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Antibiotic Resistance in Probiotic Microorganisms

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ABSTRACT

Probiotics are widely used in different forms of food or food supplements due to their health benefits. Probiotics consumption has seen an increase over the years. The main species used in probiotic products are *Lactobacillus* and *Bifidobacterium*, along with other species such as *Bacillus*. Generally, probiotic microorganisms are accepted as safe even though they are resistant to several antibiotics. Some probiotic strains with intrinsic antibiotic resistance may be beneficial in regenerating gut microbiota during antibiotic therapy. However, the antibiotic resistance genes identified in probiotic microorganisms may carry the risk of the transfer of resistance genes to pathogens, raising concerns. For instance, tetracycline resistance genes have often been detected in probiotic organisms *Bifidobacterium* and *Lactobacillus*. The antibiotic resistance genes carried on mobile genetic elements create reservoirs for pathogen resistance. This transfer of resistant genes to opportunistic pathogens and their spread may pose great danger. Hence, the purpose of this review was to assess the presence of antibiotic resistance in probiotic microorganisms and the potential transfer of the resistant genes to pathogens or commensal bacteria in the intestine.

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Introduction

The word probiotic means “for life”. The term was used by Lily and Stillwell in 1965, who defined probiotics as substances supporting the growth of other microorganisms. The World Health Organization (WHO) defines probiotics as live microorganisms that provide a beneficial effect to the host when administered in appropriate amounts (FAO/WHO, 2001). Various probiotic species have been reported in the prevention of several diseases, such as cancer and antibiotic-associated diarrhea. It also improves intestinal health and lactose metabolism, enhances the immune response, and reduces serum cholesterol. However, these health benefits are strain-specific (Kechagia et al., 2013; Krupodorova et al., 2022). Several studies have reported the health benefits of consuming probiotics. Evivie et al. (2017) reported that *Lactobacillus acidophilus* and *Lb. casei* delayed the progression of diabetes while *Lactobacillus* GG and *Lb. rhamnosus* GG species were found to reduce the risk of allergic disease (Abatenh et al., 2018). Probiotic *Enterococcus faecium* inhibited the replication of the swine flu virus and protected the host cells from infection (Wang et al., 2013). The mood-enhancing effect of consuming yogurt containing *Lb. casei* (Cerdó et al., 2017) has also been reported, along with the effects of *Lactobacillus* and *Bifidobacterium* species in preventing dental caries (Jain and Sharma, 2012). The first known benefits of probiotics were shown in gastrointestinal tract diseases, including Crohn’s disease, ulcerative colitis, and obesity (Markowiak and Śliżewska, 2017). The mechanism of action of probiotics can be explained as an increase in the number of beneficial bacteria and/or reductionin the number of pathogenic bacteria in the intestine. With the health benefits of probiotic products being demonstrated in clinical trials, a worldwide increase was observed in their consumption (Sharma et al., 2014).

The probiotic market involves fermented milk or cereal food products and supplements, which are sold in the form of capsules or tablets. Probiotic food products mainly consist of dairy products such as yogurt and kefir. Besides, they include probiotic ice cream, probiotic cheese, breakfast cereals, and infant formula. Probiotic food products constitute 60–70% of the functional food market, with their market valued at USD 46.17 billion in 2017, which is expected to reach USD 69.29 billion by 2023. This

exhibits a compound annual growth rate (CAGR) of 7.0% compared to the year 2018 (Misra et al., 2021).

Lactic acid bacteria (LAB) have been safely used in fermented foods for many years under the GRAS (Generally Regarded as Safe) and QPS (Qualified Presumption of Safety) status provided by the FDA (Food and Drug Administration) and EFSA (European Food Safety Authority) (EFSA, 2021). Additionally, LAB isused as a probiotic food supplement because it is a natural member of the intestinal microbiota having GRAS status (Fraqueza, 2015).

The most common microorganisms used in probiotic products belong to *Bifidobacterium*, *Lactobacillus*, *Lactococcus*, and *Streptococcus* spp. On the other hand, the genetic relatedness and phylogeny of the species within the present genus *Lactobacillus* and its sister taxa in the *Lactobacillaceae* and *Leuconostocaceae* were re-evaluated. In this re-evaluation, the criteria such as average nucleotide identity, average amino acid identity, core-gene average amino acid identity, core genome phylogeny, signature genes, and metabolic or ecological were based on (Zheng et al., 2020). *Saccharomyces cerevisiae*, *Bacillus*, *Propionibacterium*, and *Enterococcus* are also considered probiotics. However, these products have safety concerns since these genera also contain many pathogenic species, especially *Enterococcus*. The non-pathogenic strain *Escherichia coli* Nissle 1917 (EcN) is the most widely used probiotic because of its beneficial effect on the homeostasis of intestinal microbiota (Sharma et al., 2014). Some of the commercially used probiotic strains are listed in Table 1. According to legal regulations, probiotic products may have $>10^6$–10^8 CFU/g or $>10^8$–10^{10} CFU/g of viable cells, which are considered adequate (Kim et al., 2018).

Although probiotic cultures are generally considered safe for human consumption, some concerns related to the safety of probiotics do exist. The three primary risks against probiotics safety are as follows: 1) the occurrence of diseases, such as bacteremia or endocarditis; 2) lead toxicity or metabolic activity; 3) the transfer of antibiotic-resistant genes (Sharma et al., 2014). WHO has warned about antibiotic resistance reaching dangerously high levels worldwide. Since probiotics are the potential transferring source of antibiotic resistance in the gastrointestinal tract, the primary safety concern of probiotics remains antibiotic resistance. (WHO, 2014). Therefore, it is significant to determine the transferable antibiotic resistance of probiotics. Hence, we aimed to summarize the antibiotic resistance profile of LAB and commercial probiotic strains along with the potential transfer of antibiotic resistance to pathogens and other commensal microbiota.

Table 1. Details of commercially available probiotic strains

Probiotic strains	Company	References
Lactobacillus rhamnosus GG	Valio Dairy, Helsinki (Finland)	Raja and Arunachalam (2011)
Lactobacillus johnsonii Lal	Nestle, Lausanne (Switzerland)	Raja and Arunachalam (2011)
Lactobacillus acidophilus	Rhodia, Madison (USA)	Raja and Arunachalam (2011)
Lactobacillus delbruekii	Meiji Milk Products (Tokyo, Japan)	Raja and Arunachalam (2011)
Lactobacillus casei Shirota	Yakult (Tokyo, Japan)	Raja and Arunachalam (2011)
Saccharomyces boulardii	Biocodex, Seattle (USA)	Raja and Arunachalam (2011)
Lactobacillus casei DN 014001	Danone (France)	Raja and Arunachalam (2011)
Bifidobacterium longum BB536	Morinaga Milk Industry (Japan)	Raja and Arunachalam (2011)
Enterococus LAB SF 68	Bioflorin,Cerbios-Pharma	Sharma et al. (2014)
Escherichia coli Nissile 1917	Mutaflor,Ardeypharm	Sharma et al. (2014)
Saccharomyces boulardii	Biocodex, Seattle (USA)	Sharma et al. (2014)
Bifidobacterium infantis 35624	Align, Procter &Gamble	Sharma et al. (2014)
Bifidobacterium lactis HN019 (DR10)	Howaru Bifido, Danisco	Sharma et al. (2014)
Bifidobacterium lactis Bb-12	Chr. Hansen (MilwaukeeWI)	Sharma et al. (2014)
Lactobacillus fermentum VRI003 (PCC)	Probiomics (Eveleigh,Australia)	Tiwari et al. (2012)
Lactobacillus salivarius UCC118	University College (Cork,Ireland)	Tiwari et al. (2012)
Bifidobacterium infantis 35264	Procter and Gamble (Mason OH)	Tiwari et al. (2012)
Bifidobacterium longum BB536	Morinaga Milk Industry o., Ltd. (Japan)	Tiwari et al. (2012)
Bacillus cereus	Bactisubtil (France)	Lee et al. (2019)
Bacillus subtilis	Bio-Kult (Protexin), UK	Lee et al. (2019)
Bacillus clausii	Domuvar (Bio Progress SpA., Italy)	Lee et al. (2019)
Bacillus coagulans, *Lactobacillus rhamnosus*	Kevika (USA)	Lillo-Pérez et al. (2021)
Lactobacillus reuteri MM53	Rela (Sweden)	Lillo-Pérez et al. (2021)
Lactobacillus plantarum 299v	GoodBelly (USA)	Lillo-Pérezet al. (2021)
Lactobacillus paracasei and *Lactobacillus plantarum*	Healthy life probiotic (Australia)	Lillo-Pérez et al. (2021)
Lactobacillus plantarum 299v	Proviva (Sweden)	Lillo-Pérez et al. (2021)
Lactobacillus paracasei	Malee probiotic juices (Thailand)	Lillo-Pérez et al. (2021)
Lactobacillus rhamnosus GG, *Propionibacterium freudenreichii*	Gefilus (Finland)	Lillo-Pérez et al. (2021)

Mechanisms of Antibiotic Resistance

Bacteria exhibit two major resistance mechanisms against antibiotics, namely intrinsic or acquired resistance. The mechanisms in specific bacterial species depend on the antibiotics, their target location in the host, the bacterial species, and their association with the plasmid or chromosomal mutation (Sharma et al., 2014). Intrinsic resistance is an inherent trait characteristic of a species or genus, which is encoded chromosomally, whereas the acquired resistance is attained either through genetic mutations or the acquisition of foreign DNA from other bacteria. The intrinsic resistance can be described by four different mechanisms, including enzymatic inactivation, alteration of outer membrane permeability by an active efflux pump system, change in the bacterial target location, and regulation of intracellular metabolism (Meral and Korukluoğlu, 2014).

