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Friend or foe? A critical evaluation of compositional quality and antibiotic resistance profiles of probiotic dietary supplements in Türkiye

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RESEARCH ARTICLE

Abstract

This study analyzed 10 commercial probiotic dietary supplements for the enumeration and identification of lactobacilli and bifidobacteria, as well as their antibiotic resistance profiles. The isolated strains were identified using molecular methods, and their resistance to 18 antibiotics was assessed using the disc diffusion method. Four of the tested products had a lower number of viable bacteria than stated on the label. A total of 13 presumptive lactobacilli and bifidobacteria strains were identified using molecular methods. The results showed discrepancies between the bacterial species listed on the labels of some products and the actual strains present. All of the *Lactobacillus* strains were resistant to methicillin, cefoxitin, and vancomycin. Furthermore, low levels of resistance to cefazolin, enrofloxacin, ciprofloxacin, norfloxacin, kanamycin, and trimethoprim was observed in *Lactobacillus* spp. All *Bifidobacterium* strains were resistant to methicillin and vancomycin. In addition, *Bifidobacterium* spp. strains that were resistant to cefazolin, cefoxiti, kanamycin, norfloxacin, ampicillin, clindamycin, enrofloxacin, trimethoprim, and ciprofloxacin were determined. Multidrug resistance was found in all *Lactobacillus* and *Bifdobacterium* strains. Finally, MDR rates were found to be 100% in both *Bifidobacterium* and *Lactobacillus* species. The MAR index indicated a high-risk source of contamination for most strains, with 11 out of 13 strains exceeding the threshold of 0.2. These findings emphasize the critical role of precise labeling in fostering consumer trust and enabling informed decision-making. Antibiotic resistance should be regarded a significant part of the safety assessment of probiotics. Novel approaches will be essential for addressing MDR bacteria. MAR index findings highlight the need for stricter quality control in probiotic product labeling and a closer examination of antibiotic resistance in probiotic strains, given their potential implications for health and safety.

Keywords: Label correctness, antibiotic resistance, probiotics dietary supplements, *Bifidobacterium* spp., *Lactobacillus* spp.

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Introduction

Microorganisms are ubiquitous components of the biosphere, colonizing both biotic and abiotic habitats. The human gut, in particular, hosts an incredibly complex ecosystem formed through microbial colonization. These microorganisms are essential for maintaining the host's physiological balance through symbiotic interactions (Requena *et al.*, 2018). The growing understanding of the complex interplay between the microbiome and host health has prompted a renewed interest in manipulating the gut microbiome for therapeutic purposes. This brings the concept of probiotics (Latin for "for life"), an old expression of the modern age, defining the bacterial association that modulates the gut microbiota and promotes health, which is rooted in the early 20th century with the works of Ilya Metchnikoff (Brunser and Gotteland, 2010). Probiotic research encompasses a multifaceted approach, such as (i) the establishment of rigorous selection criteria for probiotic strains (of human origin, able to survive under host gastrointestinal system conditions, have specific health effects when consumed, suitable for industrial scale production, able to survive under storage conditions, etc.), (ii) the isolation of elite probiotic strains (Lactic acid bacteria: *Lactobacillus* spp., *Bifidobacterium* spp., *Streptococcus* spp., *Lactococcus lactis,* and some species of *Enterococcus* spp.) (Argyri *et al.*, 2013), spore-forming species: *Bacillus* spp. (Cutting, 2011), nonpathogen yeast: *Saccharomyces cerevisiae boulardii* (Vohra *et al.*, 2016), and (iii) the elucidation of their potential health benefits at various dosage levels (Requena *et al.*, 2018).

The COVID-19 pandemic has catalyzed more rapid growth in the global probiotic market, which was already expanding (Misra *et al.*, 2021). Previously consumed by individuals seeking to alleviate digestive issues or adopt a healthier lifestyle, probiotics have become a first-line choice for consumers aiming to bolster their immune systems in the wake of the pandemic. Although SARS-CoV-2 is the causative agent of severe acute respiratory syndrome, it has been reported that it can also induce gastrointestinal infections (Nayebi *et al.*, 2022). Oral probiotics have been shown to exhibit antiviral effects and improve gut health to restore homeostasis (Hung *et al.*, 2021), leading to their recommendation as adjunctive therapy for COVID-19 (Xavier-Santos *et al.*, 2022). In this context, while probiotics are generally thought to inhibit microbial adhesion, enhance intestinal barrier function, and strengthen the immune system (Stavropoulou and Bezirtzoglou, 2020), they are also reported to exert specific effects, including modulation of cytokine production by influencing intestinal epithelial cells, increased IgA secretion, activation of phagocytosis, modulation of regulatory T cell function, promotion of dendritic cell maturation, reinforcement of mucosal barriers, and reduction of viral entry (Bottari *et al.*, 2021; Patra *et al.*, 2021). These mechanisms are believed to facilitate viral clearance and prevent bacterial coinfections associated with COVID-19 (Patra *et al.*, 2021). In addition to consumer demands, the probiotic market, restricted to a narrow product range, has experienced significant expansion during the pandemic, driven by the introduction of new product varieties and the growth of e-commerce platforms. In this context, the probiotic market projections indicate a market value of 77.09 billion USD by 2025 (Baral *et al.*, 2021).

Consumers may prefer commercial probiotic dietary supplements over other probiotic forms because of their ease of transportation, consumption, dosage control, and longer shelf life (Zheng *et al.*, 2017). Probiotic dietary supplements, which come in various formats such as capsules, tablets, powders, and liquids, typically contain millions to billions of commercially manufactured probiotic bacteria, often representing a diverse combination of genera and species (Meybodi *et al.*, 2017).

While the ideal dosage of probiotics remains a subject of ongoing research, the recommended daily intake of probiotics ranges from 10^6 to 10^9 CFU/mL or g viable microorganisms. The optimal dosage of probiotics may fluctuate based on the specific strain, the intended health outcomes, the administration duration, the probiotic product type, and the probiotic strain's viability (Aureli *et al.*, 2010; Martinez *et al.*, 2015; Mazzantini *et al.*, 2021). On the other side, the various factors, including exposure to water, oxygen, strong acids, bile, heat, etc., during storage and oral administration, may also influence the viability and dosage levels of probiotics (Russell *et al.*, 2011; Wang *et al.,* 2022a). Given the strain-specific nature of probiotic efficacy and viability, rigorous identification and characterization of candidate probiotic strains is imperative (Soccol *et al.*, 2014).

In 2017, the Council for Responsible Nutrition (CRN) and the International Probiotics Association (IPA) issued guidelines for probiotic labelling build upon the FAO/WHO guidelines (2002) by providing more specific recommendations tailored to the United States regulatory frameworks. Aiming to ensure consumers have access to accurate and informative labelling for probiotic products, both guidelines emphasize the importance of taxonomic identification, recommended serving size, health claims, storage conditions, and manufacturer contact information. CRN/IPA also introduces the concept of "quantitative declaration" (the explicit indication of the viable cell count in colony-forming units) and declaration of the total count of microorganisms for multispecies formulations (Council for Responsible Nutrition and International Probiotics Association, 2017).

For the reasons discussed above, accurate labelling of commercial probiotic products is paramount to

empowering consumers to make informed choices (Korona-Glowniak *et al.*, 2019; Martinez *et al.*, 2015). A consensus among researchers highlights the prevalence of inaccuracies in probiotic product labelling regarding the overestimation of viable cell counts and the misidentification of probiotic strains (Lugli *et al.*, 2019; Mazzantini *et al.*, 2021; Morovic *et al.*, 2016).

