



GLOBAL MEDICAL DISCOVERY



INVESTIGATION OF THE ANTIBACTERIAL ACTIVITY OF A SHORT CATIONIC PEPTIDE AGAINST MULTIDRUG-RESISTANT *KLEBSIELLA PNEUMONIAE* AND *SALMONELLA TYPHIMURIUM* STRAINS AND ITS CYTOTOXICITY ON EUKARYOTIC CELLS.

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Abstract

With the growing microbial resistance to conventional antimicrobial agents, the development of novel and alternative therapeutic strategies are vital. During recent years novel peptide antibiotics with broad spectrum activity against many Gram-positive and Gram-negative bacteria have been developed. In this study, antibacterial activity of CM11 peptide (WKLFKKILKVL-NH₂), a short cecropin-melittin hybrid peptide, is evaluated against antibiotic-resistant strains of *Klebsiella pneumoniae* and *Salmonella typhimurium* as two important pathogenic bacteria. To appraise the antibacterial activity, minimal inhibitory concentration (MIC), minimal bactericidal concentration (MBC) and bactericidal killing assay were utilized with different concentrations (2-128 mg/L) of peptide. To evaluate cytotoxic effect of peptide, viability of RAJI, HeLa, SP2/O, CHO, LNCAP cell lines and primary murine macrophage cells were also investigated with MTT assay in different concentrations (3-24 and 0.5-16 mg/L, respectively). MICs of *K. pneumoniae* and *S. typhimurium* isolates were in range of 8-16 and 4-16 mg/L, respectively. In bactericidal killing assay no colonies were observed at 2X MIC for *K. pneumoniae* and *S. typhimurium* isolates after 80-90 min, respectively. Despite the fact that CM11 reveals no significant cytotoxicity on RAJI, HeLa, SP2/O, and CHO cell lines beneath 6 mg/L at first 24 and 48 h, the viability of LNCAP cells are about 50 % at 3 mg/L, which indicates strong cytotoxicity of the peptide. In addition, macrophage toxicity by MTT assay showed that LD₅₀ of CM11 peptide is 12 µM (16 mg/L) after 48 h while in this concentration after 24 h macrophage viability was about 70 %.

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Additional Information

This research was based on our previous study that for the first time we evaluated antibacterial activity of CM11 and CM15 peptides against antibiotic resistance isolates of five pathogenic bacteria including *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Vibrio cholerae*, *Acinetobacter baumannii*, and *Escherichia coli* which is published in the journal of *probiotics and antimicrobial proteins* (June 2012). Our studies demonstrated the effective antibacterial activity of these peptides against five pathogenic bacteria

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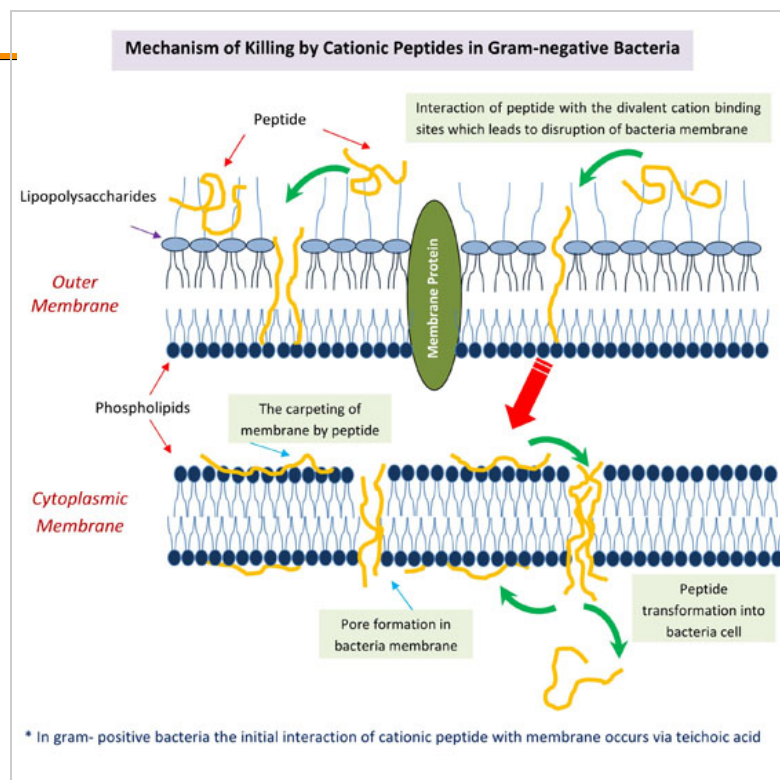
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with the same ranges of inhibitory values (MIC 8 mg/L and MBC 32 mg/L) in early 24 h but after 48 h the MIC and MBC remained constant for CM11 peptide, while for CM15 peptide these parameters were not stable. Results highlighted bacteriostatic potential of CM11 peptide even after 48 h with a remarkable stability in environment of the experiments. So based on these results, we investigated antibacterial activity of CM11 peptide against multi-drug resistant *Klebsiella pneumoniae* and *Salmonella typhimurium* strains.



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