

TITLE: SYNERGISTIC EFFECT BETWEEN A BACTERICION NISIN AND CONVENCIONAL ANTIMICROBIAL DRUGS FRONT *Staphylococcus aureus* MRSA

Autors: Alves, F.C.B. ¹, Albano, M.¹, Andrade, B.F.M.T.¹ Cunha, M.L.R.S.¹, Barbosa, L.N.², Fernandes Junior, A.¹

Instituição: ¹ Department of Microbiology and Immunology. Biosciences Institute of Botucatu-UNESP, Universidade Estadual Paulista (Rubião Junior s/n- Cep: 18.610-307- Botucatu-SP)

² CEVAP- Center for the Study of Venoms and Venomus Animals – UNESP- Universidade Estadual Paulista (Fazenda Experimental Lageado- Rua José Barbosa de Barros, 1780. Cep:18.618-970- Botucatu-SP).

Introduction: The microorganisms resistant to antimicrobial drugs, such as *Staphylococcus aureus*, are the public health problem worldwide, and this has stimulated research aimed at new pharmaceuticals. One strategy is the possibility of combination of conventional drugs with natural antimicrobials, that can serve as alternatives to treatment. Antimicrobial peptides such as nisin (bacteriocin already used in the food industry as a preservative) are produced by bacteria and called bacteriocins; they are defined as a heterogeneous group with bactericidal action on various types of bacteria. The objective of this study was to analyze a potential synergy between nisin and conventional antimicrobial drugs for potentiation of drug effect.

Materials and Methods: The bacteriocin nisin and six antibiotics (Tetracycline, Vancomycin, Polymyxin B, Cephalothin, Ciprofloxacin and Oxacillin) were analyzed for their potential synergy against *Staphylococcus aureus* MRSA ATCC by Time kill curve methodology, with prior determination of minimum inhibitory concentration (MIC) of antibiotics. Proportions of nisin $\frac{1}{4}$ + $\frac{1}{4}$ antimicrobial drugs were compared in relation to the control and the MIC of each antimicrobial. For 24 hours in 7 different times was performed counting the colony forming units (CFU / mL). For it was considered: reduction of 3 or more log of CFU / mL as bactericidal effect.

Results: The antimicrobial drugs tested in its MIC against *S. aureus* MRSA, the one that did not get the effect was oxacillin, while Ciprofloxacin had bactericidal action after treatment and the other drugs had bacteriostatic. Nisin had bactericidal action. The combinations tested between drugs and nisin ($\frac{1}{4}$ + $\frac{1}{4}$) were bacteriostatic effect are: Vancomycin / nisin and Tetracycline / nisin; while other combinations (Polymyxin B / nisin Cephalothin / nisin Ciprofloxaxina / oxacillin and nisin) showed after 24 hours of bactericidal effect. **Conclusion:** Natural products such as nisin can potentiate the effect of traditional antibiotics using a lower dose of these drugs and overcome resistance mechanisms as is the case of *S. aureus* against oxacillin. However more studies are needed to determine the mechanism of action of these combinations.

Key words: Antimicrobials, Nisin, Resistance, *Staphylococcus aureus* MRSA, Synergism

Acknowledgments: CAPES