The escalating global prevalence of antibiotic resistance has raised concerns. In the concept of probiotics, the precautionary assessment that candidate probiotic bacteria selected for use do not harbor transferable antibiotic resistance genes is strongly emphasized by the FAO/WHO (2001). While probiotic strains of *Lactobacillus* and *Bifidobacterium* are generally regarded as genetically stable, the presence of high concentrations of probiotics in dietary supplements could create potential risks for antibiotic resistance (Zheng *et al.*, 2017). In recent years, emerging evidence suggests that the potential for microorganisms in probiotic dietary supplements may serve as reservoirs for antibiotic resistance genes (Aziz *et al.*, 2022; Gundogdu *et al.*, 2023; Wong *et al.*, 2015). This has raised significant concerns regarding the risk of horizontal gene transfer of antibiotic resistance determinants from probiotics to opportunistic pathogens within the intestinal microbiota (Aziz *et al.*, 2022).

The primary objective of this study was to quantitatively enumerate and identify the *Lactobacillus* and *Bifidobacterium* strains present in commercially available probiotic dietary supplements widely marketed in Türkiye, and to assess previews of their resistance to clinically relevant antibiotics.

Materials and Methods

Sampling

A total of 10 samples were randomly purchased from retailers in Ankara, Türkiye. Seven different brands (A–G) of probiotic dietary supplements, marketed in sachet, capsule, tablet, and drop formulations, were subjected to analysis. Table 1 lists the product brand codes (A–G), sample numbers, types of products, and probiotic culture(s) claimed on the label. The samples, preserved in their original manufacturer-sealed packaging, were transported to the laboratory, maintaining cold chain requirements and aseptic conditions. The supplements were stored at 4°C and examined before expiration.

Microbial reference strains

To ensure the consistency and accuracy of assays, *Lactiplantibacillus plantarum* (formerly *Lactobacillus plantarum*) LMG2003, *Latilactobacillus sakei* (formerly *Lactobacillus sakei*) NCDO2714, *Bifidobacterium longum*, *Staphylococcus aureus* ATCC25923, and *Escherichia coli* LMG3083 (ETEC) were used as reference strains and kindly obtained from the culture collection of Microbiology Laboratory, Department Engineering, Faculty of Food Engineering, Ankara University.

Preparation of diluents

One gram or one milliliter of each probiotic dietary supplement was thoroughly suspended in 99 mL of Mitsuoka Buffer (4.5 g potassium dihydrogen phosphate, 6.0 g disodium hydrogen phosphate, 0.5 g L-cysteine HCl, 0.5 g Tween-80) and subsequently incubated for 30 minutes at 37°C. Serial dilutions were performed up to 10^{-7}, utilizing Mitsuoka Buffer as the diluent medium (Champagne *et al.*, 2011; Vinderola *et al.*, 2019).

Enumeration and isolation of *Lactobacillus* and *Bifidobacterium* species

For isolation of *Lactobacillus* spp., 0.1 mL of each dilution was aseptically inoculated on MRS Agar (de Man Rogosa Sharpe; Merck™, Germany) supplemented with 0.05% sistein and incubated under controlled conditions at 37°C for 72 hours. Post-incubation, the viable cell count was determined by enumerating the colonies on agar plates with a colony range of 30–300, using a Quebec colony counter. The results were expressed as colony-forming units per dose (CFU/dose). Selected five representative colonies were transferred to MRS broth (Merck™, Germany) and incubated at 37°C for 18–24 hours (Todorov *et al.*, 1999).

For isolation of *Bifidobacterium* spp., one milliliter of each dilution was inoculated to the sterile Petri dishes and poured over with melted MRS-NNLP agar supplemented with 100 µg/mL neomycin sulfate, 15 µg/mL nalidixic acid, 3 mg/mL lithium chloride, 200 µg/mL paramomycin sulfate, and 0.5 g/mL L-cysteine HCl. The plates were incubated anaerobically at 37°C for 72 hours using an anaerobic jar (GENbag anaer from bioMérieux). Post-incubation, the viable cell count was determined by enumerating the colonies on agar plates with a colony range of 30–300, using a Quebec colony counter. The results were expressed as colony-forming units per dose (CFU/dose). Selected five representative colonies were transferred to MRS+0.05% sistein broth (Merck™, Germany) and incubated at 37°C for 18–24 hours under anaerobic conditions (Todorov *et al.*, 1999). For each microbial group, the experiments were repeated in triplicate.

Following microscopic examination to elucidate their morphological characteristics, presumptive *Lactobacillus* spp. and *Bifidobacterium* spp. isolates were stored at –20°C using MRS broth and MRS+0.05% sistein broth, respectively. Both media contained 40% (*v/v*) glycerol (Merck™, Germany) for cryoprotection.

Phenotypic and molecular identification of isolates

The identification of isolates employed a multifaceted approach, encompassing both phenotypic and genotypic characterization. Phenotypic characterization of *Lactobacillus* and *Bifidobacterium* isolates involved a preliminary evaluation, including assessment of cellular morphology, Gram staining reaction, and catalase activity, as described by Temiz (1999). Gram-positive, catalase-negative, rod-shaped isolates obtained from MRS agar supplemented with 0.05% cysteine were tentatively identified as members of the genus *Lactobacillus*. Gram-positive, catalase-negative isolates exhibiting a bifurcated morphology reminiscent of branching were tentatively classified as members of the genus *Bifidobacterium* from MRS-NNLP agar. The molecular identification of the strains was achieved by 16S rRNA gene sequencing, following the protocol detailed below.

Genomic DNA was extracted from the isolates using the Cell CV mini kit (Gene All, Catalog No: 106-101), and DNA concentration and purity were evaluated spectrophotometrically using a NanoDrop ND-2000 spectrophotometer (Thermo Fischer Scientific, Waltham, MA, USA). The resulting DNA samples were stored at –20°C. Amplification of the 16S rRNA gene region was conducted using polymerase chain reaction (PCR). The 2×PCR Master Mix (WizPure, Catalog No: 1401) was employed with an Applied Biosystems™ Pro Flex Thermal Cycler. Universal primers 27F (5'-AGAGTTTGATCMTGGCTCAG-3') and 1492R (5'-CCGTCAATTCCTTTRAGTTT-3') were amplified. Each 20 µL PCR reaction comprised 10 µL of 2×PCR Master Mix, 0.5 µL each of forward and reverse primers (100 pmol each), 2 µL of genomic DNA (100 ng/µL), and nuclease-free water to final volume. The PCR amplification protocol consisted of 35 cycles, each comprising the following steps: (i) the initial denaturation step at 95°C for 5 minutes to denature the double-stranded DNA template fully, (ii) the denaturation step at 95°C for 30 seconds to ensure complete denaturation of the template DNA, (iii) the annealing step at 52°C for 30 seconds to facilitate specific primer annealing to the target 16S rRNA gene region, (iv) the extension step at 72°C for 30 seconds to allow Taq polymerase to extend the annealed primers and amplify the target DNA, and (v) the final extension step at 72°C for 5 minutes to ensure complete extension of all amplicons. DNA fragments were electrophoresed in 1% (*w/v*) agarose gels to verify successful amplification. The O'Gene RulerTM 1000-bp DNA ladder (Fermentas, Finland) served as a size marker. To evaluate the integrity of the amplified DNA fragments, ethidium bromide staining (0.2 µg/mL) was followed by visualization under ultraviolet (UV) illumination using a Kodak Gel Logic 200 Imaging System (Kodak, USA). Subsequent purification using ExoSAP-IT Express PCR Cleanup Reagents (Thermo Fisher Scientific, Catalog No: 75001.200.UL) eliminated residual primers and unincorporated dNTPs, the purified DNA to be submitted for sequencing at Atlas Biotechnology (Ankara, Türkiye). To elucidate the taxonomic identity of the isolates, the generated 16S rRNA gene sequences were subjected to a comparative analysis against the National Center for Biotechnology Information (NCBI) 16S rRNA sequence database utilizing the Basic Local Alignment Search Tool (BLAST) program. *L. plantarum* LMG2003 and *B. longum* were employed as control strains to validate the accuracy of the identification process.