Horizontal gene transfer (HGT) refers to the transfer of genetic material between the same or different species. Whereas, mutations may cause genetic replacements in many genome regions with only a minor role in improving resistance. Thus, enteric bacteria may acquire resistance via mutation or horizontal transfer of resistance genes from other enteric bacteria (Sharma et al., 2014). The horizontal transfer of resistant genes within species and genera involves three main mechanisms, namely conjugation, transformation, and transduction. Furthermore, these mechanisms involve plasmids, transposons, integrons, and bacteriophages to play essential roles as mobile genetic elements, which include antibiotic resistance genes responsible for transferring genetic material within and between the species (Huddleston, 2014).

The primary mechanism of the horizontal transfer of plasmids (Huddleston, 2014) involves conjugation. The role of conjugation in horizontal gene transfer is to transfer DNA between different bacterial species. The major three incidents of conjugation are as follows: 1) cell-to-cell communication, 2) copulation-double formation, and 3) transfer of plasmid DNA via the conjugative pilus (Huddleston, 2014). Several researchers have reported the transfer of antibiotic resistance genes in LAB through conjugative transposons, which include tetracycline, chloramphenicol, kanamycin, and erythromycin(Imperial and Ibana, 2016). Transduction involves the transfer of resistance genes through bacteriophage. Whereas, transformation involves the transfer of resistant genes to the bacterial cell through free DNA (Meral and Korukluoğlu, 2014).

Antibiotic Resistance in LAB

The development and preservation of the properties of fermented food and feeds, including the structural property, aroma, and flavor, are attributed to the production potential of LAB's exopolysaccharide (EPS), organic acids, polyols, aromatic compounds, and bacteriocins. The potential of LAB in industrial applications is highlighted by its safe documentation status (GRAS), wide tolerance to different stress environments, simple metabolism, and ability to metabolize different carbon sources widely. The probiotic perspective proposed since the first half of the 20th century has led to a greater focus on the probiotic potentials of LAB. However, the identification of antibiotic-resistant LAB strains and the possibility of transferring resistant genes to pathogens have raised concerns (Fraqueza, 2015). Antibiotic resistance may be intrinsic, acquired, and/or mutational, with transposons and conjugative plasmids being prevalent in LAB (Sharma et al., 2014).

The most common resistant genes in LAB include *tet(M)* and *erm(B)* (Wang et al., 2020). Besides, the resistance genes *erm(A), erm(C),* and *erm(T)* are also uncommonly detected in lactobacilli and *Streptococcus thermophilus* (Nawaz et al., 2011). According to Li and colleagues (2020), LAB is usually resistant to vancomycin, streptomycin, gentamicin, teicoplanin, kanamycin, bacitracin, furantoin, norfloxacin, sulfadiazine, cefoxitin, metronidazole, and trimethoprim. Imperial and Ibana (2016) reported intrinsic resistance in the LAB against bacitracin, kanamycin, teicoplanin, vancomycin, and beta-lactams. *Lactococcus* spp., *Leuconostoc* spp., and *Lactobacillus* spp. are found to be highly resistant to cefoxitin, while many species of lactobacilli, except *Lb. delbrueckii* subsp. *bulgaricus*, *Lb. acidophilus*, *Lb. johnsonii*, and *Lb. crispatus*, are intrinsically resistant to glycopeptides (Sharma et al., 2014).

Generally, *Lactobacillus* species are susceptible to antibiotics, such as tetracycline, erythromycin, and chloramphenicol, that inhibit protein syntheses (Fraqueza, 2015). They are also sensitive to penicillin but significantly resistant to cephalosporins. Intrinsic resistance to colistin has been reported in different lactobacilli (Das et al., 2020). *Lactobacillus* species tend to show intrinsic resistance against ciprofloxacin, co-trimoxazole, and nalidixic acid which are not transferable horizontally (Kumari et al., 2022). Many strains belonging to the genus *Lactobacillus* are intrinsically resistant to vancomycin and are widely used as probiotics to prevent *Clostridium difficile* infection (Goldstein et al., 2015). For instance, Nawaz et al. (2011) determined that although *Lactobacillus* strains did not carry the acquired resistant gene *van(B)*, they were intrinsically resistant to vancomycin. Fu et al. (2022) showed that *Lb. plantarum* ZJ2868 was also resistant to vancomycin. Klare et al. (2007) found that probiotic *Lb. rhamnosus* L-015 and L-455 and *Lb. paracasei* L-005 were highly resistant to streptomycin. Moreover, *Lb. rhamnosus*, *Lb. paracasei*, *Lb. plantarum*, and *Lb. acidophilus* were intrinsically resistant to fusidic acid while *Lb. reuteri* was sensitive to it.

Zago et al. (2011) showed that *Lb. plantarum* strains isolated from cheese were sensitive to erythromycin, chloramphenicol, and gentamicin. Similarly, another study also detected the susceptibility of *Lb. plantarum* strain to tetracycline, erythromycin, chloramphenicol, and gentamicin (Gupta and Tiwari, 2014). Furthermore, the probiotic strain *Lb. rhamnosus* GG ATCC 53103 showed susceptibility to ciprofloxacin, erythromycin, amoxicillin/clavulanic acid, and tetracycline (Drago et al., 2011). Hoque et al. (2010) reported that the *Lactobacillus* spp. isolated from Bogra yogurt of Bangladesh was resistant to nalidixic acid, kanamycin, cefradine, metronidazole, and tetracycline but susceptible to azithromycin, gentamicin, amoxicillin, and clindamycin. The researchers also isolated *Lactobacillus* spp. from yogurt of the Khulna region and found it resistant to

metronidazole, tetracycline, kanamycin, azithromycin, nalidixic acid, amoxicillin, and cefradine and susceptible to clindamycin and gentamicin. Andriani et al. (2021) showed that *Lactobacillus* strains were resistant to ciprofloxacin and aminoglycosides and varying grades of chloramphenicol and tetracycline but were sensitive to erythromycin, amoxicillin, and clindamycin. *Lactobacillus* strains were also detected to be free of transposable elements, gene transfer agents, and plasmids.

Lactobacillus spp. consisted of tetracycline-resistant genes encompassing *tet(M), tet(O), tet(Q), tet(W), tet(S), tet(K), tet(36), tet(L), tet(Z),* and *tet(O/W/32/O/W/O),* and aminoglycoside resistance genes including *aph(200), lnu(A), aph(2), ant(6), aaa(60),aph(3)-IIIa,* and *aac(6)* (Das et al., 2020; Fatahi-Bafghi et al., 2022). Fatahi-Bafghi et al. (2022) identified *tet(L), tet(W),* and *(Tmt)dfrG* genes in probiotic *Lb. reuteri*. Guo and colleagues reported (2017) that *Lb. plantarum, Lb. casei*, and *Lb. helveticus* strains were resistant to vancomycin but sensitive to gentamicin, linezolid, neomycin, erythromycin, and clindamycin. The genes *van(X), van(E), gyr(A),* and *tet(M)* were identified in *Lactobacillus* strains. Specifically, *msrC, van(X),* and *dfrA* genes were reported in *Lb. plantarum*, *S. thermophilus*, and *Lactococcus lactis* strains, respectively (Liu et al., 2009).

Neut et al. (2017) showed intrinsic resistance in the *S. thermophilus* strain against metronidazole, while another study showed resistance against ciprofloxacin in the *S. thermophilus* strain isolated from a probiotic product (Ashraf and Shah, 2011). Koçak and Çifci (2020) found that *Lb. acidophilus* strains were resistant to ampicillin, enrofloxacin, oxytetracycline erythromycin, lincomycin, neomycin, and trimethoprim/sulfamethoxazole. However, all these strains were sensitive to amoxicillin.

The *Lc. lactis* strain was found to be resistant to erythromycin and tetracycline. Some strains were susceptible to ampicillin, amikacin, erythromycin, gentamicin, imipenem, oxacillin, penicillin, pipericillin, sulfonamides, tetracycline, chloramphenicol, trimethoprim/sulfamethoxazole, and vancomycin but were intrinsically resistant to rifamycin, colistin pipemidic acid, and fosfomycin (Sharma et al., 2014). Zhang et al. (2022) detected that *Lb. fermentum* YLF016 was resistant to streptomycin, vancomycin, kanamycin, gentamicin, and ciprofloxacin but was sensitive to chloramphenicol, clindamycin, cephalexin, penicillin, amoxicillin, ampicillin, cefradine, tetracycline, and erythromycin.

Sabir et al. (2010) showed that the strains isolated from kefir, including *Lb. acidophilus* Z1L, *Lb. helveticus* Z5L, *Lb. casei* Z7L, *Pediococcus dextrinicus* ZN1P, *P. acidilactici* ZN10P, *P. pentosaceus* ZN13P, *Lc. cremoris* Z11S, and *Lc. lactis* Z3S were susceptible to ampicillin. Another study reported that *Lactobacillus*, *Streptococcus*, and *Lactococcus* possessed intrinsic resistance to streptomycin, with genes *erm(B)* and *msrA/B* being detected in both *Lactobacillus* and *Streptococcus* species (Toomey et al., 2010). Sharma et al. (2016) assessed antibiotic resistance in strains isolated from commercial probiotic preparations, including *Lb. rhamnosus, Lb. acidophilus, Lb. casei, Lb. reuteri, Lb. plantarum,* and *Lb. fermentum*. The isolates showed high resistance to nalidixic acid, vancomycin, kanamycin, teicoplanin, co-trimoxazole, amikacin, streptomycin, norfloxacin, cefepime, and nitrofurantoin. However, they showed a low level of resistance against tobramycin, gentamicin, ampicillin, cefaclor, methicillin, penicillin, tetracycline, levofloxacin, azithromycin, chloramphenicol, amoxiclav, sulbactam, oxacillin, ofloxacin, ciprofloxacin, cloxacillin, and novobiocin. These isolates were also found susceptible to ceftriaxone, ceftazidime, cefadroxil, cefotaxime, cephalothin, cefoperazone, and netilmicin.

Generally, antibiotic resistance is not transferable in LAB, but it is transferable to pathogens by genes carried on plasmids (Fatahi-Bafghi et al., 2022). Furthermore, *Lactococcus* spp. and *S. thermophilus* are reported to carry and transfer antibiotic-resistant genes (Meral and Korukluoğlu 2014).

