Pengembangan model penapisan virtual berbasis artificial intelligence dengan metode klasifikasi untuk identifikasi inhibitor dipeptidil peptidase-IV = Virtual screening model development using artificial intelligence with classification method to identify new inhibitor dipeptidyl peptidase-IV.

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Abstrak

Diabetes melitus tipe 2 (DMT2) merupakan salah satu tipe diabetes yang telah menjadi permasalahan besar dalam dunia kesehatan. Salah satu pengobatan DMT2 yang mendegrasi enzim glukagon dan meningkatkan sekresi insulin adalah inhibitor Dipeptidil Peptidase-IV (DPP-IV). Inhibitor DPP-IV yang sudah digunakan memiliki efek samping yang bahaya, seperti pankreatitis akut, arthalagia, dan gagal jantung. Pada penelitian ini, dilakukan pengembangan model Virtual Screening (VS) menggunakan teknologi Artificial Intelligence (AI) untuk identifikasi inhibitor DPP-IV yang berpotensi. Pengembangan model VS dilakukan menggunakan konsep machine learning (ML) dan deep learning (DL). Pada penelitian ini, dilakukan 18 pengembangan model ML dan 8 model DL. Model VS DPP-IV yang optimal merupakan DNN dengan fitur Fingerprint dengan nilai parameter statistik lebih tinggi dari threshold VS optimal yaitu 0,85, dengan akurasi 0,91554, presisi 0,90815, sensitivitas 0,92319, selektivitas 0,90801, dan nilai F1 0,9156. Hyperparameter optimal model VS adalah tiga layer dengan jumlah neuron 2.000, 1.000, 100; nilai dropout 0; ukuran batch size 256; jumlah epoch 100; kecepatan learning rate 0,0001; dan tipe activation function merupakan RELU. Model VS DPP-IV dilakukan ujicoba terhadap database bindingDB dan didapat 24 ligan potensi. Berdasarkan perbandingan nilai binding affinity 24 ligan potensi terhadap ligan inhibitor DPP-IV menggunakan penambatan molekular, didapat satu ligan potensi berinteraksi dengan situs aktif S2 dan tujuh ligan potensi berinteraksi dengan situs aktif S3. Ligan tersebut memiliki nilai binding affinity lebih rendah dari ligan inhibitor DPP-IV yang FDA-approved dan lebih rendah dari -8 kcal/mol. Hasil ini menunjukkan bahwa model VS DPP-IV menggunakan AI dapat menjadi metode virtual screening dalam identifikasi inhibitor DPP-IV yang baru.

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Diabetes mellitus type 2 (DMT2) is one of diabetes type that has been causing problems in the health sector. One of the DMT2 medications that can degrade glucagon enzyme and increase insulin secretion is a Dipeptydil Peptidase-IV (DPP-IV) inhibitor. However, DPP-IV inhibitor drugs result in unexpected side effects such as acute pancreatitis, arthralgia, and heart failure. This research developed a virtual screening (VS) model using Artificial Intelligence (AI) to identify potential DPP-IV inhibitors. VS models that were developed were 18 ML models and 8 DL models. DNN with fingerprint features was the VS model best optimal with statistical parameters that exceeds the optimum VS threshold value, which is 0,85, with

accuracy 0,91554, precision 0,90815, sensitivity 0,92319, selectivity 0,90801, and F1 score 0,9156. Optimum VS model hyperparameter used a three-layered neuron with the neuron amount of each layer were 2000, 1000, and 100; zero dropout, 256 batch size, 100 epochs, learning rate 0,0001 with RELU as activation function. DPP-IV VS model was used to predict potential ligands using bindingDB and showed 24 ligands with an AI confidence level above 0.98. Based on the binding affinity comparison with DPP-IV inhibitors by molecular docking, it resulted one ligand interacting with active site S2 and seven ligands interacting with active site S3. These ligands had lower binding affinity value compared to FDA-approved DPP-IV inhibitor by docking. The result of this research showed that the DPP-IV VS model using AI could be a new VS model in identifying new DPP-IV inhibitors.