Assessment of antibiotic resistance testing

Antibiotic resistance of *Lactobacillus* and *Bifidobacterium* strains was conducted using the Kirby–Bauer disk diffusion method on Mueller–Hinton agar (Merck, Germany), as described by Bauer *et al.* (1966). Commercially available antibiotic discs (Oxoid, UK) were employed to assess resistance to a diverse panel of 18 commonly prescribed antibiotics, and the tests were performed in duplicate. The antibiotics employed in the study encompassed the following classes: (i) Beta-lactams: Ampicillin (10 µg/disc), methicillin (5 µg/disc), penicillin G (10 µg/disc), cefazolin (30 µg/disc), cefoxitin (30 µg/disc), (ii) Glycopeptides: Vancomycin (30 µg/disc), (iii) Aminoglycosides: Gentamicin (10 µg/disc), kanamycin (30 µg/disc), streptomycin (10 µg/disc), (iv) Phenicols: Chloramphenicol (30 µg/disc), (v) Lincosamides: Clindamycin (2 µg/disc), (vi) Macrolides: Erythromycin (15 µg/disc), (vii) Tetracyclines: Tetracycline (30 µg/disc), (viii) Fluoroquinolones: Enrofloxacin (5 µg/disc), Ciprofloxacin (5 µg/disc), Norfloxacin (10 µg/disc), (ix) Rifamycins: Rifampin (5 µg/disc), and (x) Trimethoprim: Trimethoprim (5 µg/disc). The plates with antibiotic discs were incubated at room temperature for at least 20 minutes prior to incubation at 37°C for 24–48 hours. Following incubation, the diameters of the inhibition zones were measured, and isolates were categorized as susceptible, intermediate, or resistant based on the criteria established by the Clinical Laboratory Standards Institute (CLSI, 2016) and Charteris *et al.* (1998). *L. plantarum* LMG2003, *L. sakei* NCDO2714, *B. longum*, *S. aureus* ATCC 25923, and *E. coli* LMG3083 (ETEC) were included in the testing as quality control strains.

Isolates exhibiting resistance to three or more antibiotic classes were considered multidrug-resistant (MDR). The MAR index was also calculated using the formula described by Krumperman (1983): MAR index = number of antibiotics to which an isolate is resistant/total number of antibiotics tested.

Statistical analysis

Statistical analyses were conducted using SPSS version 26. Analysis of variance (ANOVA) was employed to evaluate differences between antibiotic groups. A p-value less than 0.05 was considered statistically significant.

Results

Enumeration and identification of *Lactobacillus* and *Bifidobacterium* species

A total of 10 probiotic food supplements including four sachets, three capsules, two tablets, and one drop are reported in Table 1 in terms of enumeration and identification of the contained lactobacilli and bifidobacteria. The agents and their labeled per dose composition were as follows: **A1**, *Lactobacillus acidophilus, Lactobacillus rhamnosus* (new name *Lacticaseibacillus rhamnasus*), *Lactobacillus casei* (new name *Lacticaseibacillus casei*), *Bifidobacterium bifidum*, 5×10^9 CFU/dose; **B2**, *Streptococcus thermophilus, B.bifidum, Bifidobacterium infantis, B. longum, Lactobacillus helveticus, L. acidophilus, Lactobacillus bulgaricus* (new name *Lactobacillus delbrueckii subsp. bulgaricus)* (800 mg); **C3**, *L. plantarum* 299v, 10^{10} CFU/dose; **C4**, *L. plantarum* HEAL9, *Lactobacillus paracasei* (new name *Lacticaseibacillus paracasei*) n8700:2, 10^9 CFU/dose; **D5**, *L. acidophilus* L1, *L. rhamnosus* liobif, *B. longum* LBL-01, *Saccharomyces boulardii,* 10×10^9 CFU/dose; **E6**, *S. thermophilus, L. plantarum, B. longum, Bifidobacterium breve,* 2.3×10^9 CFU/dose; **E7**, *B. infantis, B.breve, B. longum, B. bifidum,* 5×10^8 CFU/dose; **E8**, *Enterococcus faecium, L. acidophilus, L. rhamnosus, B. longum, B. bifidum,* 2.5×10^9; **F9**, *Bifidobacterium animalis* spp. *lactis* B94, 5×10^9 CFU/dose; **G10**, *L. acidophilus* La-14, *L. helveticus*, *L. rhamnasus* Lr-32, *B. longum* BI-05, *B. infantis* Bi-26, *Bifidobacterium lactis* BI-04, *Bacillus subtilis*, *B.bifidum* Bb-06, *L. plantarum* Lp-115, *L. bulgaricus* Lb-87, *Lactobacillus reuteri* (new name *Limosilactobacillus reuteri*) 1E1, *L. paracasei* Lpc-37, *Lactobacillus brevis* Lbr-35, *S. thermophilus* St-21, 10×10^9 CFU/dose. According to the label, 2 of 10 products contained monoculture bifidobacteria (E7, F9), 2 products contained monoculture lactobacilli (C3, C4), and 6 of them included mixed cultures.

The labeled number of cells and the counts (CFU) obtained for a unit dose (one capsule, one sachet, one tablet, or six drops) of each product can also seen in Table 1. Bacterial enumeration revealed that A1, E6, E7, and F9 have a lower content of viable cells than claimed. C3, C4, D5, E8, and G10 products were in agreement with their labels in the aspect of viable amount of bacteria. B2 packaging claimed a weight rather (800 mg) than a unit concentration and was found to have 6×10^7 CFU/dose *Lactobacillus* spp., 1.2×10^7 CFU/dose *Bifidobacterium* spp. None of the products that claimed to contain monocultures *Bifidobacterium* (E7, F9) were detected in bifidobacteria, but all products that claimed to contain monocultures *Lactobacillus* (C3, C4) contained the claimed culture concentration.

Thirteen presumptive lactobacilli or bifidobacteria strains were purely isolated and were phenotypically characterized. All the isolates were found to be Gram positive and catalase negative. Next, eight lactobacilli isolates and five bifidobacteria isolates were identified at the species level (Table 2). A1 and D5 evaluated were incompatible with the bacterial species claimed on the label. A1 product contained *Lacticaseibacillus paracasei* subsp. *tolerans* rather than *L. acidophilus*, *L. rhamnasus,* or *L. casei* mentioned on the label; similarly, the D5 contained *B. infantis* instead of *B. longum* stated on the label.

Lactiplantibacillus plantarum and *Lacticaseibacillus rhamnosus* were formerly known as *Lactobacillus plantarum* and *Lactobacillus rhamnosus*, respectively (Echegaray *et al.*, 2022; Mathipa-Mdakane and Thantsha, 2022; Zheng *et al.*, 2020). Table 2 shows that up-to-date names are not reflected in C3, C4, D5, E6, E8, and G10 products' label information.

