Evaluation of the antibacterial activity of synthetic compounds against KPC-producing Klebsiella pneumoniae

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Antimicrobial resistance is one of the major global public health challenges of the 21st century, compromising therapeutic efficacy and increasing the morbidity and mortality associated with bacterial infections. Among clinically relevant pathogens, carbapenem-resistant *Klebsiella pneumoniae* is included in the critical priority group of the World Health Organization due to its rapid dissemination and the scarcity of effective therapeutic options. In this scenario, medicinal chemistry represents an important strategy for the discovery of new molecules with antibacterial potential. Therefore, this study investigated the antibacterial activity of seven synthetic compounds (FN-8, RIF-03, RIF-05, RIF-18, BR010660, BR010496, and BR010349) against two reference strains and four human clinical isolates of KPC-producing *K. pneumoniae*. Antibacterial activity was evaluated by determining the minimum inhibitory concentration (MIC) using the broth microdilution method, according to the Clinical and Laboratory Standards Institute (CLSI), followed by minimum bactericidal concentration (MBC) determination and classification of the antibacterial effect by subculture. Overall, the investigated compounds showed limited activity, with MIC values ranging from 64 to 128 µg/mL. Among the tested molecules, FN-8 was the most promising, demonstrating activity against five of the six strains evaluated. For *K. pneumoniae* (ATCC 700603), the MIC was 64 µg/mL, whereas for clinical isolates 4752925, 4757071, 4741321, and 4657000 the MIC was 128 µg/mL, with confirmed bactericidal effect in all cases. RIF-05 was active only against the clinical isolates 4752925 and 4757071, with MIC equal to 128 µg/mL and bacteriostatic effect in both cases. In contrast, RIF-03, RIF-18, BR010660, BR010496, and BR010349 showed no antibacterial activity within the tested concentration range, with MIC values > 128 µg/mL. Taken together, the findings demonstrate the modest antibacterial activity of FN-8 against KPC-producing *K. pneumoniae* and highlight the challenge of developing new active compounds against this multidrug-resistant pathogen. Nevertheless, FN-8 may represent a relevant lead structure for future molecular optimization. Further studies involving structural modifications, synergism combinations with conventional antimicrobials, mechanistic investigation, toxicity assays, and validation in biological models are warranted to explore its therapeutic potential.

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