Components of essential oils - A promise land to combat methicillin-resistant *Staphylococcus aureus* related diabetic foot wound infections

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Abstract

Diabetic foot ulcers (DFUs) are a complication that often arises in diabetic patients. Treatment of DFUs commonly relies on antibiotics. However, these ulcers are frequently colonized by antibiotic-resistant strains, such as methicillin-resistant *Staphylococcus aureus* (MRSA). Consequently, administering higher concentrations of antibiotics would most likely aggravate the ongoing problem of antimicrobial resistance and lead to cytotoxic effects in patients. Therefore, new alternatives to antibiotics are required. Thus, this work evaluated the role of selected sesquiterpenoids (farnesol, α-bisabolol and nerolidol) in the potentiation of the antimicrobial effect of commercial antibiotics (oxacillin and methicillin).

First, it was evaluated the minimum inhibitory and bactericidal concentrations (MIC and MBC) of the molecules against a MRSA clinical isolate from a diabetic foot wound, and their potentiation effect on oxacillin and methicillin, through the disc diffusion method. Their ability to eradicate pre-established biofilms of the same isolate was also evaluated in terms of biofilm mass removal (% BMR), biofilm metabolic activity reduction (% BAR) and decrease in the culturability of biofilm cells (log CFU/mL reduction).

Results indicate that farnesol was able to restore the effects of both methicillin and oxacillin. Biofilm experiments show that sesquiterpenoids by themselves have a greater effect than the antibiotics. From the perspective of antibiotics, 5 out of 6 combinations led to an increase in the value of % BMR, whereas 4 out of 6 were related to a higher reduction in biofilm metabolic activity. Furthermore, all combinations showed a significant reduction in the values of log CFU/mL. Overall, the combinations between antibiotics and sesquiterpenoids led to an increase in the antimicrobial effect of antibiotics, thus demonstrating the great potential of phytochemicals combined with antibiotics to combat multi-drug resistance wound infections.