
Bacteriocins: From Isolation to Innovation – Harnessing Natural Peptides Against Multidrug-Resistant Pathogens

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Résumé

The growing threat of multidrug-resistant (MDR) bacteria is making it increasingly difficult to treat infections with standard antibiotics. As these pathogens continue to evolve and resist multiple drug classes, there's an urgent need to explore new antimicrobial strategies. In this context, bacteriocins (small, naturally occurring peptides produced by bacteria) are emerging as promising alternatives due to their targeted activity and low potential for resistance development. In this study, we focused on five clinically relevant MDR pathogens: *Pseudomonas aeruginosa*, *Enterococcus faecalis*, *Staphylococcus epidermidis*, *Escherichia coli*, and *Klebsiella pneumoniae*. Strains from these species were successfully isolated from clinical sources and selected for their resistance to multiple antibiotic classes. To identify potential bacteriocins with antimicrobial activity, we isolated lactic acid bacteria (LAB) from diverse Moroccan fermented matrices. Purification of the active peptides was performed using cation-exchange chromatography (SP Sepharose), followed by semi-preparative and analytical C18 reversed-phase HPLC. Structural characterization was conducted using MALDI-TOF mass spectrometry, leading to the identification of several peptides-specifically pediocin PA-1, plantaricin, and a modified form of the class IIb bacteriocins L50A and L50B. However, in the antibacterial tests, we only used pediocin PA-1, modified forms of L50A/L50B, and a commercial Nisin A (used as a control). Clear inhibitory effects were observed particularly against MDR *P. aeruginosa*, *S. epidermidis*, and *E. faecalis*, with certain combinations showing enhanced activity, suggesting potential synergy. No antimicrobial effects were observed against *E. coli* and *K. pneumoniae* under the tested conditions. These findings support the idea that bacteriocins may be useful additions to the antimicrobial arsenal, especially against Gram-positive pathogens and certain Gram-negative strains such as *P. aeruginosa*. Their use in combination with conventional antibiotics could be a promising strategy to lower the minimum inhibitory concentration (MIC) and improve treatment efficacy against resistant infections.

Mots-Clés: Multidrug resistance, Bacteriocins, HPLC, MIC.

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