TITLE: SELECTION OF PHENOLIC COMPOUNDS WITH POTENTIAL ANTI-QUORUM SENSING ACTIVITY BY MOLECULAR DOCKING WITH CviR PROTEIN OF *Chromobacterium violaceum*

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ABSTRACT:
Bacteria have a communication process that allows them to collectively modify behavior in response to changes in cell density, activating or repressing gene expression, in a mechanism called quorum sensing (QS). The phenotypes regulated by QS contribute to pathogenesis since they are related to the production of virulence factors such as toxins, proteases, biofilm formation, synthesis of antibiotics, motility, among others. *Chomobacterium violaceum* is a QS model bacterium in which the CviI-CviR system produces and responds to the signal molecule *N*-hexanoyl-homoserine lactone (C6-HSL), activating or inhibiting the transcription of virulence genes, mainly the purple pigment violacein which presents antimicrobial activity. Studies indicate that phenolic compounds may inhibit QS communication. This work aimed to evaluate by molecular docking the interaction of six structures of CviR proteins from *C. violaceum* ATCC 31532 and *C. violaceum* ATCC 12472, available in the Protein Data Bank (PDB ID: 3QP1, 3QP2, 3QP4, 3QP5, 3QP6, 3QP8) with 80 phenolic compounds, as well as 14 acyl homoserine lactones (AHLs) and 7 furanones. The CLC Drug Discovery Workbench 4.0 software was used for molecular docking. Among the evaluated AHLs, the best binding scores were with the CviR structure 3QP6, as follows: -87.18 for *N*-dodecanoyl-DL-homoserine lactone, -88.97 for *N*-(3-hydroxydodecanoyl)-DL-homoserine lactone, and -89.6 for *N*-(3-oxododecanoyl)-L-homoserine lactone. Demethoxycurcumin, bisdemethoxycurcumin, dihydrocapsaicin, matairesinol, capsaicin, curcumin and secoisolariciresinol were prominent in all six structures of CviR. These compounds are classified as flavonoids, curcuminoids, capasaicinoids, xanthones and lignans. The best binding scores were -85.33 for demethoxycurcumin and -83.36 for bisdemethoxycurcumin with 3QP6. These compounds had better binding scores than known QS inhibitor 4-bromo-5-(bromomethylene)-3-dodecyl-2(5H)-furanone which was the furanone with the higher observed binding score (-75.52). The molecular docking results suggest that phenolic compounds could be able to bind to CviR protein of *C. violaceum*, suggesting their potential as QS inhibitors. These results can direct studies for the identification of new compounds inhibiting QS regulated phenotypes.

Keywords: AHLs, curcumin, quorum quenching, autoinducer molecules.

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