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Mosloflavone attenuates the quorum sensing controlled virulence phenotypes and biofilm formation in *Pseudomonas aeruginosa* PAO1: *In vitro*, *in vivo* and *in silico* approach

Sairengpuii Hnamte[a], Paramanantham Parasuraman[a], Sampathkumar Ranganathan[b], Dinakara Rao Ampasala[b], Dhanasekhar Reddy[c], Ranjith N. Kumavath[c], Kitlangki Suchiang[d], Saswat Kumar Mohanty[d], Siddhardha Busi[a,*]

[a] Department of Microbiology, School of Life Sciences, Pondicherry University, Puducherry, India
[b] Centre for Bioinformatics, School of Life Sciences, Pondicherry University, Puducherry, 605 014, India
[c] Department of Genomic Sciences, School of Biological Sciences, Central University of Kerala, Kasaragod, India
[d] Department of Biochemistry and Molecular Biology, School of Life Sciences, Pondicherry University, Puducherry, India

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ABSTRACT

Quorum sensing (QS) is the cell density dependent communication network which coordinates the production of pathogenic determinants in majority of pathogenic bacteria. *Pseudomonas aeruginosa* causes hospital-acquired infections by virtue of its well-defined QS network. As the QS regulatory network in *P. aeruginosa* regulates the virulence determinants and antibiotic resistance, attenuating the QS system seems to be influential in developing next-generation anti-infective agents. In the current study, the QS attenuation potential of a flavonoid, mosloflavone was investigated against *P. aeruginosa* virulence and biofilm formation. Mosloflavone inhibited the pyocyanin production, LasB elastase and chitinase by 59.52 ± 2.74, 35.90 ± 4.34 and 61.18 ± 5.52% respectively. The QS regulated biofilm formation and development was also reduced when supplemented with sub-MIC of mosloflavone. The gene expression studies of mosloflavone using RT-PCR depicted its ability to down-regulate the expression levels of QS regulated virulence genes such as *lasI* (60.64%), *lasR* (91.70%), *rhlI* (57.30%), *chiC* (90.20%), *rhlA* (47.87%), *rhlR* (21.55%), *lasB* (37.80%), *phzM* (42.40%), *toxA* (61.00%), *aprA* (58.4%), *exoS* (78.01%), *algD* (46.60%) and *pelA* (50.45%). The down-regulation of QS virulence phenotypes by mosloflavone could be attributed to its binding affinity with the QS regulatory proteins, LasR and RhlR by competitively inhibiting the binding of natural autoinducers as evidenced from simulation studies. Mosloflavone also exhibited promising potential in controlling bacterial infection in *Caenorhabditis elegans* model system, *in vivo*. The *anti*-biofilm and *anti*-QS potential of mosloflavone in the current study illustrated the candidature of mosloflavone as a promising biocide.

1. Introduction

Excessive and promiscuous administration of antibiotics has compel to the advancement of multidrug resistance bacteria worldwide [1]. One of the important mechanisms for establishing such resistance by pathogenic bacteria is the formation of highly recalcitrant biofilm formation. The majority of biofilm formation is coordinated by highly organized, species-specific and cell density based called as quorum sensing (QS) [2]. It produced signaling molecule known as auto-inducers, their detection by specific receptor proteins and up-regulation of virulence factors production [3,4]. *P. aeruginosa* causes severe chronic and pulmonary infections in the immunocompromised individuals by using the highly complex QS regulatory network [5] *P.aeruginosa* QS constitutes of two components i.e., Las and Rhl system which are dependent on acyl homoserine lactone (AHL) [6]. Both the las and rhl system are correlated and coordinated the expression of different virulence factors.

The QS regulatory network is generally associated with formation and development of biofilm matrix which ultimately led to the development of multidrug resistance by minimizing the susceptibility of bacterial cells to conventional antibiotics [7]. From ancient times, plant derived phytochemicals are regarded as effective therapeutic agents

* Corresponding author. Department of Microbiology, School of Life Science Pondicherry University, Puducherry, 605014, India.
E-mail address: siddhardha.busi@gmail.com (S. Busi).

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