

Molecular Docking Study of Rosmarinic Acid and Its Analog Compounds on Sickle Cell Hemoglobin

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Abstract : Introduction: Voxelotor, also known as GBT 440, binds to the alpha cleft in HbS tetramers and promotes the stability of the relaxed or oxygenated state of HbS. This process hinders the conformational change of the HbS tetramers into the deoxygenated state. Voxelotor prevents interactions between HbS tetramers in the deoxygenated state, ultimately inhibiting the polymerization of HbS tetramers and resulting in significant clinical improvements, particularly in raising hemoglobin levels in patients. In this study, we have explored the use of herbal compound models, such as rosmarinic acid and compounds with similar structures that exhibit high binding affinity to Voxelotor's hemoglobin binding site. Materials and methods: The molecular model of hemoglobin (PDB: 5E83) was initially obtained from the RCSB PDB database. In addition, we collected 453 ligand models with structural similarity to rosmarinic acid from the PubChem database. To prepare these models for molecular docking, we utilized the Molegro Virtual Docker tool. Subsequently, we used the SwissADME web tool to predict the physicochemical properties and pharmacokinetics of these compounds. Results: We investigated the affinity and binding site of 453 compounds similar to rosmarinic acid on the hemoglobin model (PDB: 5E83). Our focus was on the alpha cleft between two alpha chains of the hemoglobin model (PDB: 5E83). The results showed that most compounds had molecular weights above 500 daltons, and some exhibited acceptable hydrophobicity. Furthermore, their solubility in aqueous solutions was good. None of the compounds were able to cross the blood-brain barrier or have gastrointestinal absorption. However, they did have varying inhibitory effects on CYP2C9 cytochromes. The skin penetration rate was generally low. Conclusion: Through our study, we identified three compounds (CID: 162739375, CID: 141386569, and CID: 24015539) with promising potential for further research. These compounds demonstrated high binding affinity to the hemoglobin model, favorable dissolution and digestive absorption rates, as well as suitable hydrophobicity, making them ideal candidates for continued laboratory investigation.

Keywords : voxelotor, binding site, hemoglobin, rosmarinic acid

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