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Synergism of cationic antimicrobial peptide WLBU2 with antibacterial agents against biofilms of multi-drug resistant Acinetobacter baumannii and Klebsiella pneumoniae

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Abstract: Purpose: The activity of the cationic antimicrobial peptide WLBU2 was evaluated against planktonic cells and biofilms of multi-drug resistant (MDR) Acinetobacter baumannii and Klebsiella pneumoniae, alone and in combination with classical antimicrobial agents. Methods: Control American type culture collection (ATCC) strains and MDR clinical isolates of A. baumannii and K. pneumoniae were utilized. The minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) of WLBU2 alone and in combination with antimicrobials were determined by classical methods. The Calgary biofilm device was used to determine the minimum biofilm eradication concentration (MBEC). The MTT assay was used to determine cytotoxicity of agents on eukaryotic cells. The electrophoretic mobility shift assay was used to evaluate ability of WLBU2 to bind bacterial DNA. Results: The WLBU2 MIC and MBC values were identical indicating bactericidal activity. The MIC/MBC values ranged from 1.5625-12.5 ?M. At these concentrations, Vero cells and human skin fibroblasts were viable. The MBEC of WLBU2 ranged from 25-200 ?M. A significant loss of eukaryotic cell viability was observed at the MBEC range. The combination of sub-inhibitory concentrations of WLBU2 with amoxicillin-clavulanate or ciprofloxacin for K. pneumoniae, and with tobramycin or imipenem for A. baumannii, demonstrated synergism, leading to a significant decrease in MIC and MBEC values for some isolates and ATCC strains. However, all combinations were associated with considerable loss in eukaryotic cells? viability. WLBU2 did not demonstrate ability to bind bacterial plasmid DNA. Conclusion: WLBU2 in combination with antimicrobials holds promise in eradication of MDR pathogens.