm 2.1\%$, 72 h). It was concluded that NCIMB-5221 strains could potentially be considered as biotherapeutic agent against CRC.

Other investigators documented that *Lb. fermentum* NCIMB-5221 has a significant antioxidant, anti-proliferative, and pro-apoptotic effect on CRC cells, principally when used in combination with *Lb. acidophilus* ATCC 314 (La-Lf). The anti-cancer activity of La-Lf co-culture was significantly enhanced in vitro with significant reduced proliferation ($3'8.8 \pm 6.9\%$, $p = .009$) and increased apoptosis (413 RUL, $p < .001$) toward cancer cells, as well as significant protection of normal colon cell growth from toxic treatment ($18.6 \pm 9.8\%$, $p = .001$) (Kahouli et al. 2017). The concomitant administration of *Lb. fermentum* and *Lb. plantarum* showed a synergistic impact for the control of colorectal cancer in mice. An increase in body weight, a decrease in ammonia concentration, a decrease in β glucosidase and β glucuronidase enzyme activity and a reduction in the number of crypts (level of inhibition of about 90%) in the mice in the pre-carcinogen-induced group was reported

when compared to these variables in the post-carcinogen-induced group (Asha 2012a).

Lactobacillus fermentum *and immune health*

Investigators have reported the immunological effects of *Lb. fermentum* among healthy adults and infants. Specifically, oral administration of lactobacilli enhanced both innate and adaptive immunity by increasing IgA synthesis, which may contribute to the LAB anti-infectious properties in combating infectious diarrhea (Kaila et al. 1992) and improved the function of natural killer (NK) cells (Nagao et al. 2000). A human RCT performed by Olivares et al. (2007) determined that oral administration of *Lb. fermentum* CECT-5716 enhances the immunologic response of an influenza vaccine (12% increase in specific antibodies) and protects against subsequent infection by increasing the Th-1 response and virus-neutralizing antibodies (37.5% reduction in the incidence of an influenza-like illness). The vaccination stimulated an increase in Th-1 cytokines and in T-helper and T-cytotoxic proportions; however, some of these increases were significantly higher after administration of *Lb. fermentum* CECT-5716-probiotic group (10 billion CFU). Remarkably, antibody induction was observed in the probiotic group with a significant increase in antigen-specific IgA. Similarly, probiotic *Lb. fermentum* VRI-003 (PCC®) enhances the mucosal immune system of elite athletes. Probiotic (PCC®) given at a daily dose of 1.26×10^{10} (as a freeze-dried powder in gelatin capsules), elicited a significant increase in whole-blood culture interferon gamma (IFNγ), compared with placebo used as control treatment (Cox et al. 2010). Recently, Lim et al. (2017) reported that *Lb. fermentum* IM12 attenuates inflammation in mice by inhibiting the NF-κB-STAT3 signaling pathway. Oral administration of probiotic IM12 (0.2×10^9, 1×10^9 or 5×10^9 CFU/mouse, once a day for 3 days) in mice with carrageenan-induced hind-paw edema (CIE) significantly suppressed the increase of edema volume. The treatment also activated nuclear factor kappa beta (NF-κB) and the signal transducer and activator of transcription 3 (STAT3). *Lb. fermentum* CECT-5716 could support the natural and acquired immune response which was shown by an activation of the NK cells and T-reg cells *in vitro* (Perez-Cano, Dong, and Yaqoob 2010).

Recently, the probiotic strain *Lb. fermentum* UCO-979C was reported to differentially modulate the immune response of intestinal epithelial cells (IECs) via Toll-like receptor 4 (TLR4) activation and through the modulation of TLR negative regulators expression (Garcia-Castillo et al. 2019). And, this has been demonstrated in vivo to increase intestinal IgA (Garcia-Castillo et al. 2019).

Lactobacillus fermentum *cholesterol-lowering effect*

Human cardiovascular and coronary artery disease risks are correlated with high cholesterol levels and are significant health concerns (Ait Seddik et al. 2017). LAB have been demonstrated to have cholesterol-reducing effects in many studies and the capability of probiotic *Lactobacillus* strains to remove cholesterol from media, especially under simulated intestinal conditions, demonstrates their potential use as cholesterol-lowering agents (Zhuang et al. 2012; Tomaro-Duchesneau et al. 2014; Bendali et al. 2017). Tomaro-Duchesneau et al. (2015) reported that *Lb. fermentum* NCIMB (5221 and 2797) can offer multiple advantages, such as cholesterol assimilation, colon epithelial adhesion, and inhibition of cholesterol uptake by colon epithelial (Caco-2) cells *in vitro*. It was reported that *Lb. fermentum* NCIMB 5221 decreased cholesterol uptake by about $85.98 \pm 2.07\%$ comparatively to the untreated group in animal models. Among artificially induced hyperlipidemia imprinting control region (ICR) mice, *Lb. fermentum* SM-7 in feed was able to reduce cholesterol by 66.8% while also reducing total triglyceride levels, low-density lipoprotein (LDL), cholesterol concentrations, and atherogenic index (Pan, Zeng, and Yan 2011). Utilizing human volunteers Kullisaar et al. (2016) reported that the level of LDL cholesterol as well as total cholesterol and oxLDL decreased significantly in all participants and high-density lipoprotein (HDL) cholesterol showed a tendency of improvement after 4 weeks of consumption of *Lb. fermentum* ME3 containing the food supplement Reg'Activ Cholesterol.

Lactobacillus fermentum *and food processes*

Bioprocessing (fermentation) has been used to produce a wide range of foods and food ingredients ever since the earliest recorded food preservation by humans. Bioprocessing technology has developed this further, with specialized production of food and feed ingredients or processing aids (Bernardeau, Guguen, and Vernoux 2006). *Lactobacilli* are microorganisms that are extensively used in food microbiology as technological starters among fermented products, for preserving food by inhibiting contamination causing foodborne illness or food spoilage and as probiotics due to their strain-specific, health-improving properties (Arena et al. 2016). LAB producing exopolysaccharides (EPS) have received attention in recent years, due to their useful role in improvement of physical, rheological, and sensory properties of fermented milks such as dahi, yoghurt, lassi, and cultured buttermilk (Behare et al. 2013). *Lb. fermentum* is an exopolysaccharides (EPS) producing and heterofermentative LAB (Leo et al. 2007; Dan et al. 2009). Low fat artisanal cheese (dahi) prepared using the EPS producing strain *Lb. fermentum* V10 exhibited optimum acid production, less whey separation, high viscosity, increased adhesiveness and stickiness, decreased firmness conversely to non-inoculated cheese (Behare et al. 2013). Recently, Nielsen et al. (2017) reported that in a fermented milk product, *Lb. fermentum* (10^7 CFU/g) is capable of helping maintain a pH above 4.0 when stored for at least 14 days at 25 °C.

Owusu-Kwarteng et al. (2015) reported *Lb. fermentum* as functional starter cultures, with inherent functional characteristics contributing to more organoleptic, nutritional, and technological or health-promoter benefits (probiotics). For instance, the application of *Lb. fermentum* strains were able

to enrich, in situ, the riboflavin content of fermented foods of cereal origin, as reported by Russo et al. (2014). Also, *Lb. fermentum* produces antimicrobial substances to inhibit the growth of spoilage and/or pathogenic bacterial strains (Barman et al. 2017). The production of lactic acids leads to a decrease in pH value in the intestine by which pathogenic microorganism growth is reduced compared to controls. *Lb. fermentum* CECT-5716 also increases the membrane permeability of Gram-negative bacteria, thereby reducing their viability and enhancing their exposure to bactericidal compounds (Olivares et al. 2006).

Since *Lb. fermentum* is also present in fermented plant material, it constitutes a part of the bioprocessing phenomenon occurring in their transformation (Madoroba et al. 2011; Oguntoyinbo et al. 2011; Illeghems et al. 2012). Among plants by-products, chocolate is a product of cocoa bean fermentation where *Lb. fermentum* is reported as the predominating bacterial species (Lefeber et al. 2010). Sawadogo-Lingani et al. (2007) reported that *Lb. fermentum* is the dominating LAB species for Sorghum (*Sorghum caffrorumor* and *S. vulgare*), an alcoholic beverage produced by malting and characterized by a two-stage (lactic followed by alcoholic) fermentation (Tamang, Watanabe, and Holzapfel 2016).