Antibiotic resistance

The antibiotic resistance of eight *Lactobacillus* and five *Bifidobacterium* probiotic strains from probiotic food supplements were analyzed by the disc diffusion method and were classified as either resistant (R), intermediate (I), or susceptible (S) based on the inhibition zone measured. A summary of the antibiotic resistance of *Lactobacillus* and *Bifidobacterium* isolates were reported in Table 3 and Table 4, respectively.

According to our results, all of the *Lactobacillus* strains were resistant to methicillin, cefoxitin, and vancomycin. Furthermore, resistance to cefazolin (37.5%), enrofloxacin (25%), ciprofloxacin (50%), norfloxacin (50%), kanamycin (37.5%), and trimethoprim (37.5%) was also observed, although at slightly lower levels. In contrast, none of the lactobacilli strains were resistant to ampicillin, chloramphenicol, clindamycin, erythromycin,

Table 1. Declared and actual counts of viable bacteria in commercially available probiotic dietary supplements.

Product brand code	Sample No.	Preparation form	Declared total count (CFU/Dose)	Labelled probiotic culture(s)	Viable microbial species (CFU/dose)	
					0.05% cysteine-MRS agar	MRS-NNLP agar
A	1	Sachet	5×10^9	*Lactobacillus acidophilus* *Lactobacillus rhamnosus* *Lactobacillus casei* *Bifidobacterium bifidum*	$8.4\times10^6\pm1.89$	$2.73\times10^5\pm2.09$
B	2	Sachet	NS[a]	*Streptococcus thermophilus* *Bifidobacterium bifidum* *Bifidobacterium infantis* *Bifidobacterium longum* *Lactobacillus helveticus* *Lactobacillus acidophilus* *Lactobacillus bulgaricus*	$6\times10^7\pm2.52$	$1,2\times10^7\pm1.99$
C	3	Capsules	10^{10}	*Lactobacillus plantarum* 299v	$5\times10^{10}\pm2.22$	–
	4	Tablets	10^9	*Lactobacillus plantarum* HEAL9 *Lactobacillus paracasei* 8700:2	$3.9\times10^9\pm2.11$	–
D	5	Capsules	10×10^9	*Lactobacillus acidophilus* L1 *Lactobacillus rhamnosus* liobif *Bifidobacterium longum* LBL-01 *Saccharomyces boulardii*	$4.5\times10^9\pm1.68$	$3.25\times10^9\pm2.52$
E	6	Tablets	$2,3\times10^9$	*Streptococcus thermophilus* *Lactobacillus plantarum* *Bifidobacterium longum* *Bifidobacterium breve*	$4.45\times10^8\pm2.18$	$2.9\times10^8\pm1.02$
	7	Drops	5×10^8	*Bifidobacterium infantis* *Bifidobacterium breve* *Bifidobacterium longum* *Bifidobacterium bifidum*	–	ND
	8	Sachet	$2,5\times10^9$	*Enterococcus faecium* *Lactobacillus acidophilus* *Lactobacillus rhamnosus* *Bifidobacterium longum* *Bifidobacterium bifidum*	$1.8\times10^9\pm2.33$	$4\times10^7\pm1.16$
F	9	Sachet	5×10^9	*Bifidobacterium animalis* spp. *lactis* B94	–	ND
G	10	Capsules	10×10^9	*Lactobacillus acidophilus* La-14 *Lactobacillus helveticus* *Lactobacillus rhamnasus* Lr-32 *Bifidobacterium longum* BI-05 *Bifidobacterium infantis* Bi-26 *Bifidobacterium lactis* BI-04 *Bacillus subtilis* *Bifidobacterium bifidum* Bb-06 *Lactobacillus plantarum* Lp-115 *Lactobacillus bulgaricus* Lb-87 *Lactobacillus reuteri* 1E1 *Lactobacillus paracasei* Lpc-37 *Lactobacillus brevis* Lbr-35 *Streptococcus thermophilus* St-21	$3.5\times10^9\pm1.51$	$1.85\times10^8\pm1.96$

ND: Not Determined; NS[a]: Not Stated.

Table 2. Comparison of label claims with identification of probiotic microorganisms isolated from probiotic dietary supplements by sequence analysis of the 16S rRNA gene.

Isolate codes	Species identification based on sequence of 16S rRNA gene	Claimed probiotic culture on the label
A1 Lb	*Lacticaseibacillus paracasei* subsp. *tolerans*	*Lactobacillus acidophilus* *Lactobacillus rhamnasus* *Lactobacillus casei*
A1 Bf	*Bifidobacterium bifidum*	*Bifidobacterium bifidum*
B2 Lb	*Lactobacillus acidophilus*	*Lactobacillus acidophilus* *Lactobacillus helveticus* *Lactobacillus bulgaricus*
B2 Bf	*Bifidobacterium longum*	*Bifidobacterium bifidum* *Bifidobacterium infantis* *Bifidobacterium longum*
C3 Lb	*Lactiplantibacillus plantarum*	*Lactobacillus plantarum* 299v
C4 Lb	*Lactiplantibacillus plantarum*	*Lactobacillus plantarum* HEAL9 *Lactobacillus paracasei* 8700:2
D5 Lb	*Lacticaseibacillus rhamnosus*	*Lactobacillus acidophilus* L1 *Lactobacillus rhamnasus* liobif
D5 Bf	*Bifidobacterium infantis*	*Bifidobacterium longum* LBL-01
E6 Lb	*Lactiplantibacillus plantarum*	*Lactobacillus plantarum*
E6 Bf	*Bifidobacterium breve*	*Bifidobacterium longum* *Bifidobacterium breve*
E8 Lb	*Lacticaseibacillus rhamnosus*	*Lactobacillus acidophilus* *Lactobacillus rhamnasus*
G10 Lb	*Lactiplantibacillus plantarum*	*Lactobacillus acidophilus* La-14 *Lactobacillus helveticus* *Lactobacillus rhamnasus* Lr-32 *Lactobacillus plantarum* Lp-115 *Lactobacillus bulgaricus* Lb-87 *Lactobacillus reuteri* 1E1 *Lactobacillus paracasei* Lpc-37 *Lactobacillus brevis* Lbr-35
G10 Bf	*Bifidobacterium lactis*	*Bifidobacterium longum* BI-05 *Bifidobacterium infantis* Bi-26 *Bifidobacterium lactis* BI-04 *Bifidobacterium bifidum* Bb-06

gentamicin, penicillin G, rifampin, streptomycin, and tetracycline. *L. paracasei* subsp. *tolerans* strain was found to be resistant to cefoxitin, methicillin, and vancomycin, while being susceptible to ampicillin, cefazolin, chloramphenicol, ciprofloxacin, clindamycin, enrofloxacin, erythromycin, gentamicin, penicillin G, streptomycin, rifampin, tetracycline, and trimethoprim. *L. acidophilus* strain was resistant to cefoxitin, methicillin, trimethoprim, and vancomycin, while susceptible to ampicillin, cefazolin, chloramphenicol, ciprofloxacin, clindamycin, erythromycin, gentamicin, penicillin G, rifampin, streptomycin, and tetracycline. All *L. plantarum* strains were resistant to vancomycin, methicillin, cefoxitin, ciprofloxacin, and norfloxacin. Furthermore, the resistance to cefazolin (50%), enrofloxacin (50%), kanamycin (50%), and trimethoprim (25%) were also observed. However, none of the strains were found to be resistant to ampicillin, chloramphenicol, clindamycin, erythromycin, gentamicin, rifampin, penicillin G, tetracycline, and streptomycin. All *L. rhamnosus* strains were resistant to vancomycin, methicillin, and cefoxitin. In addition, the resistance to cefazolin (50%), kanamycin (50%), and trimethoprim (50%) were detected. Contrarily, none of the strains was found to be resistant to ampicillin, chloramphenicol, ciprofloxacin, clindamycin, enrofloxacin, erythromycin, gentamicin, norfloxacin, rifampin, penicillin G, tetracycline, and streptomycin.

