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Original article

Antibiotic susceptibility of probiotic strains: Is it reasonable to combine probiotics with antibiotics?

Sensibilité des souches de probiotiques aux antibiotiques : est-il raisonnable de les associer?

C. Neut , S. Mahieux , L.J. Dubreuil *

Inserm, U995, Lille inflammation research international center (LIRIC), university of Lille, 59006 Lille, France

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Abstract

Objective. – The main goal of this study was to determine the in vitro susceptibility of strains collected from marketed probiotics to antibiotics used to treat community-acquired infections.

Methods. – The minimum inhibitory concentrations (MICs) of 16 antibiotics were determined using a gradient strip (E test) or the agar dilution method for fidaxomicin.

Results. – The probiotics demonstrated various antibiotic patterns. Bacterial probiotics are generally susceptible to most prescribed antibiotics orally administered, whereas yeast probiotics, such as *Saccharomyces boulardii*, are resistant.

Conclusion. – Special attention must be paid to co-prescriptions of antibiotics and probiotics to ensure that the probiotic strain is not susceptible.

Keywords: Antibiotic susceptibility; Probiotics

Résumé

Objectifs. – Le but de cette étude consistait à déterminer la sensibilité in vitro de souches commerciales de probiotiques commercialisées aux antibiotiques prescrits dans le traitement des infections communautaires.

Méthodes. – Les concentrations minimales inhibitrices (CMI) de 16 antibiotiques ont été déterminées à l'aide d'une méthode en gradient (E test) ou par dilution en gélose pour la fidaxomicine.

Résultats. – Les probiotiques présentaient différents profils de sensibilité. D'origine bactérienne, ils sont généralement sensibles aux antibiotiques les plus prescrits par voie orale tandis que les probiotiques d'origine fongique, comme *Saccharomyces boulardii*, y sont résistants.

Conclusion. – Lors d'un traitement antibiotique, le choix du probiotique devrait tenir compte de la sensibilité de celui-ci aux antibiotiques.

Mots clés : Sensibilité aux antibiotiques ; Probiotiques

1. Introduction

Antibiotics are the most effective drugs available to treat bacterial infections. However, diarrhea remains one of the most common adverse events associated with antibiotics: the so-called antibiotic-associated diarrhea (AAD) that occurs in 5 to 39% of cases [1,2]. The mean duration of AAD is approximately seven days, but this event can last for up to 10 days or longer for 19% of patients who receive antibiotics [3]. If possible, the antibiotic treatment is discontinued; however, in most clinical situations, the severity of the infection or the comorbidities require further treatment, resulting in extended hospital stays, increased medical care costs, and increased diagnostic procedures [4].

* Corresponding author. Laboratoire de microbiologie clinique, faculté de pharmacie, 3, rue du Professeur-Laguesse, 59006 Lille cedex, France.
E-mail address: luc.dubreuil@univ-lille2.fr (L.J. Dubreuil).

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In addition to treating bacterial infections, the use of broad-spectrum antibiotics leads to (as collateral damage) the disruption of the protective host microbiota, which results in AAD [4]. The more severe the alteration of the gut microbiota by a given antibiotic, the more likely it is to cause AAD.

AAD may allow opportunistic pathogens to colonize the gut and can result in increased susceptibility to subsequent disease. Of particular importance is *Clostridium difficile*-associated diarrhea (CDAD), which occurs in approximately 20% of AAD patients who have contracted more severe illnesses with this life-threatening pathogen [1,2,5].

The overuse or inappropriate use of antibiotics has led to the emergence of resistant bacteria and to increased opportunities for horizontal gene transfer, with major implications for the emergence of resistance [6].

