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ORIGINAL ARTICLE **OPEN ACCESS**

Virtual Screening of Gentiobiose Treat for Breast Cancer Based on Molecular Docking Modeling

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ABSTRACT
The breast cancer cell (MCF7 cell) protein and the ligand Gentiobiose were used in a molecular docking investigation. Those compounds' greatest binding affinity would be -8. MET2846, IIE2873, GLU2828, PRO2825, UNK1, and ASN2881 are the residues that interact with the macromolecule's active site. The Root Mean Square Deviation value can also be used to study the interaction of protein and ligand in various conformations. The tiny chemical is strongly linked to the Breast cancer cell's active regions. Gentiobiose is a medication that is effective in the treatment of breast cancer.
Keywords : *Molecular docking, Gentiobiose, Breast Cancer, Active sites, Residues.*

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INTRODUCTION

Cancer is currently one of the major causes of death from diseases around the world, and without additional improvements and screening in producing new treatments to treat this sickness, it is expected to remain the leading cause of death from diseases in the coming years [1, 2]. Current-cure treatments diagnose breast cancer or metastatic breast cancer as an incurable disease. Breast cancer is the most frequent malignant disease in women, with over 400 fatalities each year [3, 4]. Because current therapies are limited by the formation of treatment-resistant cancer cells, mortality from this type of cancer remains high [5, 6]. BC starts off as a local disease, but it can spread to other parts of the body via metastases, such as lymph nodes and organs [7].

This process involves the expression of a number of genes that control cancer cell survival and invasion. Immunotherapy, surgery, radiation, and chemotherapy are commonly used in the treatment of breast cancer [8]. The inhibition or activation of a protein or pathway as a therapeutic impact in a medical condition is frequently the initial step in research [9, 10]. Indeed, selecting a target, which can be a variety of biological entities such as proteins, RNA, and genes that can be picked by ioinformatics analysis [11], is an important part of the research process. The potential drug molecule must have access to an ideal target, and the binding drug–target complex must elicit a biological response. The goal of this research is to determine the binding affinity, interactions, binding distances, and key amino acid residues involved in docking molecule binding. The molecules were docked using molecular docking software (Protein: human 3-alpha hydroxysteroid dehydrogenase type 3 and ligand: Gentiobiose).

The affinity of an association and the conditions for creating a complex are determined by the binding free energy of target–drug interactions [12]. Because of its low molecular weight, the tiny molecule attaches quickly to the receptor molecule [13]. As a result, atomic docking could be a useful tool for discovering treatments for breast cancer and other disorders. The potential therapeutic molecule must be able to access an ideal target, and the drug–target combination that binds to it must induce a biological response. The purpose of this study is to figure out what factors influence docking molecule binding, such as binding affinity, interactions, binding distances, and important amino acid residues. Molecular docking software was used to dock the compounds (Protein: human 3-alpha hydroxysteroid dehydrogenase type 3 and ligand: Gentiobiose).

MATERIALS AND METHODS

Protein Preparation

The crystal structure of human 3-alpha hydroxysteroid dehydrogenase type 3 (PDB ID:4XO6) was downloaded in PDB format from the Protein Data Bank (PDB) database for molecular docking. With a resolution of 1.20Ao[14], it is an X-Ray diffracted structure. The discovery studio software was used to remove side chains, water molecules, and other ligands from the protein structure (Figure1). Finally, for docking compatibility, it was converted to PDBQT format [15].

Ligand Preparation

Gentiobiose(PubChem CID:3D 441422)(Figure 2) was chosen as the ligand for our docking and was retrieved in SDF format as a 3D structure from the PubChem database. Open babel software was used to convert it to PDB format. The energy was reduced and the tiny molecule was converted to a PDBQT format [16].

Molecular Docking

Autodock vina is one of the greatest molecular docking programmes available. The docking's major molecules were acquired and readied for docking. The molecules' format was altered to make docking easier. 15.9353, -1.5377, and 2.998 were used to centre the grid box, which was 72X64X25 in size. 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 visualisations of the interactions.

