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Identifying analogues of 2-deoxyglucose, alpha-d-glucose and beta-d-glucose-6-phosphate as potential inhibitors of human hexokinase ii for the development of anti-dengue therapeutics (Article)

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Abstract

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The human hexokinase isoform II (HKII) is one of the important enzymes for dengue virus (DENV) replication and thus has been suggested as a potential therapeutic target for DENV drug development. In this work, compounds were identified using Ultrafast Shape Recognition with CREDO Atom Types (USRCAT) by utilizing both HKII's substrate and product; alpha-D-glucose (GLC) and beta-D-glucose-6-phosphate (BG6), as well as a known HKII's inhibitor, 2-deoxyglucose (2DG), as the query molecules. The analogues of the three query molecules were subsequently docked against the HKII's crystal structure (PDB ID: 2NZT) by using Auto Dock 4 program on Chain B, where the active sites and strong bonds were located. Among the top-ranked compounds, Compound 4 (ZINC26898487), which was the most similar to 2DG, showed the best binding energy (-7.63 kcal/mol) and contained two H bonds. Compound 9 (ZINC16930948), an analogue of GLC emerged as the best inhibitor candidate because it had six H bonds. Similarly, among the molecules similar to BG6, Compound 14 (ZINC4403351) had been suggested as a potential inhibitor because it contained four strong H bonds. All compounds were predicted to be non-toxic, based on Toxicity Estimation Software Tool (TEST) analysis. By providing these valuable findings, this study has paved the way for the discovery of compounds that should be further tested for the development of anti-dengue drugs.

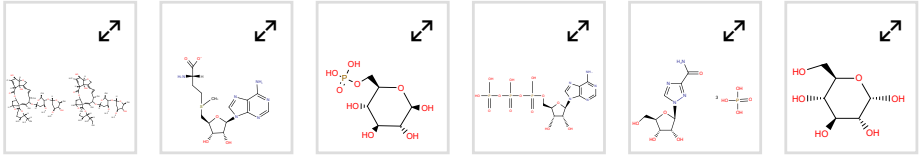
SciVal Topic Prominence

Topic: Dengue Virus | Flavivirus | NS2B-NS3 protease

Prominence percentile: 98.348

Chemistry database information

Substances View all substances (9)



Author keywords

2-deoxyglucose | Alpha-D-glucose | Beta-D-glucose-6-phosphate | Human Hexokinase II (HK2) | Ligand-based screening | Structure-based screening | Toxicity test

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