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ORIGINAL ARTICLE **OPEN ACCESS**

In Silico Analysis of Gentiobiose Treats for Lung Cancer

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ABSTRACT
Lung cancer is one of the dangerous diseases that have resulted in a significant mortality rate in recent decades around the world. As a result, developing an effective treatment for this disease is critical. Lung cancer cell protein and the ligand Gentiobiose were used in this molecular docking. As a result, the protein and ligand have interacted with a binding score of -7 and 9 interactions, respectively. TRP227, TYR55, ASP50, HIS117, UNK1, PRO2025, and GLU2828 were the amino acid residues that interacted with a small molecule. The values of the Root Mean Square Deviation are also determined. As a result, Gentiobiose will be used to treat lung cancer.
Keywords : *Lung Cancer, Gentiobiose, Aminoacid residues, Molecular docking.*

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INTRODUCTION

Cancer is one of the world's most common diseases, with a high fatality rate. Every year, around 16 percent of all cancer patients die from the disease [1]. Lung cancer affects more people than prostate, breast, and colon cancer combined [2]. Lung cancer is the second most common malignancy in both men and women [3]. Nonsmall cell lung cancer [NSCLC] is a frequent subtype of lung cancer that accounts for 85-90 percent of new cases [4, 5]. The Epidermal Growth Factor [EGFR][6] is responsible for about 62 percent of NSCLC.

Chemical medicine is currently an excellent treatment option for any type of cancer [7]. Many resistance proteins, including LRP and MDR, may be used to treat NSCLC in the future [8, 9]. The LRP was found in abundance in the cytoplasm and nuclear envelope of lung cancer cells [10]. Clinical trials for medications made from natural sources have been disappointing [11]. In recent decades, network pharmacology has emerged as a new science capable of analyzing drug action mechanisms [12], identifying pharmaceuticals [13], and better explaining the mechanism of interaction molecules and cellular pathways. Molecular docking technology is a useful tool for modernization research since it allows for virtual drug screening [14].

MATERIAL AND METHODS

Protein Preparation

Protein was downloaded from the Protein Data Bank [PDB] database as one of the key molecules for molecular docking. The crystal structure of CPd8, an X-ray diffracted structure with a resolution of 2.84Ao [PDB ID: 7DN4], was downloaded [15]. The discovery studio file [Figure1] was used to eliminate additional components from the macromolecule, such as heat atoms, water molecules, and ligand groups. The data is then transformed to PDBQT [16].

Ligand Preparation

The tiny molecule was found in the PubChem database and downloaded. Gentiobiose was found as a three-dimensional structure with the CID 3D 441422 [Figure2]. It was initially saved in SDF format and then converted to PDB format using Open Babel. For autodock compatibility, the energy was reduced and translated to PDBQT format [17].

Docking Protocol

Autodock vina is one of the greatest molecular docking programs available. On autodock vina, the major compounds for molecular docking were downloaded and pre-processed. A grid box with dimensions of 62X58X25 and 72.3995, -18.7200, and 9.81 was produced and centered. Docking was performed after selecting the docking macromolecule and ligand. The MD's findings were saved in a discovery studio file. Protein and ligand interactions with their molecular surfaces, known as H-bonds, were recorded as PNG files. JPEG files were used to save the 2d interactions and various visualizations of the interactions.

RESULTS AND DISCUSSION

Lung cancer has a high malignancy, a bad prognosis, and a short survival rate. Patients with advanced cancer have predictive biomarkers, and targeted therapy or immunotherapy, when compared to chemotherapy, will improve quality of life [18]. Recently, there has been a surge in interest in using natural substances to treat cancer patients that express P-GP constitutively and are resistant to several chemotherapy drugs. Animals are not poisonous to some of these phytochemicals [19]. Two methods increase the accumulation and efficacy of chemotherapeutic agents: [a] functional inhibition of P-GP mediated transport [20] and [b] reduction of P-GP expression [21]. The main mechanism of MDR is to keep cellular drug accumulation below the hazardous level.

Molecular docking is a structure-based drug design strategy that predicts the affinity and binding pattern of ligands and receptors, speeds up drug design and screening, and provides a foundation for future experimental detection [22]. To investigate the stability and flexibility of ligand-target complexes in a given system, molecular dynamics simulations are used [23-24]. As a result, the crystal structures of CPd8 and Gentiobiose were used in Molecular Docking. The protein and ligand were converted to PDBQT format for autodock compatibility. Gentiobiose's energy minimization is 378.53. -7 are the highest binding score.

