Antibiotic potential of some synthesized derivatives of C-9154 antibiotic

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Abstract

Structural modification of the C-9154 antibiotic in an attempt to simultaneously improve its activity and lower its toxicity led to the synthesis of an analogue of the C-9154 antibiotic and six derivatives of this analogue. The significant reduction of the polarity of the synthesized analogue in the derivatives to increase permeability across cell membranes was achieved by conversion of the highly polar carboxylic group to the nonpolar ester functional groups. The compounds were synthesized by condensation of 4-nitroaniline with maleic anhydride and then conversion of the terminal carboxylic acid functional group to an ester functional group using a thionyl chloride-mediated esterification. The in vitro biological activity using gram positive bacteria (MRSA, S. pyogenes, B. subtilis, and C. ulcerans), gram negative bacteria (E. coli, P. mirabilis, P. aeruginosa, S. typhii, S. dysenteriae, and K. pneumonia and some fungi (C. albicans, A. nigre and T. rubrum), showed that the derivatives were more active than their respective analogue and significantly better than the standard antibiotics (Sparfloxacin and Fluconazole) used for comparison, establishing their potential or use as antibiotics. The derivatives exhibited activity at concentrations as low as 0.625µg/mL while the analogue was active at 2.5µg/mL. These values were higher than results obtained for the standard drugs which showed activity at concentrations of 5 µg/mL. The derivatives however did not show activity against A. nigre whereas the analogue was active against it.

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