All *Bifidobacterium* strains were resistant to methicillin and vancomycin. Frequent resistance was seen against cefazolin (80%), cefoxitin (80%), kanamycin (60%), and norfloxacin (60%). Furthermore, resistance to ampicillin (40%), clindamycin (20%), enrofloxacin (40%), trimethoprim (20%), and ciprofloxacin (20%) was also observed. None of the *Bifidobacterium* strains were found to be resistant against chloramphenicol, erythromycin, gentamicin, penicillin G, rifampin, streptomycin, and tetracycline.

Table 3. Antibiotic resistance profiles of *Lactobacillus* spp. to 18 antibiotics.

	Groups		Beta lactam			Cephalosporin		Phenicol	Fluoroquinolone			Lincosamide	Macrolide	Aminoglycoside			Rifamycin	Tetracycline	Trimethoprim	Glycopeptide
	Antibiotic		Ampicillin	Methicillin	Penicillin G	Cefazolin	Cefoxitin	Chloramphenicol	Enrofloxacin	Ciprofloxacin	Norfloxacin	Clindamycin	Erythromycin	Gentamicin	Kanamycin	Streptomycin	Rifampin	Tetracyline	Trimethoprim	Vancomycin
Lacticaseibacillus paracasei subsp. *tolerans* (n: 1)	R	n	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1
		%	0	100	0	0	100	0	0	0	0	0	0	0	0	0	0	0	0	100
	I	n	0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0	0
		%	0	0	0	0	0	0	0	0	100	0	0	0	100	0	0	0	0	0
	S	n	1	0	1	1	0	1	1	1	0	1	1	1	0	1	1	1	1	0
		%	100	0	100	100	0	100	100	100	0	100	100	100	0	100	100	100	100	0
Lactobacillus acidophilus (n: 1)	R	n	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	1
		%	0	100	0	0	100	0	0	0	0	0	0	0	0	0	0	0	100	100
	I	n	0	0	0	0	0	0	1	0	1	0	0	0	1	0	0	0	0	0
		%	0	0	0	0	0	0	100	0	100	0	0	0	100	0	0	0	0	0
	S	n	1	0	1	1	0	1	0	1	0	1	1	1	0	1	1	1	0	0
		%	100	0	100	100	0	100	0	100	0	100	100	100	0	100	100	100	0	0
Lactiplantibacillus plantarum (n: 4)	R	n	0	4	0	2	4	0	2	4	4	0	0	0	2	0	0	0	1	4
		%	0	100	0	50	100	0	50	100	100	0	0	0	50	0	0	0	25	100
	I	n	0	0	2	1	0	0	1	0	0	0	0	0	2	3	0	2	0	0
		%	0	0	50	25	0	0	25	0	0	0	0	0	50	75	0	50	0	0
	S	n	4	0	2	1	0	4	1	0	0	4	4	4	0	1	4	2	3	0
		%	100	0	50	25	0	100	25	0	0	100	100	100	0	25	100	50	75	0
Lacticaseibacillus rhamnosus (n: 2)	R	n	0	2	0	1	2	0	0	0	0	0	0	0	1	0	0	0	1	2
		%	0	100	0	50	100	0	0	0	0	0	0	0	50	0	0	0	50	100
	I	n	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
		%	50	0	0	0	0	0	0	0	0	0	0	0	50	0	0	0	0	0
	S	n	1	0	2	1	0	2	2	2	2	2	2	2	0	2	2	2	1	0
		%	50	0	100	50	0	100	100	100	100	100	100	100	0	100	100	100	50	0
Total (n: 8)	R	n	0	8	0	3	8	0	2	4	4	0	0	0	3	0	0	0	3	8
		%	0	100	0	37.5	100	0	25	50	50	0	0	0	37.5	0	0	0	37.5	100
	I	n	1	0	2	1	0	0	2	0	2	0	0	0	5	3	0	2	0	0
		%	12.5	0	25	12.5	0	0	25	0	25	0	0	0	62.5	37.5	0	25	0	0
	S	n	7	0	6	4	0	8	4	4	2	8	8	8	0	5	8	6	5	0
		%	87.5	0	75	50	0	100	50	50	25	100	100	100	0	62.5	100	75	62.5	0

The diameters of the zones were compared with the diameters of the European Committee on Antimicrobial Susceptibility Testing (EUCAST 2021), Clinical Laboratory Standards Institute (CLSI 2016), and Charteris *et al.* (1998).
S:Susceptible, I:Intermediate resistant, R:Resistant.

Table 4. Antibiotic resistance profiles of *Bifidobacterium* spp. to 18 antibiotics.

	Groups		Beta lactam			Cephalosporin		Phenicol	Fluoroquinolone			Lincosamide	Macrolide	Aminoglycoside			Rifamycin	Tetracycline	Trimethoprim	Glycopeptide
	Antibiotic		Ampicillin	Methicillin	Penicillin G	Cefazolin	Cefoxitin	Chloramphenicol	Enrofloxacin	Ciprofloxacin	Norfloxacin	Clindamycin	Erythromycin	Gentamicin	Kanamycin	Streptomycin	Rifampin	Tetracyline	Trimethoprim	Vancomycin
Bifidobacterium bifidum (n: 1)	R	n	1	1	0	1	1	0	1	0	1	1	0	0	0	0	0	0	0	1
		%	100	100	0	100	100	0	100	0	100	100	0	0	0	0	0	0	0	100
	I	n	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		%	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	S	n	0	0	1	0	0	1	0	1	0	0	1	1	1	1	1	1	1	0
		%	0	0	100	0	0	100	0	100	0	0	100	100	100	100	100	100	100	0
Bifidobacterium longum (n: 1)	R	n	0	1	0	1	1	0	0	0	0	0	0	0	1	0	0	0	1	1
		%	0	100	0	100	100	0	0	0	0	0	0	0	100	0	0	0	100	100
	I	n	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		%	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	S	n	1	0	1	0	0	1	1	1	1	1	1	1	0	1	1	1	0	0
		%	100	0	100	0	0	100	100	100	100	100	100	100	0	100	100	100	0	0
Bifidobacterium infantis (n: 1)	R	n	1	1	0	1	1	0	0	0	0	0	0	0	1	0	0	0	0	1
		%	100	100	0	100	100	0	0	0	0	0	0	0	100	0	0	0	0	100
	I	n	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		%	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	S	n	0	0	1	0	0	1	1	1	1	1	1	1	0	1	1	1	1	0
		%	0	0	100	0	0	100	100	100	100	100	100	100	0	100	100	100	100	0
Bifidobacterium breve (n: 1)	R	n	0	1	0	1	1	0	1	1	1	0	0	0	1	0	0	0	0	1
		%	0	100	0	100	100	0	100	100	100	0	0	0	100	0	0	0	0	100
	I	n	0	0	1	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0
		%	0	0	100	0	0	0	0	0	0	100	0	0	0	100	0	0	0	0
	S	n	1	0	0	0	0	1	0	0	0	0	1	1	0	0	1	1	1	0
		%	100	0	0	0	0	100	0	0	0	0	100	100	0	0	100	100	100	0
Bifidobacterium lactis (n: 1)	R	n	0	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1
		%	0	100	0	0	0	0	0	0	100	0	0	0	0	0	0	0	0	100
	I	n	0	0	0	0	1	0	1	1	0	0	0	0	0	0	0	0	1	0
		%	0	0	0	0	100	0	100	100	0	0	0	0	0	0	0	0	100	0
	S	n	1	0	1	1	0	1	0	0	0	1	1	1	1	1	1	1	0	0
		%	100	0	100	100	0	100	0	0	0	100	100	100	100	100	100	100	0	0
Total (n: 5)		n	2	5	0	4	4	0	2	1	3	1	0	0	3	0	0	0	1	5
	R	%	40	100	0	80	80	0	40	20	60	20	0	0	60	0	0	0	20	100
		n	0	0	1	0	1	0	1	1	0	1	0	0	0	1	0	0	1	0
	I	%	0	0	20	0	20	0	20	20	0	20	0	0	0	20	0	0	20	0
		n	3	0	4	1	0	5	2	3	2	3	5	5	2	4	5	5	3	0
	S	%	60	0	80	20	0	100	40	60	40	60	100	100	40	80	100	100	60	0