Lactobacillus fermentum bacteriocinogenic strains

Like other lactobacilli, many *Lb. fermentum* strains produce antimicrobial peptides, bacteriocins, which are ribosomal synthesized peptides produced by both Gram-negative and Gram-positive bacteria (Drider and Rebuffat 2011). These compounds were found to be involved in the antimicrobial activities observed for lactobacilli strains in food bio-preservation and in the biomedical field (Mokoena 2017; Singh 2018). Although most of the bacteriocinogenic lactobacilli strains are isolated from various sources, including meat, fish, fruits, vegetables and milk (Ait Seddik et al. 2017; Mokoena 2017), *Lb. fermentum*, producing such antimicrobial compounds, are mostly isolated from fermented food, raw milk, human vaginal microbiota, the oral ecosystem, breast milk or gastrointestinal tract (von Mollendorff, Todorov, and Dicks 2006; Ilayajara, Radhamadhavan, and Nirmala 2011; Kaewnopparat et al. 2013; Kaur et al. 2013a; Riaz, Nawaz, and Hasnain 2010; Sabia et al. 2014; Zahid et al. 2015; Morovic 2017a). Interestingly, bibliographic references related to bacteriocinogenic *Lb. fermentum* strains are less abundant comparatively to other species such as *Lb. plantarum*, *Lb. gasseri* or *Lb. salivarius*. In the first report on an antagonistic *Lb. fermentum* strain, the latter was isolated from human saliva and was able to produce a proteinaceous inhibitory compound (De Klerk and Coetzee 1961). Later De Klerk and Smit (1967), published a report on the same *Lb. fermentum* strain, mentioning the production of an antimicrobial lipid-carbohydrate heat stable complex. The characterization of this inhibitory compound has resulted in identification of at least 16 amino acids in the peptide and was sensitive to proteolytic enzymes (Trypsin and Pepsin) but remained insensitive to lysozyme (De Klerk and Smit 1967). This inhibitory compound, called bacteriocin 466, was later reported to have similar characteristics as lactacin 27 produced by *L. helviticus* (Upreti and Hinsdill 1975). Still in terms of bacteriocins production by this species, Yan and Lee (1997) identified a bacteriocin, fermenticin B, produced by *Lb. fermentum* Beijerinck CCRC 14018. This bacteriocin showed the common characteristic of small bacteriocins, with a molecular size less than 3–5 kDa with heat and pH stability as well as sensitivity to the action of proteolytic enzymes.

Bacteriocins produced by LAB generally have a narrow activity spectrum (Soomro, Masud, and Anwaar 2002), nevertheless some bacteriocins produced by *Lb. fermentum* strains designated as fermenticins are endowed with wide spectrum activities. This is the case of fermenticin L23 and fermenticin SD11, which were reportedly inactivated both Gram-positive and Gram-negative bacteria, and even were active against some fungi (Pascual et al. 2008; Wannun, Piwat, and Teanpaisan 2016). The first report establishing antagonistic activity was provided by Aslim et al. (2005), who isolated from various dairy products several lactobacilli strains, including *Lb. fermentum* 25 with antagonism toward Gram-positive *Staphylococcus aureus*, and against Gram-negative pathogens such as *Escherichia coli* and *Yersinia enterocololitica*. These activities were ascribed to production of bacteriocin-like inhibitory substance which was unique for its heat-stability and structurally for its high molecular size of 29 kDa based on the SDS-PAGE data. The antimicrobial activity was reportedly a potential large bacteriocin relative to the majority of LAB bacteriocins from previous publications (Aslim et al. 2005). Furthermore, Klayraung and Okonogi (2009) described the mode of action of a bacteriocin produced by two *Lb. fermentum* strains FTL2311 and FTL10BR isolated from Miang, a traditional Thai fermented tea leaves. These strains were active against *Listeria monocytogenes* DMST 17303, *Salmonella* Typhi DMST 5784, *Shigella sonnei* DMST 561 (ATCC 11060) and *Staphylococcus aureus* subsp. *aureus* DMST 6512. Scanning Electron Microscopy (SEM) images revealed that the inhibitory compounds from *Lb. fermentum* strains FTL2311 and FTL10BR targeted the cell membrane ultrastructure leading to disruption and shrinking of the pathogenic bacteria cells (Klayraung and Okonogi 2009). However, the lack of data on the characterization of the inhibitory compounds from these strains did not allow their classification.

Interestingly, von Mollendorff, Todorov, and Dicks (2006) described two strains reported as *Lb. fermentum* JW11BZ and JW15BZ isolated from Boza, a Balkan fermented food. The inhibitory activity was expressed in a strain-dependent manner against one Gram-negative bacterium *Klebsiella pneumoniae* (strain referred as *K. pneumoniae* 30) and other bacteria including *Listeria* spp. as well as other LABs, mostly *Enterococcus* and *Lactobacillus* strains. The biochemical characterization of these inhibitory compounds resulted in identification of a low molecular size peptide of approximatively 2.3–3.3 kDa. Because of the increase in bacterial antibiotic resistance worldwide during the last decades, different alternatives are currently being

Table 2. Characteristics of some bacteriocins produced by *Lb. fermentum* strains.

Strain	Origin	Bacteriocins characteristics	Sensitive bacteria	Reference
Lb. fermentum 25	Fermented dairy product	Large peptide of 29 kDa	*S. aureus*, *E. coli*, *Yersinia enterocolitica*	Aslim et al. (2005)
Lb. fermentum Lf3	Fecal sample	Estimated molecular weight on SDS-PAGE (104 kDa)	*Vibrio cholerae* subsp. *inaba*, *Shigella dysenteriae*	Asha (2012b)
Lb. fermentum SK5	Vagina of healthy women	ND	*E. coli*, *G. vaginalis*	Kaewnopparat et al. (2013)
Lb. fermentum HV6b	Human vaginal ecosystem	Fermenticin HV6b Class IIa	*Bacillus fragilis*, *B. ovatus*, *B. vulgatus*, *Candida albicans*, *C. sporogenes*, *E. coli*, *Enterococcus faecalis*, *G. vaginalis*, *Klebsiella pneumoniae*, *Leuconostoc mesenteroides*, *L. monocytogenes*, *Mariniluteicoccus flavus*, *Neisseria. gonorrhoeae*, *N. mucosa*, *P. aeruginosa*, *P. mirabilis*, Staphylococci, Streptococci, *Salmonella typhi*, *Vibrio cholerae*.	Kaur et al. (2013a, b)
Lb. fermentum L23	Vagina of healthy women	Bacteriocin L23 (7kDa)	Gram-positive and Gram-negative food spoilage and pathogenic bacteria, *C. albicans*, *C. glabrata* *Proteus* and clinical strains of *C. albicans*	Pascual et al. (2008)
Lb. fermentum 466	Human saliva	Bacteriocin 466 (>16 aminoacids)	Other LAB	De Klerk and Smit (1967)
Lb. fermentum	Milk product	Approximatively 8 kDa	*E. coli*, *S. aureus*, *S.* typhi, *Pseudomonas* and *Klebsiella*	Saranya and Hemashenpagam (2011)
Lb. fermentum SBS001	Marine water sample	Large peptide (78 kDa)	*Kleibsiella oxytoca*, *P. aeruginosa*, *E. coli*, *S. paratyphi*, *P. mirabilis*, *V. cholerae*, *K. pneumoniae*.	Singh et al. (2013)
Lb. fermentum JW11BZ and JW15BZ	Boza brevage	BacJWBZ, bacJW15BZ (2 to 3kDa)	LAB, *Streptococcus* sp. TL2R, *S. caprinus*, *L. innocua*	von Mollendorff, Todorov, and Dicks (2006)
Lb. fermentum SD11	Human saliva	Fermenticin SD11 (≈33 kDa)	LAB, *Streptococcus mutans*, *S. sobrinus*, *C. albicans*, *Flavo*bacterium *nucleatum*, *Porphyromonas gingivalis*	Wannun, Piwat, and Teanpaisan (2016)
Lb. fermentum GA715	Goat milk	Fermenticin SA715 (≈2 kDa)	*Micrococcus luteus* ATCC 10240, *Corynebacterium* spp. GH17, *Bacillus cereus* ATCC, *P. aeruginosa* PA7 and *E. coli* UT181	Wayah and Philip (2018)
Lb. fermentum Beijerinck CCRC 14018	Collection of Culture and Research Center (CCRC) Taiwan	Fermenticin B (<3 kDa)	LAB, *Micrococcus luteus*	Yan and Lee (1997)
Lb. fermentum CS57	Vaginal secretion	Peptide (>30 kDa)	*S. agalactiae*, *C. albicans*	Sabia et al. (2014)

