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Editorial

Quorum Sensing Inhibitors: Noble Prospect Anti-Pathogenic Drugs for Future

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Received: June 03, 2022; **Published:** June 29, 2022

In the quest of getting breakthroughs for the problem of emerging drug resistance, scientists are engaged in intensive research to develop non-antibiotic agents to encounter mechanisms of drug resistance. One such prospect is detection of Quorum sensing (QS) inhibitor drugs which produce synergistic effects when combined with antimicrobial drugs. Quorum sensing in simple terms can be understood as intercellular communication within the bacterial population. This intracellular communication aids individual cells to sense alteration in the surrounding environment and modulate its gene expression and growth accordingly and simultaneously communicate it to other sister cells. This communication is mediated by production and detection of extracellular messenger molecules called Autoinducers. Autoinducers II mediated by LuxS protein are messengers which mediates interspecies communication. Accumulation of autoinducers molecules in close proximity to bacterial growth alter expression of genes which favors the survival and growth of bacteria. Gene expression controlled by quorum sensing includes secretion of virulence factors, biofilm production, sporulation, growth inhibition and competence. Control of a wide array of gene expression, especially virulence factor secretion and biofilm production makes quorum sensing inhibition a potential strategy to develop drugs which can reduce the risk of emergence of drug resistance. There are more than seventy pathogenic gram negative bacteria capable of producing biofilms. These biofilms are an important strategy of bacteria to survive antibiotic concentration. Both gram negative and gram positive bacteria possess different strategies for quorum sensing. Quorum sensing of gram positive bacteria is mediated by autoinducing peptides and of gram negative bacteria is mediated by comparatively small molecules like acyl-homoserine lactones (AHLs). Kaufmann., *et al*. [1] reported the ability of Pseudomonas strain to produce autoinducers having antibacterial and antifungal properties. Till then several studies have identified various QS inhibitor molecules/anti QS drugs and some of these QS inhibitors have reached the phase of preclinical trials.

There are four major mechanisms to inhibit quorum sensing viz QS receptor inactivation or antagonism, QS signal synthesis inhibition, degradation of QS signals and target antibodies for QS blockage [2]. Flavonoids, N-decanoyl-L-homoserine benzyl ester and meta-bromothiolactone has demonstrated ability to reduce expression of virulence genes of *Pseudomonas aeruginosa* after binding to QS receptor [3,4]. Similarly, Acyl-homoserine lactone (AHLs) molecules participate in synthesis and regulation of QS signals and AHLS inhibition by immucillin A, butyryl-SAM, S-adenosylhomocysteine and sinofungin has demonstrated inhibition of release of QS-mediated virulence factors by *Pseudomonas aeruginosa*. Certain bacteria derived enzymes like lactonase, oxidoreductase, acylase and dioxygenase effectively disrupts AHLs and decreases the expression of virulence factors viz lectin A, pyocyanin and rhamnolipid. Lactonase has demonstrated an increase in antibiotic sensitivity to *Pseudomonas aeruginosa* and *Acinetobacter baumannii*. Certain studies have reported efficacy of antibodies against QS signaling molecules to attenuate inflammatory response of host cells. All these Quorum sensing inhibitors have ability to modulate growth, virulence factors and biofilm production of pathogenic bacteria but none of them shows bactericidal activities like most antibiotics, therefore scientists start investigating QS inhibitors with synergistic effects to antibiotics. Such QS inhibitors can be used

in combination with antibiotics and will decrease the risk of drug resistance. QS Inhibitors farnesol and hamamelitannin significantly increase the antibiotic sensitivity of β-lactam antibiotics to *Staphylococcus aureus* [5]. N-(2-pyrimidyl) butylamine shows a similar increase in sensitivity of ciprofloxacin and tobramycin against *Pseudomonas aeruginosa*. Curcumin supplementation has shown synergistic effects of gentamicin and azithromycin against *Pseudomonas aeruginosa* [2].

Knowledge of researchers around the globe about the complex mechanism of quorum sensing and its role in intraspecies, interspecies and pathogen host interaction is in its nascent stage. Still success achieved till date has established QS inhibitors as potential strategies to decrease the risk of emergence of drug resistance. Stability and QS inhibitors associated adverse effects are major hindrance in extensive application of QS inhibitors in clinical use but for sure it will improve as the understanding of QS mechanisms will improve. Coating of QS inhibitor acylase over various devices to prevent growth of *Pseudomonas aeruginosa* has been widely practiced in hospital care [6]. Acylase is one example of successful practical application of QS inhibitors in the field of medicine and can be credited as sound start in emergence of QS inhibitors drugs. More intensive researches are required to develop QS inhibitor drugs as a practical non-antibiotic strategy to encounter antibiotic resistance for future [7].

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Volume 7 Issue 7 July 2022