

Analisis Selektivitas Inhibitor Dipeptidil Peptidase-IV (DPP-IV) terhadap *Parabacteroides goldsteinii* dan *Bacteroides fragilis* secara In-silico = Selectivity Analysis of Dipeptidyl Peptidase-IV (DPP-IV) Inhibitor against *Parabacteroides goldsteinii* and *Bacteroides fragilis* in In-silico

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Abstrak

ABSTRAK

Diabetes melitus tipe 2 (DMT2) adalah jenis diabetes yang paling umum di dunia. Baris kedua pengobatan DMT2 yang dapat menghambat pelepasan glukagon dan meningkatkan sekresi insulin adalah inhibitor DPP-IV. Enzim DPP-IV yang terdapat dalam tubuh manusia dapat diproduksi oleh tubuh sendiri atau dari bakteri yang terdapat di usus, seperti *Parabacteroides goldsteinii* dan *Bacteroides fragilis*. Dalam penelitian ini dilakukan penyelarasan sekuens bakteri dan pemodelan homologi. Docking makromolekul DPP-IV manusia dan model bakteri dilakukan terhadap setiap situs aktif DPP-IV manusia menggunakan aplikasi PyRx. Persentase kemiripan urutan antara DPP-IV manusia dan model DPP-IV bakteri (% urutan yang dipertahankan;% dari semua urutan), *P.goldsteinii* (46,15%, 24,18%) dan *B. fragilis* (92,31%; 20, 04%). Parameter optimasi untuk molecular docking DPP-IV yaitu kotak grid dengan ukuran 50x50x50 unit dengan jarak spasi 0,375 dan evaluasi energi sebesar 5.000.000. Berdasarkan hasil analisis nilai indeks selektivitas diperoleh senyawa penghambat DPP-IV yaitu gemigliptin yang relatif selektif pada *P.goldsteinii* dengan nilai indeks selektivitas $1,34 \times 10^{-4}$ dan retagliptin yang relatif selektif pada *B. fragilis* dengan nilai indeks selektivitas $0,05 \times 10^{-4}$ diantara 16 ligan lain pada tiga sisi aktif enzim DPP-IV. Hasil ini menunjukkan bahwa gemigliptin dan retagliptin dapat digunakan sebagai data pendukung dalam perancangan molekul baru dan perkembangannya sebagai penghambat DPP-IV selektif untuk pasien diabetes melitus tipe 2 (DMT2).

ABSTRACT

Diabetes mellitus type 2 (T2DM) is the most common type of diabetes in the world. The second line of T2DM treatment that can inhibit glucagon release and increase insulin secretion are DPP-IV inhibitors. The DPP-IV enzyme found in the human body can be produced by the body itself or from bacteria found in the intestines, such as *Parabacteroides goldsteinii* and *Bacteroides fragilis*. In this study, bacterial sequence alignment and homology modeling were carried out. Docking of human DPP-IV macromolecules and bacterial models was carried out against each active human DPP-IV site using the PyRx application. Percentage of sequence similarity between the human DPP-IV and the bacterial DPP-IV model (% retained sequences;% of all sequences), *P.goldsteinii* (46.15%, 24.18%) and *B. fragilis* (92.31%; 20, 04%). The optimization parameters for the DPP-IV molecular docking are a grid box with a size of 50x50x50 units with a spacing of 0.375 and an energy evaluation of 5,000,000. Based on the results of the selectivity index value analysis, the DPP-IV inhibitor compound was obtained, namely gemigliptin which was relatively selective in *P.goldsteinii* with a selectivity index value of 1.34×10^{-4} and retagliptin which was relatively selective in *B. fragilis* with a selectivity index value of 0.05×10^{-4} . among 16 other ligands on the three

active sites of the DPP-IV enzyme. These results indicate that gemigliptin and retagliptin can be used as supporting data in the design of new molecules and their development as selective DPP-IV inhibitors for type 2 diabetes mellitus (T2DM) patients.