ABSTRAK

STUDI *IN SILICO* AKTIVITAS ANTIDIABETES SENYAWA KOMPLEKS Zn(II)-FENILALANIN, Zn(II)-TIROSIN DAN PIOGLITAZON TERHADAP PROTEIN 4L7F

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Diabetes melitus merupakan penyakit metabolik kronis yang ditandai oleh peningkatan kadar glukosa darah akibat gangguan produksi maupun sensitivitas insulin. Keterbatasan efektivitas dan efek samping terapi konvensional, seperti pioglitazon, mendorong pengembangan alternatif berbasis *metallotherapy*, khususnya kompleks logam seng (Zn) dengan ligan asam amino. Penelitian ini bertujuan mengevaluasi potensi kompleks Zn(II)-fenilalanin dan Zn(II)-tirosin sebagai kandidat antidiabetes melalui pendekatan *in silico* dengan target protein MAPK8 (PDB ID 4L7F).

Metode yang digunakan meliputi analisis farmakokinetik berdasarkan *Lipinski's Rule of Five*, *Pre-ADME*, dan Protox, serta uji *molecular docking* menggunakan *AutoDock Vina* untuk menilai afinitas pengikatan, energi ikatan, RMSD, dan interaksi residu aktif. Hasil analisis menunjukkan bahwa kedua senyawa memenuhi kriteria *Lipinski's Rule of Five*, memiliki absorpsi yang baik, distribusi stabil, serta profil toksisitas yang aman.

Hasil *docking* menunjukkan bahwa Zn(II)-tirosin memiliki energi ikatan paling rendah sebesar -13,00 kkal/mol, diikuti Zn(II)-fenilalanin sebesar -10,00 kkal/mol, sedangkan pioglitazon sebagai kontrol memiliki energi -8,7 kkal/mol. Interaksi kompleks Zn(II) dengan residu aktif protein lebih kuat dan beragam dibandingkan kontrol positif, sehingga meningkatkan kestabilan ikatan. Berdasarkan hasil analisis ini, kedua kompleks berpotensi sebagai agen antidiabetes, dengan Zn(II)-tirosin menunjukkan aktivitas paling optimal.

Kata kunci: Diabetes melitus, *Molecular docking*, Pioglitazon, Protein MAPK8, Zn(II)-fenilalanin, Zn(II)-tirosin

ABSTRACT

IN SILICO STUDY OF ANTIDIABETIC ACTIVITY OF Zn(II)-PHENYLALANINE, Zn(II)-TYROSINE COMPLEXES AND PIOGLITAZON AGAINST 4L7F PROTEIN

By

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Diabetes mellitus is a chronic metabolic disease characterized by elevated blood glucose levels due to impaired insulin production and/or sensitivity. The limited effectiveness and side effects of conventional therapies, such as pioglitazon, have encouraged the development of alternative approaches based on metallotherapy, particularly zinc (Zn) complexes with amino acid ligands. This study aims to evaluate the potential of Zn(II)-phenylalanine and Zn(II)-tyrosine complexes as antidiabetic candidates through an *in silico* approach targeting the MAPK8 protein (PDB ID: 4L7F). The methods include pharmacokinetic analysis based on Lipinski's Rule of Five, Pre-ADME, and Protox, as well as molecular docking using AutoDock Vina to assess binding affinity, binding energy, RMSD, and interactions with active site residues. The results show that both compounds meet Lipinski's criteria, exhibit good absorption, stable distribution, and a safe toxicity profile. Docking analysis indicates that Zn(II)-tyrosine has the lowest binding energy (-13.00 kcal/mol), followed by Zn(II)-phenylalanine (-10.00 kcal/mol), while pioglitazon as the control shows -8.7 kcal/mol. The interactions of Zn(II) complexes with active site residues are stronger and more diverse than the control, enhancing binding stability. Therefore, both complexes have potential as antidiabetic agents, with Zn(II)-tyrosine demonstrating the most optimal activity.

Keywords: Diabetes mellitus, Molecular docking, Pioglitazon, MAPK8 protein, Zn(II)-phenylalanine, Zn(II)-tyrosine