Theoretical investigation of antimicrobial property of native histatin-3 and its four mutants via molecular Dynamics simulation method

Zahra Tavakoli[1], Karim Mahnam*[2], Behnaz Saffar[1]

1 . Faculty of Science, Department of Genetics, Shahrekord University, Shahrekord, Iran

2. Biology Department, Faculty of Sciences, Shahrekord University, Shahrekord, Iran

* Corresponding Author Karim Mahnam**:** karimmahnam93@gmail.com

Abstract: Cationic antimicrobial peptides are a class of small positively charged, broad-spectrum peptides that are known as potential next-generation antibiotics [1]. Histatin-3 (HTN3) cationic antimicrobial peptide is a 32-amino acid rich in histidine, secreted by salivary glands [2]. In this study, in order to investigate the antimicrobial activity of HTN3, its native and Asp1Ala, Gly9Trp, Phe14Ile and Asp1Ala+Gly9Trp mutants of this peptide in the presence of sodium dodecyl sulfate (SDS) micelle were subjected to molecular dynamics simulation. The structures were simulated once with SDS micelle and once without it. Simulations were performed by the GROMACS 5 under Amber99 force field and the TIP4P water model for 50 ns. Also binding free energy calculations were done by g_mmpbsa software. Analyses were carried out during the last 30 nanoseconds. The results of potential energy, RMSD, temperature, Rg, and SASA indicated that the systems reached to equilibrium. According to the results of MM/PBSA, the best structure, is Asp1Ala+Gly9Trp mutation because it has the least binding free energy to SDS micelle. Therefore it can be concluded that this peptide has the most antimicrobial activity rather than native and other mutated peptides. Also, the difference of amount of SASA (ΔSASA) is high in the free state and in the presence of micelle in Asp1Ala+Gly9Trp, which indicates that this peptide has a stronger binding to the SDS micelle.

Keywords: Antimicrobial peptides; HTN3; SDS micelle; MM/PBSA; molecular dynamics simulation

References

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