# Effect of Acetylation of Substance P on the Binding to NK1 Receptor by Molecular Dynamics Simulation

Samira Davoudmanesh [a*], Jafar Mohammadian Mosaabadi [b]
[a,b]Department of Biochemistry-Biophysics, Faculty of Bioscience and Biotechnology, Malek Ashtar University of Technology, Tehran, Iran
[*]Corresponding author.
samiradavoodmanesh@yahoo.com

**Abstract:** The main object of this study is modification of Lysine amino acid of substance P (SP) by acetyl group. Conformational dynamics of native and modified peptide and their complex with the NK1 receptor is considered by MD simulations. It is obtained that acetylation of SP causes stability in peptide structure, but decreases the tendency of modified SP to bind to the NK1 receptor and consequently decreases the stability of complex structures. RMSD of native SP (~0.33nm) is about twice larger than modified SP (~0.18 nm) while, RMSD for receptor in complex with native SP shows the value of ~0.3 nm, and for the receptor in complex with modified SP display ~0.35 nm, that showed high stability of acetylated SP and receptor in compare with native SP. Also such changes are observed in RMSF and secondary structure of complex. Binding free energy of native and acetylated SP with NK1 receptor also is compared; ΔGbind for binding of acetylated Substance P to the NK1 is -64.46 kJ mol-1 , while it is -264.52 kJ mol-1 for native Substance P to NK1. According to these results, acetylation of lysine decreases the binding affinity of modified SP to the NK1 receptor compared to native SP. In other words, acetylation SP form weak interactions with the NK1 receptor compared to native substance P,which can cause pathologic effects by increasing the amount of free acetylated substance p in plasma.

**Keywords:** Substance p; NK1 receptor; Acetylation; Acetyl; MD Simulation; Binding affinity.