considered to address this issue. The use of probiotics stands as one potential alternative but also LAB bacteriocins are emerging as a new group of therapeutic agents (Drider et al. 2016; Vieco-Saiz et al. 2019). Currently, most published studies on LAB bacteriocins have been focused on biomedical applications, searching for alternative strategies against cancer, systemic infections, oral-care, vaginal infections, contraception, skincare, and emerging multidrug resistant bacteria (Al Atya et al. 2016a, 2016b; López-Cuellar, Rodríguez-Hernández, and Chavarría-Hernández 2016; Kang et al. 2017). To highlight this point, studies as that published by Riaz, Nawaz, and Hasnain (2010) described antagonistic activities of *Lb. fermentum* 45 against cephalosporin resistant *E. coli* isolated from a patient in a Lahor hospital (Pakistan). This inhibition was ascribed to production of a heat stable bacteriocin (Riaz, Nawaz, and Hasnain 2010). Since then, investigations addressing suitability of bacteriocinogenic strains as alternatives to treat infections or as probiotics promoting the health of the host have increased (Cotter, Ross, and Hill 2013; Allen et al. 2014). Remarkably, many *Lb. fermentum* strains were assessed as protective against urinary tract and oral infections, vaginosis (Ilayajara, Radhamadhavan, and Nirmala 2011; Kaur et al. 2013a, 2013b; Asha 2012b; Adebayo, Afolabi, and Akintokun 2014; Wannun, Piwat, and Teanpaisan 2016; Ouarabi et al. 2019) and mainly against multidrug resistant strains including MRSA or against pathogenic yeasts such as *Candida albicans* or *C. glabrata* (Pascual et al. 2008; Zahid et al. 2015) as reported in Table 2. Kaur et al. (2013a) showed the spectra of Fermenticin HV6b, a class IIa bacteriocin produced by *Lb. fermentum* HV6b MTCC 10770 isolated from human vaginal ecosystem. Indeed, Fermenticin HV6b reported antagonistic activities against many pathogenic microorganisms associated with vaginal infections such as *Bacteroides*, *Gardnerella vaginalis*, *Mobiluncus*, Staphylococci, and Streptococci (Kaur et al. 2013a, 2013b).

Tulumoğlu, Kaya, and Şimşek (2014) investigated two strains of *Lb. fermentum* LP3 and LP4 isolated from

a traditional Tulum Turkish cheese, which were selected for their antagonistic effect towards a set of pathogenic microorganisms. Moreover, the authors established the probiotic potential of both *Lb. fermentum* LP3 and LP4. In addition to producing potent inhibitory compounds, these strains have fulfilled the criteria to be considered as potential probiotics (Tulumoğlu, Kaya, and Şimşek 2014). A previous study by Kaewnopparat et al. (2013) established that a bacteriocinogenic strain *Lb. fermentum* SK5, with high adhesion abilities to Caco-2, HT-29, and HeLa epithelial cells prevented binding and growth of *E. coli* and *G. vaginalis* onto intestinal and vaginal epithelial cells therefore providing a protective barrier against these pathogens. The study by Kaewnopparat et al. (2013) revealed the potential of *Lb. fermentum* SK5 to reduce the proliferation of some pathogens potentially via co-aggregation traits. Also, *Lb. fermentum* SK5 produces a potent BLS. Taken together, these studies indicate that the *Lb. fermentum* SK5 strain is a good candidate for probiotic development mainly for its protective claims against GI and vaginal microbial infections (Kaewnopparat et al. 2013).

The use of bacteriocinogenic *Lb. fermentum* strains for food preservation was reported also for use in several dairy products, vegetables, fruits or juices (Saranya and Hemashenpagam 2011; Nithya et al. 2012; Adebayo, Afolabi, and Akintokun 2014; Adedokun et al. 2016; Wayah and Philip 2018). These investigators studied the effect of these *Lb. fermentum* strains and their bacteriocins to control a wide range of spoilages microorganisms such as *E. coli*, *S. aureus*, *Salmonella typhi*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Bacillus cereus*, *L. monocytogenes*, and *Micrococcus luteus* (Nithya et al. 2012; Wayah and Philip 2018). These bacteriocins reportedly also had anti-biofilm inhibitory activities (Rybalchenko et al. 2015). Most of the recently identified bacteriocins have a wide activity spectra, including antagonism against Gram-positive and Gram-negative pathogens, and likely against pathogenic yeasts. Nevertheless, a number of these molecules are high molecular size, up to 30 kDa, as depicted in Table 2. Despite these unusual biochemical characteristics, bacteriocin-like activities from *Lb. fermentum* strains need to be investigated to gather insights into characterization of potential new antimicrobials and their mechanisms of action. Even so, all the studies performed on bacteriocinogenic *Lb. fermentum* strains provide promising beneficial applications in food preservation and medical areas.

A recently developed *in silico* genome approach has allowed investigators to assess the probiotic-associated traits after analysis of the genome of *Lb. fermentum* 3872 strain (Lehri, Seddon, and Karlyshev 2017a). Indeed, upon a comparative genomic analysis, several genes contributing to probiotic properties such as those coding for mucus and collagen-binding proteins, exopolysaccharides and a putative class III bacteriocin were reported (Lehri, Seddon, and Karlyshev 2017a, 2017b).

Lactobacillus fermentum cell factories

Lactobacilli and pediococci are being developed as cell factories to produce a variety of various metabolites and biofuels such as alcohol because of their tolerance to low pH or high alcohol concentrations. *Lb. fermentum* among other lactobacilli are homolactic, but can produce alcohol as a metabolic byproduct. However, the bacterium was not resistant to ethanol and low pH, but apparently will replicate in the presence of 5% NaCl (Bosma, Forster, and Nielsen 2017). Another potential health benefit of LAB is the production of vitamins such as riboflavin and overproduction of this metabolite could potentially be utilized as cell factories (Arena et al. 2014; Thakur, Tomar, and De 2016). Reportedly, riboflavin production in *Lb. fermentum* KTLF1 occurs in MRS medium (Thakur and Tomar 2016) and Jayashree, Jayaraman, and Kalaichelvan (2010) reported an efficient riboflavin-producing bacterium *Lb. fermentum* strain MTCC 8711 produced 2.29 mg/l of riboflavin in chemically defined media after 24 h. Moreover, *Lb. fermentum* can be genetically engineered for production of mannitol and pure L-lactic acid or pyruvate (Aarnikunnas et al. 2003) which opens the possibility for further research in the over production of metabolites by this bacterium as well as other LABs.

Conclusions

In conclusion, *Lb. fermentum* could potentially be more widely utilized as a probiotic to control gastrointestinal infections due to *Campylobacter jejuni* (Lehri, Seddon, and Karlyshev 2017b) and other foodborne bacterial disease agents. Additional benefits include applications to reduce inflammation during colitis (Rodríguez-Nogales et al. 2017) and provide alternative antimicrobials against other pathogens such as multi-resistant *Staphylococcus aureus* (Kang et al. 2017). Importantly, *Lb. fermentum* has also been investigated as a potential anti-cancer treatment (Liu et al. 2019), even as an anti-aging agent (Hor et al. 2019; Schifano et al. 2019) and as a potential anti-diabetic in combination with other LAB (Yadav et al. 2018). Although the investigations are preliminary and were completed in animal models, these results indicate potential future use as treatments among humans. The antimicrobial activities due to bacteriocins produced by *Lb. fermentum* have been reported herein and further add to the list of positive effects produced by this bacterium to improve human and animal health.

Acknowledgements

YB and DD would like to thank la region des Hauts-de-France for providing funds.

Funding

Funded by Région des Hauts de France through ALIBIOTECH CPER/FEDER project (2016-2020).

References

Aarnikunnas, J., N. Von Weymarn, K. Rönnholm, M. Leisola, and A. Palva. 2003. Metabolic engineering of *Lactobacillus fermentum*

for production of mannitol and pure L-lactic acid or pyruvate. *Biotechnology and Bioengineering* 82 (6):653–63. doi: 10.1002/bit.10615.

Adebayo, F. A., O. R. Afolabi, and A. K. Akintokun. 2014. Antimicrobial properties of purified bacteriocins produced from *Lactobacillus casei* and *Lactobacillus fermentum* against selected pathogenic microorganisms. *British Journal of Medicine and Medical Research* 4 (18):3415–31. doi: 10.9734/BJMMR/2014/8584.

Adedokun, E. O., I. A. Rather, V. K. Bajpai, and Y. H. Park. 2016. Biocontrol efficacy of *Lactobacillus fermentum* YML014 against food spoilage moulds using the tomato puree model. *Frontiers in Life Science* 9 (1):64–8. doi: 10.1080/21553769.2015.1084951.

Ait Seddik, H., F. Bendali, F. Gancel, I. Fliss, G. Spano, and D. Drider. 2017. *Lactobacillus plantarum* and its probiotic and food potentialities. *Probiotics and Antimicrobial Proteins* 9 (2):111–22. doi: 10.1007/s12602-017-9264-z.