RESULTS AND DISCUSSION

Around 80% of breast cancer cells are oestrogen receptor-positive, with 65 percent also being progesterone receptor-positive, while 13% of total breast cancer cells are oestrogen receptor-positive but progesterone receptor-negative, and 2% are oestrogen receptor-negative but progesterone receptor-positive. Drug discovery is a labor-intensive and time-consuming process. A new medicine takes an average of 10–15 years to create. Because of its low cost and risk-free properties, drug repositioning, or the use of old treatments for new conditions, is an effective technique [17]. In order to develop an effective treatment against breast cancer, molecular docking was performed in a computer. Autodock tools were used to perform molecular docking investigations, and Gentiobiose was docked with human 3-alpha hydroxysteroid dehydrogenase type 3 (PDB ID:4XO6).

The energy minimization of the ligand Gentiobiose would be 378.53 if protein and ligand were preprocessed. The maximum negative protein binding affinity will be -8. The discovery studio file was used to examine the interactions between proteins and ligands. The distances between H bonds in various aminoacids were computed. MET2846, IIE2873, GLU2828, PRO2825, UNK1, and ASN2881 are key residues in interactions. H-bond distances and H-bond interaction residues were measured (Table 1). The root mean square deviation will be 0 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), were in agreement (Table 2). Protein-ligand interactions (Lupeol) were studied (Figures 3, 4, 5, 6, 7, 8, and 9). It is also displayed in other charts such as the Ramachandran plot (Figure 10), the Hydrophobicity plot (Figure 11), and several contact plots such as the CAlpha plot (Figure 12), the CBeta plot (Figure 13), the Sidechain plot (Figure 14), the H bond plot (Figure 15), and the Residue plot (Figure 16). (Figure 16). As a result, Gentiobiose is an excellent breast cancer treatment.

Table 1. The molecular docking studies of compounds with human 3-alpha hydroxysteroid dehydrogenase type 3

S. No	Compound name	Docking score	H-Bond Interaction	Distance
1.	Gentiobiose	-8	MET2846 IIE2873 GLU2828 PRO2825 UNK1 ASN2881	2.86 2.36 2.38 2.63 2.17 2.63 1.52 2.48

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
Protein_A_Gentiobiose_uff_E=378.53	-8	0	0
	-8	6.9	1.215
	-8	6.323	1.734
	-7.9	6.598	1.383
	-7.8	3.672	1.931
	-7.8	3.934	2.185
	-7.7	7.238	1.931
	-7.6	6.245	3.406
	-7.5	2.843	2.091

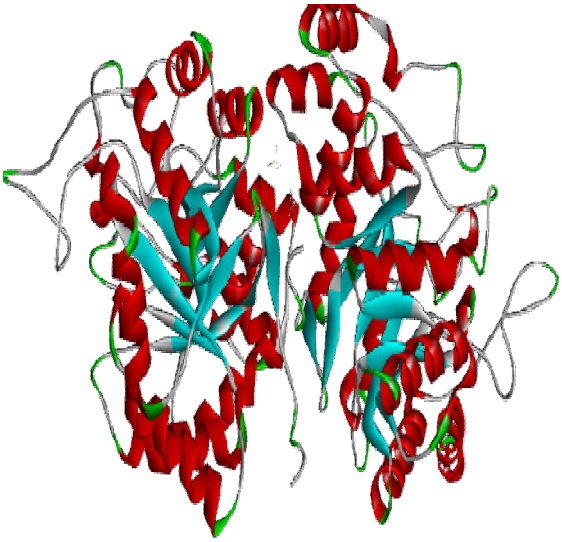

Figure 1 shows the 3D structure of human 3-alpha hydroxysteroid dehydrogenase type3

