

TITLE: Evaluation of antimicrobial and modulatory activity on virulence genes of methicillin-resistant *Staphylococcus aureus*

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ABSTRACT:

Staphylococcus aureus is responsible for community- and hospitals-acquired infections and can also cause diseases in animals. The antimicrobials bacterial resistance, especially methicillin-resistant *S. aureus* (MRSA), is a worldwide health problem that promote research in the search for new treatments, such as natural products. The use of essential oils like citral is an alternative to antibiotics. The aim of this study was to analyze the action of citral essential oil (EOC) on the microorganism inhibition, biofilm formation inhibition and expression of virulence genes modulation. For the study nine isolates of MRSA were used. Thus, minimum inhibitory (MIC) and bactericidal concentration (MBC) were determined through the microdilution assay using citral at different concentrations (4%, 2%, 1%, 0.5%, 0.25%, 0.12% and 0.06%). Values between 0.5% and 4% were found for MIC and between 1% and 4% for MBC. The EOC activity at 2.5% (concentration determined from the growth curve) was evaluated to analyze the inhibition of biofilm formation in the initial and mature stages. Citral had higher activity in the strains at the initial stage of biofilm formation. The effect of EOC in subinhibitory concentration (0.25%) on expression of virulence genes such as enterotoxin (*seg*, *sei* and *sej*), exfoliative toxins (*eta* and *etb*) and genes involved in the biofilm formation (*icaA* e *icaD*) was analyzed using RT-qPCR. The essential oil increased the expression of enterotoxins *seg* and *sei* and downregulated the expression of the *icaA* and *icaD* genes. No activity on the exfoliative toxin genes was observed. The citral showed antimicrobial and antibiofilm activity, besides acting on the regulation of some virulence genes, being promising in the search for new alternatives of treatment for MRSA infections.

Keywords: antimicrobial; biofilm; citral; *Staphylococcus aureus*.

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