Abstract

Background and Purpose: Diabetes mellitus is a multifactorial and metabolic disorder. The alpha-glucosidase enzyme in the epithelium of the small intestine is responsible for the digestion of carbohydrates. Inhibiting this enzyme by preventing the digestion of carbohydrates can reduce postprandial hyperglycemia. Designing and reporting new compounds with coumarin and triazole core, using virtual screening, is an optimal, simple and low-cost method and can be useful in inhibiting alpha-glucosidase enzyme.

Materials and Methods: First, the crystallographic structure of alpha-glucosidase enzyme with identifier code 3A4A was obtained from Protein Data Bank (PDB). Then, a library of 1922 chemical compounds that were structurally similar to the main triazole and coumarin skeletons was formed from the PubChem database. Various filters were applied to compounds by PyRx0.8 software and Molinspiration, SwissADME and admetSAR servers. Finally, the binding energy and interaction of the compounds were checked by Autodock 4.2 software.

Results: Among the compounds in the library, eight compounds passed the mentioned filters successfully. Then, molecular docking was performed on these compounds. Among the eight docked compounds, four compounds with the identification codes of CID_132277006, CID_1534998, CID_110745226 and CID_122233777 were introduced as the best compounds with binding energy of -9.19, -8.89, -8.71 and -8.49 kcal/mol respectively. Examining the results of molecular docking showed that amino acids Arg442, Gln279, Ser241, His351, Lys156, Asp352, Glu277, Arg315, Asp242, Phe303, Ser157, Asn415, Glu411, Phe314, Tyr158, Ser240, Asp215 and Val216 have a higher importance in the formation of compounds complex with the active site of alpha-glucosidase enzyme.

Conclusion: It seems that the hydrophobic bond and on the next level the hydrogen bond, then the cation-π bond are important for the interaction of the compounds with the active site of alpha-glucosidase enzyme.

Keywords: alpha-glucosidase, coumarin, triazole, virtual screening, molecular docking