Human apo-myoglobin structural stability in the presence of ligands: a molecular dynamics study

Joulia Alizadeh-Rahrovi[1,2], Azadeh Ebrahim-Habibi[1,2]

1.Biosensor Research Center, Endocrinology and Metabolism Molecular-Cellular Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran.

2.Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

A protein's structure defines its interactions with other molecules. Indeed structure integrity is of high importance for a protein proper function. Environmental factors affecting proteins structure may lead to conformational disorders by causing functional changes. Thus, it is important to investigate factors that influence structure stability of proteins, particularly the proteins which play crucial roles in biological systems. Myoglobin (Mb), a globular metalloprotein, is noteworthy due to its role in oxygen transport in muscle cells which occurs through its heme prosthetic group. Influence of substitution of some small molecules such as Nile red instead of heme in different environmental conditions has been studied previously [1, 2].

In the present study, the 3-D x-ray crystallographic structure of human Mb with the PDB code of 3RGK has been used after applying required modifications [3]. Using docking methods, small molecules structurally similar to Nile red were replaced in the heme binding site of Mb. The systems were set in a periodic box and SPC water model was selected as the solvent. Next, molecular dynamics simulation (MDS) at 500K was performed on the structures with the use of GROMACS and the GROMOS96 53a6 force field. Analysis of the trajectories was made and RMSD, hydrophilic and hydrophobic areas, secondary structure (SS) percentages, and energies were extracted for each protein-ligand complex. Finally, ligands with high overall rank were selected according to a decision matrix incorporating these parameters. Pharmacophore features of these ligands may be used to seek for other more potent compounds.

[1] E. Polverini, G. Cugini, F. Annoni, S. Abbruzzetti, C. Viappiani, T. Gensch, Biochemistry, **2006**,45, 5111-5121.
[2] M. Azami-Movahed, S. Shariatizi, M. Sabbaghian, A. Ghasemi, A. Ebrahim-Habibi, M. Nemat-Gorgani, Int J Biochem Cell Biol, **2013**, 45, 299–307.
[3] J. Alizadeh-Rahrovi, A. Shayesteh, A. Ebrahim-Habibi, J BiolPhys, **2015**, 41, 349–366.