Al Atya, A.K., H. Abriouel, I. Kempf, E. Jouy, E. Auclair, A. Vachée, and D. Drider. 2016a. Effects of colistin and bacteriocins combinations on the *in vitro* growth of *Escherichia coli* strains from Swine origin. *Probiotics and Antimicrobial Proteins* 8 (4):183–90. doi: 10.1007/s12602-016-9227-9.

Al Atya, A. K., Y. Belguesmia, G. Chataigne, R. Ravallec, A. Vachée, S. Szunerits, R. Boukherroub, and D. Drider. 2016b. Anti-MRSA activities of enterocins DD28 and DD93 and evidences on their role in the inhibition of biofilm formation. *Frontiers in Microbiology* 7:817. doi: 10.3389/fmicb.2016.00817.

Allen, H. K., J. Trachsel, T. Looft, and T. A. Casey. 2014. Finding alternatives to antibiotics. *Annals of the New York Academy of Sciences* 1323 (1):91–100. doi: 10.1111/nyas.12468.

Arena, M. P., P. Russo, V. Capozzi, P. López, D. Fiocco, and G. Spano. 2014. Probiotic abilities of riboflavin-overproducing *Lactobacillus* strains: A novel promising application of probiotics. *Applied Microbiology and Biotechnology* 98 (17):7569–81. doi: 10.1007/s00253-014-5837-x.

Arena, M. P., A. Silvain, G. Normanno, F. Grieco, D. Drider, G. Spano, and D. Fiocco. 2016. Use of *Lactobacillus plantarum* strains as a bio-control strategy against food-borne pathogenic microorganisms. *Frontiers in Microbiology* 7:464. doi: 10.3389/fmicb.2016.00464.

Arroyo, R., V. Martín, A. Maldonado, E. Jiménez, L. Fernandez, and J. M. Rodriguez. 2010. Treatment of infectious mastitis during lactation: Antibiotics versus oral administration of Lactobacilli isolated from breast milk. *Clinical Infectious Diseases* 50 (12):1551–8. doi: 10.1086/652763.

Asha, G. D. 2012a. Synergistic impact of *Lactobacillus fermentum, Lactobacillus plantarum* and vincristine on 1,2-dimethylhydrazine-induced colorectal carcinogenesis in mice. *Experimental and Therapeutic Medicine* 3:1049–54.

Asha, G. D. 2012b. Antagonistic properties of *Lactobacillus fermentum* and *L. plantarum* with potential intestinal pathogens; purification and characterization of bacteriocin isolated from curd and fecal samples. *Advance Journal of Food Science and Technology* 4:265–9.

Aslim, B., Z. N. Yuksekdag, E. Sarikaya, and Y. Beyatli. 2005. Determination of the bacteriocin-like substances produced by some lactic acid bacteria isolated from Turkish dairy products. *LWT – Food Science and Technology* 38 (6):691–4. doi: 10.1016/j.lwt.2004.08.001.

Barman, S., R. Ghosh, S. Sengupta, and N. C. Mandal. 2017. Long term storage of post-packaged bread by controlling spoilage pathogens using *Lactobacillus fermentum* C14 isolated from homemade curd. *PLoS One* 12 (8):e0184020. doi: 10.1371/journal.pone.0184020.

Barone, R., F. Rappa, F. Macaluso, C. C. Bavisotto, C. Sangiorgi, G. Di Paola, G. Tomasello, V. Di Felice, V. Marcianò, F. Farina., et al., 2016. Alcoholic liver disease: A mouse model reveals protection by *Lactobacillus fermentum*. *Clinical Translational Gastroenterology* 7:138.

Behare, P. V., R. Singh, R. Nagpal, and K. H. Rao. 2013. Exopolysaccharides producing *Lactobacillus fermentum* strain for enhancing rheological and sensory attributes of low-fat dahi. *Journal of Food Science and Technology* 50 (6):1228–32. doi: 10.1007/s13197-013-0999-6.

Bendali, F., K. Kerdouche, S. Faradji-Hamma, and D. Drider. 2017. *In vitro* and *in vivo* cholesterol lowering ability of *Lactobacillus pentosus* KF923750. *Beneficial Microbes* 8 (2):271–80. doi: 10.3920/BM2016.0121.

Bernardeau, M., M. Guguen, and J. P. Vernoux. 2006. Beneficial lactobacilli in food and feed: Long-term use, biodiversity and proposals for specific and realistic safety assessments. *FEMS Microbiology Reviews* 30 (4):487–513. doi: 10.1111/j.1574-6976.2006.00020.x.

Bintsis, T. 2018. Lactic acid bacteria: Their applications in foods. *Journal of Bacteriology and Mycology* 5:1065.

Bosma, E.F., J. Forster, and A. T. Nielsen. 2017. Lactobacilli and pediococci as versatile cell factories – Evaluation of strain properties and genetic tools. *Biotechnology Advances* 35 (4):419–42. doi: 10.1016/j.biotechadv.2017.04.002.

Byoung-Kook, K., L. In-Ock, T. Pei-Lei, E. Ju-Young, H. Jae-Kwan, and K. Sae-Hun. 2017. Protective effect of *Lactobacillus fermentum* LA12 in an alcohol-induced rat model of alcoholic steatohepatitis. *Korean Journal for Food Science of Animal Resources* 37:931–9.

Cao, L., Y. Xiaojun, S. Feifei, L. Chanjuan, and Y. Junhu. 2012. Lactobacillus strain with high adhesin stimulates inotestinal mucin expression in broiler. *The Journal of Poultry Science* 49 (4):273. doi: 10.2141/jpsa.0110146.

Cholakov, R., Y. Tumbarski, V. Yanakieva, I. Dobrev, Y. Salim, and Z. Denkova. 2017. Antimicrobial activity of *Leuconostoc lactis* strain BT17, isolated from a spontaneously fermented cereal beverage (boza). *Journal of Microbiology, Biotechnology and Food Sciences* 7 (1):47–9. doi: 10.15414/jmbfs.2017.7.1.47-49.

Coton, M., F. Berthier, and E. Coton. 2008. Rapid identification of the three major species of dairy obligate heterofermenters *Lactobacillus brevis*, *Lactobacillus fermentum* and *Lactobacillus parabuchneri* by species-specific duplex PCR. *FEMS Microbiology Letters* 284 (2):150–7. doi: 10.1111/j.1574-6968.2008.01206.x.

Cotter, P. D., R. P. Ross, and C. Hill. 2013. Bacteriocins – A viable alternative to antibiotics? *Nature Reviews Microbiology* 11 (2):95. doi: 10.1038/nrmicro2937.

Cox, A. J., D. B. Pyne, P. U. Saunders, and P. A. Fricker. 2010. Oral administration of the probiotic *Lactobacillus fermentum* VRI-003 and mucosal immunity in endurance athletes. *British Journal of Sports Medicine* 44 (4):222–6. doi: 10.1136/bjsm.2007.044628.

Dal Bello, F., and C. Hertel. 2006. Oral cavity as natural reservoir for intestinal lactobacilli. *Systematic and Applied Microbiology* 29 (1):69–76. doi: 10.1016/j.syapm.2005.07.002.

Dan, T., K. Fukuda, M. Sugai-Bannai, N. Takakuwa, H. Motoshima, and T. Urashima. 2009. Characterization and expression analysis of the exopolysaccharide gene cluster in *Lactobacillus fermentum* TDS030603. *Bioscience, Biotechnology, and Biochemistry* 73 (12):2656–64. doi: 10.1271/bbb.90502.

Datta, P., V. Gupta, G. K. Mohi, J. Chander, and A. K. Janmeja. 2017. *Lactobacillus coryniformis* causing pulmonary infection in a patient with metastatic small cell carcinoma: Case report and review of literature on *Lactobacillus* pleuro-pulmonary infections. *Journal of Clinical and Diagnostic Research* 11 (2):DE01–DE05. doi: 10.7860/JCDR/2017/22837.9391.

De Klerk, H. C., and J. N. Coetzee. 1961. Antibiosis among lactobacilli. *Nature* 192 (4800):340. doi: 10.1038/192340a0.

De Klerk, H. C., and J. A. Smit. 1967. Properties of a *Lactobacillus fermentum* bacteriocin. *Journal of General Microbiology* 48:309–16. doi: 10.1099/00221287-48-2-309.

De Vuyst, L., G. Vrancken, F. Ravyts, T. Rimaux, and S. Weckx. 2009. Biodiversity, ecological determinants, and metabolic exploitation of sourdough microbiota. *Food Microbiology* 26 (7):666–75. doi: 10.1016/j.fm.2009.07.012.

Doron, S., and D. R. Snydman. 2015. Risk and safety of probiotics. *Clinical Infectious Diseases* 60 (suppl_2):S129–S34. doi: 10.1093/cid/civ085.