Probiotics are one approach to preserve colonization resistance and reduce AAD episodes. General practitioners and pharmacists may suggest the use of probiotics. Probiotics are live organisms that, when administered in adequate amounts, confer a health benefit to the host [7]. Guidelines have been issued on the use of probiotics. The European Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the North American Society for Pediatric Gastroenterology (ESPGHAN) recommends using two probiotics to prevent AAD in children: the *Saccharomyces boulardii* yeast and the *Lactobacillus rhamnosus* GG bacterium [8]. Only *S. boulardii* is recommended for preventing *C. difficile*-associated diarrhea.

Effects of antibiotics on pathogenic bacteria have been extensively studied, although only few studies focused on probiotic bacteria. Moreover, while these studies aimed to describe the susceptibility of potentially new probiotic strains, healthcare professionals lack information on the antibiotic susceptibility of commercially available probiotics [9]. Indeed, we were unable to find literature data on the resistance level of these probiotic isolates to antibiotics that are among the most commonly prescribed antibiotics for community-acquired infections.

Therefore, we determined the antibiotic susceptibility of 16 bacterial strains together with one strain of fungal origin to a panel of 16 selected antibiotics. Fidaxomicin was added and studied separately because this drug is used to treat severe diarrhea due to the production of toxins by *C. difficile*.

2. Materials and methods

2.1. Strains

The strains used in this study were isolated from the main marketed probiotics (registered drugs or food supplements) and are listed in Table 1. The purity of the strains was checked again before the antimicrobial susceptibility test was performed. *Escherichia coli* ATCC 25922, *Staphylococcus aureus* ATCC 29213, and *Bacteroides fragilis* ATCC 25285 were added as control strains.

Table 1
Origins of the probiotic isolates used in this study.
Origine des probiotiques dans cette étude.

Probiotic	Strain	Company (brand)
Lactobacillus reuteri Protectis	DSM 17938	BioGaia AB (BioGaia Probiotic drops)
Lactobacillus casei var *rhamnosus*	Lcr35	PROBIONOV (Bacilor)
Lactobacillus acidophilus	LA-5	Mayoly Spindler (ProbioLog) Sandoz (Linex)
Bifidobacterium lactis	BB-12/DSM 15954	Mayoly Spindler Versale Pharma (Bacilac infantis) Sandoz (Linex) Johnson & Johnson (Immoflora)
Bifidobacterium longum	LA 101	PiLeJe (Lactibiane référence, Lactibiane enfant)
Lactobacillus helveticus	LA 102	PiLeJe (Lactibiane référence, Lactibiane enfant)
Lactococcus lactis	LA 103	PiLeJe (Lactibiane référence, Lactibiane enfant)
Streptococcus thermophilus	LA 104	PiLeJe (Lactibiane référence, Lactibiane enfant)
Lactobacillus rhamnosus	LA 801	PiLeJe (Lactibiane référence, Lactibiane ATB)
Lactobacillus casei var. *rhamnosus* GG	ATCC 53103/LMG18243	Versale Pharma (Bacilac infantis) Laboratoire Nutergia (Ergyphylus plus, Ergyphilus confort) Chr Hansen/Valio (LGG)
Bacillus clausii OC	Unknown strain	Sanofi-Aventis (Enterogermina)
Bacillus clausii NR	Unknown strain	Sanofi-Aventis (Enterogermina)
Bacillus clausii SIN	Unknown strain	Sanofi-Aventis (Enterogermina)
Bacillus clausii T	Unknown strain	Sanofi-Aventis (Enterogermina)
Lactobacillus paracasei	Unknown strain	Laboratoire Nutergia (Ergyphilus plus)
Lactobacillus acidophilus	Unknown strain	Laboratoire Nutergia (Ergyphilus plus, Ergyphilus confort)
Bifidobacterium bifidum	Unknown strain	Laboratoire Nutergia (Ergyphilus plus, Ergyphilus comfort)
Saccharomyces boulardii	CNCM I-745	Biocodex (Ultra Levure)

Table 2
Activity of seven ß-lactams against probiotic isolates (MIC in mg/L).
Activité de sept ß-lactamines sur les souches de probiotique (CMI en mg/L).

