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

Daniavi Nayunda, author

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 x10-4 dan retagliptin yang relatif selektif pada B. fragilis dengan nilai indeks selektivitas 0,05 x10 -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 x10-4 and retagliptin which was relatively selective in B. fragilis with a selectivity index value of 0.05 x10-4. 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.