Drider, D., F. Bendali, K. Naghmouchi, and M. L. Chikindas. 2016. Bacteriocins: Not only antibacterial agents. *Probiotics and Antimicrobial Proteins* 8 (4):177–82. doi: 10.1007/s12602-016-9223-0.

Drider, D., and Rebuffat, S. (Eds.). 2011. *Prokaryotic antimicrobial peptides: From genes to applications*. New York: Springer Science Business Media. 451 pp.

EFSA. 2007. Introduction of a Qualified Presumption of Safety (QPS) approach for assessment of selected microorganisms referred to EFSA – Opinion of the Scientific Committee. *EFSA Journal* 587: 1–16.

Franko, B., M. Vaillant, C. Recule, E. Vautrin, J. P. Brion, and P. Pavese. 2013. *Lactobacillus paracasei* endocarditis in a consumer of probiotics. *Médecine et Maladies Infectieuses* 43 (4):171–3. doi: 10.1016/j.medmal.2013.01.007.

Franz, C. M., M. E. Stiles, K. H. Schleifer, and W. H. Holzapfel. 2003. Enterococci in foods – A conundrum for food safety. *International Journal of Food Microbiology* 88 (2–3):105–22. doi: 10.1016/S0168-1605(03)00174-0.

Fuochi, V., G. L. Volti, and P. M. Furneri. 2017. Probiotic properties of *Lactobacillus fermentum* strains isolated from human oral samples and description of their antibacterial activity. *Current Pharmaceutical Biotechnology* 18 (2):138–49. doi: 10.2174/1389201017666161229153530.

Furrie, E. 2005. Probiotics and allergy. *Proceedings of the Nutrition Society* 64 (4):465–9. doi: 10.1079/PNS2005466.

Garcia-Castillo, V., R. Komatsu, P. Clua, Y. Indo, M. Takagi, S. Salva, M.A. Islam, S. Alvarez, H. Takahashi, A. Garcia-Cancino, H. Kitazawa, and J. Villena. 2019. Evaluation of the Immunomodulatory Activities of the Probiotic Strain Lactobacillus fermentum UCO-979C. *Frontiers in Immunology 10*:1376. doi: 10.3389/fimmu.2019.01376.

Gardiner, G. E., C. Heinemann, M. L. Baroja, A. W. Bruce, and D. Beuerman. 2002b. Persistence of *Lactobacillus fermentum* RC-14 and *Lactobacillus rhamnosus* GR-1 but not *L. rhamnosus* GG in the human vagina as demonstrated by Randomly Amplified Polymorphic DNA. *Clinical and Vaccine Immunology* 9:92–6. doi: 10.1128/CDLI.9.1.92-96.2002.

Gardiner, G. E., C. Heinemann, M. L. Baroja, A. W. Bruce, D. Beuerman, J. Madrenas, and G. Reidac. 2002a. Oral administration of the probiotic combination *Lactobacillus rhamnosus* GR-1and *L. fermentum* RC-14 for human intestinal applications. *International Dairy Journal* 1:191–6. doi: 10.1016/S0958-6946(01)00138-8.

Gil-Campos, M., M. A. Lopez, M. V. Rodriguez-Benítez, J. Romero, I. Roncero, M. D. Linares, J. Maldonado, E. López-Huertas, R. Berwind, K. L. Ritzenthaler, et al. 2012. *Lactobacillus fermentum* CECT 5716 is safe and well tolerated in infants of 1-6 months of age: A randomized controlled trial. *Pharmacological Research* 65 (2): 231–8. doi: 10.1016/j.phrs.2011.11.016.

Gleeson, M., N. C. Bishop, M. Oliveira, and P. Tauler. 2011. Daily probiotic's (*Lactobacillus casei* Shirota) reduction of infection incidence in athletes. *International Journal of Sport Nutrition and Exercise Metabolism* 21 (1):55–64. doi: 10.1123/ijsnem.21.1.55.

Haghighat, L., and N. F. Crum-Cianflone. 2016. The potential risks of probiotics among HIV-infected persons: Bacteraemia due to *Lactobacillus acidophilus* and review of the literature. *International Journal of STD & AIDS* 27 (13):1223–30. doi: 10.1177/0956462415590725.

Hempel, S., S. Newberry, A. Ruelaz, Z. Wang, J. N. Miles, M. J. Suttorp, B. Johnsen, R. Shanman, W. Slusser, N. Fu., et al. 2011. Safety of probiotics used to reduce risk and prevent or treat disease. *Evidence Report Technology Assessment* 200:1–645.

Hor, Y. Y., C. H. Ooi, B. Y. Khoo, S. B. Choi, A. Seeni, S. Shamsuddin, C. E. Oon, K. L. Ong, W. S. Jeong, and M. T. Liong. 2019. *Lactobacillus* strains alleviated aging symptoms and aging-induced metabolic disorders in aged rats. *Journal of Medicinal Food* 22 (1): 1–13. doi: 10.1089/jmf.2018.4229.

Ilayajara, R., P. A. Radhamadhavan, and C. B. Nirmala. 2011. Assessment for potential use of bacteriocin producing *Lactobacillus fermentum* isolated from human milk for preventing urinary tract infections. *Journal of Pharmacy Research* 4:3445–7.

Illeghems, K., L. De Vuyst, Z. Papalexandratou, and S. Weckx. 2012. Phylogenetic analysis of a spontaneous cocoa bean fermentation metagenome reveals new insights into its bacterial and fungal community diversity. *PLoS One* 7 (5):e38040. doi: 10.1371/journal.pone.0038040.

Isolauri, E., M. Juntunen, T. Rautanen, P. Sillanaukee, and T. Koivula. 1991. A human *Lactobacillus* strain (*Lactobacillus casei* sp strain GG) promotes recovery from acute diarrhea in children. *Pediatrics* 88 (1):90–7.

Jayashree, S., K. Jayaraman, and G. Kalaichelvan. 2010. Probiotic properties of the riboflavin producing *Lactobacillus fermentum* strain isolated from yoghurt sample. *Journal of Biotechnology* 2:11–6.

Jayashree, S., R. Karthikeyan, S. Nithyalakshmi, J. Ranjani, P. Gunasekaran, and J. Rajendhran. 2018. Anti-adhesion property of the potential probiotic strain *Lactobacillus fermentum* 8711 against Methicillin-Resistant *Staphylococcus aureus* (MRSA). *Frontiers in Microbiology* 9:411–20. doi: 10.3389/fmicb.2018.00411.

Kaban, G., and M. Kaya. 2008. Identification of lactic acid bacteria and Gram-positive catalase-positive cocci isolated from naturally fermented sausage (sucuk). *Journal of Food Science* 73 (8):M385–8. doi: 10.1111/j.1750-3841.2008.00906.x.

Kaewnopparat, S., N. Dangmanee, N. Kaewnopparat, T. Srichana, M. Chulasiri, and S. Settharaksa. 2013. *In-vitro* probiotic properties of *Lactobacillus fermentum* SK5 isolated from vagina of a healthy woman. *Anaerobe* 22:6–13. doi: 10.1016/j.anaerobe.2013.04.009.

Kahouli, I., M. Malhotra, C. Tomaro-Duchesneau, L. S. Rodes, M. A. Alaoui-Jamali, and S. Prakash. 2015. Identification of *Lactobacillus fermentum* strains with potential against colorectal cancer by characterizing short chain fatty acids production, anti-proliferative activity and survival in an intestinal fluid: *In vitro* analysis. *Journal of Bioanalysis & Biomedicine* 7:4.

Kahouli, I., M. Malhotra, S. Westfall, M. A. Alaoui-Jamali, and S. Prakash. 2017. Design and validation of an orally administrated active *L. fermentum-L. acidophilus* probiotic formulation using colorectal cancer Apc Min/+ mouse model. *Applied Microbiology and Biotechnology* 101 (5):1999–2019.

Kaila, M., E. Isolauri, E. Soppi, E. Virtanen, S. Laine, and H. Arvilommi. 1992. Enhancement of the circulating antibody secreting cell response in human diarrhea by a human *Lactobacillus* strain. *Pediatric Research* 32 (2):141–4. doi: 10.1203/00006450-199208000-00002.

Kang, M. S., H. S. Lim, J. S. Oh, Y. J. Lim, K. Wuertz-Kozak, J. M. Harro, M. E. Shirtliff, and Y. Achermann. 2017. Antimicrobial activity of *Lactobacillus salivarius* and *Lactobacillus fermentum* against *Staphylococcus aureus*. *Pathogens and Disease* 75 (2). doi: 10.1093/femspd/ftx009.

