Modelling of the structure-activity relationships between the cannabinoid Cb1 and Cb2 receptors and cannabinoid ligands

Fatima Sapundzhi[1], Tatyana Dzimbova[1,2], Nevena Pencheva[1], Peter Milanov[1,3]

[1] South-West University "Neofit Rilski", Blagoevgrad, Bulgaria
sapundzhi@swu.bg

[2] Institute of Molecular Biology, Bulgarian Academy of Sciences, Sofia, Bulgaria

[3] Institute of Mathematics and Informatics, Bulgarian Academy of Sciences, Sofia, Bulgaria

Keywords: cannabinoid CB1 and CB2 receptors, cannabinoid ligands, drug-receptor interactions, docking, QSAR, binding site.

The 3D models of the human cannabinoid receptor type 1 (CB1) and type 2 (CB2) were built by homology modeling. The models were developed by using multiple sequence alignment.

The prediction of the drug-receptor interactions and their corresponding binding free energy is a difficult problem in the structure-based drug design. Molecular docking approaches were used to propose the binding mode and underlying interactions as well as to provide an evaluation of ligand affinity. The cannabinoid system was studied by means of molecular docking techniques by using the 3D models of the CB1 and CB2 receptors and some known cannabinoid ligands. Once the final models were obtained, molecular docking simulations were performed by using GOLD 5.2 program to predict putative binding site and potential ligand-receptor interactions such as hydrophobic interactions, hydrogen-bonding, etc..

The obtained results could be used in further experiments in quantitative structure-activity relationship (QSAR) and a design of new potential and selective cannabinoid ligands.

Acknowledgements: This work is partially supported by the project of the Bulgarian National Science Fund, entitled: Bioinformatics research: protein folding, docking and prediction of biological activity, NSF I02/16, 12.12.14.