A discovery studio file was used to assess the docking outcomes. The H-bond was estimated using the distances between the amino acid residues in the protein. TRP227, TYR55, ASP50, HIS117, UNK1, PRO2025, and GLU2828 were identified to be significant residues in interactions. H-bond distances and H-bond interaction residues were measured (Table 1). The root means square deviation value will be zero in those conformations. The binding affinity of those compounds with the macromolecule in various conformations, as well as the Root Mean Square Deviation (RMSD) values of the interacting molecules (Protein and Ligand), agreed (Table 2).

Table 1. The molecular docking studies of compounds with the crystal structure of CPd8

S. No	Compound name	Docking score	H-Bond Interaction	Distance
1.	**G**entiobiose	-7	TRP227 TYR55 ASP50 HIS117 UNK1 PRO2025 GLU2828	2.77 2.82 2.15 3.00 2.25 2.43 2.17 2.63 2.38

Table 2 shows the various binding affinity and root mean square deviation (RMSD) Upper and Lower Bound values of Gentiobiose

Ligand	**Binding Affinity**	**rmsd/ub**	**rmsd/lb**
pro7dn4_A_Gentiobiose_uff_E=378.53	-7	0	0
	-6.5	6.951	1.952
	-6.3	3.388	1.698
	-6.3	7.243	1.303
	-6.1	4.354	2.249
	-6	3.682	2.336
	-5.9	3.848	2.077
	-5.9	4.91	2.375
	-5.8	7.551	1.964

Protein-ligand interactions (Gentiobiose) were studied (Figures 3, 4, 5, 6, 7and 8). It can also be seen in different charts such as the Ramachandran plot (Figure9), the Hydrophobicity plot (Figure10), and some contact plots such as the CAlpha plot (Figure11), the CBeta plot (Figure12), the Sidechain plot (Figure13), the H bond plot (Figure14), and the Residue plot (Figure15) (Figure15). As a result of the MD simulation, Gentiobiose is a promising medication for lung cancer.