The diameters of the zones were compared with the diameters of the European Committee on Antimicrobial Susceptibility Testing (EUCAST 2021), Clinical Laboratory Standards Institute (CLSI 2016), and Charteris *et al.* (1998).
S:Susceptible, I:Intermediate resistant, R:Resistant.

Table 5. Comprehensive overview of the MAR index and MDR of strains.

Strains	Antibiotic Resistance[a]	MAR[b] Index	Resistance (%)[c]				
			Resistance to 3 Antibiotics	Resistance to 4 Antibiotics	Resistance to 5 Antibiotics	Resistance to ≥6 Antibiotics	Total
Lacticaseibacillus paracasei subsp. *tolerans* A1	3	0.16	3	—[d]	—[d]	—[d]	**1 (12.5%)**
Lactobacillus acidophilus B2	4	0.22	—[d]	4	—[d]	—[d]	**2 (25.0%)**
Lacticaseibacillus rhamnosus D5	4	0.22	—[d]	4	—[d]	—[d]	
Lacticaseibacillus rhamnosus E8	5	0.27	—[d]	—[d]	5	—[d]	**1 (12.5%)**
Lactiplantibacillus plantarum C3	6	0.33	—[d]	—[d]	—[d]	6	**4 (50.0%)**
Lactiplantibacillus plantarum C4	7	0.38	—[d]	—[d]	—[d]	7	
Lactiplantibacillus plantarum E6	7	0.38	—[d]	—[d]	—[d]	7	
Lactiplantibacillus plantarum G10	7	0.38	—[d]	—[d]	—[d]	7	
***Lactobacillus* spp. (n:8)**			**1 (12.5 %)**	**2 (25.0 %)**	**1 (12.5 %)**	**4 (50.0 %)**	**8 (100.0%)**
Bifidobacterium bifidum A1	8	0.44	—[d]	—[d]	—[d]	8	**4 (80.0%)**
Bifidobacterium longum B2	6	0.33	—[d]	—[d]	—[d]	6	
Bifidobacterium infantis D5	6	0.33	—[d]	—[d]	—[d]	6	
Bifidobacterium breve E6	8	0.44	—[d]	—[d]	—[d]	8	
Bifidobacterium lactis G10	3	0.16	3	—[d]	—[d]	—[d]	**1 (20.0%)**
***Bifidobacterium* spp. (n:5)**			**1 (20.0 %)**	—[d]	—[d]	**4 (80.0 %)**	**5 (100.0%)**

[a] Antibiotic resistance spectrum of isolates. [b]MAR: Multiple antibiotic resistance index. [c]Percentage resistance was determined by dividing the number of resistant isolates by the total number of isolates per genus. [d]No isolates were resistant.

B. bifidum strain was resistant to ampicillin, cefazolin, cefoxitin, clindamycin enrofloxacin, methicillin, norfloxacin, and vancomycin. *B. longum* strain was resistant to cefazolin, cefoxitin, kanamycin, methicillin, trimethoprim, and vancomycin. *B. infantis* strain was resistant to ampicillin, cefazolin, cefoxitin, kanamycin, methicillin, and vancomycin. *B. breve* strain was resistant to cefazolin, cefoxitin, ciprofloxacin, enrofloxacin, kanamycin, methicillin, norfloxacin, and vancomycin. *B. lactis* was resistant to methicillin, norfloxacin, and vancomycin.

The MDR defined as the resistance to three or more antimicrobial agents was found in all *Lactobacillus* and *Bifdobacterium* strains. *L. paracasei* subsp. *tolerans* strain was resistant to three antibiotics, one *L. acidophilus* and one *L. rhamnosus* strains were resistant to four antibiotics, one *L. rhamnosus* strain was resistant to five antibiotics, one *L. plantarum* strain was resistant to six antibiotics, and three *L. plantarum* strains were resistant to seven antibiotics. When the antibiotic resistance levels of the lactobacilli species were compared, *L. plantarum* strains showed a more resistant phenotype than other lactobacilli strains. Moreover, *B.lactis* strain was resistant to three antibiotics, *B. infantis* and *B. longum* strains were resistant to six antibiotics, and *B. breve* and *B. bifidum* strains were resistant to eight antibiotics. The majority of bifidobacteria isolates were resistant to six antibiotics and eight antimicrobials. In this study, MDR rates were found to be 100% in *Bifidobacterium* spp. and 100% in *Lactobacillus* spp. (Table 5). The data of the resistance in *Bifidobacterium* spp. and *Lactobacillus* spp. strains against antibiotics were statistically significant ($p<0.001$). The MAR index of the present study was notably unique for each isolate (Table 5). While 11 strains tested in the present study showed a MAR index of higher than 0.2, indicating a high-risk source of contamination, 2 strains showed a MAR index of lower than 0.2.

Discussion

Given the global surge in probiotic consumption, it is imperative to ensure that probiotic products are accurately labelled and contain well-documented strains, considering both safety and efficacy. The efficacy of probiotics often depends on strain-specific characteristics and the viability of the microorganisms upon reaching the gut (Korona-Glowniak *et al.*, 2019; Temmerman *et al.*, 2003). Manufacturers should adhere to rigorous labelling standards, identifying the genus, species, and strain of microorganisms in commercial probiotic formulations. Moreover, the labelled quantity of viable microorganisms should be guaranteed throughout the product's shelf life under the specified storage conditions (FAO/WHO, 2002; Council for Responsible Nutrition and International Probiotics Association, 2017).

A significant discrepancy was observed between the labelled content and the actual microbial composition of five out of the ten probiotic products examined in this study. Our results corroborate previous studies by Aureli *et al.* (2010), Lugli *et al.* (2019), Kesavelu *et al.* (2020), and Syromyatnikov *et al.* (2022), which have reported inconsistencies between the labeled claims and the actual microbial content of probiotic products, including variations in the number, purity, type, and viability of microorganisms.