Under *in vitro* conditions, the *erm(B)* gene from *Lb. lactis* and *S. thermophilus* could be transferred *to Listeria monocytogenes* through plasmid (Varankovich et al., 2015). However, Flórez and Mayo (2017) determined that the *tet(S)* or *erm(B)* genes were not transferred from *S. thermophilus* to *Lb. delbrueckii* during yogurt production and storage. Besides, lactobacilli acquired resistant genes from enterococci through *Tn916-Tn1545* and *Tn1546* type transposons and plasmids (Abriouel et al., 2015). Another study reported the transfer of erythromycin resistance from *Lb. plantarum* strain M345 to *Lb. rhamnosus, Lc. lactis, L. innocua, E. faecalis*, and *L. monocytogenes* through pLFE1 plasmid (Varankovich et al., 2015). The transfer of *tet(M)* genes from *Lactobacillus* to *E. faecalis* and *Lc. lactis* has also been observed (Das et al., 2020). Nawaz et al. (2011) reported the transfer of *erm(B)* gene from *Lb. fermentum* NWL24 and *Lb. salivarius* NWL33, and the transfer of *tet(M)* gene from *Lb. plantarum* NWL22 and *Lb. brevis* NWL59 to *E. faecalis* 181. Egervärn et al. (2010) investigated the transferability of tetracycline-resistant gene *tet(W)*from the probiotic *Lb. reuteri* ATCC 55730 strain to the enterococci, bifidobacteria, and lactobacilli strains in the human gut without any transfer of *tet(W)* gene.

Antibiotic Resistance in *Enterococcus*

Enterococci are opportunistic pathogens that commonly cause nosocomial infections. Enterococcal strains may develop resistance to a range of antibiotics in certain conditions, where resistant genes are encoded by transferable genetic elements. Particularly, vancomycin resistance can cause significant problems worldwide. Since enterococci had a higher possibility of acquiring antibiotic-resistant genes compared to others in the same niche, their safety as probiotics is discussed in the literature (Franz et al., 2011; Dinçer and Kıvanç, 2021).

Chromosomally encoded intrinsic antibiotic resistance was reported in enterococci against lincosamide, sulfonamide, cephalosporin, some β-lactams, and aminoglycosides. Furthermore, enterococci could acquire resistance from other microorganisms against erythromycin, chloramphenicol, aminoglycosides, rifampicin, tetracycline, ampicillin, penicillin, glycopeptides (vancomycin, teicoplanin), and fluoroquinolones through plasmids or transposons (Braïek and Smaoui, 2019).

Enterococcus strains isolated from food are usually sensitive to clinically suitable antibiotics, including

gentamicin, ampicillin, and vancomycin (Dinçer and Kıvanç, 2021). For instance, Nami et al. (2019) analyzed the antibiotic susceptibility of *Enterococcus* isolated from dairy products and found that all strains were sensitive to vancomycin, gentamicin, and chloramphenicol. Guo et al. (2016) reported that *Enterococcus* strains were resistant to gentamicin but susceptible to penicillin G, ampicillin, and erythromycin with no detection of any antibiotic-resistant genes. Contrastingly, Nascimento and colleagues (2019) showed that all *Enterococcus* spp. were resistant to kanamycin and vancomycin, with many strains also resistant to gentamicin, streptomycin, and clindamycin. Furthermore, the strains *E. durans* SJRP14, *Enterococcus* spp. SJRP11 and SJRP 125, and *E. faecium* SJRP28 and SJRP69 were found resistant to erythromycin. Overall, all strains were resistant to at least a minimum of two groups of antibiotics, with 93.75% of them displaying multi-drug resistance.

A recent study showed that all strains of *E. faecalis* and *E. faecium* isolated from traditional white cheeses were highly susceptible to vancomycin (Oruc et al., 2021). Similarly, another study reported the susceptibility of *E. faecium* strains isolated from the probiotic product to vancomycin, gentamicin, ampicillin, cefaclor, cefotaxime, ciprofloxacin, and erythromycin (Ashraf and Shah, 2011).

The resistance genes *van(A), van(B), van(C), van(D), van(E), van(G), tet(L), tet(M), erm(B),* and *msrA/B* were detected in *Enterococcus* species, with *van(A)* gene found to bethe most prevalent (Ashraf and Shah, 2011; Oruc et al., 2021). The genes *msrC, van(X),* and *dfrA* (Liu et al., 2009) were identified in *E. faecium*, with the gene *van(A)* being detected both on chromosome and plasmid (Ashraf and Shah, 2011).

Dinçer and Kıvanç (2021) tested the antibiotic resistance of three potential probiotic strains of *E. faecium* isolated from 'pastırma' and found that all were susceptible to netilmicin sulfate, ciprofloxacin, gentamicin, and penicillin G. However, the strain 29-P2 was found resistant only to vancomycin. Additionally, 168-P6 and 277-S3 strains were found resistant to erythromycin, streptomycin, and kanamycin. Zommiti et al. (2018) showed that *E. faecium* strains were susceptible to ampicillin, chloramphenicol, gentamicin, tetracycline, and vancomycin but resistant to ofloxacin and erythromycin. Similarly, Shi et al. (2020) showed that *E. faecium* strain was susceptible to amoxicillin–clavulanate potassium, phosphonomycin, vancomycin, ampicillin, cefaclor, chloromycetin, and cefalexin but resistant to neomycin, doxycycline, gentamicin, norfloxacin, tetracycline, cefalotin, polymyxin B, and cefotaxime. Koçak and Çifci (2020) reported that the isolates of *E. faecium* had the antibiotic resistance occurrence rates of 95%, 90%, 80%, 55%, 45%, and 10% against ampicillin and neomycin, erythromycin, amoxicillin/clavulanic acid and oxytetracycline, lincomycin, enrofloxacin, and trimethoprim/sulfamethoxazole and amoxicillin, respectively.

The transfer of resistance genes by *Enterococcus* spp. was reported by Meral and Korukluoğlu (2014). For instance, *in vivo* and *in vitro* studies in mice showed that the vancomycin resistance gene (*vanA*) from enterococci was transferred to a commercial *Lb. acidophilus* strain (Ashraf and Shah, 2011). One study has also reported the transfer of vancomycin resistance from enterococci to *Staphylococcus aureus* strains (Hanchi et al., 2018). Similarly, other studies have shown the transfer of antibiotic resistance between the enterococci strains through conjugation (Wang et al., 2020).

Antibiotic Resistance in *Bifidobacterium*

Bifidobacterium species were reported to have intrinsic resistance to ciprofloxacin, nalidixic acid, mupirocin, streptomycin, and aminoglycosides. Additionally, lincosamides, macrolides, streptogramin B, and tetracycline-resistant genes were also detected in the transposons of *Bifidobacterium* (Imperial and Ibana, 2016). Bifidobacteria are generally susceptible to chloramphenicol but mostly resistant to aminoglycosides (Mayrhofer et al., 2011). *Bifidobacterium* species are also reported to be resistant to gentamicin (Ku et al., 2020). Ünal Turhan and Enginkaya (2016) reported that *Bifidobacterium* isolated from probiotic foods were resistant to vancomycin, tetracycline, ampicillin, and ciprofloxacin but susceptible to erythromycin, gentamicin, chloramphenicol, and nitrofurantoin. Similarly, Mayrhofer et al. (2011) reported that *Bifidobacterium* strains were also resistant to kanamycin and neomycin.

Studies have identified the genes *tet(W), tet(M), tet(O),* and *erm(X)* in *Bifidobacterium* (Raeisi et al., 2018). Rozman et al. (2020) detected acquired *tet(W)* gene in *Bifidobacterium animalis* subsp. *lactis.* Furthermore, the prevalence of *tet(W)* was higher in tested bifidobacteria than in lactobacilli. The most common determinant of resistance in *Bif. animalis* subsp. *lactis* was the *tet(W)* gene, which was sometimes found in transposons as well (Gueimonde et al., 2010). Raeisi et al. (2018) reported no transfer of the gene *tet (W)*from the isolates of *Bif. animalis* subsp. *lactis* to the *Enterococcus* species.

Fatahi-Bafghi et al. (2022) detected the resistance gene *tet(W)* in the mobile element of probiotic *Bif. animalis* subsp. *lactis* and *Bif. longum*. They also observed the transfer of this resistance gene to other bacteria. Contrastingly, another study revealed high resistance levels of *Bif. animalis* subsp. *lactis* AD011 to tetracycline. However, the plasmid carrying the transmissible antibiotic resistance gene was not found. Therefore, *Bif. lactis* could be used as a safe probiotic microorganism to benefit human health (Ku et al., 2020).

Probiotic strain *Bif. breve* in Yakult was found resistant to streptomycin due to chromosomal mutation in the gene *rps(L),* but the resistant gene was not transferable to other bacterial species (Ashraf and Shah, 2011). Similarly, the gene *tet(O)* was also identified in probiotic *Bif. breve* (BR03 NZ_CP034770) (Fatahi-Bafghi et al., 2022). Wei et al. (2012) reported that the strain *Bif. longum* JDM301 was intrinsically resistant to ciprofloxacin, amikacin, gentamicin, and streptomycin but susceptible to vancomycin, amoxicillin, cephalothin, chloramphenicol, erythromycin, ampicillin, cefotaxime, rifampicin, imipenem, and trimethoxime. They also identifieda tetracycline-resistant gene in this strain with the possibility of risk of transfer. Thus, the study concluded that the *Bif. longum* JDM301 used as a probiotic strain needs careful safety screening.

Xiao et al. (2010) assessed the antibiotic susceptibility of bifidobacterial strains in the Japanese market. A total of 23 strains were isolated from probiotic products and tested for susceptibility to 15 antibiotics. The strains were generally found susceptible to chloramphenicol, ampicillin, vancomycin, and linezolid, with intrinsic resistance to aminoglycoside. All the strains were resistant to tetracycline with the gene *tet(W)* being detected in *Bif. animalis* subsp. *lactis*. The study indicated that although *Bifidobacterium* strains may not be considered safety risk, the *tet(W)* gene in some strains may require experimental validation.

