Original Article

The Journal of Antibiotics **70**, 832-844 (July 2017) | doi:10.1038/ja.2017.55

Synthesis and biological evaluation of indole core-based derivatives with potent antibacterial activity against resistant bacterial pathogens

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The emergence of drug resistance in bacterial pathogens is a growing clinical problem that poses difficult challenges in patient management. To exacerbate this problem, there is currently a serious lack of antibacterial agents that are designed to target extremely drug-resistant bacterial strains. Here we describe the design, synthesis and antibacterial testing of a series of 40 novel indole core derivatives, which are predicated by molecular modeling to be potential glycosyltransferase inhibitors. Twenty of these derivatives were found to show in vitro inhibition of Gram-positive bacteria, including methicillin-resistant Staphylococcus aureus. Four of these strains showed additional activity against Gram-negative bacteria, including extended-spectrum beta-lactamase producing Enterobacteriaceae, imipenem-resistant Klebsiella pneumoniae and multidrug-resistant Acinetobacter baumanii, and against Mycobacterium tuberculosis H37Ra. These four compounds are candidates for developing into broad-spectrum anti-infective agents.

The Journal of Antibiotics ISSN 0021-8820 EISSN 1881-1469