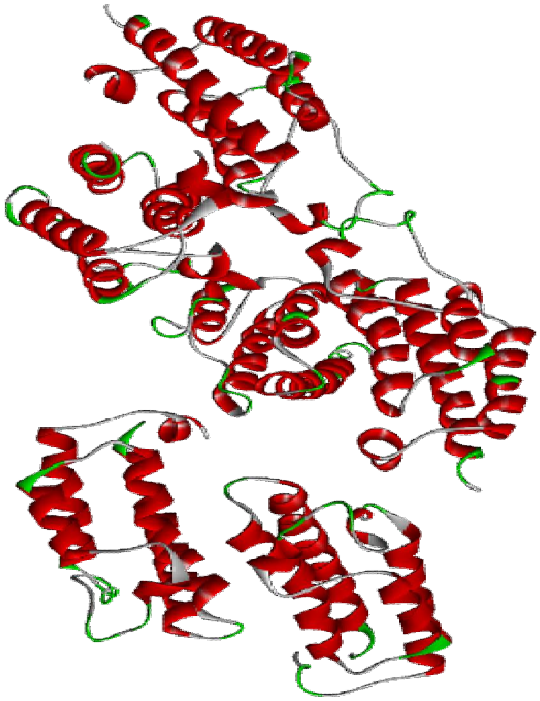

Figure 1 shows 3d structure of crystal structure of CPd8

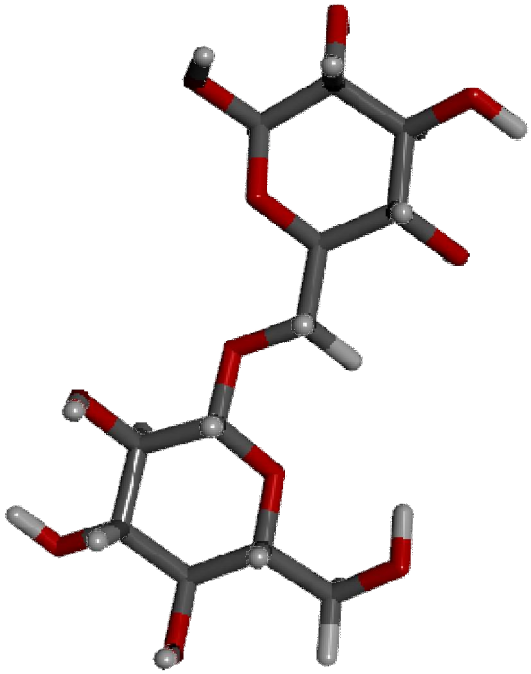

Figure 2 shows the 3d structure of Gentiobiose

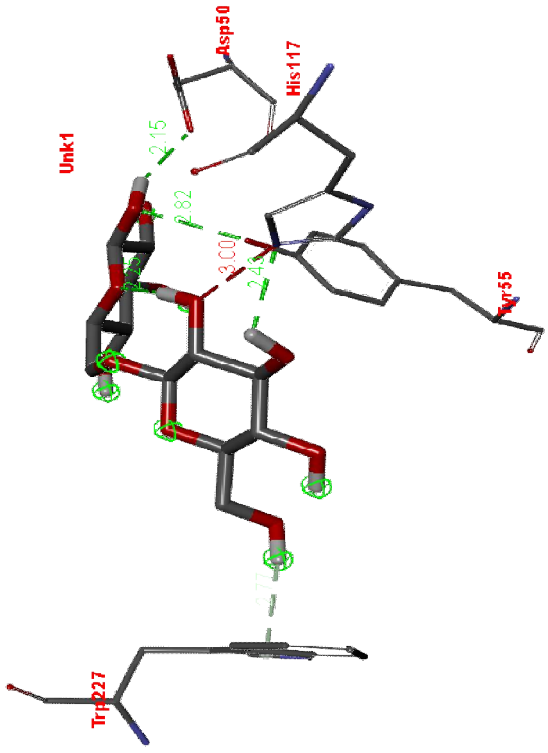

Figure 3 shows the interaction of Gentiobiose with the crystal structure of CPd8

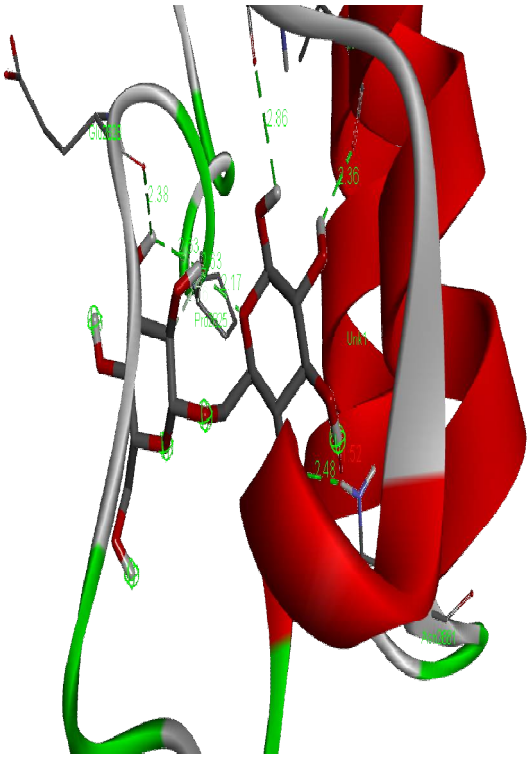

Figure 4 shows the interaction of Gentiobiose with the crystal structure of CPd8 with a receptor