	PG	OX	AC	XL	XM	PX	IX
Antibiotic breakpoints (mg/L)	0.25/2	0.25/2	2/8	2/8	4/8	1/1	1/1
Strains							
Lactococcus lactis LA 103	0.094	1.5	0.047	0.047	0.064	0.38	2
Lactobacillus reuteri Protectis DSM 17938	>32	>256	24	12	4	64	>256
Lactobacillus casei var *rhamnosus* Lcr35	0.38	6	0.5	0.75	4	>256	>256
Lactobacillus acidophilus LA-5	0.19	3	1.5	0.5	1	1	3
Lactobacillus helveticus LA 102	0.064	0.38	0.064	0.064	0.5	2	3
Lactobacillus rhamnosus LA 801	0.5	6	0.5	0.5	3	>256	>256
Lactobacillus rhamnosus GG ATCC 53103	0.125	2	0.38	0.38	0.75	4	24
Lactobacillus paracasei Unknown strain	0.75	4	2	2	4	64	>256
Lactobacillus acidophilus Unknown strain	0.064	1.5	0.094	0.19	0.047	4	6
Bacillus clausii O/C Unknown strain	0.19	8	0.094	0.023	64	96	64
Bacillus clausii N/R Unknown strain	0.125	8	0.094	0.047	24	64	64
Bacillus clausii SIN Unknown strain	0.38	8	0.094	0.047	128	128	>256
Bacillus clausii T Unknown strain	0.19	6	0.125	0.047	64	64	64
Streptococcus thermophilus LA 104	0.047	1	0.047	0.064	<0.016	0.094	0.25
Bifidobacterium bifidum Unknown strain	<0.016	0.125	<0.016	<0.016	<0.016	0.38	0.75
Bifidobacterium lactis BB12	0.032	0.38	0.047	0.032	0.125	0.5	3
Bifidobacterium longum LA101	0.25	2	0.25	0.19	0.75	4	48
Saccharomyces boulardii CNCM I-745	>32	>256	>256	>256	>256	>256	>256

Abbreviations given by the E test manufacturer. PG: benzylpenicillin; OX: oxacillin; AC: amoxicillin; XL: amoxicillin combined with clavulanic acid; XM: cefuroxime; PX: cefpodoxime; IX: cefixime.

2.2. Preparation of the inoculum

Each isolate was subcultured in Mueller Hinton broth for aerobic bacteria (24 hrs), as recommended by the European Committee for Antibiotic Susceptibility Testing (EUCAST) [10], and in *Brucella* broth (Difco, Becton Dickinson, Le Pont de Claix, France) for strict anaerobes (48 hrs), as recommended by the Clinical Laboratory Standards Institute (CLSI) [11].

The final inoculum was obtained by diluting the previous subcultures in the same liquid media to reach a turbidity equal to the 1 McFarland standard (ca. 1 to 1.5 × 10^8 CFU/mL).

2.3. Plate inoculation and minimum inhibitory concentration (MIC) determination

Using a cotton swab, the previous suspension was inoculated onto Columbia blood agar (5% horse blood), and after 5 minutes of drying an E test strip (BioMérieux, France) was placed on the agar surface. For the aerobic bacteria, the plates were incubated at 36–37 °C for 24 hours; meanwhile, the anaerobic strains were incubated in an anaerobic chamber (Don Whitley, AES, Combourg, France) at 35–36 °C for 48 hours. Columbia blood agar is the medium recommended by the E Test manufacturer. The highest concentration tested corresponded to the highest value on the scale for each individual E test strip.

2.4. MIC determination for fidaxomicin

Fidaxomicin strips are not yet marketed; therefore, we determined the fidaxomicin MICs using an agar dilution reference method (M11A7 from CLSI). The inoculum was prepared in *Brucella* broth by diluting a 48-hour subculture to reach a turbidity equal to the 0.5 McFarland standard. The strains were inoculated onto *Brucella* agar supplemented with 5% lysed horse blood. A Mast Multipoint Inoculator was used to deliver an inoculum of ca. 10^5 CFU/spot. The reading was performed after 48 hours of incubation at 35 °C in a Don Whitley anaerobic chamber.