Antibiotic Resistance in *Bacillus*

Many studies have revealed the intrinsic resistance of *Bacillus* species to penicillin and ampicillin (Mohkam et al., 2016). However, the *Bacillus* species lacks the mobile elements accountable for the transfer of antibiotic-resistant genes. Hence, antibiotic resistance in *Bacillus* spp. was not considered a safety issue since the resistance genes were not readily transferable to other microorganisms (Saroj and Gupta, 2020).

Neut et al. (2017) found that *Bacillus* strains isolated from probiotic food supplements were intrinsically resistant to macrolides, cephalosporins, metronidazole, and clindamycin but susceptible to all penicillins, streptogramin, fluoroquinolones (ciprofloxacin and levofloxacin), co-trimoxazole, and doxycycline. Another study determined that *Bacillus* strains showed high levels of resistance to kanamycin, ampicillin, and methicillin but were susceptible to chloramphenicol, streptomycin, tetracycline, norfloxacin, rifampicin, neomycin, nalidixic acid, and co-trimoxazole (Samanta et al., 2012).

Although plasmids are common in *Bacillus*, conjugation transfers are rarely observed between *Bacillus subtilis* strains and other bacteria (Dai et al., 2012). The plasmid encoding *erm(C)*, *tet(L)*, and *tet(M)* genes were located within the conjugative transposon *Tn5397* of *B. subtilis*. Other tetracycline-resistant genes such as *tet(K)* were also identified from some isolates of *Bacillus*. Furthermore, the presence of *cfr*-like genes was observed in several *Bacillus* species. Specific antibiotic defense mechanisms involving the aminoglycoside-resistant genes (*aadD2*), chloramphenicol acetyl transferase genes, *cat (Bcl)*, or beta-lactamase were identified in the probiotic strain *B. clausii*. The *erm(34)* gene was detected in the probiotic strain *B. clausii* DSM8716 (Gueimonde et al., 2013). The genes *(Bla)bla-1*, *(Bla)bla2*, and *(Fcyn)fosBx1* were reported on the chromosome of probiotic *Bacillus* spp. (Fatahi-Bafghi et al., 2022). Plasmids encoding tetracycline-resistant genes were also determined in *B. cereus* species (Ashraf and Shah, 2011).

Anokyewaa et al. (2021) investigated the antibiotic resistance of *Bacillus* isolated from commercial aquaculture probiotics in China. *B. cereus* CMPF 4 and *B. paranthracis* CMPF 41 were determined to be resistant to β-lactam antibiotics, including penicillin, ampicillin, oxacillin, cefuroxime, ceftriaxone, and minocycline. Although *B. clausii* strains were resistant to erythromycin, cephalosporins, cycloserine, kanamycin, tobramycin, and amikacin, their resistance genes were not transferable to other organisms (Cutting, 2011). Jeong et al. (2017) demonstrated that all *B. licheniformis* strains were susceptible to gentamicin, kanamycin, tetracycline, and vancomycin but intrinsically resistant to chloramphenicol and streptomycin. Hamdy et al. (2017) reported that the strains *B. subtilis* BS3 and *B. licheniformis* BL31 were sensitive to ampicillin, kanamycin, vancomycin, streptomycin, and gentamicin but had no mobile elements. The *erm* gene was detected in *B. clausii* strains and was considered safe due to no risk of transferability (Lee et al., 2019).

B. coagulans strains were susceptible to ampicillin, chloramphenicol, ciprofloxacin, clindamycin, erythromycin, gentamicin, kanamycin, rifampin, streptomycin, tetracycline, and vancomycin. Its highest susceptibility was observed against tetracycline (Saroj and Gupta 2020; Altun and Erginkaya, 2021). A study investigating the potential probiotic properties of *B. coagulans* CGMCC 9951 revealed that the strain was susceptible to amikacin, bacitracin, cephalothin, chloramphenicol, penicillin G, erythromycin, gentamicin, neomycin, and streptomycin. The strain was also moderately susceptible to vancomycin, amoxicillin, flavomycin, and oxytetracycline (Gu et al., 2015). Similarly, *B. coagulans* T242 was reported as sensitive to amoxicillin, amikacin, tetracycline, chloramphenicol, and rifampin, with intermediate sensitivity to ciprofloxacin and erythromycin (Sui et al., 2020).

Antibiotic Resistance in Other Probiotic Strains

S. cerevisiae and *S. boulardii* (nom. inval.) species are clinically demonstrated yeasts used in probiotics (Fakruddin et al., 2017). The probiotic strain *S. cerevisiae* showed resistance to erythromycin, gentamicin, chloramphenicol, tetracycline, and ampicillin (Fernandez-Pacheco et al., 2018). In the study of Poloni et al. (2017) reported that *S. cerevisiae* was resistant to ampicillin, streptomycin, gentamicin, neomycin, norfloxacin, penicillin G, sulfonamide, and trimethoprim. Another study revealed a potentially probiotic strain *S. cerevisiae* IFST 062013, isolated from fruit, which was resistant to tetracycline, ampicillin, gentamicin, penicillin, polymyxin B, and nalidixic acid (Fakruddin et al., 2017). Neut and colleagues (2017) showed that *S. boulardii* (nom. inval) strains were intrinsically resistant to benzylpenicillin, oxacillin, amoxicillin, cefuroxime, cefixime, macrolides, azithromycin, clarithromycin, lincosamide, clindamycin, streptogramin, fluoroquinolones, ciprofloxacin, levofloxacin, and co-trimoxazole.

C. butyricum MIYAIRI 588® (CBM 588®) strain has been developed as a probiotic for human and animal food. It showed susceptibility to all clinically used antibiotics, except aminoglycoside (gentamicin, kanamycin, and streptomycin) (Isa et al., 2016). The probiotic *E. coli* Nissle 1917 strain is genetically stable and intrinsically resistant to clindamycin, erythromycin, metronidazole, penicillin G, rifampicin, and vancomycin (Altuntaş et al., 2017). The chromosome of probiotic *E. coli* Nissle 1917 NZ_CP007799 was detected with the resistance genes Penicillin_Binding_Protein, *ampC2*, and *ampH* (Fatahi-Bafghi et al., 2022).

Table 2. Antibiotic resistance profiles of commercially available probiotic strains

CPS	Probioticstrainused	Antibioticresistance	Location	R
Probiotic strain	*Lactobacillus salivarius* BFE 7441	Ciprofloxacin, Erythromycin, Gentamicin, Streptomycin	*erm(B)*-chromosome	1
Probiotic product	*Lactobacillus salivarius*	Erythromycin,Gentamicin, Vancomycin	-	2
Probiotic product	*Streptococcus thermophilus*	Ciprofloxacin	-	2
Probiotic product	*Lactobacillus paracasei*, *Lactobacillus plantarum*	Vancomycin	-	2
Probiotic product	*Lactobacillus. acidophilus*, *Lactobacillus paracasei*	Gentamicin	-	2
Fermented milk	*Lactobacillus plantarum*	Vancomycin	*van(X)*	3
Isolated from the gastrointestinal microbiome of people	Lactobacillus *casei/paracasei* K 3Sh24, *Lactobacillus helveticus* NNIE, *Lactobacillus helveticus* Er 317/402.	Tetracycline	*tet(M)*-transposon	4
ProbioticYogurt	*Lactobacillus kefiri* NWL78	Tetracycline	*tet(S)*	5
Italian and Argentinean cheeses	*Lactobacillus plantarum* Lp804, *Lactobacillus plantarum* Lp805	Tetracycline	*tet(M)*	6
Probiotic strain	*Lactobacillus reuteri*	A1	-	7
Probiotic strain	*Bifidobacterium longum* JDM301	A2	ND	8
Naturally fermented olives	*Lactobacillus casei* Shirota	Erythromycin, Tetracycline	ND	9
Cheese	*Bacillus flexus* Hk1	Penicillin, Methicillin, Ampicillin, Co-Trimoxazole	-	10
Probiotic strain	*Bacillus coagulans*	Penicillin, Methicillin, Co-Trimoxazole	-	10
Probiotic strain	*Enterococcus faecalis*129 *BIO 3B-R*, *Enterococcus faecalis BIO-4R*, *Enterococcus faecalis PCR*	Beta-lactams	-	11
Fermented food	*Lactobacillus plantarum* LD1	Kanamycin	-	12
Probiotic product	*Lactobacillus plantarum* CICC 23180	β-lactam	*blr*-plasmid	13
Dairy samples	*Lactobacillus* isolates LBS 1, *Lactobacillus* isolates LBS 2	Co-trimoxazole, Amoxycillin, Vancomycin	-	14
Probiotics of dietary supplements (U.S.A)	*Lactobacillus acidophilus*, *Lactobacillus salivarius*, *Bifidobacterium bifidum*, *Streptococcus thermophilus*	Vancomycin, Gentamycin, Streptomycin, Ciprofloxacin	-	15
Probiotics of dietary supplements (Malaysia)	*Bifidobacterium longum*, *Bifidobacterium bifidum*, *Bifidobacterium infantis*, *Lactobacillus bulgaricus*, *Lactobacillus rhamnosus*, *Lactobacillus casei*, *Lactobacillus acidophilus*	Vancomycin, Streptomycin, Aztreonam, Gentamycin, Ciprofloxacin	-	15
Probiotics of dietary supplements (Austria)	*Bifidobacterium longum*, *Bifidobacterium bifidum*, *Lactobacillus gasseri*	Vancomycin, Streptomycin, Aztreonam, Gentamycin, Ciprofloxacin	-	15
Probiotic product	*Lactobacillus plantarum* (CECT 7527, CECT 7528)	Clindamycin, Kanamycin	ND	16
Probiotics food supplements	*Bifidobacterium lactis* BB-12/DSM 15954, *Bifidobacterium longum* LA 101, *Bifidobacterium bifidum*	Ciprofloxacin	-	17
Probiotics food supplements	*Lactococcus lactis* LA 103	Ciprofloxacin, Co-Trimoxazole, Metronidazole	-	17
Probiotic drop	*Lactobacillus reuteri*Protectis DSM 17938	Penicillins	-	17
Yogurt drink sample	*Bifidobacterium* C	Erythromycin	*erm(B)*	18
Indigenous milk of different animals	*Lactobacillus pentosus* MMP4	A3	-	19
Mozzarella cheese	*Lactobacillus casei, Lactobacillus fermentum*	Vancomycin	ND	20
Probiotic strain	*Lactobacillus plantarum* 299v	Aminoglycosides, Vancomycin, Metronidazole,	-	21
Commercial food products	*Lactobacillus* E	Erythromycin, Tetracycline, Vancomycin	*tet(M)*,*erm(B)*	22
Commercial food products	*Lactobacillus* D	Erythromycin, Tetracycline, Vancomycin	*erm(B)*	22
Jugcheese, a type of Iranian traditional cheese	*Lactobacillus brevis* KMJC1, *Lactobacillus acidipiscis* KMJC2, *Lactobacillus curvatus* KMJC3, *Lactobacillus plantarum* KMJC4	Vancomycin, Kanamycin, Streptomycin	-	23
Camel milk	*Lactococcus lactis*(cam 12), *Enterococcus lactis*(cam 14), *Lactobacillus plantarum*(cam 15)	Chloramphenicol, Lincomycin	-	24
Probiotic isolate	*Enterococcus lactis* JDM1	Macrolid, Fluoroquinolone, Aminoglycoside	L1	25
Commercial probiotic lozenges	*Lactobacillus paracasei*, *Lactobacillus reuteri*, *Lactobacillus sakei*, *Lactobacillus salivarius*, *Lactobacillus reuteri* DSM 17938, *Lactobacillus reuteri* ATCC PTA 5289, *Lactobacillus brevis* CECT 7480, *Lactobacillus plantarum* CECT 7481	Trimethoprim	*dfrD*-plasmid	26
Commercial probiotic lozenges	*Lactobacillus acidophilus* HA-122, *Lactobacillus casei* HA-108, *Lactobacillus rhamnosus* HA-111, *Lactobacillus salivarius* HA-188	Macrolide, Chloramphenicol, Trimethoprim	L2	26
Commercial probiotic lozenges	*Lactobacillus paracasei*, *Lactobacillus reuteri*	Chloramphenicol, Aminoglycoside, Vancomycin	L3	26