Our study's findings align with those of cross-national investigations, which, as summarized below, have demonstrated discrepancies between the declared and actual microbial composition of commercial probiotic dietary supplements from various geographical regions. The study conducted by Temmerman *et al.* (2003) on 55 European probiotic products revealed that food supplements generally exhibited lower viable bacterial counts compared to dairy-based products. While a study by Drago *et al.* (2010) found that four out of thirteen probiotic supplements in the United States met their label claims, a subsequent study by Morovic *et al.* (2016) revealed that 33% of samples contained fewer viable bacteria than labelled or were mislabelled. A survey of probiotic dietary supplements in the United Kingdom conducted by Fredua-Agyeman *et al.* (2016) revealed that only three out of seven (43%) products contained the claimed concentration of probiotic bacteria. In addition, none of the multispecies products contained all of the labelled probiotic strains. Studies conducted in Bulgaria and China have demonstrated significant discrepancies between probiotic dietary supplements' labels and actual microbial content. Respectively, Marinova *et al.* (2019) found that only 10 out of a certain number of products contained the claimed 10^8 to 10^{10} CFU/g of probiotic bacteria, and none of the commercial products contained all labelled LAB species. In addition, some products were found to contain unacceptable microorganisms. Similarly, Ullah *et al.* (2019) reported that 29.41% of the capsule and sachet-based probiotic products in their study contained inaccurate or lower CFU counts, while 23.52% did not comply with the labelled microbial composition. Recent research by Anisimova *et al.* (2022) revealed inconsistencies between certain labelled probiotic products and the actual microbial composition. Some samples were labelled as multispecies formulations but were found to contain only a single species of lactobacilli. In addition, other samples contained species that differed from those claimed by the manufacturers. Similarly, a study conducted by Gundogdu *et al.* (2023) on probiotic products in Türkiye found discrepancies between the label and actual content in 17 examined products. These findings align with our results, highlighting the prevalence of mislabelling and misidentification of probiotic strains in the market.

Our findings align with previous studies by Chen *et al.* (2014) and Lewis *et al.* (2016), which demonstrated that *Bifidobacterium* species were either absent or present in low numbers in products labeled as containing these bacteria. Similarly, Aureli *et al.* (2010) reported the frequent mislabeling of probiotic products, with *B. bifidum* often claimed but rarely detected, and when detected, found to be nonviable.

Suboptimal processing techniques can compromise the viability of microorganisms, while inadequate packaging, storage, and transportation conditions can further reduce bacterial survival. Consequently, careful consideration must be given to selecting strains that are robust to manufacturing processes or optimize manufacturing processes to accommodate sensitive strains. Bifidobacterial species, in particular, are more susceptible to adverse manufacturing and storage conditions than other bacterial strains (Drago *et al.*, 2010; Fredua-Agyeman *et al.*, 2016).

Probiotic bacteria can exhibit either resistance or sensitivity to antibiotics, depending on the presence or absence of resistance genes in their genome, plasmid-based antibiotic resistance genes, or intrinsic resistance mechanisms. The transfer of antibiotic resistance determinants from probiotic bacteria to the intestinal microbiota and potential opportunistic pathogens poses a significant health concern. Consequently, the long-term consumption of probiotic dietary supplements and foods warrants careful consideration because of the potential risk of disseminating antibiotic resistance (Jose *et al.*, 2015; Shahali *et al.*, 2023).

In the present study, the antibiotic resistance profiles of eight *Lactobacillus* strains and five *Bifidobacterium* strains isolated from probiotic food dietary supplements were evaluated. Notably, all tested strains demonstrated resistance to multiple antibiotics (three or more), revealing a pattern of MDR. These findings are consistent with previous research by Anisimova *et al.* (2022) and Sharma *et al.* (2016), which also reported widespread antibiotic resistance among probiotic lactobacilli strains.

All *Lactobacillus* strains in our study exhibited resistance to vancomycin, consistent with the findings of Wong *et al.* (2015), Wang *et al.* (2022b), and Zavišić *et al.* (2023). However, in contrast to our results, lower levels of resistance to vancomycin were reported by Sharma *et al.* (2016) and Anisimova *et al.* (2022), who observed resistance rates of 76% and 79%, respectively. In alignment with our findings, Han *et al.* (2015) determined that all *L. plantarum* and *L. rhamnosus* strains exhibited resistance to vancomycin. Similarly, Hammad and Shimamoto (2010) reported high levels of vancomycin resistance in *L. plantarum* strains. The resistance of lactobacilli to vancomycin is widely regarded as intrinsic, chromosomally encoded, and nontransferable (Anisimova and Yarullina, 2019). Zaviši´c *et al.* (2023) reported that all *Lactobacillus* isolates were resistant to cefoxitin, consistent with the findings of our study. However, in contrast to our results, Sharma *et al.* (2016) observed lower levels of resistance to methicillin. Contrary to the findings of Zaviši´c *et al.* (2023), none of the *Lactobacillus* strains isolated in our study exhibited resistance to penicillin. Similarly, Sharma *et al.* (2016) reported that most *Lactobacillus* strains displayed low levels of resistance to penicillin. In agreement with our results, Guo *et al.* (2017) found that all *Lactobacillus* strains were susceptible to gentamicin, whereas Turhan and Enginkaya (2016) reported that 20% of *Lactobacillus* spp. isolates were resistant to this antibiotic. Furthermore, the susceptibility of *Lactobacillus* strains to erythromycin and clindamycin observed in our study aligns with the findings of Sharma *et al.* (2016) and Guo *et al.* (2017). Turhan and Enginkaya (2016) also found that all *Lactobacillus* isolates were susceptible to chloramphenicol and erythromycin, consistent with our results. However, they reported higher resistance rates to tetracycline (20%), ampicillin (20%), gentamicin (20%), and ciprofloxacin (80%) compared to our findings. The resistance of *Lactobacillus* isolates to cefazolin in our study was 37.5%, closely aligning with the 32% reported by Anisimova *et al.* (2022). In contrast, Han *et al.* (2015) reported higher incidences of resistance to penicillin G (37.9%), ampicillin (34.5%), streptomycin (93.1%), kanamycin (100%), tetracycline (10.3%), chloramphenicol (10.3%), gentamicin (86.2%), and rifampin (34.5%). In our study, *L. acidophilus* strains were susceptible to ampicillin, chloramphenicol, erythromycin, rifampin, and tetracycline, consistent with the findings of Zhou *et al.* (2005) and Turhan and Enginkaya (2016). Similarly, Zhou *et al.* (2005) and Temmerman *et al.* (2003) observed that *L. acidophilus* strains were susceptible to penicillin, aligning with our findings. However, Zhou *et al.* (2005) reported resistance to kanamycin and streptomycin in *L. acidophilus* strains, which contradicts our results. Conversely, Selvin *et al.* (2020) found *L. acidophilus* to be resistant to ampicillin and *L. rhamnosus* resistant to erythromycin, contrasting with our study. Similarly, Kim *et al.* (2020) observed resistance in *L. rhamnosus* MG316 to kanamycin and chloramphenicol, while in our study, all *L. rhamnosus* strains were sensitive to chloramphenicol, and only one of two strains exhibited resistance to kanamycin. Anisimova and Yarullina (2019) reported that none of the *L. plantarum* strains were resistant to ampicillin, erythromycin, chloramphenicol, or tetracycline and that all strains exhibited resistance to ciprofloxacin and norfloxacin, consistent with our results. In addition, 10 of 11 strains were resistant to vancomycin, aligning with our findings. Gupta and Tiwari (2014) observed that the *L. plantarum* LD1 strain was resistant to kanamycin but sensitive to tetracycline,

erythromycin, chloramphenicol, and gentamicin, which aligns with our findings that all *L. plantarum* strains were sensitive to erythromycin, chloramphenicol, and gentamicin. However, in our study, two of four *L. plantarum* strains exhibited resistance to kanamycin.