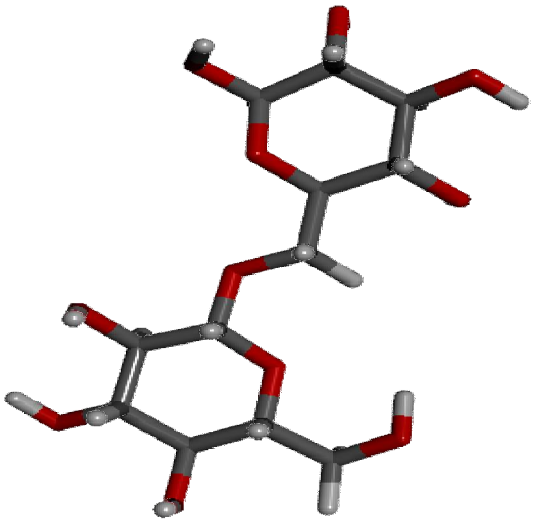

Figure 2 shows the 3D structure of Gentiobiose

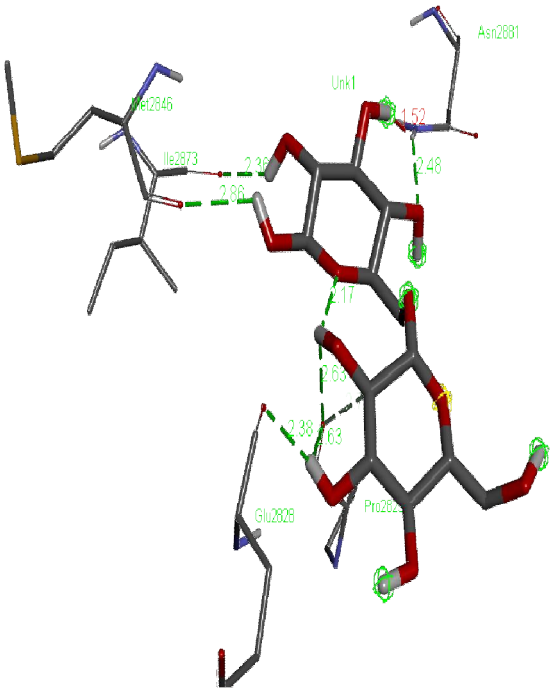

Figure 3 shows the interaction of Gentiobiose and human 3-alpha hydroxysteroid dehydrogenase type 3

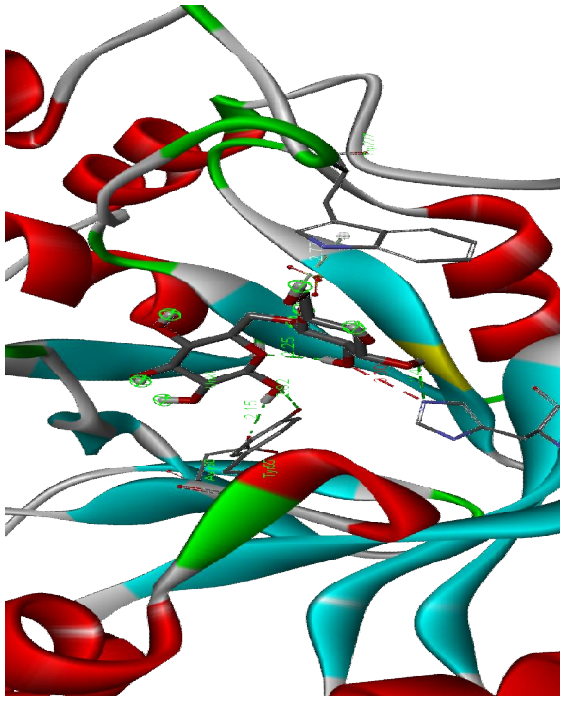

Figure 4 shows the interaction of Gentiobiose and human 3-alpha hydroxysteroid dehydrogenase type 3

5. 6.