CPS: Commercial probioticproducts/strain; R: References; 1: Hummel et al. (2007); 2: Blandino et al. (2008); 3: Liu et al. (2009); 4: Botinaet al. (2011); 5: Nawaz et al. (2011); 6: Zagoet al. (2011); 7: Singh et al. (2012); 8: Wei et al. (2012); 9: Argyri et al. (2013); 10: Nithya and Halami (2013); 11: Yamaguchi et al. (2013); 12: Guptaand Tiwari (2014); 13: Han et al. (2015); 14: Kumar and Kumar (2015); 15: Wong et al. (2015); 16: Mukerji et al. (2016); 17: Neut et al. (2017); 18: Aarif and Weerasooriya (2019); 19: Choudhary et al. (2019); 20: de Souza et al. (2019); 21: Klarin et al. (2019); 22: Priyadarshana and Daniel (2019); 23: Mahmoudi et al. (2021); 24: Sharma et al. (2021); 25: Fu et al. (2022); 26: Wang et al. (2022); A1: Polymyxin B, Gentamycin, Cefazolin, Ampicillin, Kanamycin, Amikacin, Vancomycin; A2: Ciprofloxacin, Amikacin, Gentamicin, Streptomycin; A3: Chloramphenicol, Novobiocin, Methicillin, Tetracycline, Streptomycin, Erythromycin, Penicillin, Fusidic Acid; L1: efmA, aac(6')-Ii, msrC-chromosome; L2: mefA, cat-TC-plasmid, dfrD-plasmid; L3: cat-TC-plasmid, aadE, van(X); *cat:*chloramphenicol*; erm:* erythromycin*; tet:* tetracycline*; lnu(A):* lincosamide*; van:* vancomycin*; blr:* β-lactam*; efmA:* macrolide*; aac(6´)-Ii:* aminoglycoside*; msrC :* macrolide*; dfrA/dfrD:* trimethoprim *; mefA:* erythromycin*; aadE:* streptomycin; (-): not studied; ND: not determined

Antibiotic Resistance in Commercial Probiotic Strains

With time, widespread and wrong usage of antibiotics has led to the creation of a reservoir of antibiotic-resistant genes in microorganisms. The resistance to antibiotics and, more importantly, the potential transfer of antibiotic resistance to pathogens and commensal bacteria in the gut poses a serious threat worldwide. Although the *Lactobacillus* and *Bifidobacterium* strains in commercial probiotics are accepted as highly genetically stable, there is a need to evaluate the risk of transfer of antibiotic-resistant genes during the production and storage conditions of probiotics. Determining the inability to transmit or accept antibiotic-resistant genes becomes essential in assessing the safety of probiotics for human consumption (Wong et al., 2015; Ku et al., 2020). Probiotic microorganisms with non-transmissible antibiotic resistance do not generally pose a safety risk. Therefore, while selecting probiotic strains, it is suggested to ensure that the transferable resistance genes encoding resistance to clinical drugs are not carried by the probiotic bacteria (FAO/WHO, 2001).

Antibiotic resistance in probiotics may be "intrinsic" or "acquired." Intrinsic resistance may be a desirable trait during antibiotic treatment because such probiotics may help restore the host gut microflora. Whereas, acquired resistance in probiotic strains presents a significant potential for horizontal spread of resistant genes than enabling intrinsic resistance. It is essential to evaluate antibiotic resistance in probiotic strains to distinguish between intrinsic and acquired resistance, which helps in identifying the strains correctly (Li et al., 2020).

Probiotics have shown resistance to several classes of antibiotics, including glycopeptides, aminoglycosides, monobactams, and fluoroquinolones (Zheng, 2017). Additionally, some probiotic strains were identified with antibiotic-resistant genes in their plasmids, which could be transferred horizontally to pathogens. Hence, there is a need to identify antibiotic resistance in commercial probiotic strains (Ku et al., 2020). Antibiotic resistance profiles of some commercial probiotic strains are listed in Table 2.

Probiotics, except the ones with yeast, are usually susceptible to most antibiotics applied orally. So far, most of the acquired antibiotic-resistant genes in LAB and bifidobacteria have been tetracycline-and erythromycin-resistant genes (Neut et al., 2017). Fatahi-Bafghi et al. (2022) found that the *tet(W)* resistance gene was common in probiotic species *Bifidobacterium* and *Lactobacillus*.

A study evaluated the genotypic and phenotypic stability of a probiotic nominee strain, *Lb. rhamnosus* PRSF-L477, which was found to be genetically stable. Although the *tet(W)* gene was found on the chromosome of *Bif. animalis* subsp. *lactis* Bb-12, the probability of its transfer from Bb-12 to other microorganisms was considered low. The PROSAFE project detected the minimal inhibitory concentrations (MICs) of 16 antimicrobials in 473 LAB isolates, including the genera *Lactobacillus*, *Pediococcus,* and *Lactococcus*. Although *Lactobacillus* strains showed high resistance to streptomycin, PCR results showed no resistant gene. The project concluded that testing antimicrobial susceptibility was essential in assessing the safety of LAB due to the presence of acquired-resistant genes in isolates derived from probiotics (Sanders et al., 2010). Wong et al. (2015) investigated five commercially available probiotic dietary supplements and reported that probiotics of the whole group of products were resistant to vancomycin while few were resistant to streptomycin, aztreonam, gentamicin, orciprofloxacin based on their group.

Hammad and Shimamoto (2010) revealed that the isolates obtained from 40 commercially available Japanese probiotic supplements did not carry antibiotic-resistant genes and showed low natural resistance to tested antibiotics. The probiotics evaluated within the scope of this study were reported to be risk-free. Besides, the isolated probiotic strains were not suitable for probiotic-antibiotic combination therapy due to their sensitivity to clinically used antibiotics.

A recent study conducted by Baumgardner and colleagues (2021) reported transferrable *tet(M) ,tet(K), erm(B), erm(T), sul1, sul2,* and *dfrG* resistant genes in commercial animal probiotics. Another important finding of the study was the determination of the transferable gene *van(A)* in probiotics marketed for application in animal foods.

Conclusion

Many probiotic strains were reported to have intrinsic or acquired resistance to antibiotics. Antibiotic-resistant genes were also identified on mobile genetic elements in typical probiotics. Recent studies have reported antibiotic resistance in probiotics. The significant safety problem of probiotics is the transfer of antibiotic-resistant genes to pathogenic and commensal organisms. Since the consumption of probiotics has notably increased worldwide, it becomes mandatory to assess their safety. Therefore, it is essential to determine the antibiotic resistance profiles and transferable antibiotic resistance among the strains used as probiotics.

References

Aarif TI, Weerasooriya P. 2019. Identification of the genus *Bifidobacterium* in commercially available yogurt drink products and determination of their antibiotic resistance genes. GARI Int. J. Multidisip. Res., 4(7): 109-120.

Abatenh E, Gizaw B, Tsegay Z, Tefera G, Aynalem E. 2018. Health benefits of probiotics. J. Bacteriol. Infec. Dis., 2(1): 8-27.