2.5. Antibiotic testing and clinical categorization of the strains

The MICs were determined for 13 of the most prescribed antibiotics in community settings: benzylpenicillin; oxacillin (isoxazolyl penicillin); amoxicillin (aminopenicillin) alone or combined with clavulanic acid; cefuroxime (second-generation cephalosporin); cefpodoxime and cefixime (oral third-generation cephalosporins); clarithromycin and azithromycin (macrolides); clindamycin (lincosamide); quinupristin/dalfopristin (a streptogramin analogue of oral pristinamycin); ciprofloxacin and levofloxacin (fluoroquinolones); doxycycline (tetracycline); co-trimoxazole (a combination of trimethoprim and sulfamethoxazole, a sulfonamide) and metronidazole (5 nitroimidazole). The strains were categorized as susceptible or resistant, according to their EUCAST breakpoints [12].

Fidaxomicin, an antibiotic mainly used in hospitals to treat diarrhea and pseudomembranous colitis related to toxin production by *C. difficile*, was tested separately. It is not yet possible to proceed to the clinical categorization of fidaxomicin because EUCAST decided not to give the breakpoint due to the variation in MICs between studies. Low solubility in water or broth media prevents researchers from determining MICs > 128 mg/L.

Table 3
Activity of macrolides, fluoroquinolones, cyclins, sulfonamides, and metronidazole against probiotic isolates (MIC in mg/l).
Activité des macrolides, fluoroquinolones, cyclines, sulfamides et métronidazole sur les souches de probiotique (CMI en mg/L).

Strains	AZ	CH	CM	QDA	CI	LE	DC	TS	MZ
Antibiotic breakpoints (mg/L)	1/2	1/2	0.25/0.5	1/2	0.5/1	1/2	1/2	2/4	4/4
Strains									
Lactococcus lactis LA 103	0.19	0.047	0.094	1	1.5	0.5	0.047	> 32	> 256
Lactobacillus reuteri Protectis DSM 17938	0.19	0.016	< 0.016	0.38	> 32	6	> 256	> 32	> 256
Lactobacillus casei var *rhamnosus* Lcr35	> 256	> 256	> 256	0.5	> 32	0.75	1	> 32	> 256
Lactobacillus acidophilus LA-5	0.023	< 0.016	0.75	0.75	> 32	> 32	1	> 32	> 256
Lactobacillus helveticus LA 102	< 0.016	< 0.016	0.032	0.19	> 32	> 32	0.38	> 32	> 256
Lactobacillus rhamnosus LA 801	0.25	0.19	0.25	0.5	> 32	> 32	1	> 32	> 256
Lactobacillus rhamnosus GG ATCC 53103	0.38	0.125	0.047	0.25	0.5	0.75	0.25	> 32	> 256
Lactobacillus paracasei Unknown strain	> 256	> 256	0.25	0.5	> 32	1	1	> 32	> 256
Lactobacillus acidophilus Unknown strain	0.25	0.023	0.19	0.19	> 32	> 32	0.75	> 32	> 256
Bacillus clausii O/C Unknown strain	> 256	> 256	32	1.5	0.125	0.19	0.25	0.16	> 256
Bacillus clausii N/R Unknown strain	> 256	> 256	96	1.5	0.25	0.25	0.094	0.023	> 256
Bacillus clausii SIN Unknown strain	> 256	> 256	> 256	1	0.125	0.25	0.19	0.023	> 256
Bacillus clausii T Unknown strain	> 256	> 256	> 256	2	0.125	0.25	0.19	0.023	> 256
Streptococcus thermophilus LA 104	0.064	< 0.016	< 0.016	0.032	0.75	1	0.094	1.5	> 256
Bifidobacterium bifidum Unknown strain	0.19	0.023	0.032	0.19	4	0.75	0.25	0.25	1.5
Bifidobacterium lactis BB12	0.125	0.023	< 0.016	0.047	1.5	2	3	< 0.002	1
Bifidobacterium longum LA101	0.5	0.032	0.064	0.032	3	1.5	0.5	2	1
Saccharomyces boulardii CNCM I-745	> 256	> 256	> 256	> 32	> 32	> 32	> 256	> 32	> 256

