Farnesol as a prospective antimicrobial agent against *Staphylococcus epidermidis*

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Objectives: *Staphylococcus epidermidis* is now among the most important pathogenic agents responsible for bloodstream nosocomial infections and for biofilm formation on indwelling medical devices. Its increasing resistance to common antibiotics is a challenge for the development of new antimicrobial agents. Accordingly, the goal of this study was to evaluate the effect of farnesol, a natural sesquiterpenoid, on *Staphylococcus epidermidis* biofilm cells and compare this one with the effect of vancomycin, one of the most frequently used antibiotics to treat resistant nosocomial infections. Another aim of this work was to determine if subjecting *S. epidermidis* cells to farnesol they acquire resistance.

Methods: A 24 h kinetic study was performed using vancomycin at the peak serum concentration (40mg/L) and farnesol at concentrations of 30, 100, 200 and 300 microM. The growth inhibition effect of farnesol and vancomycin on biofilm cells of *S. epidermidis* was assessed by XTT (the reduction of this tetrazolium salt is a measure of cellular activity and is easily assessed by colorimetry) and Crystal Violet, which measures total biomass of biofilm. The biofilm cells were analysed by confocal laser scanning microscopy after being stained with Live/Dead. Resistance to farnesol and vancomycin was tested growing *S. epidermidis* planktonic cells in sub-inhibitory concentrations of farnesol and vancomycin and then subjecting these cells to inhibitory concentrations of both antimicrobial agents during 24 hours. After that, cellular activity was assessed by XTT. This was repeated for 5 consecutive

days.

Results: Both tested agents act at the cell wall level, vancomycin inhibits the biosynthesis of bacterial cell wall, while farnesol is considered to disrupt the normal barrier function of the cell membrane. Interestingly, farnesol at a concentration higher than 200 microM displayed the same or higher effectiveness of vancomycin at peak serum concentration. In fact, the response of the strains tested was very similar for both farnesol (>200 microM) and vancomycin. Regarding cells resistance to farnesol, the results point out to a slight increase of tolerance but not to an acquired resistance, because the percentage of inhibition was steady along the time.

Conclusions: Overall, the results indicate a potential antibacterial effect of farnesol against *S. epidermidis*, and therefore the possible action of this molecule on the prevention of *S. epidermidis* related infections.