Kaur, B., P. Balgir, B. Mittu, A. Chuahan, B. Kumar, and N. Garg. 2013a. Antimicrobial spectrum of Anti-*Gardnerella vaginalis* bacteriocin producing *Lactobacillus fermentum* HV6b against bacterial vaginosis associated organisms. *American Journal of Drug Discovery and Development* 3 (1):1–12. doi: 10.3923/ajdd.2013.1.12.

Kaur, B., P. P. Balgir, B. Mittu, B. Kumar, and N. Garg. 2013b. Biomedical applications of fermenticin HV6b isolated from *Lactobacillus fermentum* HV6b MTCC10770. *BioMed Research International* 2013:1. doi: 10.1155/2013/168438.

Klayraung, S., and S. Okonogi. 2009. Antibacterial and antioxidant activities of acid and bile resistant strains of *Lactobacillus fermentum* isolated from miang. *Brazilian Journal of Microbiology* 40 (4): 757–66. doi: 10.1590/S1517-83822009000400005.

Kullisaar, T., K. Zilmer, T. Salum, A. Rehema, and M. Zilmer. 2016. The use of probiotic *L. fermentum* ME-3 containing Reg'Activ Cholesterol supplement for 4 weeks has a positive influence on blood lipoprotein profiles and inflammatory cytokines: An open-label preliminary study. *Nutrition Journal* 15 (1):93.

Lara-Villoslada, F., S. Sierra, M. P. Díaz-Ropero, J. M. Rodríguez, J. Xaus, and M. Olivares. 2009. Safety assessment of *Lactobacillus fermentum* CECT5716, a probiotic strain isolated from human milk. *Journal of Dairy Research* 76 (2):216–21.

Lefeber, T., M. Janssens, N. Camu, and L. De Vuyst. 2010. Kinetic analysis of strains of lactic acid bacteria and acetic acid bacteria in cocoa pulp simulation media toward development of a starter culture for cocoa bean fermentation. *Applied and Environmental Microbiology* 76 (23):7708–16. doi: 10.1128/AEM.01206-10.

Lehri, B., A. M. Seddon, and A. V. Karlyshev. 2017a. Potential probiotic-associated traits revealed from completed high quality genome sequence of *Lactobacillus fermentum* 3872. *Standards in Genomic Sciences* 12 (1):19. doi: 10.1186/s40793-017-0228-4.

Lehri, B., A. M. Seddon, and A. V. Karlyshev. 2017b. *Lactobacillus fermentum* 3872 as a potential tool for combatting *Campylobacter jejuni* infections. *Virulence* 8 (8):1753–60. doi: 10.1080/21505594.2017.1362533.

Leo, F., S. Hashida, D. Kumagai, K. Uchida, H. Motoshima, I. Arai, S. Asakuma, K. Fukuda, and T. Urashima. 2007. Studies on a neutral exopolysaccharide of *Lactobacillus fermentum* TDS030603. *Journal of Applied Glycoscience* 54 (4):223–9. doi: 10.5458/jag.54.223.

Lim, S. M., H. M. Jang, S. E. Jang, M. J. Han, and D. H. Kim. 2017. *Lactobacillus fermentum* IM12 attenuates inflammation in mice by inhibiting NF-kappaB-STAT3 signalling pathway. *Beneficial Microbes* 8 (3):407–19. doi: 10.3920/BM2016.0156.

Liu, B., J. Zhang, R. Yi, X. Zhou, X. Long, Y. Pan, and X. Zhao. 2019. Preventive effect of *Lactobacillus fermentum* CQPC08 on 4-nitroquinoline-1-oxide induced tongue cancer in C57BL/6 mice. *Foods* 8 (3):93.

López-Cuellar, M. D. R., A. I. Rodríguez-Hernández, and N. Chavarría-Hernández. 2016. LAB bacteriocin applications in the last decade. *Biotechnology & Biotechnological Equipment* 30 (6):1039–50. doi: 10.1080/13102818.2016.1232605.

Lopez-Huertas, E. 2015. Safety and efficacy of human breast milk *Lactobacillus fermentum* CECT5716. A mini review of studies with infant formulae. *Beneficial Microbes* 6:219–24.

Madoroba, E., E. T. Steenkamp, J. Theron, I. Scheirlinck, T. E. Cloete, and G. Huys. 2011. Diversity and dynamics of bacterial populations during spontaneous sorghum fermentations used to produce ting, a South African food. *Systematic and Applied Microbiology* 34 (3):227–34.

Maldonado, J., F. Cañabate, L. Sempere, F. Vela, A. R. Sánchez, E. Narbona, E. López-Huertas, A. Geerlings, A. D. Valero, M. Olivares., et al. 2012. Human milk probiotic *Lactobacillus fermentum* CECT5716 reduces the incidence of gastrointestinal and upper respiratory tract infections in infants. *Journal of Pediatric Gastroenterology and Nutrition* 54 (1):55–61. doi: 10.1097/MPG.0b013e3182333f18.

Maldonado-Lobón, J. A., M. Gil-Campos, J. Maldonado, E. López-Huertas, K. Flores-Rojas, A. D. Valero, M. V. Rodríguez-Benítez, O. Bañuelos, F. Lara-Villoslada, J. Fonollá, et al. 2015. Long-term safety of early consumption of *Lactobacillus fermentum* CECT5716: A 3-year follow-up of a randomized controlled trial. *Pharmacological Research* 95–96:12–9. doi: 10.1016/j.phrs.2015.01.006.

Martín, R., S. Langa, C. Reviriego, E. Jimínez, M. L. Marín, J. Xaus, L. Fernández, and J. M. Rodríguez. 2003. Human milk is a source of lactic acid bacteria for the infant gut. *The Journal of Pediatrics* 143 (6):754–8. doi: 10.1016/j.jpeds.2003.09.028.

Meini, S., R. Laureano, L. Fani, C. Tascini, A. Galano, A. Antonelli, and G. M. Rossolini. 2015. Breakthrough *Lactobacillus rhamnosus* GG bacteremia associated with probiotic use in an adult patient with severe active ulcerative colitis: Case report and review of the literature. *Infection* 43 (6):777–81. doi: 10.1007/s15010-015-0798-2.

Melo, T. A., T. F. Dos Santos, L. R. Pereira, H. M. Passos, R. P. Rezende, and C. C. Romano. 2017. Functional profile evaluation of *Lactobacillus fermentum* TCUESC01: A new potential probiotic strain isolated during Cocoa fermentation. *Biomed Research International* 2017:1. doi: 10.1155/2017/5165916.

Mikelsaar, M., and M. Zilmer. 2009. *Lactobacillus fermentum* ME-3 – An antimicrobial and antioxidative probiotic. *Microbial Ecology in Health and Disease* 21 (1):1–27.

Mokoena, M. P. 2017. Lactic acid bacteria and their bacteriocins: Classification, biosynthesis and applications against uropathogens: A mini review. *Molecules* 22 (8):1255. doi: 10.3390/molecules22081255.

Morovic, W. 2017a. Analysis of taxonomy and genomic safety for *Lactobacillus fermentum* SBS-1 (DGCC 1925). Internal Technical Report No. 01811536, DuPont.

Morovic, W. 2017b. *In-silico* comparison of *Lactobacillus fermentum* SBS-1 metabolic functions to public strains. Internal Technical Report No. 0186049, DuPont

Nagao, F., M. Nakayama, T. Muto, and K. Okumura. 2000. Effects of a fermented milk drink containing *Lactobacillus casei* strain shirota on the immune system in healthy human subjects. *Bioscience, Biotechnology, and Biochemistry* 64 (12):2706–8. doi: 10.1271/bbb.64.2706.

Nazir, Y., S. A. Hussain, A. B. Hamid, and S. Song. 2018. Probiotics and their potential preventive and therapeutic role for cancer, high serum cholesterol, and allergic and HIV disease. *Biomed Research International* 2018:1. doi: 10.1155/2018/3428437.

Nielsen, C., M. Lykke, T. Hornbaek, P. Rasmussen, and L. Poulsen. (2017). *Lactobacillus fermentum* bacteria reducing the concentration of acetaldhehyde. CHR. HANSEN A/S (Boege Alle 10-12, 2970 Hoersholm, 2970, DK) WO/2017/037058.

Nielsen, D. S., O. D. Teniola, L. Ban-Koffi, M. Owusu, T. S. Andersson, and W. H. Holzapfel. 2007. The microbiology of Ghanaian cocoa fermentations analysed using culture-dependent and culture-independent methods. *International Journal of Food Microbiology* 114 (2):168–86. doi: 10.1016/j.ijfoodmicro.2006.09.010.