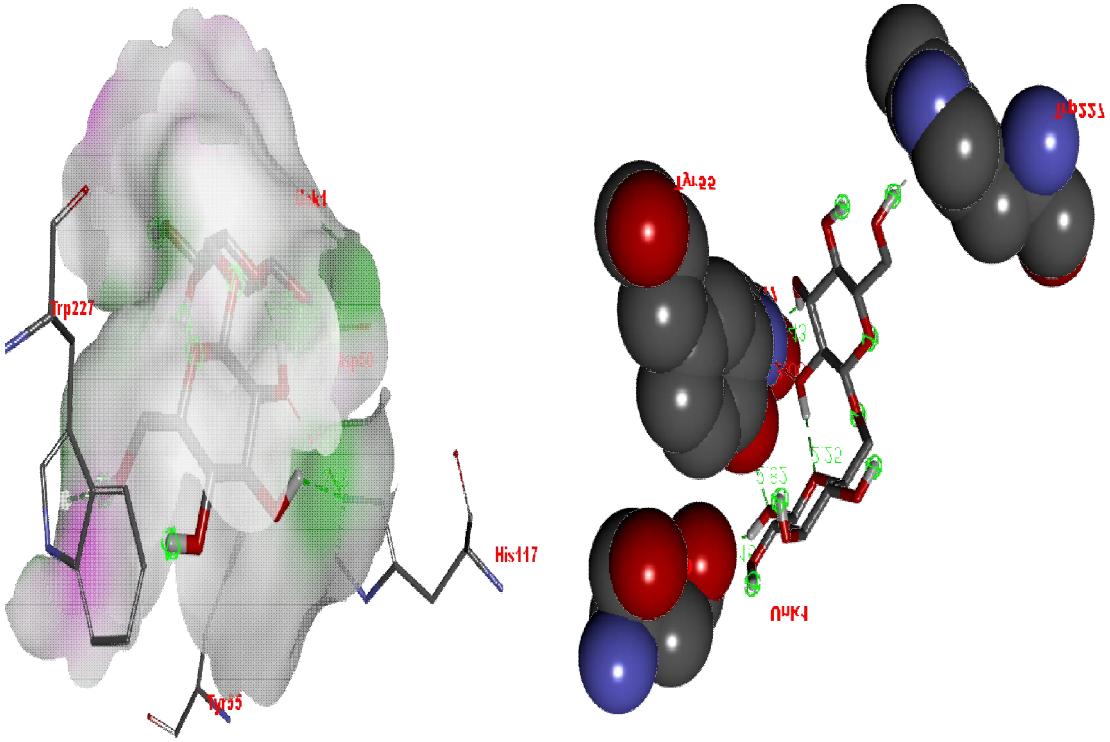

Figure 5,6 shows the interaction of Gentiobiose with the crystal structure of CPd8

