STUDI PENAMBATAN DAN DINAMIKA MOLEKULER SENYAWA DERIVAT ISOTIOSIANAT TERHADAP PROTEIN *QseC* SEBAGAI UPAYA PENEKANAN VIRULENSI *Escherichia coli* O157:H7

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ABSTRAK

Protein QseC berperan sebagai sensor utama pada sistem *two-component signaling Escherichia coli* O157:H7 dan mengaktifkan regulasi virulensi sebagai respon terhadap AI-3, epinefrin, dan norepinefrin. Penelitian ini menganalisis afinitas dan kestabilan pengikatan derivat isotiosianat terhadap QseC menggunakan pendekatan *in silico* untuk menilai potensi senyawa tersebut sebagai inhibitor antivirulensi. Model QseC dibangun menggunakan AlphaFold dan divalidasi melalui pLDDT, pTM, PAE, Ramachandran, dan MolProbity. Penambatan molekuler dilakukan terhadap LED209 sebagai kontrol positif serta lima derivat isotiosianat, yaitu alil isotiosianat, benzil isotiosianat, fenetil isotiosianat, fenil isotiosianat, dan sulforafen. Hasil penambatan dilanjutkan dengan simulasi dinamika molekuler selama 2 *ns* untuk mengevaluasi kestabilan kompleks melalui energi potensial, RMSD, RMSF, dan profil ikatan hidrogen. Hasil penambatan menunjukkan bahwa LED209 memiliki energi bebas ikatan terbaik ($\Delta G \approx -9{,}86$ kkal/mol), sedangkan derivat isotiosianat menunjukkan afinitas sedang (ΔG –3,58 hingga –5,60 kkal/mol). Simulasi dinamika molekuler menunjukkan bahwa seluruh kompleks berada dalam kondisi energi stabil tanpa perubahan struktural besar, dengan ikatan hidrogen ligan isotiosianat yang bersifat lebih dinamis dibandingkan LED209. Hasil ini menunjukkan bahwa derivat isotiosianat mampu mengenali kantung pengikatan QseC, namun masih memerlukan optimasi struktur untuk meningkatkan potensi penghambatan.

Kata kunci: Dinamika molekuler, Isotiosianat, Penambatan molekuler, QseC

MOLECULAR DOCKING AND DYNAMICS STUDY OF ISOTHIOCYANATE DERIVATIVE COMPOUNDS AGAINST QSEC PROTEIN AS AN EFFORT TO SUPPRESS THE VIRULENCE OF ESCHERICHIA COLI O157:H7

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ABSTRACT

QseC functions as the primary sensor in the two-component signaling system of *Escherichia coli* O157:H7 and activates virulence regulation in response to AI-3, epinephrine, and norepinephrine. This study analyzes the binding affinity and stability of isothiocyanate derivatives toward QseC using an *in silico* approach to evaluate their potential as antivirulence inhibitors. The QseC model was constructed using AlphaFold and validated through pLDDT, pTM, PAE, Ramachandran, and MolProbity assessments. Molecular docking was performed on LED209 as a positive control and five isothiocyanate derivatives, namely allyl isothiocyanate, benzyl isothiocyanate, phenethyl isothiocyanate, phenyl isothiocyanate, and sulforaphane. Docking results were followed by a 2 ns molecular dynamics simulation to evaluate complex stability through potential energy, RMSD, RMSF, and hydrogen-bond profiles. Docking analysis showed that LED209 exhibited the best binding free energy ($\Delta G \approx -9.86$ kcal/mol), whereas the isothiocyanate derivatives demonstrated moderate affinity (ΔG –3.58 to –5.60 kcal/mol). Molecular dynamics simulations showed that all complexes remained energetically stable without significant structural changes, with hydrogen bonds formed by isothiocyanate ligands exhibiting more dynamic behavior compared to LED209. These findings indicate that isothiocyanate derivatives are able to recognize the QseC binding pocket, although further structural optimization is required to enhance their inhibitory potential.

Keywords: Isothiocyanates, Molecular docking, Molecular dynamics, QseC