Секция «Биоинформатика»

In silico study of the interaction of morin with LasR ligand-binding domain by molecular modeling methods

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Flavonoids are widely distributed in the plant kingdom and known for their numerous roles in plant physiology. They exhibit a large spectrum of biological activities, such as anti-atherogenic,antioxidant, anticancer, anti-inflammatory and antimicrobial activity. Some of them including morin are also inhibitors of virulence of pathogenic bacteria by interfering with quorum sensing (QS) mechanisms and attenuating the production of virulence factors in bacteria, such as adhesins and sortases [1]. N-3-oxo-dodecanoyl homoserine lactone (3OC12-HSL) is one of the autoinducers in signaling network of the opportunistic pathogen Pseudomonas aeruginosa and activator of the transcriptional regulator LasR (R protein) [2].

The aim of this work was to study the direct interaction of morin with LasR ligand-binding domain (LBD) and the comparison with the 3OC12-HSL-LasR complex. The interactions of morin and 3OC12-HSL with LBD of LasR have been computationally investigated. Docking and molecular dynamic (MD) simulations have been carried out by Autodock Vina[3] and GROMACS software packages [4]. The formation of complexes of these compounds, its structural stability and dynamics were validated through molecular dynamics simulation.

The results show that morin interacts with LBD of LasR. The conformation of the complex bound to morin is different from that of the complex with 3OC12-HSL and it's visible in the RMSD profile (Fig. 1). The 3OC12-HSL-complex model is close to the x-ray experimental data. The energetic analysis of the model structures gives detailed insight into the interactions involved in the stabilization of the spatial parameters of the complex. Simulation results of root-square mean deviation (RMSD) indicate on the stability of the formed complexes (Fig.1). Binding of morin with LasR ligand-binding domain and the displacement of the alanine residue compared with the 3OC12-HSL-complex , that could inhibit the dimerization of the complex and may explain its antibacterial activity (Fig.2). Thus, the results of this study may shed light on the understanding of possible mechanisms of anti-QS action of morin.

Thus the anti-infective strategy based on natural products represents a new therapeutic approach in the biomedical field and ecologic alternatives to antibiotics with the advantage that bioactive compounds are not growth inhibitors and selection factors.

Источники и литература

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Слова благодарности

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Иллюстрации

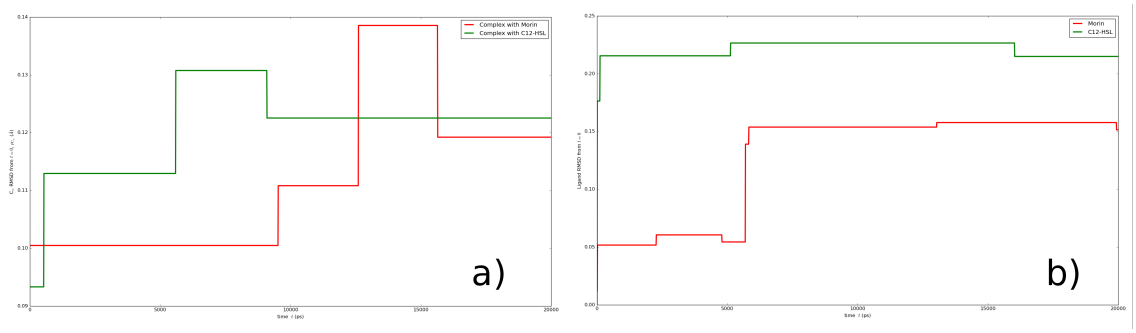

Рис. 1. RMSD profiles of simulated complexes. Green color line represents molecular complex with 3OC12-HSL while red color line represents the complex with morin. a) LasR LBD b) Ligands

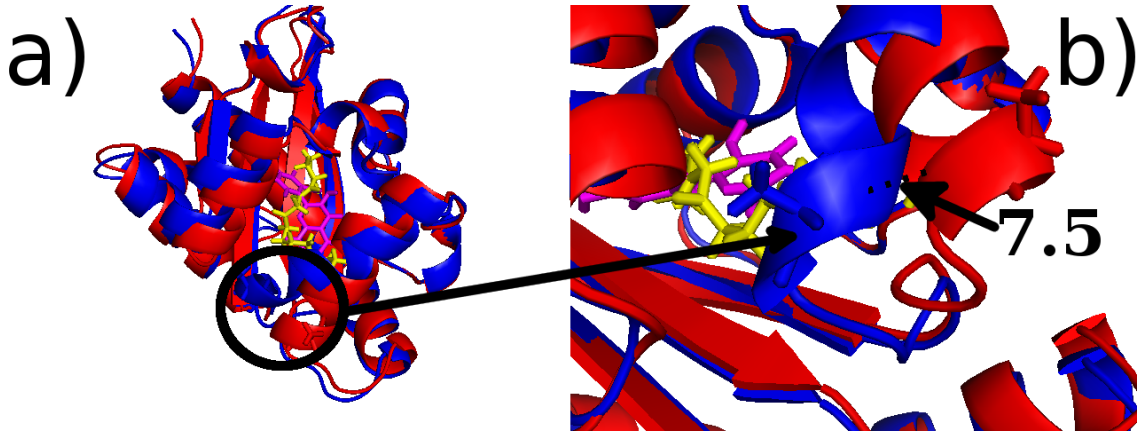

Рис. 2. 3D structures of complexes with LasR LBD. Blue and yellow colors represent molecular complex with 3OC12-HSL while red and magenta colors represent the complex with morin. a) overall complexes b) displacement of ALA 107 residue in LasR-morin complex.