Nithya, K., D. Senbagam, B. Senthilkumar, N. Udhayashree, and R. Gurusamy. 2012. Characterization of bacteriocin producing lactic acid bacteria and its application as a food preservative. *African Journal of Microbiological Research* 6:1138–46.

Oguntoyinbo, F. A., P. Tourlomousis, M. J. Gasson, and A. Narbad. 2011. Analysis of bacterial communities of traditional fermented West African cereal foods using culture independent methods. *International Journal of Food Microbiology* 145 (1):205–10. doi: 10.1016/j.ijfoodmicro.2010.12.025.

Olivares, M., M. P. Díaz-Ropero, R. Martín, J. M. Rodríguez, and J. Xaus. 2006. Antimicrobial potential of four *Lactobacillus* strains isolated from breast milk. *Journal of Applied Microbiology* 101 (1):72–9. doi: 10.1111/j.1365-2672.2006.02981.x.

Olivares, O., M. P. Díaz-Ropero, S. Sierra, F. Lara-Villoslada, J. Fonollá, M. Navas, J. M. Rodríguez, and J. Xaus. 2007. Oral intake of *Lactobacillus fermentum* CECT5716 enhances the effects of influenza vaccination. *Nutrition* 23 (3):254–60. doi: 10.1016/j.nut.2007.01.004.

Ouarabi, L., Y. Ait Chait, H. Ait Seddik, D. Drider, and F. Bendali. 2019. Newly Isolated *Lactobacillus* strains from Algerian human vaginal microbiota: *Lactobacillus fermentum* strains relevant probiotic's candidates. *Probiotics and Antimicrobial Proteins* 11 (1):43–54. doi: 10.1007/s12602-017-9360-0.

Owusu-Kwarteng, J., K. Tano-Debrah, F. Akabanda, and L. Jespersen. 2015. Technological properties and probiotic potential of *Lactobacillus fermentum* strains isolated from West African fermented millet dough. *BMC Microbiology* 15 (1):261. doi: 10.1186/s12866-015-0602-6.

Pan, D. D., X. Q. Zeng, and Y. T. Yan. 2011. Characterisation of *Lactobacillus fermentum* SM-7 isolated from koumiss, a potential probiotic bacterium with cholesterol-lowering effects. *Journal of the Science of Food and Agriculture* 91 (3):512–8. doi: 10.1002/jsfa.4214.

Pascual, L. M., M. B. Daniele, W. Giordano, M. C. Pájaro, and I. L. Barberis. 2008. Purification and partial characterization of novel bacteriocin L23 produced by *Lactobacillus fermentum* L23. *Current Microbiology* 56 (4):397. doi: 10.1007/s00284-007-9094-4.

Peran, L., D. Camuesco, M. Comalada, A. Nieto, A. Concha, J. L. Adrio, M. Olivares, J. Xaus, A. Zarzuelo, and J. Galvez. 2006. *Lactobacillus fermentum*, a probiotic capable to release glutathione, prevents colonic inflammation in the TNBS model of rat colitis. *International Journal of Colorectal Disease* 21 (8):737–46. doi: 10.1007/s00384-005-0773-y.

Perez-Cano, F. J., H. Dong, and P. Yaqoob. 2010. *In vitro* immunomodulatory activity of *Lactobacillus fermentum* CECT5716 and *Lactobacillus salivarius* CECT5713: Two probiotic strains isolated from human breast milk. *Immunobiology* 215:996–1004. doi: 10.1016/j.imbio.2010.01.004.

Popova, B., D. Mitev, and A. Nikolov. 2016. The role of mother's Milk and breast feeding. Medical problems during the lactation period *Lactobacillus fermentum* – A new approach towards the prevention and the treatment of acute and subacute mastitis. *Akush Ginekol (Sofiia)* 55:47–52.

Qian, Y., H. Suo, M. Du, X. Zhao, J. Li, J. G. Li, J. L. Song, and Z. Liu. 2015. Preventive effect of *Lactobacillus fermentum* Lee on activated carbon-induced constipation in mice. *Experimental and Therapeutic Medicine* 9 (1):272–8. doi: 10.3892/etm.2014.2064.

Riaz, S., S. K. Nawaz, and S. Hasnain. 2010. Bacteriocins produced by *L. fermentum* and *L. acidophilus* can inhibit cephalosporin resistant *E. coli*. *Brazilian Journal of Microbiology* 41 (3):643–8. doi: 10.1590/S1517-83822010000300015.

Rodríguez-Nogales, A., F. Algieri, J. Garrido-Mesa, T. Vezza, M. P. Utrilla, N. Chueca, F. Garcia, M. Olivares, M. E. Rodríguez-Cabezas, and J. Gálvez. 2017. Differential intestinal anti-inflammatory effects of *Lactobacillus fermentum* and *Lactobacillus salivarius* in DSS mouse colitis: Impact on microRNAs expression and microbiota composition. *Molecular Nutrition & Food Research* 61 (11):1700144. doi: 10.1002/mnfr.201700144.

Rossi, F., C. Amadoro, and G. Colavita. 2019. Members of the *Lactobacillus* genus complex (LGC) as opportunistic pathogens: A review. *Microorganisms* 7 (5):126. doi: 10.3390/microorganisms7050126.

Russo, P., V. Capozzi, M. P. Arena, G. Spadaccino, M. T. Dueñas, P. López, D. Fiocco, and G. Spano. 2014. Riboflavin overproducing strains of *Lactobacillus fermentum* for riboflavin enriched bread. *Applied Microbiology and Biotechnology* 98 (8):3691–700. doi: 10.1007/s00253-013-5484-7.

Rybalchenko, O. V., V. M. Bondarenko, O. G. Orlova, A. G. Markov, and S. Amasheh. 2015. Inhibitory effects of *Lactobacillus fermentum* on microbial growth and biofilm formation. *Archives of Microbiology* 197 (8):1027–32. doi: 10.1007/s00203-015-1140-1.

Sabia, C., I. Anacarso, A. Bergonzini, R. Gargiulo, M. Sarti, C. Cond, P. Messi, S. de Niederhausern, R. Iseppi, and M. Bondi. 2014. Detection and partial characterization of a bacteriocin-like substance produced by *Lactobacillus fermentum* CS57 isolated from human vaginal secretions. *Anaerobe* 26:41–5. doi: 10.1016/j.anaerobe.2014.01.004.

Salazar-Lindo, E., D. Figueroa-Quintanilla, M. I. Caciano, V. Reto-Valiente, G. Chauviere, P. Colin, and Lacteol Study Group. 2007. Effectiveness and safety of *Lactobacillus* LB in the treatment of mild acute diarrhea in children. *Journal of Pediatric Gastroenterology and Nutrition* 44 (5):571–6. doi: 10.1097/MPG.0b013e3180375594.

Saranya, S., and N. Hemashenpagam. 2011. Antagonistic activity and antibiotic sensitivity of lactic acid bacteria from fermented dairy products. *Advances in Applied Science Research* 2:528–34.

Sawadogo-Lingani, H., V. Lei, B. Diawara, D. S. Nielsen, P. L. Møller, A. S. Traoré, and M. Jakobsen. 2007. The biodiversity of predominant lactic acid bacteria in dolo and pito wort for the production of sorghum beer. *Journal of Applied Microbiology* 103 (4):765–77. doi: 10.1111/j.1365-2672.2007.03306.x.

Schifano, E., P. Zinno, B. Guantario, M. Roselli, S. Marcoccia, C. Devirgiliis, and D. Uccelletti. 2019. The foodborne strain *Lactobacillus fermentum* MBC2 triggers pept-1-dependent pro-longevity effects in *Caenorhabditis elegans*. *Microorganisms* 7 (2):45. doi: 10.3390/microorganisms7020045.

Sharma, R., R. Kapila, M. Kapasiya, V. Saliganti, G. Dass, and S. Kapila. 2014. Dietary supplementation of milk fermented with probiotic *Lactobacillus fermentum* enhances systemic immune response and antioxidant capacity in aging mice. *Nutrition Research* 34 (11):968–81. doi: 10.1016/j.nutres.2014.09.006.

Singh, R., K. Sivasubramani, S. Jayalakshmi, S. Satheesh Kumar, and C. Selvi. 2013. Isolation and production of bacteriocin by marine *Lactobacillus fermentum* SBS001. *International Journal of Current Microbiology and Applied Science* 2:67–73.

Singh, V. P. 2018. Recent approaches in food bio-preservation – A review. *Open Veterinary Journal* 8 (1):104–11. doi: 10.4314/ovj.v8i1.16.

So, S. S., M. L. Wan, and H. El-Nezami. 2017. Probiotics-mediated suppression of cancer. *Current Opinion in Oncology* 29:62–72. doi: 10.1097/CCO.0000000000000342.

