Poster 6

Efficacy of selected phenolic acids in inhibiting the LasI/LasR and PQS quorum sensing pathways of *Pseudomonas aeruginosa*

Miguel M. Leitão ^{1,2,3}, Fernanda Borges ³, Manuel Simões ^{1,2,4} and Anabela Borges ^{1,2,4,*}

¹ LEPABE—Laboratory for Process Engineering, Environment, Biotechnology and Energy, Faculty of Engineering, University of Porto, Rua Dr. Roberto Frias, 4200-465 Porto, Portugal

² ALICE—Associate Laboratory for Innovation in Chemical Engineering, Faculty of Engineering, University of Porto, Rua Dr. Roberto Frias, s/n, 4200-465 Porto, Portugal

³ CIQUP—Department of Chemistry and Biochemistry, Faculty of Sciences, University of Porto, Porto, Portugal

⁴ DEQ—Department of Chemical Engineering, Faculty of Engineering, University of Porto, Rua Dr. Roberto Frias, s/n, 4200-465 Porto, Portugal

* Correspondence: apborges@fe.up.pt

Abstract

Background: Quorum sensing (QS) is a bacterial intercellular communication mechanism mediated by extracellular signalling molecules known as autoinducers [1]. LasI/LasR and pseudomonas quinolone signalling (PQS) are fundamental components of the QS system in Pseudomonas aeruginosa. These systems perform a crucial role in the regulation of gene expression in response to cell density, coordination of biofilm formation, and expression of virulence factors, as well as antimicrobial resistance [2]. Therefore, the use of QS inhibitors (QSI), especially those that interact with multiple QS systems, could be a promising strategy, not only because it can increase the efficacy of bacterial infection treatment, but also because it reduces the selective pressure for the development of resistance [2]. In particular, phenolic acids are a group of plant secondary metabolites (*i.e.* phytochemicals) that exhibit a broad spectrum of antibacterial activity and have excellent properties in modulating bacterial cell-cell communication [3]. Objective: In this study, the efficacy of ferulic acid and sinapic acid in disrupting the LasI/LasR and PQS-QS system of P. aeruginosa was investigated. Methods: The efficacy of phenolic acids (ferulic and sinapic acids) as QSI of P. aeruginosa was investigated using bioreporter strains (P. aeruginosa PA14wild type, PA14-R3, PAO1-wild type, and PAO1-CTX). For this purpose, the ability to inhibit the production of the autoinducers N-acyl-homoserine lactone (AHL) and PQS as well as the QS responses mediated by AHL were evaluated by a high-throughput QS inhibition screening system based on a co-cultivation assay. Results: Phenolic acids have the potential to inhibit the LasI/LasR and PQS systems by more than 85%, even at subinhibitory concentrations. In addition, reductions of 80% were observed in the production of AHL by the LasI/LasR system of P. aeruginosa. Conclusions: This study has shown that the phenolic acids tested are promising as inhibitors of LasI/LasR and PQS, allowing them to reduce the pathogenicity/virulence of P. aeruginosa.

Keywords: antibiofilm activity; biofilm infections; ferulic acid; sinapic acid; quorum sensing inhibition

Acknowledgments

This research was funded by national funds through FCT/MCTES (PIDDAC): LEPABE, UIDB/00511/2020 (DOI: 10.54499/UIDB/00511/2020) and UIDP/00511/2020 (DOI: 10.54499/UIDP/00511/2020) and ALiCE, LA/P/0045/2020 (DOI: 10.54499/LA/P/0045/2020). Miguel Leitão acknowledges an individual PhD fellowship (2021.07145.BD) from FCT.

References

- 1.Borges, A., et al., Furvina inhibits the 3-oxo-C12-HSL-based quorum sensing system of *Pseudomonas aeruginosa* and QS-dependent phenotypes. Biofouling, 2017. 33(2): p. 156-168.
- 2. Gonçalves, A.S., *et al.*, The action of phytochemicals in biofilm control. Natural Product Reports, 2023. 40(3): p. 595-627.
- 3.Borges, A., *et al.*, Evaluation of the effects of selected phytochemicals on quorum sensing inhibition and in vitro cytotoxicity. Biofouling, 2014. 30(2): p. 183-195.



In Scientific Letters, works are published under a CC-BY license (Creative Commons Attribution 4.0 International License at https://creativecommons.org/licenses/by/4.0/), the most open license available. The users can share (copy and redistribute the material in any medium or format) and adapt (remix, transform, and build upon the material for any purpose, even commercially), as long as they give appropriate credit, provide a link to the license, and indicate if changes were made (read the full text of the license terms and conditions of use at https://creativecommons.org/licenses/by/4.0/).