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Designing Novel Inhibitors of α-Glucosidase: An application of Quantitative structure activity relationship, Homology Modeling and Virtual Screening

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Abstract

Diabetes is an important emerging health concern. α-Glucosidase is a prime drug target of Diabetes Mellitus and its inhibitors are used as a treatment to delay carbohydrate digestion by inhibiting catalytic pocket of α-glucosidase. With the aim to design novel α-glucosidase inhibitors, we applied three folds ligand (LB-) and structure based (SB-) virtual screening (VS) protocol. Initially quantitative structure activity relationship (QSAR) modeling was performed. The QSAR model was developed by thirty-four known inhibitors and scrutinized by a test set. The QSAR model showed excellent q2 (0.86), r2 (0.73) and RMSE (0.28) values. The high cross validation correlation coefficient (r2) and low RMSE value suggests that the model is robust enough to be validated by the test set. The test set depicted excellent prediction with q2 and r2 values of 0.89 and 0.79, respectively. The model was used for further screening of novel compound against α-glucosidase. A set of 6609 compounds was retrieved from ZINC database and subjected to SBVS. After docking, the best docked compounds were selected and their pharmacokinetic (ADMET) profile was predicted in silico. Compounds with acceptable ADMET properties were taken as a test set-2 and their biological activities were predicted by QSAR model. The predicted biological activities, pharmacokinetic behavior, docking scores and protein-ligand interactions revealed that twenty-nine compounds specifically inhibit the catalytic site of α-glucosidase thus possess potential α-glucosidase inhibition in silico. These results serve as a guidelines for the rational design and development of potential novel anti-diabetic agents.

Biography:

Sobia Ahsan Halim has completed her PhD from University of Karachi, Karachi-Pakistan in 2013. She is working as an Assistant Professor in University of Nizwa, Oman. Her research interest in Computational drug designing and molecular modeling. She has published 50 papers in reputed journals and and 3 patents.

Speaker Publications:

1. Antiproliferative and Carbonic Anhydrase II Inhibitory Potential of Chemical Constituents from Lycium shawii and Aloe vera: Evidence from In Silico Target Fishing and In Vitro Testing; Pharmaceuticals (Basel). 2020 May; 13(5): 94.
2. Genome Subtraction and Comparison for the Identification of Novel Drug Targets against Mycobacterium avium subsp. Hominissuis; Pathogens. 2020 May; 9(5): 368.
3. Triterpenic Acids as Non-Competitive α-Glucosidase Inhibitors from Boswellia elongata with Structure-Activity Relationship: In Vitro and In Silico Studies. Glucosidase_Inhibitors_from_Boswellia_elongata_with_Structure-Activity_Relationship_In_Vitro_and_In_Silico_Studies; Biomolecules. 2020 May; 10(5): 751.
4. Recent advances in combinatorial cancer therapy via multifunctionalized gold nanoparticles; NANOMEDICINE, 6may 2020,VOL. 15, NO. 12
5. In Silico Modeling of Crimean Congo Hemorrhagic Fever Virus Glycoprotein-N and Screening of Anti Viral Hits by Virtual Screening; March 12, 2020.

5th Pharmaceutical Chemistry Conference; Webinar, -April 27-28, 2020.

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