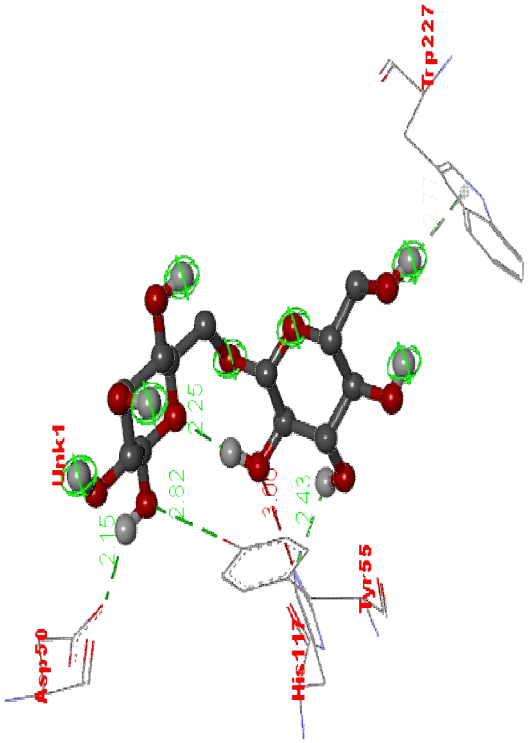

Figure 7 shows the interaction of Gentiobiose with the crystal structure of CPd8

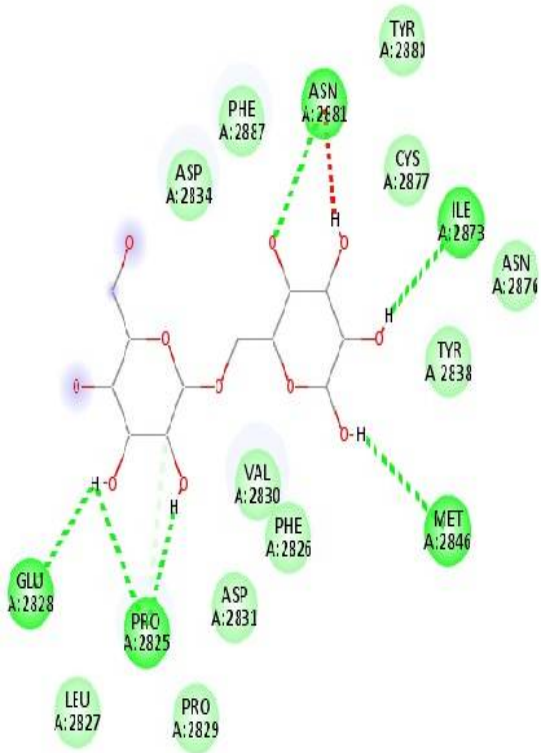

Figure 8 shows the 2d diagram of the interaction of Gentiobiose with the crystal structure of CPd8

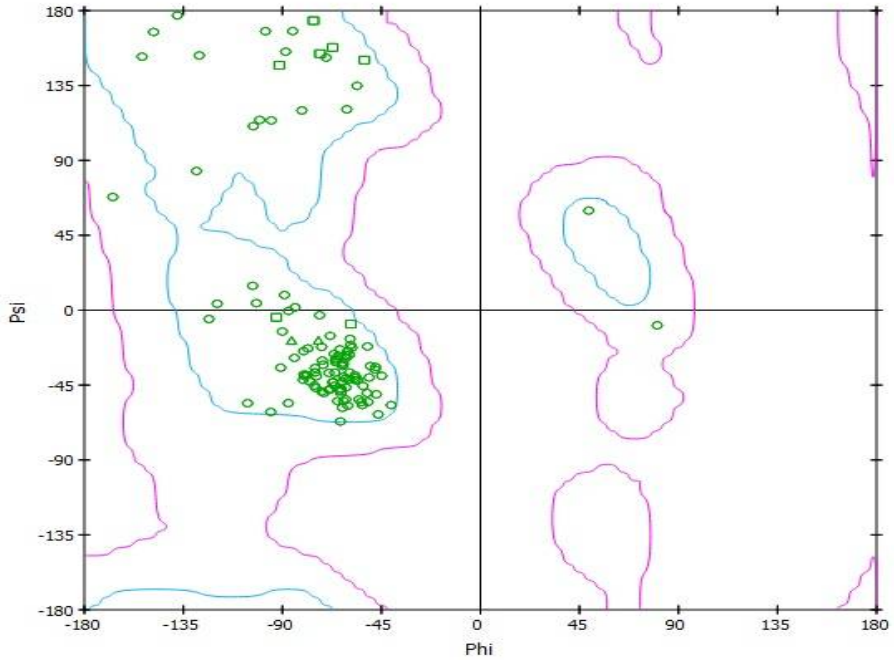

Figure 9 shows the interaction of Gentiobiose with the crystal structure of CPd8 in Ramachandran Plot

