Pengembangan Model In Silico untuk Prediksi Efikasi Senyawa *Paraboea Leuserensis* Terhadap Diabetes

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ABSTRAK

Diabetes melitus tipe 2 merupakan penyakit metabolik kronis yang ditandai dengan peningkatan kadar glukosa darah akibat gangguan sekresi maupun kerja insulin. Salah satu strategi terapi yang digunakan dalam pengendalian diabetes adalah penghambatan enzim α-glukosidase. Penelitian ini bertujuan untuk mengevaluasi potensi senyawa bioaktif dari tanaman Paraboea leuserensis sebagai inhibitor α-glukosidase menggunakan pendekatan in silico melalui molecular docking, analisis interaksi residu asam amino, serta evaluasi drug-likeness dan ADMET. Penelitian dilakukan secara komputasional menggunakan AutoDock Vina, Discovery Studio Visualizer, SwissADME, dan pkCSM. Protein target yang digunakan adalah enzim α-glukosidase dengan kode PDB 3L4Y. Validasi docking dilakukan melalui metode redocking dan menghasilkan nilai RMSD sebesar 1,272 Å yang menunjukkan metode valid. Senyawa uji menunjukkan kemampuan berikatan dengan sisi aktif protein target. Hasil molecular docking menunjukkan bahwa senyawa deoxyspergualin memiliki afinitas pengikatan terbaik dengan nilai binding energy sebesar -9,4 kcal/mol, lebih rendah dibandingkan acarbose (-6,8 kcal/mol) dan native ligand (-6,1 kcal/mol). Analisis interaksi menunjukkan keterlibatan residu asam amino penting pada sisi aktif enzim, seperti Asp203, Trp406, Asp542, Met444, dan His600. Evaluasi drug-likeness dan ADMET menunjukkan bahwa sebagian besar senyawa memiliki profil farmakokinetik yang cukup baik sebagai kandidat obat oral. Berdasarkan hasil penelitian, deoxyspergualin berpotensi menjadi kandidat inhibitor α-glukosidase yang menjanjikan untuk pengembangan terapi antidiabetes berbasis bahan alam.

Kata Kunci: diabetes melitus tipe 2, α-glukosidase, molecular docking, Paraboea leuserensis, in silico, ADMET.

ABSTRACT

Type 2 diabetes mellitus is a chronic metabolic disease characterized by elevated blood glucose levels due to impaired insulin secretion or action. One therapeutic strategy used in diabetes management is the inhibition of the α-glucosidase enzyme. This study aims to evaluate the potential of bioactive compounds from the plant Paraboea leuserensis as α-glucosidase inhibitors using an in silico approach through molecular docking, amino acid residue interaction analysis, as well as drug-likeness and ADMET evaluations. The study was conducted computationally using AutoDock Vina, Discovery Studio Visualizer, SwissADME, and pkCSM. The target protein used was the α-glucosidase enzyme with PDB code 3L4Y. Docking validation was performed via the redocking method and yielded an RMSD value of 1.272 Å, indicating a valid method. The test compounds demonstrated the ability to bind to the active site of the target protein. Molecular docking results showed that the deoxyspergualin compound had the best binding affinity with a binding energy of -9.4 kcal/mol, lower than that of acarbose (-6.8 kcal/mol) and the native ligand (-6.1 kcal/mol). Interaction analysis revealed the involvement of key amino acid residues in the enzyme's active site, such as Asp203, Trp406, Asp542, Met444, and His600. Drug-likeness and ADMET evaluations indicated that most compounds possess sufficiently favorable pharmacokinetic profiles as candidates for oral medications. Based on the research findings, deoxyspergualin has the potential to be a promising candidate for an α-glucosidase inhibitor in the development of natural-based antidiabetic therapies.

Keywords: type 2 diabetes mellitus, α-glucosidase, molecular docking, Paraboea leuserensis, in silico, ADMET.