

TITLE: PROMISING BACTERIOSTATIC AND BACTERICIDAL ACTIVITY OF ALKALOIDS DERIVED FROM *Theonella* sp. AGAINST *Klebsiella pneumoniae*

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ABSTRACT:

Among infectious diseases, pneumonia is reported as one of the leading causes of hospital admissions and nosocomial deaths worldwide. One of the factors responsible for this situation, making it even more alarming is the increasingly rapid appearance of antibiotic resistant bacteria available in clinical practice, mainly Gram-negative bacteria, among them *Klebsiella pneumoniae*. One potential approach to overcoming the problem of resistance is the discovery of innovative antimicrobial agents with mechanisms of action different from the usual drugs. Fifteen 3-alkylpyridine alkaloids derived from the marine sponge *Theonella* sp., had their antibacterial activity evaluated against two strains of *K. pneumoniae*: ATCC 43816 and a clinical isolate. The minimum inhibitory concentration (MIC) was determined according to Clinical and Laboratory Standards Institute (CLSI), while the minimum bactericidal concentration (MBC) was determined from the transfer of 50 μ L of the MIC to a new microplate containing 150 μ L of Mueller Hinton Broth in the wells. The plate was incubated at 35°C for 48h and MBC was defined as the lowest concentration of the tested agent capable of killing the bacterium and, consequently, preventing visible growth. Compounds and gentamicin, used as a positive control, were tested at concentrations ranging from 125 to 0.24 μ g/mL. Two of the fifteen compounds evaluated presented antibacterial activity, with MIC of 31.25 μ g/mL against the reference strain, and 62.50 μ g/mL against the clinical isolate. NQBio-002 showed MBC in the same MIC value, whereas NQBio-003 showed bactericidal activity at 125 μ g/mL for both strains. The MIC and MBC for gentamicin were both 0.49 μ g/mL for the reference strain, and 0.49 μ g/mL and 0.98 μ g/mL, respectively, for the clinical isolate. It is believed that the antibacterial activity found is due to presence of a quaternary ammonium grouping in the structure of these molecules and new tests will be necessary for confirmation of the pharmacophore group and elucidation of the mechanism of action.

Keywords: alkaloids, antibacterial, broth microdilution, *Klebsiella pneumoniae*

Development Agency: CAPES, CNPq, FAPEMIG, UFSJ.