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Structure - Activity Relationship of Mutant KatG from INH resistant *Mycobacterium tuberculosis*

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Mutation in katG gene of *Mycobacterium tuberculosis* encoding catalase-peroxidase that damage its enzyme activities is well associated with isoniazid (INH) resistance. The katG gene from INH resistant strain of *M. tuberculosis* clinical isolate L19 has been observed in previous study, carrying mutations of $G_{234}A$ and $C_{625}T$, and changed the arginine residue at position 209 with cysteine in its KatG protein. However the activities of the mutant protein has been not known yet. Expression of the katG gene L19 that was done in Escherisicia coli BL21(DE3) using pCold II-DNA generated KatG protein with 80 kDa in SDS PAGE electroforegram. The mutant protein of KatG L19 decreased 43% of catalase activity and 11% of peroxidase activity against to KatG wild type (H37RV). The model structure of the mutant KatG protein had deviation structure toward KatG wt as 0,13 for number of *Root Mean Square Deviations* (RMSD). The mutant KatG (Arg209Cys) losed two hydrogen interactions and a van der Waals bond which present in KatG wild type. In the KatG wt protein, the both hydrogen bonds was formed between the Arg209 residu to Glu201, while the van der Waals bond occured by lingking of Arg209 residu to Glu217. Disruption in the some chemical interactions might trigger the decline in catalase-peroxidase activities of mutant KatG L19 and further it bring out the INH resistance in the clinical isolate L19.

Keywords: katG, catalase-peroxdase, isoniazid resistance, *M. tuberculosis*.

Mycobacterium tuberculosis, the causing agent of tuberculosis (TB) disease, recently many strains have been found resistant to the TB drugs. This events caused the TB cases more difficult to resolve. Multi-drug resistant tuberculosis (MDR-TB) is TB resistant to at least two potent anti-TB drugs, such as isoniazid and rifampicin together, or with resistance to first-line anti-TB drugs, namely, pyrazinamide, ethambutol and streptomysin.[1] Indonesia posed the third ranks for TB cases in the world after India and China, having the total of TB burden are around 395,000 per one thousand populations in 2015 and 126,000 of them are deaths. Of TB cases, as many as 32,000 are cases of MDR-TB[1,2]. A better understanding in the antituberculous drug resistance is needed to make easy in the TB therapy.

The mechanism of drug resistance in *Mycobacterium tuberculosis* can occur in several ways, (1) a decrease in the effectiveness of the drug due to over production of its target protein,

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