Penapisan virtual berbasis farmakofor terhadap inhibitor SGLT2 dari pangkalan data herbal Indonesia = Pharmacophore based virtual screening of SGLT2 inhibitor from Indonesian herbal database

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Abstrak

ABSTRACT
Inhibitor sodium glucose co-transporter 2 (SGLT2) telah dievaluasi dalam uji klinis sebagai dasar strategi penanganan hiperglikemia pada diabetes. Namun, karena tergolong kelas obat baru antidiabetik oral, inhibitor SGLT-2 masih jarang ditemukan di Indonesia dan harga beli yang masih tinggi untuk dijangkau. Studi ini bertujuan untuk menemukan senyawa kandidat yang berpotensi mempunyai aktivitas sebagai inhibitor SGLT2 dari pangkalan data herbal Indonesia melalui pendekatan penapisan virtual berbasis farmakofor. Model farmakofor inhibitor SGLT2 dibuat dari 10 training set ligan inhibitor SGLT2 menggunakan LigandScout 4.1.5. Sepuluh model farmakofor yang terbentuk kemudian divalidasi menggunakan metode test set dan decoy set. Farmakofor model-1 merupakan model farmakofor terbaik dengan nilai 0,9080, EF1 =56,5 , EF5 = 56,5 dan AUC100 = 0,87 yang akan dijadikan model untuk penapisan virtual. Model-1 terdiri dari 1 interaksi hidrofobik, 1 cincin aromatis, 4 donor ikatan hidrogen dan 5 akseptor ikatan hidrogen. Penapisan virtual menghasilkan tiga senyawa kandidat Hits yang memiliki pharmacophore fit score terbaik terhadap model 1, yakni vitexin = 113,62; cucumerin A = 112,62; dan cucumerin B = 113,51. Sehingga dapat disimpulkan bahwa Vitexin, Cucumerin A, dan Cucumerin B berpotensi sebagai kandidat senyawa yang mempunyai aktivitas sebagai inhibitor SGLT2.
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ABSTRACT
Sodium glucose co transporter 2 SGLT2 inhibitor has been evaluated in clinical trials as the basic strategy of hyperglycemia handling in diabetes. However, because of SGLT 2 inhibitor was the new class of oral antidiabetic, it still rare in Indonesia and because of the high price. This study was intended to find compounds that capable of having activity as SGLT2 inhibitors from Indonesian herbal database through a pharmacophore based virtual screening approach. The SGLT2 inhibitor pharmacophore models was made from 10 training sets of SGLT2 ligand inhibitors using the LigandScout 4.1.5. Ten pharmacophore models which has been made were validated using test set and decoy set methods. The model 1 pharmacophore was the best model, with values of 0.9080, EF1 56.5 , EF5 56.5 and AUC100 0.87 which will serve as models for virtual screening. Model 1 consists of 1 hydrophobic interaction, 1 aromatic ring, 4 hydrogen bond donors and 5 hydrogen bond acceptors. Virtual screening showed three compounds Hits which have best pharmacophore fit scores according to model 1, they were Vitexin 113.62 Cucumerin A 112,62 and Cucumerin B 113,51. These results conclude that Vitexin, Cucumerin A, and Cucumerin B potentially have an activity as a SGLT2 inhibitor.