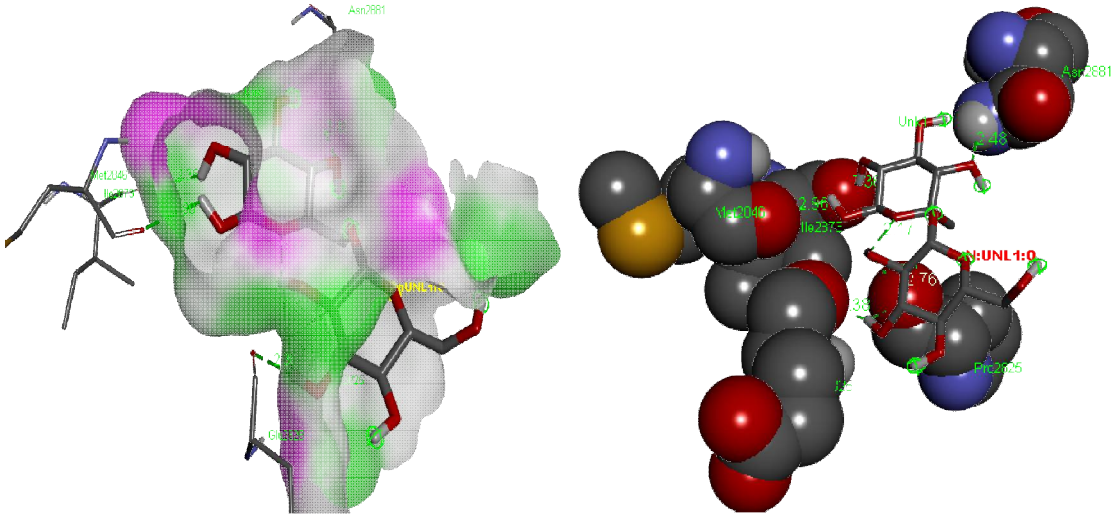

Figure 5,6 shows the interaction of Gentiobiose and human 3-alpha hydroxysteroid dehydrogenase type 3

7. 8.

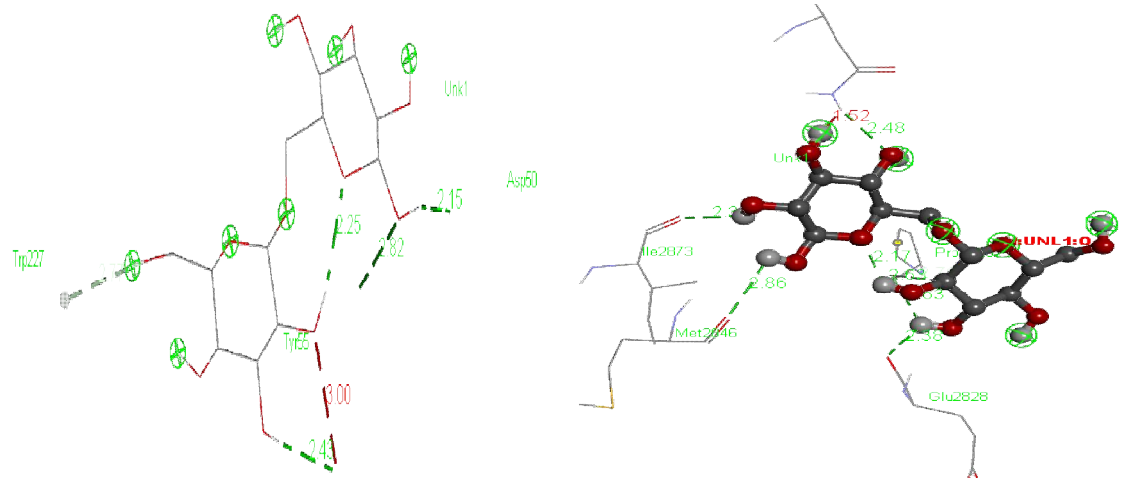

Figure 7,8 shows the interaction of Gentiobiose and human 3-alpha hydroxysteroid dehydrogenase type 3