Macrolides: AZ: azithromycin; CH: clarithromycin; lincosamide: CM: clindamycin; streptogramin: QDA: quinupristin-dalfopristin analogue of pristinamycin; fluoroquinolones: CI: ciprofloxacin; LE: levofloxacin; miscellaneous: TS: co-trimoxazole (combination of sulfamethoxazole + trimethoprim); DC: doxycycline; MZ: metronidazole.

Table 4
Activity of fidaxomicin against probiotic isolates.
Activité de la fidaxomicine sur les souches de probiotique.

Strains	Fidaxomicin MIC in mg/L
Lactococcus lactis LA 103	0.5
Lactobacillus reuteri Protectis DSM 17938	> 128
Lactobacillus casei var *rhamnosus* Lcr35	16
Lactobacillus acidophilus LA-5	0.5
Lactobacillus helveticus LA 102	16
Lactobacillus rhamnosus LA 801	0.5
Lactobacillus rhamnosus GG ATCC 53103	8
Lactobacillus paracasei Unknown strain	0.5
Lactobacillus acidophilus Unknown strain	0.5
Bacillus clausii O/C Unknown strain	0.5
Bacillus clausii N/R Unknown strain	2
Bacillus clausii SIN Unknown strain	0.5
Bacillus clausii T Unknown strain	0.5
Streptococcus thermophilus LA 104	64
Bifidobacterium bifidum Unknown strain	1
Bifidobacterium lactis BB12	8
Bifidobacterium longum LA101	16
Saccharomyces boulardii CNCM I-745	> 128

3. Results

The activities of 7 ß-lactams and 9 other antibiotics against the isolates tested are shown in Tables 2 and 3. The fidaxomicin MICs of the tested strains varied from 0.5 to 64 mg/L (Table 4).

3.1. Activity of antibiotics against Lactobacillus spp.

One strain of *L. reuteri* was resistant to penicillins and third-generation cephalosporins, but it remained susceptible to cefuroxime. Other *Lactobacillus* isolates were susceptible to benzylpenicillin, amoxicillin, and cefuroxime and, with the exception of one strain, were resistant to third-generation cephalosporins. For oxacillin, an antistaphylococcal penicillin, low-level resistance was observed (MIC 2 to 8 mg/L); a MLSb resistant phenotype (resistant to clarithromycin, azithromycin, and clindamycin and susceptible to the streptogramin) was observed in 2 of 8 tested strains. Most isolates were resistant to both ciprofloxacin and levofloxacin. One isolate was resistant to doxycycline.

The intrinsic resistance of *Lactobacillus* to metronidazole and co-trimoxazole was confirmed.

3.2. Activity of antibiotics against the Lactococcus lactis strain

The isolate was susceptible to all ß-lactams (except for cefixime) and was also resistant to ciprofloxacin, co-trimoxazole, and metronidazole.

3.3. Activity of antibiotics against Bacillus spp.

All strains were susceptible to all penicillins (except for oxacillin), fluoroquinolones (ciprofloxacin and levofloxacin), streptogramin, doxycycline, and co-trimoxazole. As usual, the *Bacillus* strains were intrinsically resistant to cephalosporins, macrolides, clindamycin, and metronidazole.

3.4. Activity of antibiotics against the Streptococcus thermophilus strain

The strain was susceptible to all tested antibiotics except for metronidazole (intrinsic resistance).

