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Molecular Modeling of the Interaction of Taxifolin with Quorum Sensing Regulator LasR of *Pseudomonas Aeruginosa*

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Pseudomonas aeruginosa is one of the most dangerous superbugs and is responsible for both acute and chronic infection. Current therapies are not effective because of biofilms that increase antibiotic resistance. Biofilm formation is regulated through a system called quorum sensing, and includes transcriptional regulators LasR and RhIR. These regulators are activated by their own natural autoinducers. Targeting quorum sensing is a promising strategy to combat bacterial pathogenicity. Flavonoids are very well known for their antimicrobial activity and inhibit *Pseudomonas aeruginosa* biofilm formation, but the mechanism of action is unknown. In the present study, we analyze the mode of interactions of LasR with taxifolin. We use a combination of molecular docking, molecular dynamics simulations to study the interaction of LasR with taxifolin. We show that taxifolin has two binding modes. One binding mode is the interaction with ligand-binding domain. The second mode is the interaction with the “bridge”, which is a cryptic site. Biochemical studies show hydroxyl group of ring A in flavonoids is necessary for inhibition. In our model the hydroxyl group ensures the formation of hydrogen bonds during the second binding mode. This study may offer insights on how taxifolin inhibits LasR and the quorum sensing circuitry.