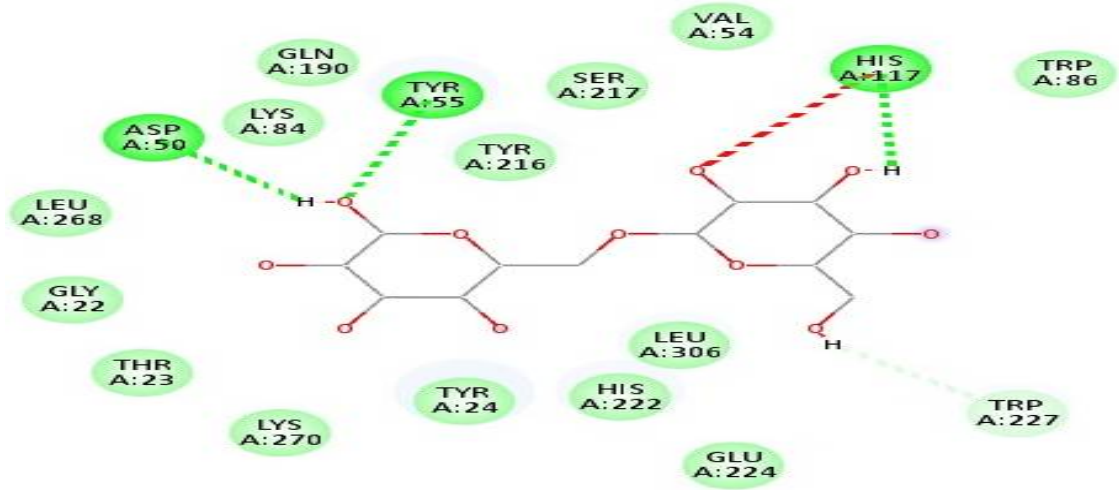

Figure 9 shows the 2D diagram of interaction of Gentiobiose and human 3-alpha hydroxysteroid dehydrogenase type 3