Abriouel H, Muñoz MDCC, Lerma LL, Montoro BP, Bockelmann W, Pichner R, Kabisch J, Cho GS, Franz CMAP, Gálvez A, Benomar N. 2015. New insights in antibiotic resistance of *Lactobacillus* species from fermented foods. Food Res. Int., 78: 465-481. doi: 10.1016/j.foodres.2015.09.016

Altun GK, Erginkaya Z. 2021. Identification and characterization of *Bacillus coagulans* strains for probiotic activity and safety. LWT–Food Sci. Technol., 15: 1-10. doi: 10.1016/j.lwt.2021.112233

Altuntaş S, Korukluoğlu M, Altuntaş V. 2017. Probiyotik *Escherichia coli* Suşu Nissle 1917. Pamukkale Univ. Muh. Bilim Derg., 23(7): 933-940. doi: 10.5505/pajes.2017.98475

Andriani D, Hasan PN, Utami T, Suroto DA, Wikandari R, Rahayu ES. 2021. Genotypic and phenotypic analyses of antibiotic resistance in İndonesian indigenous *Lactobacillus* probiotics. Appl. Food Biotechnol., 8(4): 267-274. doi: 10.22037/afb.v8i4.34448

Anokyewaa MA, Amoah K, Li Y, Lu Y, Kuebutornye FKA, Asiedu B, Seidu I. 2021. Prevalence of virulence genes and antibiotic susceptibility of *Bacillus* used in commercial aquaculture probiotics in China. Aquac., 21: 1-8. doi: 10.1016/j.aqrep.2021.100784

Argyri AA, Zoumpopoulou G, Karatzas KAG, Tsakalidou E, Nychas GJE, Panagou EZ, Tassou CC. 2013. Selection of potential probiotic lactic acid bacteria from fermented olives by in vitro tests. Food Microbiol., 33(2): 282-291. doi: 10.1016/j.fm.2012.10.005

Ashraf R, Shah NP. 2011. Review Article Antibiotic resistance of probiotic organisms and safety of probiotic dairy products. Int. Food Res. J., 18(3): 837-853.

Baumgardner RM, Berreta A, Kopper JJ. 2021. Evaluation of commercial probiotics for antimicrobial resistance genes. Can. Vet. J., 62(4): 379-383.

Blandino G, Milazzo I, Fazio D. 2008. Antibiotic susceptibility of bacterial isolates from probiotic products available in Italy. Microb. Ecol. Health Dis., 20: 199-203. doi: 10.1080/08910600802408111

Botina SG, Poluektova EU, Glazova AA, Zakharevich NV, Koroban NV, Zinchenko VV, Babykin MM, Zhilenkova OG, Amerkhanova AM, Danilenko VN. 2011. Antibiotic resistance of potential probiotic bacteria of the genus *Lactobacillus* from human gastrointestinal microbiome. Microbiol., 80(2): 164-171. doi: 10.1134/S0026261711020032

Braïek OB, Smaoui S. 2019. Enterococci: between emerging pathogens
and potential probiotics. BioMed Res. Int., 2019: 1-13. doi: 10.1155/2019/5938210

Cerdó T, Ruíz A, Suárez A, Campoy C. 2017. Probiotic, prebiotic and brain development. Nutrients, 9(11): 1247. doi: 10.3390/nu9111247

Choudhary J, Dubey RC, Sengar G, Dheeman S. 2019. Evaluation of probiotic potential and safety assessment of *Lactobacillus pentosus* MMP4 isolated from mare's lactation. Probiotics Antimicrob. Proteins, 11(2): 403-412. doi: 10.1007/s12602-018-9431-x

Cutting SM. 2011. *Bacillus* probiotics. Food Microbiol., 28(2): 214-220. doi: 10.1016/j.fm.2010.03.007

Dai M, Lu J, Wang Y, Liu Z, Yuan Z. 2012. In vitro development and transfer of resistance to chlortetracycline in *Bacillus subtilis*. J. Microbiol., 50(5): 807-812. doi: 10.1007/s12275-012-1454-5

Das DJ, Shankar A, Johnson JB, Thomas S. 2020. Critical insights into antibiotic resistance transferability in probiotic *Lactobacillus*. Nutrition, 69: 1-6. doi: 10.1016/j.nut.2019.110567

de Souza BMS, Borgonovi TF, Casarotti SN, Todorov SD, Penna ALB. 2019. *Lactobacillus casei* and *Lactobacillus fermentum* strains isolated from mozzarella cheese: probiotic potential, safety, acidifying kinetic parameters and viability under gastrointestinal tract conditions. Probiotics Antimicrob. Proteins, 11(2): 382-396. doi: 10.1007/s12602-018-9406-y

Dinçer E, Kıvanç M. 2021. In vitro evaluation of probiotic potential of *Enterococcus faecium* strains isolated from Turkish pastırma. Arch. Microbiol., 203: 2831-2841. doi: 10.1007/s00203-021-02273-y

Drago L, Rodighiero V, Mattina R, Toscano M, De Vecchi E. 2011. In vitro selection of antibiotic resistance in the probiotic strain *Lactobacillus rhamnosus* GG ATCC 53103. J. Chemother., 23(4): 211-215. doi: 10.1179/joc.2011.23.4.211

EFSA, 2021. Update of thelist of QPS-recommended biological agents intentionally added to food or feed as notified to EFSA 13: suitability of taxonomic units notified to EFSA until September 2020. Available form: https://efsa.onlinelibrary.wiley.com/doi/full/10.2903/j.efsa.2021.6377 [Accessed 20 February 2022]

Egervärn M, Lindmark H, Olsson J, Roos S. 2010. Transferability of a tetracycline resistance gene from probiotic *Lactobacillus reuteri* to bacteria in the gastrointestinal tract of humans. Antonie van Leeuwenhoek, 97(2): 189-200. doi: 10.1007/s10482–009–9401–0

Evivie SE, Huo GC, Igene JO, Bian X. 2017. Some current applications, limitations and future perspectives of lactic acid bacteria as probiotics. Food Nutr. Res., 61(1): 1318034. doi: 10.1080/16546628.2017.1318034

Fakruddin M, Hossain MN, Ahmed MM. 2017. Antimicrobial and antioxidant activities of *Saccharomyces cerevisiae* IFST062013, a potential probiotic. BMC Complement. Altern. Med., 17(1): 64. doi: 10.1186/s12906-017-1591-9

FAO/WHO, 2001. Health and nutritional properties of probiotics in food, including powder milk with live lactic acid bacteria. Report of a Joint FAO/WHO Expert Consultation on Evaluation of Health and Nutritional Properties of Probiotics in Food Including Powder Milk with Live Lactic Acid Bacteria (Cordoba, Argentina). Available from: https://www.fao.org/3/a0512e/a0512e.pdf. [Accessed 10 February 2022]

Fatahi-Bafghi M, Naseri S, Alizehi A. 2022. Genome analysis of probiotic bacteria for antibiotic resistance genes. Antonie Van Leeuwenhoek, 115(3): 375-389. doi: 10.1007/s10482-021-01703-7

Fernandez-Pacheco P, Arévalo-Villena M, Bevilacqua A, Corbo MR, Pérez AB. 2018. Probiotic characteristics in *Saccharomyces cerevisiae* strains: Properties for application in food industries. LWT-Food Sci. Technol., 97: 332-340. doi: 10.1016/j.lwt.2018.07.007

Flórez AB, Mayo B. 2017. Antibiotic resistance-susceptibility profiles of *Streptococcus thermophilus* isolated from raw milk and genome analysis of the genetic basis of acquired resistances. Front. Microbiol., 8 (2608): 1-12. doi: 10.3389/fmicb.2017.02608

Franz CM, Huch M, Abriouel H, Holzapfel W, Gálvez A. 2011. Enterococci as probiotics and their implications in food safety. Int. J. Food Microbiol., 151(2): 125–140. doi: 10.1016/j.ijfoodmicro.2011.08.014

Fraqueza MJ. 2015. Antibiotic resistance of lactic acid bacteria isolated from dry-fermented sausages. Int. J. Food Microbiol., 212: 76-88. doi: 10.1016/j.ijfoodmicro. 2015.04.035

Fu B, Huang X, Ma J, Chen Q, Zhang Q, Yu P. 2022. Characterization of an inositol-producing *Lactobacillus plantarum* strain and the assessment of its probiotic potential and antibacterial activity. LWT-Food Sci. Tehnol., 153: 112553. doi: 10.1016/j.lwt.2021.112553

Fu X, Lyu L, Wang Y, Zhang Y, Guo X, Chen Q, Liu C. 2022. Safety assessment and probiotic characteristics of *Enterococcus lactis* JDM1. Microbial Pathogen., 163: 1-8. doi: 10.1016/j.micpath.2021.105380

Goldstein EJ, Tyrrell KL, Citron DM. 2015. *Lactobacillus* species: taxonomic complexity and controversial susceptibilities. Clin. Infect. Dis., 60: 98-107. doi: 10.1093/cid/civ072

Gu SB, Zhao LN, Wu Y, Sun JR, Huang JF, Li DD. 2015. Potential probiotic attributes of a new strain of *Bacillus coagulans* CGMCC 9951 isolated from healthy piglet feces. World J. Microbiol. Biotechnol., 31(6): 851-863. doi: 10.1007/s11274-015-1838-x

Gueimonde M, Flórez AB, vanHoek AH, Stuer-Lauridsen B, Strøman P, de los Reyes-Gavilan CG, Margolles A. 2010. Genetic basis of tetracycline resistance in *Bifidobacterium animalis* subsp. *lactis*. Appl. Environ. Microbiol., 76(10): 3364-3369. doi: 10.1128/AEM.03096-09

Gueimonde M, Sánchez B, de los-Reyes CG, Margolles A. 2013. Antibiotic resistance in probiotic bacteria. Front. Microbiol., 4(202): 1-6. doi: 10.3389/fmicb.2013.00202

Guo H, Pan L, Li L, Lu J, Kwok L, Menghe B, Zhang H, Zhang W. 2017. Characterization of antibiotic resistance genes from *Lactobacillus* isolated from traditional dairy products. J. Food Sci., 82(3): 724-730. doi: 10.1111/1750–3841.13645

Guo L, Li T, Tang Y, Yang L, Huo G. 2016. Probiotic properties of *Enterococcus* strains isolated from traditional naturally fermented cream in China. Microb. Biotechnol., 9(6): 737-745. doi: 10.1111/1751-7915.12306

Gupta A, Tiwari SK. 2014. Probiotic potential of *Lactobacillus plantarum* LD1 isolated from batter of dosa, a South Indian fermented food. Probiotics Antimicrob. Proteins, 6(2): 73-81. doi: 10.1007/s12602-014-9158-2

Hamdy AA, Elattal NA, Amin MA, Ali AE, Mansour NM, Awad GE, Awad HM, Esawy MA. 2017. Possible correlation between levansucrase production and probiotic activity of *Bacillus* sp. isolated from honey and honeybee. World J. Microbiol., Biotechnol., 33(4): 69. doi: 10.1007/s11274-017-2231-8

Hammad AM, Shimamoto T. 2010. Toward a compatible probiotic-antibiotic combination therapy: assessment of antimicrobial resistance in the Japanese probiotics. J. Appl. Microbiol., 109(4): 1349-1360. doi: 10.1111/j.1365-2672.2010.04762.x

Han J, Chen D, Li S, Li X, Zhou WW, Zhang B, Jia Y. 2015. Antibiotic susceptibility of potentially probiotic *Lactobacillus* strains. Italian J. Food Sci., 27(3): 282-289. doi: 10.14674/1120-1770/ijfs.v270

Hanchi H, Mottawea W, Sebei K, Hammami R. 2018. The genus *Enterococcus*: Between probiotic potential and safety concerns—an update. Front. Microbiol., 9: 1791. doi: 10.3389/fmicb.2018.01791

Hoque MZ, Akter F, Hossain KM, Rahman MSM, Billah MM, Islam KMD. 2010. Isolation, identification and analysis of probiotic properties of *Lactobacillus* spp. from selective regional yoghurts. World J. Dairy Food Sci., 5(1): 39-46.

