In-silico Analysis of Interaction CM11 and CM15 Hybrid Antimicrobial Peptides with Bacterial Cell Membrane

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Background & Objectives: In recent decades antimicrobial peptides have gained a lot of interest due to their potential use as a new generation of antibiotics. These types of amphipathic cationic peptide target to bacterial cell membrane via pore formation. These peptides could destroy the chemical gradients of bacterial cell membrane and kill bacteria. It is important to mention that the first step of pore formation is interaction peptides to membrane surface of bacteria. In this study we applied two cecropin–melittin hybrid peptides, CM11 (WKLFKKILKVL-NH2) and CM15 (KWKLFKKIGAVLKVL-NH2) to characterize peptide-bilayer interactions.

Methods: Two cecropin–melittin hybrid peptides, CM11 and CM15, were interacted with zwitterionic membrane of dipalmitoylphosphatidylcholine (DPPC) bilayer using molecular dynamics simulation. At the first the PEP-FOLD software (www.bioserv.rpbs.univ-paris-diderot.fr/PEP-FOLD) were used to predict structure of CM11 and used SPDBV software to depicte Ramchandran plot. Finally HEX5 software was used for docking peptide via DPPC membrane (http://moose.bio.ucalgary.ca).

Results: The in-silico analysis was designed based on location and orientation of the bilayer peptide with regard to hydrogen-bond-formation patterns and electrostatics interactions. The data showed that amino acids are important in interaction with membrane bilayer. PEP-FOLD software predicted alpha-helix structure for CM11. Docking analysis by HEX5 software showed that CM11 interacted with DPPC bilayer via Trp-1, Lys-2, Lys-5, Lys-6, Leu-8, Lys-9 amino acids and CM15 interacted with DPPC bilayer via Lys-3, Lys-6, Lys-7, Ala-10, Lys-13, Val-14 amino acids. The total energy for CM11 and DPPC interaction was -450.75 and this energy for CM15 was -442.49.

Conclusion: Compression of total energy interaction between these peptides and DPPC showed CM11 with lower total energy could attach to bilayer better than CM15. In attention to this result we can predict that antimicrobial effect of CM11 is more than CM15. Also this study showed among amino acids which interact to DPPC, lysine is most common in the both peptides. If we designed peptide with more lysine amino acids which located at the side of helix, this peptide will interacted stronger with membrane and enhance antimicrobial effectiveness.

Keywords: CM11; CM15; Antimicrobial Peptide; DPPC