Sonomoto, K., and Yokota, A. (Eds.). 2011. *Lactic acid bacteria and bifidobacteria: Current progress in advanced research*, 285. Norfolk, UK: Caister Academic Press.

Soomro, A. H., T. Masud, and K. Anwaar. 2002. Role of lactic acid bacteria (LAB) in food preservation and human health – A review. *Pakistan Journal of Nutrition* 1:20–4. doi: 10.3923/pjn.2002.20.24.

Stotzer, P. O., L. Blomberg, P. L. Conway, A. Henriksson, and H. Abrahamsson. 1996. Probiotic treatment of small intestinal bacterial overgrowth by *Lactobacillus fermentum* KLD. *Scandinavian Journal of Infectious Diseases* 28 (6):615–9. doi: 10.3109/00365549609037970.

Strompfová, V., I. Kubašová, and A. Lauková. 2017. Health benefits observed after probiotic *Lactobacillus fermentum* CCM 7421 application in dogs. *Applied Microbiology and Biotechnology* 101 (16):6309–19. doi: 10.1007/s00253-017-8425-z.

Strompfová, V., A. Lauková, and D. Cilik. 2013. Synbiotic administration of canine-derived strain *Lactobacillus fermentum* CCM 7421 and inulin to healthy dogs. *Canadian Journal of Microbiology* 59 (5):347–52. doi: 10.1139/cjm-2012-0472.

Suárez-García, I., A. Sánchez-García, L. Soler, E. Malmierca, and J. Gómez-Cerezo. 2012. *Lactobacillus jensenii* bacteremia and endocarditis after dilatation and curettage: Case report and literature review. *Infection* 40 (2):219–22. doi: 10.1007/s15010-011-0182-9.

Tamang, J. P., K. Watanabe, and W. H. Holzapfel. 2016. Review: Diversity of microorganisms in global fermented foods and beverages. *Frontiers in Microbiology* 7:377. doi: 10.3389/fmicb.2016.00377.

Thakur, K., and S. K. Tomar. 2016. *In vitro* study of riboflavin producing lactobacilli as potential probiotic. *LWT – Food Science and Technology* 68:570–8. doi: 10.1016/j.lwt.2015.12.059.

Thakur, K., S. K. Tomar, and S. De. 2016. Lactic acid bacteria as a cell factory for riboflavin production. *Microbial Biotechnology* 9 (4):441–51. doi: 10.1111/1751-7915.12335.

Tiollier, E., M. Chennaoui, D. Gomez-Merino, C. Drogou, E. Filaire, and C. Y. Guezennec. 2007. Effect of a probiotics supplementation on respiratory infections and immune and hormonal parameters during intense military training. *Military Medicine* 172 (9):1006–11. doi: 10.7205/MILMED.172.9.1006.

Tomaro-Duchesneau, C., M. L. Jones, D. Shah, P. Jain, S. Saha, and S. Prakash. 2014. Cholesterol assimilation by *Lactobacillus* probiotic bacteria: An *in vitro* investigation. *BioMed Research International* 2014 (380316):1.

Tomaro-Duchesneau, C., S. Saha, M. Malhotra, M. L. Jones, L. Rodes, and S. Prakash. 2015. *Lactobacillus fermentum* NCIMB 5221 and NCIMB 2797 as cholesterol-lowering probiotic biotherapeutics: In vitro analysis. *Beneficial Microbes* 6 (6):861–9. doi: 10.3920/BM2015.0021.

Tomaro-Duchesneau, C., S. Shyamali, M. Meenakshi, M. Coussa-Charley, I. Kahouli, M. L. Jones, A. Labba, and P. Satya. 2012. Probiotic ferulic acid esterase active *Lactobacillus fermentum* NCIMB 5221 APA microcapsules for oral delivery: Preparation and *in vitro* characterization. *Pharmaceuticals (Basel)* 5 (2):236–48. doi: 10.3390/ph5020236.

Tulumoğlu, Ş., H. İ. Kaya, and Ö. Şimşek. 2014. Probiotic characteristics of *Lactobacillus fermentum* strains isolated from tulum cheese. *Anaerobe* 30:120–5. doi: 10.1016/j.anaerobe.2014.09.015.

Turpin, W., C. Humblot, and J. P. Guyot. 2011. Genetic screening of functional properties of lactic acid bacteria in a fermented pearl millet slurry and in the metagenome of fermented starchy foods. *Applied and Environmental Microbiology* 77 (24):8722–34. doi: 10.1128/AEM.05988-11.

Upreti, G. C., and R. D. Hinsdill. 1975. Production and mode of action of lactocin 27: Bacteriocin from a homofermentative *Lactobacillus*. *Antimicrobial Agents and Chemotherapy* 7 (2):139–45. doi: 10.1128/AAC.7.2.139.

Vaughan, E. E., H. G. Heilig, K. Ben-Amor, and W. M. de Vos. 2005. Diversity, vitality and activities of intestinal lactic acid bacteria and bifidobacteria assessed by molecular approaches. *FEMS Microbiology Reviews* 29 (3):477–90.

Vieco-Saiz, N., Y. Belguesmia, R. Raspoet, E. Auclair, F. Gancel, I. Kempf, and D. Drider. 2019. Benefits and inputs from lactic acid bacteria and their bacteriocins as alternatives to antibiotic growth promoters during food-animal production. *Frontiers in Microbiology* 11:10–57. doi: 10.3389/fmicb.2019.00057.

von Mollendorff, J. W., S. D. Todorov, and L. M. T. Dicks. 2006. Comparison of bacteriocins produced by lactic-acid bacteria isolated from boza, a cereal-based fermented beverage from the Balkan Peninsula. *Current Microbiology* 53 (3):209–16.

Wannun, P., S. Piwat, and R. Teanpaisan. 2016. Purification, characterization, and optimum conditions of fermencin SD11, a bacteriocin produced by human orally *Lactobacillus fermentum* SD11. *Applied Biochemistry and Biotechnology* 179 (4):572–82.

Wayah, S. B., and K. Philip. 2018. Characterization, yield optimization, scale up and biopreservative potential of fermencin SA715, a novel bacteriocin from *Lactobacillus fermentum* GA715 of goat milk origin. *Microbial Cell Factories* 17:125.

Weckx, S., R. Van der Meulen, J. Allemeersch, G. Huys, P. Vandamme, P. Van Hummelen, and L. De Vuyst. 2010. Community dynamics of sourdough fermentations as revealed by their metatranscriptome. *Applied and Environmental Microbiology* 76 (16):5402–8. doi: 10.1128/AEM.00570-10.

West, P. N., D. B. Pyne, A. W. Cripps, W. G. Hopkins, D. C. Eskesen, A. Jairath, C. T. Christophersen, M. A. Conlon, and P. A. Fricker. 2011. *Lactobacillus fermentum* (PCC®) supplementation and gastrointestinal and respiratory-tract illness symptoms: A randomised control trial in athletes. *Nutrition Journal* 10:30.

Yadav, R., D. K. Dey, R. Vij, S. Meena, R. Kapila, and S. Kapila. 2018. Evaluation of anti-diabetic attributes of *Lactobacillus rhamnosus* MTCC: 5957, *Lactobacillus rhamnosus* MTCC: 5897 and *Lactobacillus fermentum* MTCC: 5898 in streptozotocin induced diabetic rats. *Microbial Pathogenesis* 125:454–62.

Yan, T. R., and C. S. Lee. 1997. Characterization of a partially purified bacteriocin, Fermentecin B, from *Lactobacillus fermentum*. *Biotechnology Letters* 19 (8):741–4.

Zahid, M., M. Ashraf, M. Arshad, G. Muhammad, A. Yasmin, and H. M. A. Hameed. 2015. Antimicrobial activity of bacteriocins isolated from lactic acid bacteria against resistant pathogenic strains. *International Journal of Nutrition and Food Sciences* 4:326–31. doi: 10.11648/j.ijnfs.20150403.20.

Żarłok, K. 2016. *Lactobacillus fermentum* CECT5716 – Probiotic from human milk with interesting properties. *Wiadomości Lekarskie* 69 (2 Pt 2):271–5.

Zawistowska-Rojek, A., and S. Tyski. 2018. Are probiotic really safe for humans?. *Polish Journal of Microbiology* 67 (3):251–8. doi: 10.21307/pjm-2018-044.

Zhuang, G., X. M. Liu, Q. X. Zhang, F. W. Tian, H. Zhang, H. P. Zhang, and W. Chen. 2012. Research advances with regards to clinical outcome and potential mechanisms of the cholesterol-lowering effects of probiotics. *Clinical Lipidology* 7 (5):501–7. doi: 10.2217/clp.12.40.