Table 5
Susceptibility of probiotics to each antibiotic.
Sensibilité des probiotiques aux antibiotiques.

Susceptible strains S + I[a]	Penicillins				Cephalosporins		
Strains (no.)	PG	OX	AC	XL	XM	PX	IX
Lactococcus lactis (1)	1	1	1	1	1	1	0
Lactobacillus spp. (8)	7	3	7	7	8	1	0
Bacillus spp. (4)	4	0	4	4	0	0	0
Streptococcus thermophilus (1)	1	1	1	1	1	1	1
Bifidobacterium spp. (3)	3	3	3	3	3	2	1
Saccharomyces boulardii (1)	0	0	0	0	0	0	0
Total S/R (18)	16/2	8/10	16/2	16/2	13/5	5/13	2/16

Susceptible strains S + I[a]	Macrolides				Fluoroquinolones		Cyclin	Co-trimoxazole	5 nitroimidazole
	AZ	CH	CM	QDA	CI	LE	DC	TS	MZ
Lactococcus lactis (1)	1	1	1	1	0	1	1	0	0
Lactobacillus spp. (8)	6	6	6	8	1	3	7	0	0
Bacillus spp. (4)	0	0	0	4	4	4	4	4	0
Streptococcus thermophilus (1)	1	1	1	1	1	1	1	1	0
Bifidobacterium spp. (3)	3	3	3	3	0	3	2	3	3
Saccharomyces boulardii (1)	0	0	0	0	0	0	0	0	0
Total S/R (18)	11/7	11/7	11/7	17/1	6/12	12/6	15/3	8/10	3/15

S/R: number of susceptible or resistant strains, respectively. Abbreviations given by the E test manufacturer. PG: benzylpenicillin; OX: oxacillin; AC: amoxicillin; XL: amoxicillin combined with clavulanic acid; XM: cefuroxime, PX: cefpodoxime; IX: cefixime; macrolides: AZ: azithromycin; CH: clarithromycin; lincosamide: CM: clindamycin; streptogramin: QDA: quinupristin-dalfopristin analogue of pristinamycin; fluoroquinolones: CI: ciprofloxacin; LE: levofloxacin; miscellaneous: TS: co-trimoxazole (combination of sulfamethoxazole + trimethoprim); DC: doxycycline; MZ: metronidazole.
[a] S + I strains categorized as susceptible or intermediate.

3.5. Activity of antibiotics against *Bifidobacterium spp.*

The three strains were resistant to ciprofloxacin but were susceptible to levofloxacin. They were susceptible to all other tested antibiotics, including metronidazole, with the exception of two strains resistant to third-generation cephalosporins and one strain resistant to doxycycline.

3.6. Activity of antibiotics against *S. boulardii*

As usual for yeasts, the strain was naturally resistant to all tested antibiotics.

4. Discussion

Antibiotics may cause gut microbiota dysbiosis and lead to AAD. Probiotics, commonly used to prevent AAD, are live non-pathogenic bacteria that can survive in the human gut and help restore the microbiota eubiosis. The main goal of this study was to assess whether the vitality of probiotics could be affected by antibiotic intake using an in vitro study.

Our results are aligned with literature data [13] and a recent overview on probiotic strains [14] about the antibiotic susceptibility of various isolates tested in this study. The co-administration of a probiotic of bacterial origin and one of the 16 antibiotics studied led to susceptibility of the probiotic in 170 of 272 cases (62%, calculated from Table 5). Unlike *S. boulardii*, a eukaryotic probiotic strain, none of the probiotics of bacterial origins were resistant to all tested antibiotics (Fig. 1).

