Introduction

Pseudomonas aeruginosa causes serious infection diseases that vary from local to systemic infections, especially in people with immune system disorders [1,2]. This bacterium is also intrinsically resistant to many antimicrobial agents [3]. In addition to intrinsically resistant, however, the misuse of antimicrobial agents causes to increase multi-drug resistance strains [4,5]. Quorum sensing is actually a cell to cell signaling mechanism that each bacteria existing in a population respond to extracellular signals molecules (autoinducer molecules) which is produced by the bacterial cells. Quorum sensing system is regulated to expression of many bacterial genes such as genes related to virulence, antibiotic resistance, biofilm formation, toxin-antitoxin systems and others. Generally, when the concentration of autoinducer molecules came to a certain threshold, they connected to the receptor molecules (protein R). These receptor molecules are connected to autoinducer molecules (from N-terminal section) and DNA molecule (from C-terminal section) that formed receptor-autoinducer complex. The receptor-messenger complex is result in regulation of diverse bacterial genes (Fig.1,2) [6-12]. Therefore, we conducted current study for a good knowledge of these systems in the topic bacteria P. aeruginosa.

**Keywords:** Quorum sensing systems, lasIR, rhlIR, Pseudomonas aeruginosa.
Regulating quorum sensing systems in *P. aeruginosa* bacteria

The quorum sensing system is a global regulation system. Some bacterial genes are under the control of this system, and others regulated specifically. These systems are connected to *lux*-box specific sequences that in *P. aeruginosa* called *las*-box. The LasR molecule has multimer structure, but the RhlR molecule has dimer structure. However, the Las and Rhl are not compatible systems. Therefore, the RhlI-produced C4-AHL molecule cannot activate LasR, and also the LasI-produced 3-oxo-C12-AHL cannot activate RhlR. In addition, studies have been shown that many genes controlling the QS systems (Quorum sensing-controlled genes, qsc) should be classified based on temporary response patterns in the presence of Las AHL and Rhl AHL signal. Additional settings on the regulation systems of QS should be applied in different stages of bacterial life. Some *qsc* genes quickly respond to extracellular signals, while others only when bacteria are in late phase development can respond to AHL signals. Studies have been shown that *P. aeruginosa* in vitro can have a strong effect on the activation of *qsc* genes by increasing extracellular AHL molecules. However, some areas containing inhibitors that are affect on the
activating of qsc genes. Importantly, P. aeruginosa
has several global regulatory factors that influence
and regulate QS circuitry (Fig.3) [15-18].

The functions of quorum sensing systems in P. aeruginosa

In this way, mutant strains with mutations in QS genes were used. Results showed that the
mutant strains had less pathogenicity compared to wild strains. Nevertheless, the mutant strains
had effects on severity of disease that suggests these genes are not the only factor necessary for
disease but also the other factors are effective in
the development of disease [19].

The quorum sensing systems as a potential target
for antimicrobial agents

Recently, we see an increase in P. aeruginosa
strains with multiple drug resistance. Awareness
of the diverse QS systems function in bacterial
cells, it has provided these systems as unique
targets for new antimicrobial drugs. Several
components of these systems are considered as

Fig. 3. Regulation of QS systems in P. aeruginosa. Arrows in the promotor region indicate a positive regulation and
small parallel lines indicate negative regulation. The Quinolone signaling molecule 2-heptyl-3-hydroxy-4-
quinolone (PQS) molecules provide the connection between las and rhl systems [17].

Fig. 4. Different potential targets of QS systems for antimicrobial agents: antagonistic analogues (b), specific
antibodies (c), lactonases as degradation molecule (d), target the expression of QS components (e), drugs
that inhibit lasR and lasI (f), specific antisense oligonucleotides (g) [19].

ideal targets for drug development including: (1) Inhibition of activation of LasR and RhlR through AHL analogs that acts as antagonists of 3O-C12-HSL and C4-HSL molecules, (2) inhibiting of active AHL molecules by specific antibodies and (3) inhibition of las I/R and rhl I/R expression (Fig.4) [20].

**Conclusions**

*Pseudomonas aeruginosa* has two QS systems *las* and *rhl*. These systems regulate expression of many bacterial genes that affect various its physiologic functions. These systems can provide suitable targets for novel antimicrobial agents. However, there are many ambiguities about these systems that need further studies.

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**Conflict of interest**

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**References**