All *Bifidobacterium* strains in this study exhibited resistance to vancomycin, consistent with the findings of Zuo *et al.* (2016). However, this contrasts with the results of Kim *et al.* (2018), who reported that all *Bifidobacterium* spp. strains were susceptible to vancomycin. D'Aimmo *et al.* (2007) observed high resistance levels to kanamycin in bifidobacteria, aligning with our finding that 60% of the tested *Bifidobacterium* strains were resistant to kanamycin. In our study, all *Bifidobacterium* strains were susceptible to chloramphenicol, erythromycin, gentamicin, rifampin, and tetracycline. This contrasts with the results of Xu *et al.* (2018), who reported resistance rates of 8.7% to chloramphenicol, 4.35% to erythromycin, 13.04% to gentamicin, 10.87% to rifampin, and 43.48% to tetracycline among *Bifidobacterium* strains. In agreement with our findings, Kim *et al.* (2018) reported that all *Bifidobacterium* strains were susceptible to chloramphenicol, rifampin, and erythromycin, while exhibiting general resistance to kanamycin. Conversely, Yasmin *et al.* (2020) found that all *Bifidobacterium* strains were resistant to gentamicin, kanamycin, and most were resistant to streptomycin and rifampin, though all were susceptible to tetracycline, consistent with our results. Similarly, Moubareck *et al.* (2005) demonstrated that none of the tested *Bifidobacterium* strains, regardless of species, exhibited resistance to penicillin G, in alignment with our findings. Zuo *et al.* (2016) reported universal susceptibility of isolated bifidobacteria to ampicillin, while our study found that 40% of *Bifidobacterium* strains were resistant to ampicillin. Turhan and Enginkaya (2016) observed that *Bifidobacterium* strains were resistant to vancomycin, tetracycline, ampicillin, and ciprofloxacin but sensitive to chloramphenicol, erythromycin, and gentamicin. In contrast, none of the *Bifidobacterium* strains in our study exhibited resistance to tetracycline. Moubareck *et al.* (2005) found that one of fourteen *B. longum* strains and one of six *B. breve* strains were resistant to cefoxitin, while in our study, all *Bifidobacterium* species except *B. lactis* exhibited resistance to cefoxitin. Dioso *et al.* (2020) reported resistance to erythromycin, kanamycin, and vancomycin in *B. breve* strains, findings consistent with ours except for erythromycin. Similarly, *B. breve* strains were resistant to ciprofloxacin in our study, aligning with the observations of Awasti *et al.* (2016). Kim *et al.* (2020) found that *B. breve* MG729 exhibited resistance to tetracycline, whereas Kim *et al.* (2018) observed high antibiotic resistance to gentamicin and tetracycline in *B. bifidum* BGN4 and *B. longum* BORI. However, in our study, none of the *Bifidobacterium* strains exhibited resistance to tetracycline or gentamicin.

The susceptibility of *B. bifidum* strains to erythromycin, tetracycline, gentamicin, and penicillin G in our study aligns with the findings of Drago *et al.* (2013). In contrast, Wei *et al.* (2012) reported that *B. longum* JDM301 was intrinsically resistant to ciprofloxacin, gentamicin, and streptomycin while being susceptible to vancomycin and trimethoprim. In addition, Wei *et al.* (2012) observed susceptibility to chloramphenicol, erythromycin, ampicillin, and rifampin, consistent with our findings. All *B. lactis* strains were reported to be resistant to kanamycin, gentamicin, and streptomycin and susceptible to ampicillin and rifampin by Zhou *et al.* (2005), findings consistent with ours. Similarly, Temmerman *et al.* (2003) found that *B. lactis* strains were susceptible to tetracycline, chloramphenicol, erythromycin, and penicillin G, in agreement with our study. However, in our study, *B. lactis* strains exhibited resistance to vancomycin, with levels of resistance comparable to those reported by Temmerman *et al.* (2003) (50%) and Zhou *et al.* (2005) (33%).

In this study, MDR rates were found to be significantly high among the probiotic strains tested. To the best of our knowledge, this is the first study to report MDR rates in probiotic cultures isolated from commercial probiotic dietary supplements (Table 5). A key novelty of the present research lies in the calculation and reporting of the multiple antibiotic resistance (MAR) index for probiotic strains isolated from probiotic dietary supplements in Türkiye for the first time. The MAR index values in this study were distinctly unique for each isolate (Table 5). The MAR index is a crucial metric used to assess the level of antibiotic resistance in microorganisms, particularly in probiotic strains, which are commonly used in dietary supplements. This index provides an effective way to evaluate the extent of resistance, which can be a critical factor when selecting probiotics for use in commercial applications (Duche *et al.*, 2023). Several studies have reported that MAR index greater than 0.2 indicates a high-risk antibiotic-exposed source (Ayandele *et al.*, 2020; Korzeniewskan *et al.*, 2013; Okeke *et al.*, 2005). A study by Duche *et al.* (2023) showed that while probiotic strains exhibited some degree of resistance to antibiotics, their MAR index remained relatively low, suggesting a limited risk of contributing to overall antimicrobial resistance. However, a higher MAR index in probiotic strains may raise concerns about their safety and long-term use, especially when taken alongside antibiotics (Haryani *et al.*, 2023). Notably, 11 of the tested strains exhibited a MAR index greater than 0.2, indicating a high-risk source of contamination, whereas 2 strains showed a MAR index lower than 0.2. The high MAR index that was reported in the present work thus indicated a high-risk potential associated with fermented food products that could threaten human health. These findings underscore the critical importance of routine and continuous monitoring of antibiotic resistance patterns in probiotic strains

used in probiotic dietary supplements. Such measures are essential to ensure the safety and efficacy of probiotic formulations. Further research is warranted to thoroughly investigate the antibiotic resistance determinants and mechanisms in these isolates to confirm the safety of dairy-based probiotic formulations.

Conclusions

Results from this study, aimed at evaluating the compositional quality and antibiotic resistance profiles of commercial probiotic food supplements in Türkiye, revealed, through both conventional culture-based and molecular methods, that some products did not meet the label claims regarding the quantity and variety of viable microorganisms. Results from the second part of the study, which investigated the phenotypic antibiotic resistance profiles of *Lactobacillus* spp. and *Bifidobacterium* spp. strains isolated from probiotic supplements, demonstrated a high prevalence of antibiotic resistance. Despite rigorous selection criteria for candidate microorganisms based on their safety, and technological suitability, the findings indicate significant concerns in products reaching consumers. In light of the growing popularity of probiotic dietary supplements, particularly during the COVID-19 pandemic, there is an urgent need to re-evaluate the regulations governing these products to ensure the safety and efficacy of the probiotic microorganisms they contain. The findings of this study underscore the critical need for enhanced quality control measures within the probiotic industry. To address the identified shortcomings and ensure the safety and efficacy of probiotic products, the following recommendations are proposed:

(i) A comprehensive review of manufacturing processes is necessary to identify and implement strategies that minimize microbial losses, particularly for sensitive strains such as bifidobacterium, throughout the product shelf life.

(ii) Robust regulatory frameworks should be established to mandate the monitoring of the quantity and diversity of probiotic microorganisms in supplement formulations and the antibiotic resistance profiles of the included species.

(iii) Product labels for probiotic dietary supplements should clearly communicate the potential health benefits associated with the included microbial strains, emphasizing strain-specific effects supported by scientific evidence.

Ethics Approval and Consent to Participate

Not applicable.

Consent for Publication

Not applicable.

Availability of Data and Materials

All data were included in the manuscript.

Authors Contributions

Seda SEYİRT was responsible for methodology, writing of the original draft. Pınar ŞANLIBABA was concerned with conceptualization, methodology, data curation, software, writing of the original draft, and review and editing. Başar UYMAZ TEZEL was involved in conceptualization, methodology, writing of the original draft, review and editing, supervision, and funding acquisition.

Competing Interests

The authors declare that they have no competing interests.

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