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Antibacterial and Cytotoxicity Activity of Cinchona Alkaloids

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Abstract : In an attempt to identify a new class of antimicrobial agents, the antimicrobial potential of Cinchona alkaloid derivatives was evaluated. The bark of the Cinchona trees is the source of a variety of alkaloids, among which the best known are quinine, quinidine, cinchonine and cinchonidine. They are very useful as organocatalysts in stereoselective synthesis. On the other hand, quinine is traditionally used in the treatment of malaria. Furthermore, Cinchona alkaloids possess various analgesic, anti-inflammatory and anti–arrhythmic properties as well. In this work we present the synthesis of twenty quaternary derivatives of pseudo−enantiomeric Cinchona alkaloid derivatives to evaluate their antibacterial activity. Quaternization of quinuclidine moiety was carried out with groups diverse in their size. The structures of compounds were systematically modified to obtain drug-like properties with proper physical and chemical properties and avoiding toxophore. All compounds were prepared in good yields and were characterized by standard analytical spectroscopy methods (1D and 2D NMR, IR, MS). The antibacterial activities of all compounds were evaluated against series of recent clinical isolates of antibiotic susceptible Gram-positive and resistant Gram-negative pathogens by determining their zone of inhibition and minimum inhibitory concentrations. All compounds showed good to strong broad-spectrum activity, equivalent or better in comparison with standard antibiotics used. Furthermore, seven compounds exhibited significant antibacterial efficiency against Gram-negative isolates. To visualize the results, principal component analysis was used as an additional classification tool. Cytotoxicity of compounds with different cell lines in human cell culture was determined. Based on these results, substituted quaternary Cinchona scaffold can be considered as promising new class of antimicrobials and further investigations should be performed. Supported by Croatian Science Foundation, Project No 3775 ADESIRE.

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