TITLE: MELITTIN-CONJUGATED AND APITOXIN-CONJUGATED GOLD NANOPARTICLES AGAINST METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* (MRSA)

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ABSTRACT:

Bacterial resistance is a worldwide public health problem and some resistant strains have emerged, such as methicillin-resistant Staphylococcus aureus (MRSA), being a frequent cause of nosocomial and community-associated infections and may be able to produce biofilms. The search for new antimicrobial agents has been boosted, especially by natural products like the antimicrobial peptides, for example the melittin, a fraction of the bee venom. The conjugation of antimicrobial peptides with nanoparticles can generate effective administration routes, a specific targeted drug delivery system and lower cytotoxicity The aim of this study is to evaluate the antibacterial activity of melittin, apitoxin and their nanoparticles against MRSA. In the synthesis of gold nanoparticles, a solution of gold chloride trihydrate with sodium citrate addition was used, after the gold nanoparticles were stabilized, melittin and apitoxin were incorporated to form the conjugated gold nanoparticles. Resazurin assays microtiter plate (REMA) was performed for obtaining the minimum inhibitory concentration (MIC) and the minimum bactericidal concentration (MBC) of the apitoxin provided by FMVZ (UNESP, Botucatu, SP, Brazil), melittin from Sigma-Aldrich, melittin purified by CEVAP (Centro de Estudos de Venenos e Animais Peçonhentos – Botucatu, SP, Brazil) and their conjugated nanoparticles against an ATCC MRSA 33591 and a clinical isolate of MRSA. The change of color, the measures of absorbance and wavelength prove that the gold nanoparticle was formed and that the gold nanoparticles of melittin and apitoxin were conjugated. Oxacillin and cephalothin were used as positive controls. The MIC indicated that the conjugated nanoparticles showed the same performance of all the isolated products. There was no difference between the actions of the purified and Sigma's melittin and their nanoparticles. The melittin-conjugated nanoparticle (from Sigma) had a better action than the apitoxin-conjugated nanoparticle on the clinical isolate of MRSA. We can conclude that all the tested products had an antimicrobial activity against MRSA and further studies should be performed to check their cytotoxicity for the development of antibiotics to treat infectious diseases caused by these bacteria.

Keywords: *Apis mellifera*, bee venom, antibacterial activity, melittin nanoparticles.

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