Huddleston JR. 2014. Horizontal gene transfer in the human gastrointestinal tract: potential spread of antibiotic resistance genes. Infect. Drug Resist., 7: 167-176. doi: 10.2147/IDR.S48820

Hummel AS, Hertel C, Holzapfel WH, Franz CM. 2007. Antibiotic resistances of starter and probiotic strains of lactic acid bacteria. Appl. Environ. Microbiol., 73(3): 730-739. doi: 10.1128/AEM.02105-06

Imperial IC, Ibana JA. 2016. Addressing the antibiotic resistance problem with probiotics: reducing the risk of its double-edgedsword effect. Front. Microbiol., 7: 1983. doi: 10.3389/fmicb.2016.01983

Isa K, Oka K, Beauchamp N, Sato M, Wada K, Ohtani K, Nakanishi S, McCartney E, Tanaka M, Shimizu T, Kamiya S, Kruger C, Takahashi M. 2016. Safety assessment of the *Clostridium butyricum* MIYAIRI 588® probiotic strain, including evaluation of antimicrobial sensitivity and presence of *Clostridium* toxin genes in vitro and teratogenicity in vivo. Hum. Exp. Toxicol., 35(8): 818-832. doi: 10.1177/0960327115607372

Jain P, Sharma P. 2012. Probiotics and their efficacy in improving oral health: a review. J. Appl. Pharm. Sci., 2(11): 151-163. doi: 10.7324/JAPS.2012.21128

Jeong DW, Jeong M, Lee JH. 2017. Antibiotic susceptibilities and characteristics of *Bacillus licheniformis* isolates from traditional Korean fermented soybean foods. LWT-Food Sci. Technol., 75: 565-568. doi: 10.1016/j.lwt.2016.10.001

Kechagia M, Basoulis D, Konstantopoulou S, Dimitriadi D, Gyftopoulou K, Skarmoutsou N, Fakiri EM. 2013. Health Benefits of Probiotics: a review. ISRN Nutrition, 2013: 481651. doi: 10.5402/2013/481651

Kim YA, Keogh JB, Clifton PM. 2018. Probiotics, prebiotics, synbiotics and insulin sensitivity. Nutr. Res. Rev., 31(1): 35-51. doi: 10.1017/S095442241700018X

Klare I, Konstabel C, Werner G, Huys G, Vankerckhoven V, Kahlmeter G, Hildebrandt B, Muller-Bertling S, Witte W, Goossens H. 2007. Antimicrobial susceptibilities of *Lactobacillus*, *Pediococcus* and *Lactococcus* human isolates and cultures intended for probiotic or nutritional use. J. Antimicrob. Chemother., 59(5): 900-912. doi: 10.1093/jac/dkm035

Klarin B, Larsson A, Molin G, Jeppsson B. 2019. Susceptibility to antibiotics in isolates of *Lactobacillus plantarum* RAPD-type Lp299v, harvested from antibiotic treated, critically ill patients after administration of probiotics. Microbiology Open, 8(2): e00642. doi: 10.1002/mbo3.642

Krupodorova T, Barshteyn V, Sevindik M. 2022. Antioxidant and antimicrobial potentials of mycelial extracts of *Hohenbuehelia myxotricha* grown in different liquid culture media. BioTechnologia. Journal of Biotechnology Computational Biology and Bionanotechnology, 103(1): 19-28. doi: 10.5114/bta.2022.113912

Koçak Y, Çiftci A. 2020. Tavuk kökenli *Enterococcus faecium* ve *Lactobacillus* türlerinin probiyotik özelliklerinin araştırılması. J. Anatol. Environ. Animal Sci., 5(3): 356-365. doi: 10.35229/jaes.763996

Ku S, Yang S, Lee HH, Choe D, Johnston TV, Ji GE, Park MS. 2020. Biosafety assessment of *Bifidobacterium animalis* subsp. *lactis* AD011 used for human consumption as a probiotic microorganism. Food Control, 117: 106985. doi: 10.1016/j.foodcont.2019.106985

Kumar A, Kumar D. 2015. Characterization of *Lactobacillus* isolated from dairy samples for probiotic properties. Anaerobe, 33: 117-123. doi: 10.1016/j.anaerobe.2015.03.004

Kumari M, Patel HK, Kokkiligadda A, Bhushan B, Tomar SK. 2022. Characterization of probiotic lactobacilli and development of fermented soymilk with improved technological properties. LWT-Food Sci. Technol., 154: 112827. doi: 10.1016/j.lwt.2021.112827

Lee NK, Kim WS, Paik HD. 2019. *Bacillus* strains as human probiotics: characterization, safety, microbiome, and probiotic carrier. Food Sci. Biotechnol., 28(5): 1297–1305. doi: 10.1007/s10068-019-00691-9

Li T, Teng D, Mao R, Hao Y, Wang X, Wang J. 2020. A critical review of antibiotic resistance in probiotic bacteria. Food Res. Int., 136: 109571. doi: 10.1016/j.foodres.2020.109571

Lillo-Pérez S, Guerra-Valle M, Orellana-Palma P, Petzold G. 2021. Probiotics in fruit and vegetable matrices: Opportunities for nondairy consumers. LWT-Food Sci. Technol., 151: 112106. doi: 10.1016/j.lwt.2021.112106

Liu C, Zhang ZY, Dong K, Yuan JP, Guo XK. 2009. Antibiotic resistance of probiotic strains of lactic acid bacteria isolated from marketed foods and drugs. Biomed. Environ. Sci., 22: 401-412. doi: 10.1016/S0895-3988(10)60018-9

Mahmoudi M, Khomeiri M, Saeidi M, Davoodi H. 2021. *Lactobacillus* species from iranian jug cheese: identification and selection of probiotic based on safety and functional properties. Appl. Food Biotechnol., 8(1): 47-56. doi: 10.22037/afb.v8i1.29253

Markowiak P, Śliżewska K. 2017. Effects of Probiotics, Prebiotics and Synbiotics on human health. Nutrients, 9(9): 1021. doi: 10.3390/nu9091021

Mayrhofer S, Mair C, Kneifel W, Domig KJ. 2011. Susceptibility of *Bifidobacteria* of animal origin to selected antimicrobial agents. Chemother. Res. Pract., 2011: 989520. doi: 10.1155/2011/989520

Meral H, Korukluoğlu M. 2014. Laktik Asit Bakterilerinin Antibiyotik Direnç Mekanizmaları. Uludağ Üniv. Ziraat Fak. Derg., 28(2): 71-82.

Misra S, Pandey P, Mishra HH. 2021. Novel approaches for co-encapsulation of probiotic bacteria with bioactive compounds, their health benefits and functional food product development: a review. Trends Food Sci. Technol., 109: 340-351. doi: 10.1016/j.tifs.2021.01.039

Mohkam M, Rasoul-Amini S, Shokri D, Berenjian A, Rahimi F, Sadraeian M, Khalvatı B, Gholami A, Ghasemi Y. 2016. Characterization and in vitro probiotic assessment of potential indigenous *Bacillus* strains isolated from soil rhizosphere. Minerva Biotecnol., 28(1): 19-28.

Mukerji P, Roper JM, Stahl B, Smith AB, Burns F, Rae JC, Yeung N, Lyra A, Svärd L, Saarinen MT, Alhoniemi E, Ibarra A, Ouwehand AC. 2016. Safety evaluation of AB-LIFE(®) (*Lactobacillus plantarum* CECT 7527, 7528 and 7529): antibiotic resistance and 90-day repeated-dosestudy in rats. Food Chem. Toxicol., 92: 117-128. doi: 10.1016/j.fct.2016.03.018

Nami Y,Vaseghi Bakhshayesh R, Mohammadzadeh Jalaly H, Lotfi H, Eslami S, Hejazi MA. 2019. Probiotic properties of *Enterococcus* isolated from artisanal dairy products. Front. Microbiol., 10: 300. doi: 10.3389/fmicb.2019.00300

Nascimento LCS, Casarotti SN, Todorov SD, Penna ALB. 2019. Probiotic potential and safety of enterococci strains. Ann. Microbiol., 69: 241-252. doi: 10.1007/s13213-018-1412-5

Nawaz M, Wang J, Zhou A, Ma C, Wu X, Moore JE, Millar BC, Xu J. 2011. Characterization and transfer of antibiotic resistance in lactic acid bacteria from fermented food products. Curr. Microbiol., 62(3): 1081-1089. doi: 10.1007/s00284-010-9856-2

Neut C, Mahieux S, Dubreuil LJ. 2017. Antibiotic susceptibility of probiotic strains: Is it reasonable to combine probiotics with antibiotics? Méd. Mal. Infect., 47: 477-483. doi: 10.1016/j.medmal.2017.07.001

Nithya V, Halami PM. 2013. Evaluation of the probiotic characteristics of *Bacillus* species isolated from different food sources. Ann. Microbiol., 63(1): 129-137.

