

IN VITRO SYNERGISTIC EFFECT OF CITRAL IN COMBINATION WITH ANTIMICROBIAL AGENTS AGAINST MRSA STRAINS

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Resum:

Staphylococcus aureus is an important pathogen both in community acquired and nosocomial infections and the etiological agent of infections of many different tissues and organs. This microorganism has successfully evolved numerous strategies for resisting the action of antimicrobial agents. The multidrug resistant *Staphylococcus aureus* strains (MRSA) pose serious problems to hospitalized patients and their care providers. These strains have high resistance to several antimicrobial agents and, besides they have virulence factors that allow them to survive in many human systems, animals and food products. In the community, most MRSA infections are skin infections. In nosocomial environment, MRSA strains cause bacteraemia, pneumonia and surgical site infections. Facing this reality and the restricted therapy, the search for new, less toxic and more active molecules are object of several researches. Monoterpenes are secondary metabolites that have different properties, among them the antimicrobial activity. The aim of this study was to determine the antimicrobial activity of citral and linalool, and the interactions between citral and five antimicrobial agents (penicillin, oxacillin, clarithromycin, ciprofloxacin and gentamicin) against MRSA strains. Thereby, the determination of minimum inhibitory concentration (MIC) and bactericidal (MBC) was performed by broth microdilution method. The study of the interaction by checkerboard method and kinetic bactericidal by time-kill curves. The results of the interaction were expressed by calculating the fractional inhibitory concentration index (FICI). When compared to linalool, citral showed a superiority in antistaphylococcal activity. The combination of citral with antimicrobial agents resulted in partial synergism or indifferent effect. A total synergism was observed with the combination between citral/gentamicin with FICI values ranging from 0.375 to 0.5. This combination was able to decrease the number of viable cells in $\geq 2\log_{10}$ CFU/mL. This study shows that, in general citral associated with beta lactams, fluoroquinolones, aminoglycosides and macrolides act synergistically inhibit MRSA strains.

Key-words: MRSA; citral; synergism; checkerboard; bactericidal kinetics.

Promotion Agencies: CAPES, CNPq.