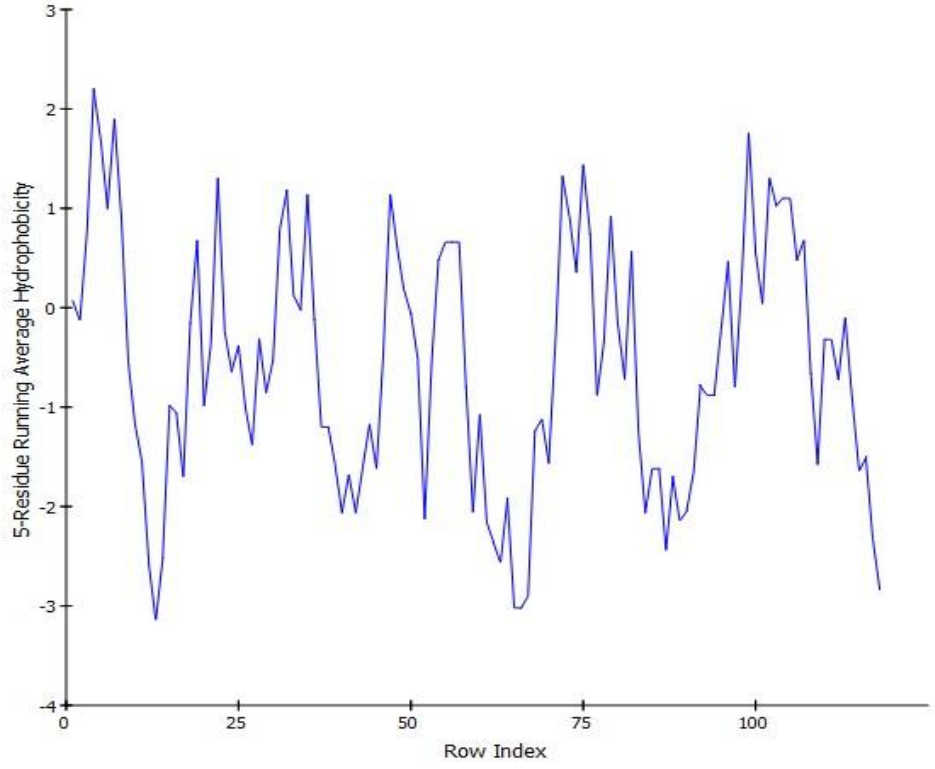

Figure 10 shows the interaction of Gentiobiose with the crystal structure of CPd8 in Hydrophobicity Plot

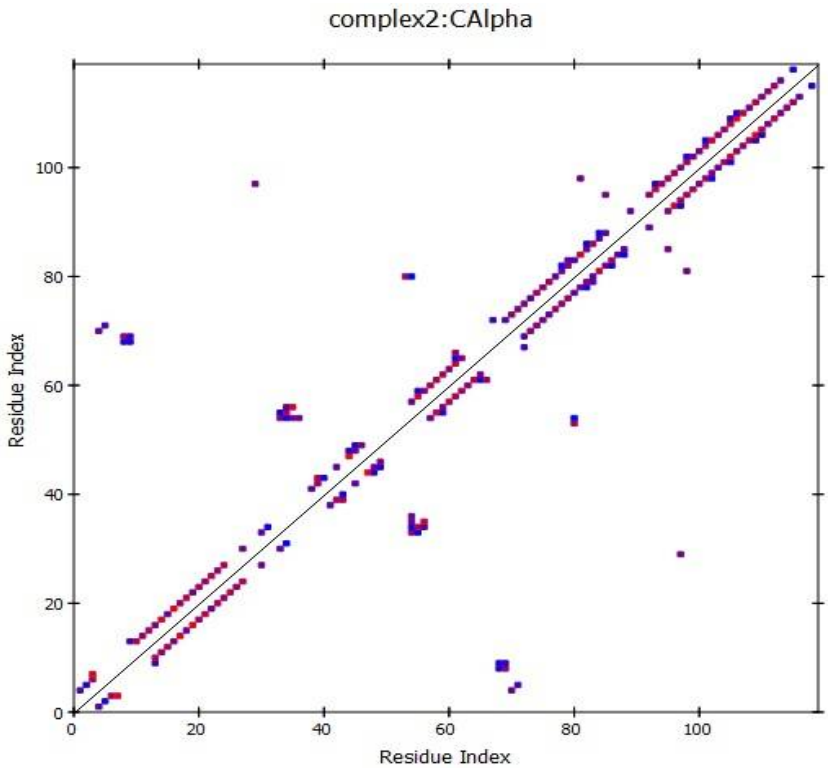

Figure 11 shows the interaction of Gentiobiose with the crystal structure of CPd8 in C-alpha Plot

