Promising antibacterial potential of synthetic peptides against KPC-producing Klebsiella pneumoniae

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Carbapenem-resistant *Klebsiella pneumoniae* (CR-Kp) is listed by the World Health Organization as a critical priority bacterial pathogen, representing a major global health threat due to high morbidity, mortality, and the scarcity of effective therapeutic options. In this context, antimicrobial peptides have emerged as promising alternatives owing to their broad-spectrum activity and reduced susceptibility to classical resistance mechanisms. This study evaluated the antibacterial activity of seven synthetic peptides against two reference strains and four clinical isolates of KPC-producing *K. pneumoniae*. Antibacterial activity was determined by minimum inhibitory concentration (MIC) using broth microdilution, followed by minimum bactericidal concentration (MBC) assessment and classification of the antibacterial effect by subculture. Overall, 57% (4/7) of the tested peptides exhibited antibacterial activity within the evaluated concentration range, showing MIC values between 8 and 128 µg/mL. Among them, TgPEP9 was the most active peptide, displaying inhibition against all tested strains, with MIC and MBC ranging from 8 to 16 µg/mL and a bactericidal effect at 8 µg/mL in four of six strains. BP100 also showed relevant activity, with MIC values ranging from 8 to 32 µg/mL and MBC values from 16 to 32 µg/mL, indicating consistent performance against clinical strains. TgPEP10 and CAAA-BP100 exhibited moderate activity, with MIC ranges of 32 to 128 µg/mL and 32 to 64 µg/mL, respectively. In contrast, TgPEP1, TgPEP2, and H1,H2,H5,H6,H9-BP100 were inactive under the tested conditions, with MIC values exceeding 128 µg/mL. Collectively, the data identify TgPEP9 and BP100 as the most promising candidates, showing consistent bactericidal activity against multidrug-resistant KPC-producing *K. pneumoniae*. These findings support the potential of synthetic peptides as alternative therapeutic strategies against KPC-producing *K. pneumoniae* infections. However, further studies are required to elucidate mechanisms of action, improve stability, and evaluate cytotoxicity and *in vivo* efficacy.

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