IN-SILICO STUDY OF THE INTERACTION OF LasR WITH LIGANDS

L. S. Hunanyan, H. V. Grabski*, S. G. Tiratsuyan
Russian-Armenian(Slavonic)University Yerevan, Armenia
*E-mail: johnwo1990@hotmail.com

In recent years, following the adoption of using various natural resources as harmless therapeutics compounds, plants widely known for the content of secondary metabolites such as flavonoids with antimicrobial activity, including quorum-sensing inhibition (QSI) [1], are very promising for anti-infective therapy. Well known flavonoids such as quercetin and morin exhibit antioxidant and anti-inflammatory activity, as well as attenuating the production of QS-controlled virulence factors in bacteria [2], such as adhesins. N-3-oxo-dodecanoyl homoserine lactone (3O-C12-HSL), one of the autoinducers in signaling network of the opportunistic pathogen *P. aeruginosa* may have a direct effect on the organism interacting with components of the immune system. The transcriptional regulator of *P. aeruginosa* LasR [3] functions in concert with 3O-C12-HSL to coordinate the expression of target genes. The aim of this work is to study the direct interaction of 3O-C12-HSL, quercetin and morin with LasR. A combination of machine learning [4], docking [5], molecular dynamic (MD) simulations [6] and homology modelling have been carried out to reveal the formation of complexes of these compounds with LasR. The structural stability and dynamics of complexes were validated through molecular dynamics simulation. For the first time it has been demonstrated the interaction of 3O-C12-HSL and morin with LasR in the loop region between the DNA binding domain (DBD) and ligand binding domain (LBD) [7], while quercetin does not interact with DBD. Preliminary results demonstrate that morin interacts with both the LBD and the DBD, mainly through A and C rings. The formation of complexes occurs through electrostatic interaction. Simulation results of root-square mean deviation (RMSD) and radius of gyration (Rg) values indicate the stability of the formed complexes. Binding of morin with the loop region may explain the high antibacterial activity compared with quercetin. Thus, the results of this study help to understand the QSI properties of flavonoids .

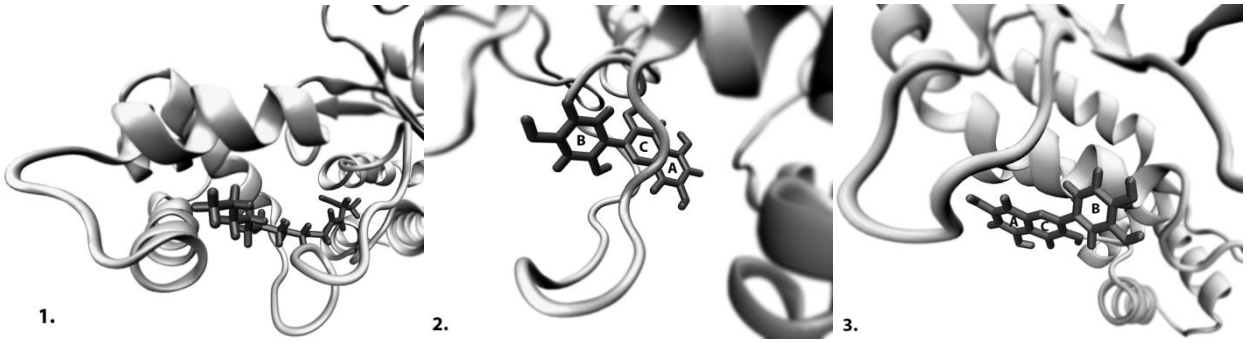

Figure 1. 3D structures of complexes of LasR with 1. HSL, 2. Morin 3. Quercetin

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