TITLE: MOLECULAR DOCKING SCREENING OF PHENOLIC COMPOUNDS WITH LasR PROTEIN OF *Pseudomonas aeruginosa*

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ABSTRACT:
Pseudomonas aeruginosa is an opportunist pathogen that causes serious diseases in both plants and animals. The expression of many virulence genes is regulated by quorum sensing (QS) in this organism, which became the main model in bacterial anti-virulence strategy studies. A complex communication network is found in *P. aeruginosa*, consisting of four interconnected QS systems: *las, rhl, pqs* and *iqs*. The *las* QS system is activated by a signal molecule called *N*-(3-oxododecanoyl)-L-homoserine lactone (3-oxo-C12-HSL) produced by LasI synthase, which is recognized by the transcriptional regulator LasR, from the LuxR family, that directs the expression of various genes. Phenolic compounds have been shown to inhibit QS phenotypes, potentially via interference with LuxR-type QS proteins. The aim of this work was to perform molecular docking of seven LasR structures of *P. aeruginosa*, available in the Protein Data Bank (PDB ID: 2UV0 6D6A, 6D6L, 6D6O, 6D6P, 6MVN and 6MVM), with 80 phenolic compounds as well as with 14 acyl homoserine lactones (AHLs) and 7 furanones. The CLC Drug Discovery Workbench 4.0 software was used for molecular docking. *N*-(3-hydroxydodecanoyl)-DL-homoserine lactone and *N*-dodecanoyl-DL-homoserine lactone exhibited good ranking for the seven structures of LasR proteins and the best binding scores were -85.54 and -82.16 with 2UV0 structure. Among the analyzed phenolic compounds, demethoxycurcumin, curcumin, bisdemethoxycurcumin, capsaicin, dihydrocapsaicin, mangostin and secoisolariciresinol were prominent in all seven structures of LasR. These compounds belong to the classes curcuminoids, capasaicinoids, xanthone and lignan. The best binding scores were -95.77 for demethoxycurcumin with 2UV0, -92.89 for curcumin with 6D6A, -92.4 for mangostin with 6D6P and -90.5 for bisdemethoxycurcumin with 6MVN. These compounds had better binding scores than 4-bromo-5-(bromomethylene)-3-dodecyl-2(5H)-furanone, which was the furanone with the higher binding score. The molecular docking results suggest that phenolic compounds may be able to bind to LasR protein of *P. aeruginosa* better than known QS autoinducer and inhibitor molecules, suggesting their potential as QS inhibitors.

Keywords: inhibitors, quorum sensing, quorum quenching, autoinducer molecules.

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