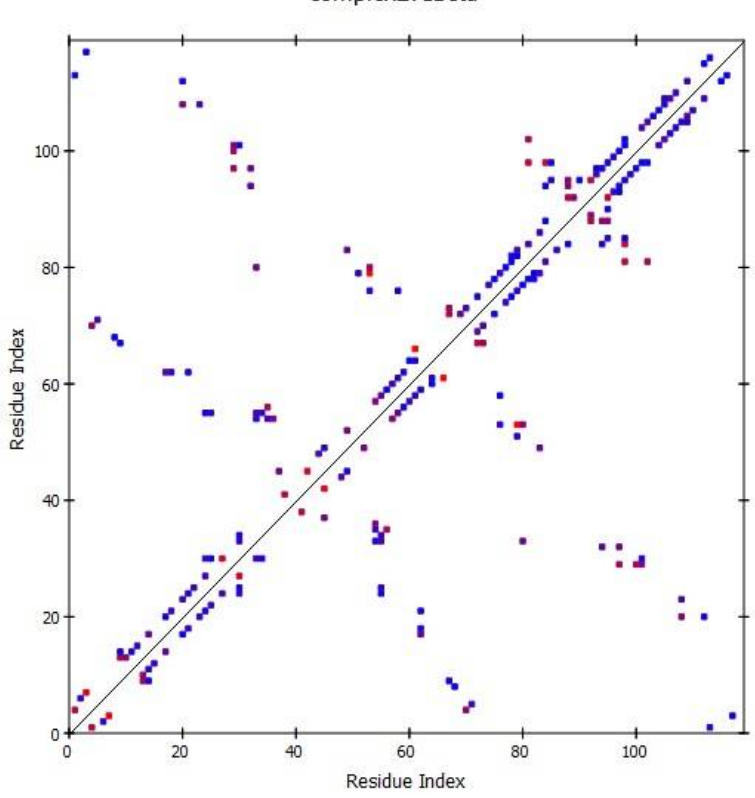

Figure 12 shows the interaction of Gentiobiose with the crystal structure of CPd8 in C-Beta Plot

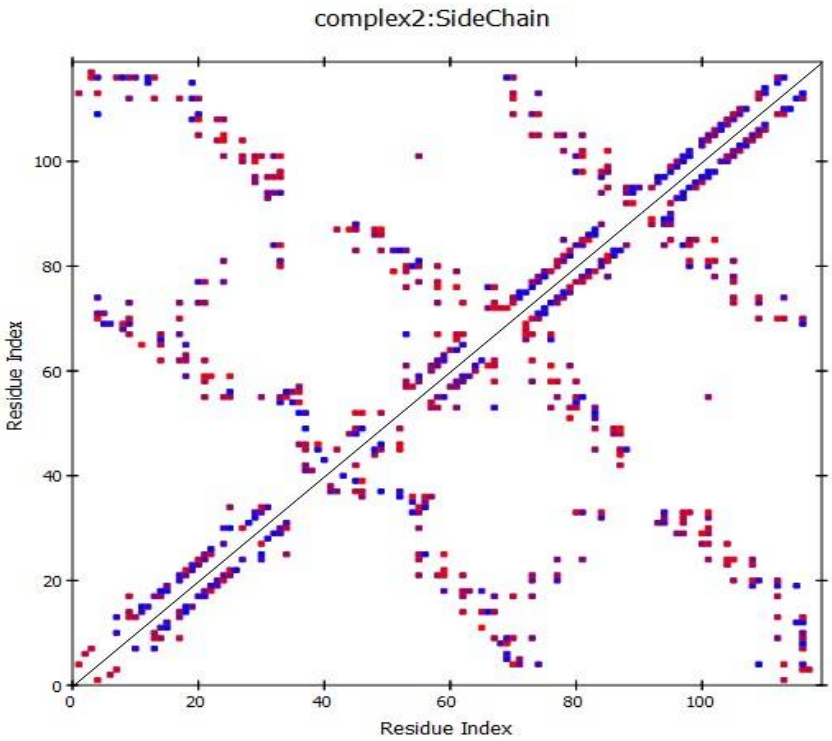

Figure 13 shows the interaction of Gentiobiose with the crystal structure of CPd8 in Sidechain Plot

