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# Virtual screening of human glyoxalase I inhibitors: A structure-based approach

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Human glyoxalase I (GlxI) is a key metalloenzyme involved in the detoxification of methylglyoxal, a cytotoxic byproduct of glycolysis. GlxI is overexpressed in many cancers and contributes to their proliferation, invasion, and drug resistance. Therefore, this enzyme is a potential target for anticancer drug discovery. In this study, we performed a virtual screening of a large library of compounds to identify novel inhibitors of GlxI. We performed molecular docking using IGEMDOCKv2.1 software to find ligands that bind to the active site of GlxI. We used *S*-*P*-bromobenzylglutathione, a known inhibitor of GlxI with a very low $K_I$ value of 83 nM [1], as a probe ligand. Docking was performed on the human GlxI structure from the Protein Data Bank entry 1qip [2] (Figure 1 shows the binding pose of the probe ligand in the active site of the enzyme). Then we used web servers to generate and search pharmacophore models based on the probe ligand). We selected the top candidates and docked them to GlxI using AutoDock Vina. We ranked the compounds by their binding energies and selected the best ones for further analysis. We evaluated the binding modes and interactions of the selected inhibitors with GlxI and compared them with the known inhibitors. We also performed ADMET prediction and drug-likeness analysis to assess the pharmacological properties of the selected inhibitors. Our results suggest that we have identified some promising candidates that can inhibit GlxI with high affinity and specificity. These compounds may serve as lead compounds for further optimization and development of novel anticancer agents.

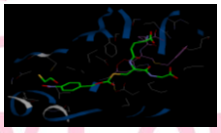


Figure 1. The binding pose of the probe ligand (pink) in the active site of the enzyme).

***Keywords:*** Glyoxalase I, Drug design, Docking, Virtual screening

**References**

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