Probiotics are mostly resistant to oxacillin and metronidazole. Oxacillin and metronidazole have a narrow spectrum of activity, primarily against *Staphylococcus* and *Streptococcus* for oxacillin; however, the activity of metronidazole is limited to strict anaerobes. Therefore, these two drugs are responsible for limited effects on the microbiota, a situation in which the requirement of probiotics may be the lowest. If we compare the results obtained for these antibiotics, bacterial probiotics are susceptible in 159 of 238 cases (67%). If one considers the eight blockbusters (amoxicillin, amoxicillin + clavulanic acid, cefuroxime, azithromycin, clarithromycin, pristinamycin, ciprofloxacin, and levofloxacin), susceptibility occurs in 102 of 136 cases (75%).

Fidaxomicin is a novel narrow-spectrum agent that has been demonstrated to be selectively active against Gram-positive anaerobes, including the main etiological agent of AAD, *C. difficile*. Considering its high cost, this drug is used to treat *C. difficile* infections when failure occurs after previous treatment with either oral vancomycin or metronidazole. As EUCAST decided not to provide a breakpoint for fidaxomicin, we were unable to determine whether the tested probiotics were susceptible or resistant. However, because of the high doses usually found in the intestine (1000 μg/mL) [15], one can imagine that fidaxomicin whose bactericidal activity occurs at a concentration of 4 × MIC, may kill most of the probiotics studied herein if they are co-administered.