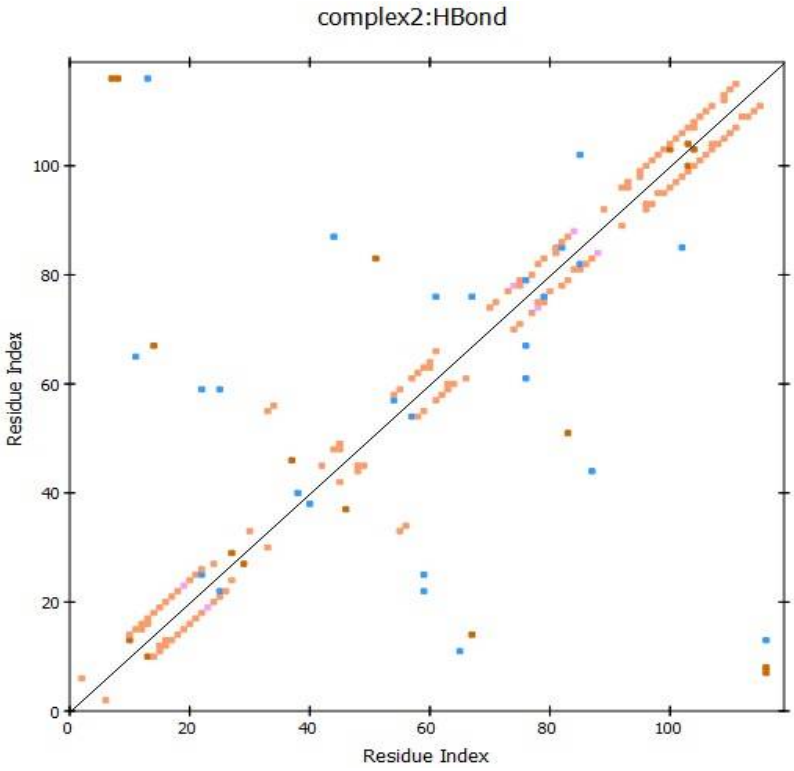

Figure 14 shows the interaction of Gentiobiose with the crystal structure of CPd8 in H-bond Plot

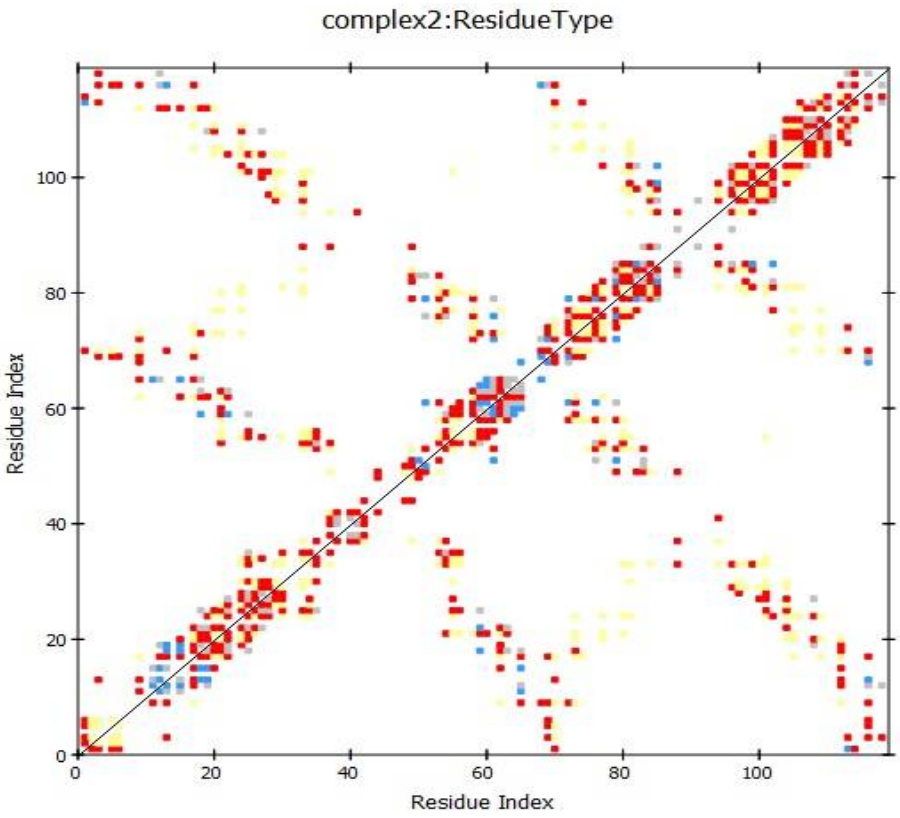

Figure 15 shows the interaction of Gentiobiose with the crystal structure of CPd8 in Residue Plot

CONCLUSION

Many medications are used to treat lung cancer, the world's second most common disease. MD modeling was used using the crystal structure of CPd8 and Gentiobiose to develop effective medication for this disease. With 9 interactions, the interacting molecules have the greatest binding affinity of -7. Many plots, such as the Ramachandran plot, were used to evaluate and prove the various conformations of these molecules. TRP227, TYR55, ASP50, HIS117, UNK1, PRO2025, and GLU2828 are the various amino acid residues in the receptor's binding site. Gentiobiose is an attractive and effective medication against Lung Cancer, as evidenced by its interactions and binding score.

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