TITLE: ANTIBACTERIAL AND MEMBRANE DISRUPTOR ACTIVITIES OF HYDROXYCHALCONES

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ABSTRACT

Numerous reasons justify the need for new antibacterial agents, such as infectious diseases are the second cause of death in the world, high rates of microbial resistance and the need for prototypes that act by different mechanisms of action in comparison to conventional drugs. Chalcones are natural products from plants that have broad pharmacological interest. Hydroxychalcones are active against Gram-positive and Gram-negative species, including *Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas aeruginosa*. This study aimed the evaluation of the antibacterial activity of a chalcone and six hydroxychalcones against *B. subtilis* (strain 168), *S. aureus* (ATCC 25923) and *P. aeruginosa* (ATCC 27853). First of all, the compounds had the antibacterial activity evaluated against the three strains at 100 μg/mL by microdilution broth method. Hydroxychalcones **3**–**6** had a percentage of bacterial growth inhibition above than 80% against *B. subtilis* and *S. aureus* and, except for compound **4**, percentage of bacterial growth inhibition above than 60% against *P. aeruginosa*. The minimum inhibitory concentration (MIC) and minimum bacterial concentration (MBC) were determined for the compounds **3**, **5** and **6** against *B. subtilis*, *S. aureus* and *P. aeruginosa* and for the compound **4** against *B. subtilis* and *S. aureus*. Hydroxychalcone **5** was the most potent against *S. aureus* and *B. subtilis*, demonstrating MIC_{50} values of 7.7 and 17.6 μg/mL, respectively. Thus, the hydroxylated chalcone **5** was submitted to septum fluorescence microscopy, which aimed to observe changes related to the formation of the divisional septum of *B. subtilis*, and to fluorescence microscopy with propidium iodide (PI), which aimed to blush cells of *B. subtilis* of red whose membrane was damaged. In septum fluorescence microscopy, compound **5** didn't affect the integrity of the septum at MIC_{50} value, but it was able to act on the septum of cell division after 15 minutes at MIC_{90} value. In fluorescence microscopy with PI, compound **5**, after 90 minutes at MIC_{50} value, caused damage to the membrane in 58.3% of the cells. In relation to the MIC_{90} value, hydroxychalcone **5**, after 30 minutes, promoted lesion of the membrane in 83.3% of the cells. The microscopy experiments suggested the primary action mechanism of compound **5** was membrane, because, at the MIC_{50} value, it was already possible to observe cell death due to membrane damage and no disturbance in the formation of septum of cell division.

Keywords: hydroxychalcone, antibacterial, microscopy, membrane disruptor

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