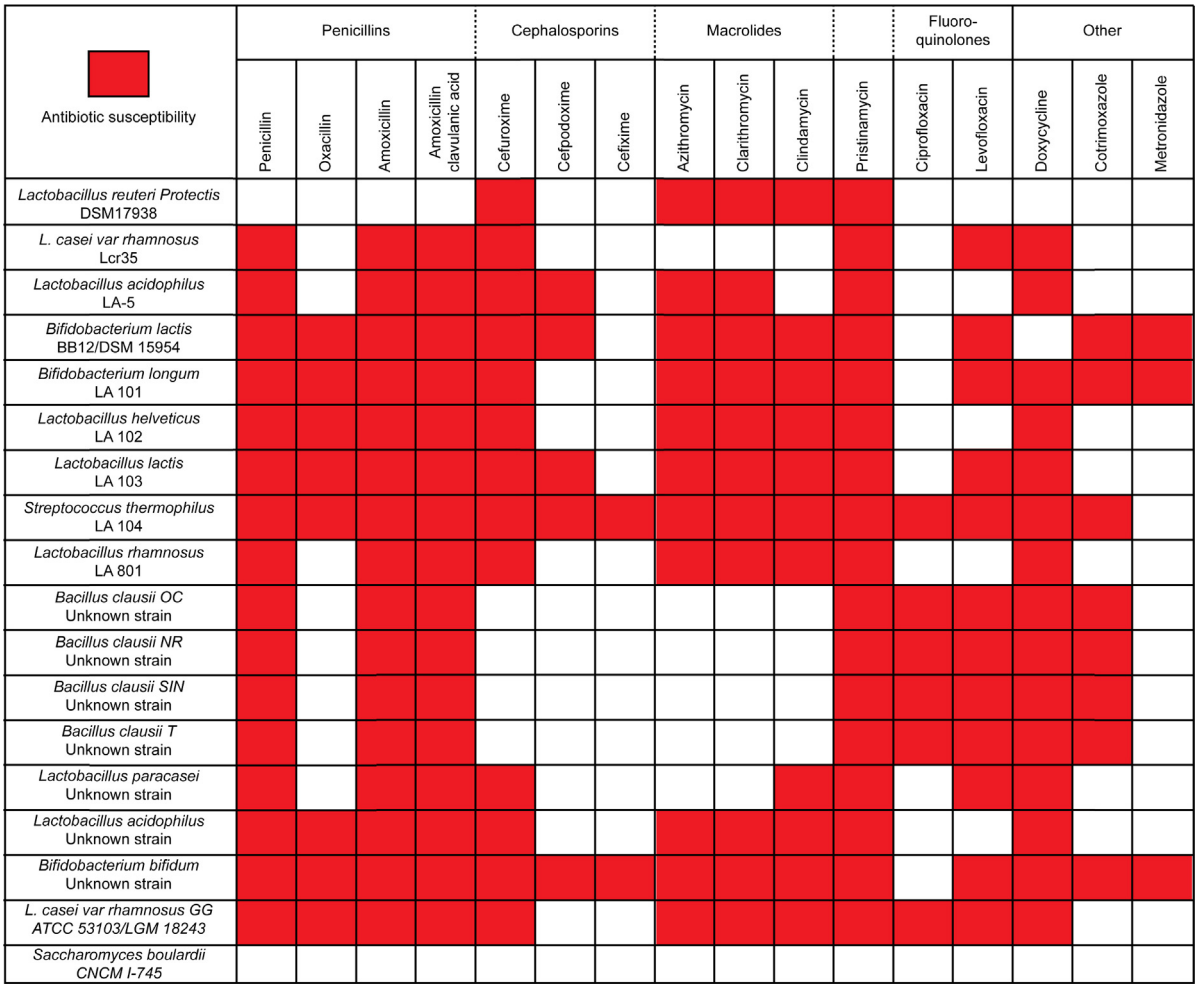

Fig. 1. Map of the antibiotic susceptibility of each probiotic strain.
Carte de sensibilité aux antibiotiques de chaque probiotique.

EUCAST defines clinical breakpoints based on the blood concentration of antibiotics. The S/I breakpoint is normally based on the standard dose, and the I/R breakpoint is based on the maximum dose. The isolates' resistance/susceptibility were determined on the basis of these breakpoints. However, antibiotic concentrations in the bowel are generally higher; for instance, a concentration of cefixime of 237–912 μg/g in the feces has been observed in patients, whereas its breakpoint is much lower than 1 mg/L [16]. The in vitro results of this study suggest that based on the high intestinal concentration of these oral antibiotics, probiotics categorized as resistant strains may be killed in situ.

According to the official definition, probiotics are "live microorganisms that, when administered in adequate amounts, confer a health benefit on the host" [7]. Ideally, a probiotic strain is unaffected by concomitant medications or antibiotics taken simultaneously with the probiotic. For example, *S. boulardii* can be administered simultaneously with oral antibiotics because only antifungal medications (not antibiotics) affect it [17].

Nevertheless, probiotics are complex, and the probiotic paradox is that both live and dead cells in probiotic products can generate beneficial biological responses [7]. However, this paradox may not apply to AAD because live probiotic cells influence both the gastrointestinal microbiota and the immune response whereas the components of dead cells exert an anti-inflammatory response in the gastrointestinal tract [18]. Moreover, the dose and the administration regimen are critical for probiotics either ingested as foods claiming health benefits or used as drugs in clinics [19]. Thus, even if high antibiotic concentrations in the gut would not kill the entire dose of the ingested probiotics, the remaining probiotics would likely not be sufficient to act, even partially.

Further in vitro studies are required to establish whether the viability and efficacy of probiotics are maintained in the presence of intestinal concentrations of antibiotics and to determine the level of probiotics when they are co-administered with antibiotics even with two hours of delay.

5. Conclusion

The co-administration of antibiotics and isolates of bacterial origin may not exert a preventive effect on AAD. Compared to bacterial probiotics, the probiotic yeast *S. boulardii* is of interest

and can be co-prescribed with oral antibiotics without being affected. Consequently, this approach prevents opportunities for horizontal gene transfer. This study emphasizes that bacterial probiotics are usually susceptible to most prescribed antibiotics administered orally. Moreover, special attention must be paid when co-prescribing antibiotics and probiotics to ensure that the probiotic strain is not also sensitive.

Contribution of authors

S. Mahieux performed the tests and was supervised by C. Neut.

C. Neut, L. Dubreuil, and the study sponsor interpreted the results (two interpretations).

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Disclosure of interest

The authors declare that they have no competing interest.

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