Oruc O, Cetin O, Darilmaz DO, Yüsekdag ZN. 2021. Determination of the biosafety of potential probiotic *Enterococcus faecalis* and *Enterococcus faecium* strains isolated from traditional white cheeses. LWT-Food Sci. Technol., 148: 111741. doi: 10.1016/j.lwt.2021.111741

Poloni V, Salvato L, Pereyra C, Oliveira A, Rosa C, Cavaglieri L, Keller KM. 2017. Bakery by-products-based feeds borne-*Saccharomyces cerevisiae* strains with probiotic and antimycotoxin effects plus antibiotic resistance properties for use in animal production. Food Chem. Toxicol., 107: 630-636. doi: 10.1016/j.fct.2017.02.040

Priyadarshana RMA, Daniel CR. 2019. Analysis of antibiotic resistance of the probiotic bacteria found in commercial food products. Vaccin. Res. Open J., 1(1): 90–97. doi: 10.17140/VROJ-4-115

Raeisi SN, Ghoddusi HB, Boll EJ, Farahmand N, Stuer-Lauridsen B, Johansen E, Sutherland JP, Ouoba LII. 2018. Antimicrobial susceptibility of bifidobacteria from probiotic milk products and determination of the genetic basis of tetracycline resistance in *Enterococcus* species after in vitro conjugation with *Bifidobacterium animalis* subsp. *lactis*. Food Control, 94: 205-211. doi: 10.1016/j.foodcont.2018.07.016

Raja BR, Arunachalam KD. 2011. Market potential for probiotic nutritional supplements in India. Afr. J. Bus. Manag., 5(14): 5418-5423. doi: 10.5897/AJBM11.494

Rozman V, Mohar-Lorbeg P, Accetto T, Bogovič Matijašić B. 2020. Characterization of antimicrobial resistance lactobacilli and bifidobacteria used as probiotics or starter cultures based on integration of phenotypic and in silico data. Int. J. Food Microbiol., 314: 108388. doi: 10.1016/j.ijfoodmicro.2019.108388

Sabir F, Beyatli Y, Cokmus C, Onal-Darilmaz D. 2010. Assessment of potential probiotic properties of *Lactobacillus* spp., *Lactococcus* spp., and *Pediococcus* spp. strains isolated from kefir. J. Food Sci., 75(9): M568-M573. doi: 10.1111/j.1750-3841.2010.01855.x

Samanta A, Bera P, Khatun M, Sinha C, Pal P, Lalee A, Mandal A. 2012. An investigation on heavy metal tolerance and antibiotic resistance properties of bacterial strain *Bacillus* sp. isolated from municipal waste. J. Microbiol. Biotech. Res., 2(1): 178-189.

Sanders ME, Akkermans LM, Haller D, Hammerman C, Heimbach J, Hörmannsperger G, Huys G, Levy DD, Lutgendorff F, Mack D, Phothirath P, Solano-Aguilar G, Vaughan E. 2010. Safety assessment of probiotics for human use. Gut Microbes, 1(3): 164-185. doi: 10.4161/gmic.1.3.12127

Saroj DB, Gupta AK. 2020. Genome based safety assessment for *Bacillus coagulans* strain LBSC (DSM 17654) for probiotic application. Int. J. Food Microbiol., 318: 108523. doi: 10.1016/j.ijfoodmicro.2020.108523

Sharma A, Lavania M, Singh R, Lal B. 2021. Identification and probiotic potential of lactic acid bacteria from camel milk. Saudi J. Biol. Sci., 28(3): 1622-1632. doi: 10.1016/j.sjbs.2020.11.062

Sharma P, Tomar SK, Goswami P, Sangwan V, Singh R. 2014. Antibiotic resistance among commercially available probiotics. Food Res. Int., 57: 176-195. doi: 10.1016/j.foodres.2014.01.025

Sharma P, Tomar SK, Sangwan V, Goswami P, Singh R. 2016. Antibiotic resistance of *Lactobacillus* sp. İsolated from commercial probiotic preparations. J. Food Saf., 36(1): 38-51. doi: 10.1111/jfs.12211

Shi Y, Zhai M, Li J, Li B. 2020. Evaluation of safety and probiotic properties of a strain of *Enterococcus faecium* isolated from chicken bile. J. Food Sci. Technol., 57(2): 578-587. doi: 10.1007/s13197-019-04089-7

Singh TP, Kaur G, Malik RK, Schillinger U, Guigas C, Kapila S. 2012. Characterization of intestinal *Lactobacillus reuteri*strains as potential probiotics. Probiotics Antimicrob. Proteins, 4(1): 47-58. doi: 10.1007/s12602-012-9090-2

Sui L, Zhu X, Wu D, Ma T, Tuo Y, Jiang S, Qian F, Mu G. 2020. In vitro assessment of probiotic and functional properties of *Bacillus coagulans* T242. Food Biosci., 36: 100675. doi: 10.1016/j.fbio.2020.100675

Tiwari G, Tiwari R, Pandey S, Pandey P. 2012. Promising future of probiotics for human health: Current scenario. Chron. Young Sci., 3(1): 17-28. doi: 10.4103/2229-5186.94308

Toomey N, Bolton D, Fanning S. 2010. Characterisation and transferability of antibiotic resistance genes from lactic acid bacteria isolated from Irish pork and beef abattoirs. Res. Microbiol., 161(2): 127-135. doi: 10.1016/j.resmic.2009.12.010

Ünal Turhan E, Enginkaya Z. 2016. Probiyotik gıdalardan izole edilen laktik asit bakterilerinin antibiyotik dirençliliklerinin belirlenmesi. PAJES, 22(7): 620-624. doi: 10.5505/pajes.2016.87369

Varankovich NV, Nickerson MT, Korber DR. 2015. Probiotic-based strategies for therapeutic and prophylactic use against multiple gastrointestinal diseases. Front. Microbiol., 6: 685. doi: 10.3389/fmicb.2015.00685

Wang X, Yang Y, Huycke MM. 2020. Risks associated with enterococci as probiotics. Food Res. Int., 129: 108788. doi: 10.1016/j.foodres.2019.108788

Wang Y, Dong J, Wang J, Chi W, Zhou W, Tian Q, Hong Y, Zhou X, Ye H, Tian X, Hu R, Wong A. 2022. Assessing the drug resistance profiles of oral probiotic lozenges. J. Oral Microbiol., 14(1): 2019992. doi: 10.1080/20002297.2021.2019992

Wang Z, Chai W, Burwinkel M, Twardziok S, Wrede P, Palissa C, Esch B, Schmidt MF. 2013. Inhibitory influence of *Enterococcus faecium* on the propagation of swine influenza a virus in vitro. PloS ONE, 8(1): e53043. doi: 10.1371/journal.pone.0053043

Wei YX, Zhang ZY, Liu C, Malakar PK, Guo XK. 2012. Safety assessment of *Bifidobacterium longum* JDM301 based on complete genome sequences. World J. Gastroenterol., 18(5): 479-488. doi: 10.3748/wig. v18.i5.479

WHO, 2014. Antimicrobial resistance: global report on surveillance. ISBN 978 92 4 156474 8. Available form: https://apps.who.int/iris/bitstream/handle/10665/112642/?sequence = 1 [Accessed 21 April 2022]

Wong A, Ngu DY, Dan LA, Ooi A, Lim RL. 2015. Detection of antibiotic resistance in probiotics of dietary supplements. Nutrition J., 14(95): 1-6. doi: 10.1186/s12937-015-0084-2

Xiao JZ, Takahashi S, Odamaki T, Yaeshima T, Iwatsuki K. 2010. Antibiotic susceptibility of bifidobacterial strains distributed in the Japanese market. Biosci. Biotechnol. Biochem, 74(2): 336-342. doi: 10.1271/bbb.90659

Yamaguchi T, Miura Y, Matsumoto T. 2013. Antimicrobial susceptibility of *Enterococcus* strains used in clinical practice as probiotics. J. Infect. Chemother., 19(6): 1109-1115. doi: 10.1007/s10156-013-0633-6

Zago M, Fornasari ME, Carminati D, Burns P, Suàrez V, Vinderola G, Reinheimer J, Giraffa G. 2011. Characterization and probiotic potential of *Lactobacillus plantarum* strains isolated from cheeses. Food Microbiol., 28(5): 1033-1040. doi: 10.1016/j.fm.2011.02.009

Zhang L, Ma H, Kulyar MF, Pan H, Li K, Li A, Mo Q, Wang Y, Dong H, Bao Y, Li J. 2022. Complete genome analysis of *Lactobacillus fermentum* YLF016 and its probiotic characteristics. Microb. Pathog., 162: 105212. doi: 10.1016/j.micpath.2021.105212

Zheng M, Zhang R, Tian X, Zhou X, Pan X, Wong A. 2017. Assessing the risk of probiotic dietary supplements in the context of antibiotic resistance. Front. Microbiol., 8: 908. doi: 10.3389/fmicb.2017.00908

Zheng J, Wittouck S, Salvetti E, Franz MAP, Harris HMB, Mattarelli P, O'Toole PW, Pot B, Peter Vandamme P, Walter J, Koichi Watanabe K, Wuyts S, Felis G, Gänzle MG, Lebeer S. 2020. A taxonomic note on the genus *Lactobacillus*: Description of 23 novel genera, emended description of the genus Lactobacillus Beijerinck 1901, and union of *Lactobacillaceae* and *Leuconostocaceae*. Int. J. Syst. Evol. Microbiol., 70: 2782-2858. doi: 10.1099/ijsem.0.004107

Zommiti M, Cambronel M, Maillot O, Barreau M, Sebei K, Feuilloley M, Ferchichi M, Connil N. 2018. Evaluation of probiotic properties and safety of *Enterococcus faecium* isolated from artisanal Tunisian meat "Dried Ossban". Front. Microbiol., 9: 1685. doi: 10.3389/fmicb.2018.01685