TITLE: EVALUATION OF THE *in vitro* ANTIBACTERIAL ACTIVITY OF PHENYLPROPANOID DERIVATIVES AGAINST BACTERIA OF THE ESKAPE GROUP

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ABSTRACT:
Multiresistant bacteria are a concern because they are frequently found in hospital environments, increasing mortality rates, costs and extent of hospital stay. The bacteria of the ESKAPE group are among the pathogens that cause nosocomial infections and they often exhibit resistance to most antimicrobials available in the clinic. Considering the need to discover new antimicrobials, the aim of this study was to evaluate the *in vitro* antibacterial activity of 30 synthetic phenylpropanoid derivatives related to eugenol against the following bacteria of the ESKAPE group: *Enterococcus faecalis* (ATCC 51299), *Staphylococcus aureus* (ATCC 29213), *Klebsiella pneumoniae* (ATCC 43816), *Acinetobacter baumannii* (ATCC 19606), *Pseudomonas aeruginosa* (ATCC 15442) and *Enterobacter cloacae* (ATCC 23355). The compounds, named DTC 01 to 30, were submitted to the broth microdilution method for determination of minimum inhibitory concentration (MIC) and minimum bacterial concentration (CBM), as described by the Clinical and Laboratory Standards Institute (CLSI). Compounds were tested at concentrations of 125 to 0.24 µg/mL and the following controls were used: negative (DMSO, used in compound dilution), positive (gentamicin for Gram-negative bacteria and amoxicillin for Gram-positive bacteria), growth (Mueller Hinton broth with inoculum), medium sterility (Mueller Hinton broth) and white sample (Mueller Hinton broth with compound). Although there are reports in the literature of antioxidant, analgesic and antimicrobial activity of phenylpropanoids, none of the evaluated compounds showed antibacterial activity at the concentrations tested. The positive controls used, as well as other controls, showed results as expected with MIC of 15.63 µg/mL against *A. baumannii*, 0.49 µg/mL against *P. aeruginosa* and *E. faecalis*, 0.24 µg/mL against *E. cloacae* and *K. pneumoniae* and 0.12 µg/mL against *S. aureus*. The CBM was determined only for the antibiotics used as control and ranged from 0.49 to 62.5 µg/mL. Modifications in the structure of molecules and insertion of new functional groups can influence the activity of synthetic compounds and frequently lead to negative results. The findings with this study, however, may orientate which structural features do not enhance antibacterial potential when searching for new drug candidates for the treatment of bacterial infections.

Keywords: ESKAPE, eugenol, phenylpropanoid derivatives, resistant bacteria

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