Form8

ABSTRACT OF DISSERTATION

Title	*pruR* and PA0065 Genes Are Responsible for Decreasing Antibiotic Tolerance by Autoinducer Analog-1 (AIA-1) in *Pseudomonas aeruginosa*
Author's Name	Muhammad Reza Pahlevi

Pseudomonas aeruginosa infection is considered a high-risk nosocomial infection and is very difficult to eradicate because of its tolerance to antibiotic treatment. A new compound, autoinducer analog-1 (AIA-1), has been demonstrated to reduce antibiotic tolerance, but its mechanisms remain unknown. This study aimed to investigate the mechanisms of AIA-1 in the antibiotic tolerance of *P. aeruginosa*. A transposon mutant library was constructed using miniTn5pro, and screening was performed to isolate high tolerant mutants upon exposure to biapenem and AIA-1. We constructed a deletion mutant and complementation strain of the genes detected in transposon insertion site determination, *pruR* and PA0066-65-64, and performed killing assays with antibiotics and AIA-1. Gene expression upon exposure to biapenem and AIA-1 and their relationship to stress response genes were analyzed. High antibiotic tolerance was observed in Tn5-*pruR* and Tn5-PA0065 transposon mutants and their deletion mutants, Δ*pruR* and ΔPA0066-65-64. Complemented strains of *pruR* and PA0066-65-64 with their respective deletion mutants exhibited suppressed antibiotic tolerance. It was determined that deletion of PA0066-65-64 increased *rpoS* expression, and PA0066-65-64 affects antibiotic tolerance via the *rpoS* pathway. Additionally, antibiotics and AIA-1 were found to inhibit *pruR* and PA0066-65-64. This study proposed that *pruR* and PA0066-65-64 are members of the antibiotic tolerance suppressors.

Keywords: antibiotic tolerance; *Pseudomonas aeruginosa*; autoinducer analog-1; *pruR*; PA0066-65-64