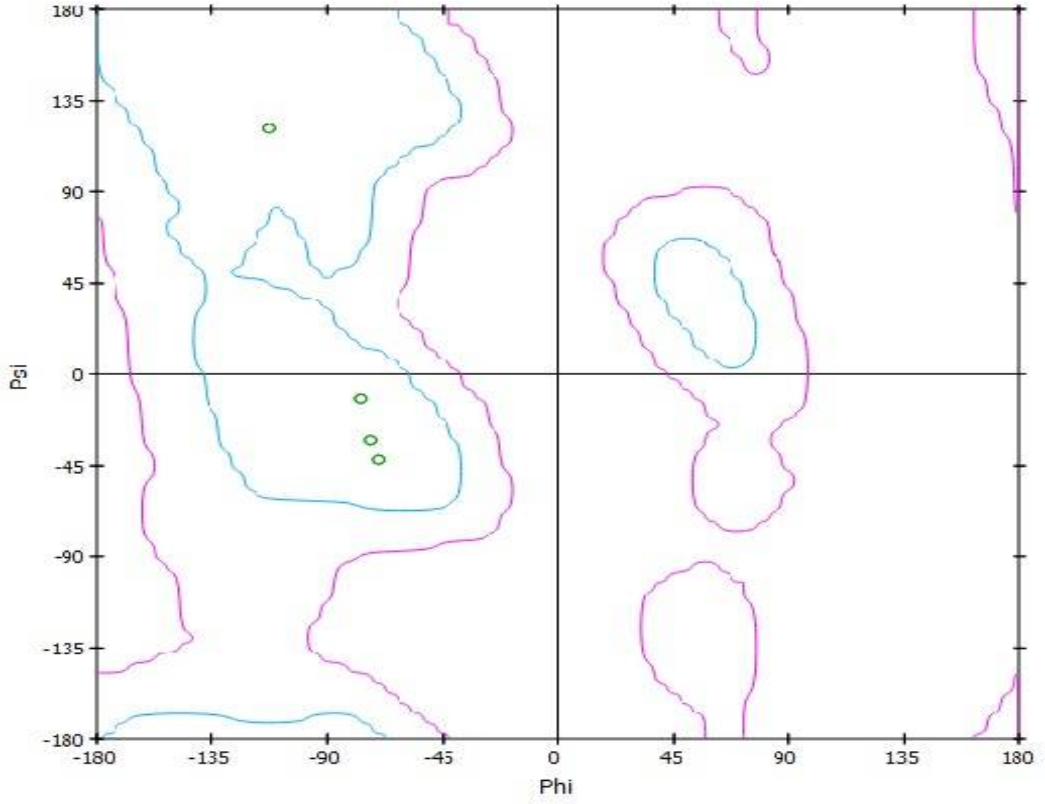

Figure 10 shows the interaction of Gentiobiose and human 3-alpha hydroxysteroid dehydrogenase type 3 in Ramachandran Plot

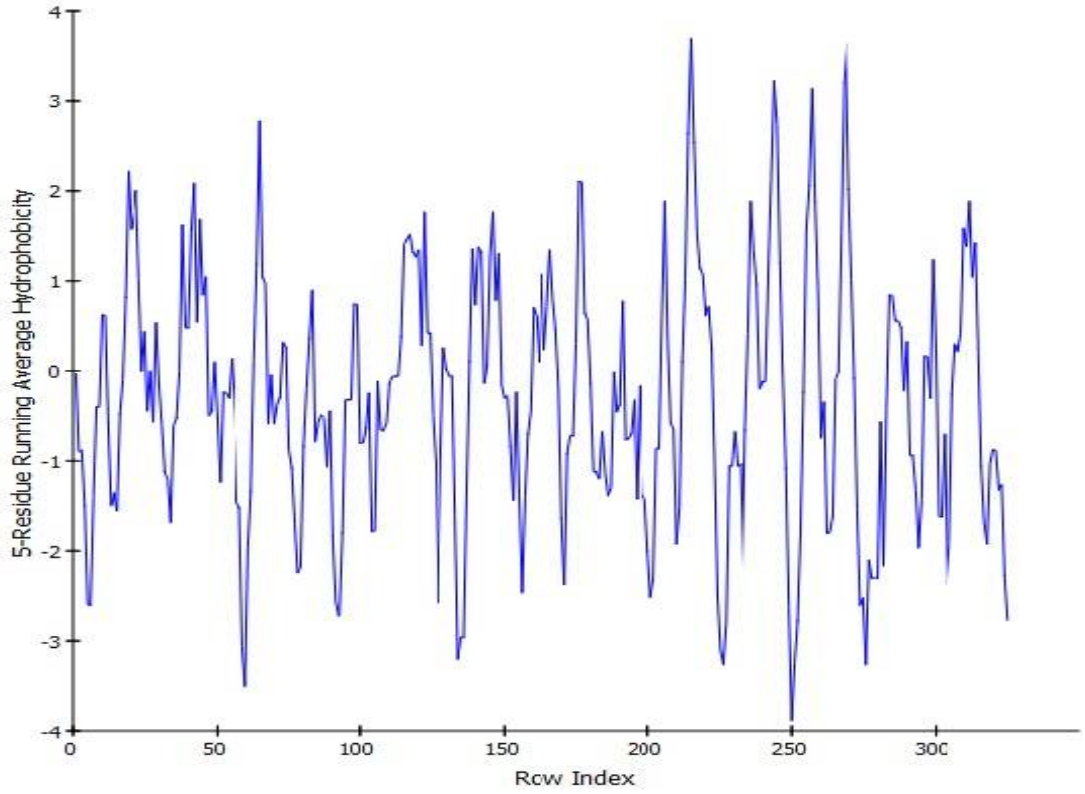

Figure 11 shows the interaction of Gentiobiose and human 3-alpha hydroxysteroid dehydrogenase type 3 in Hydrophobicity Plot

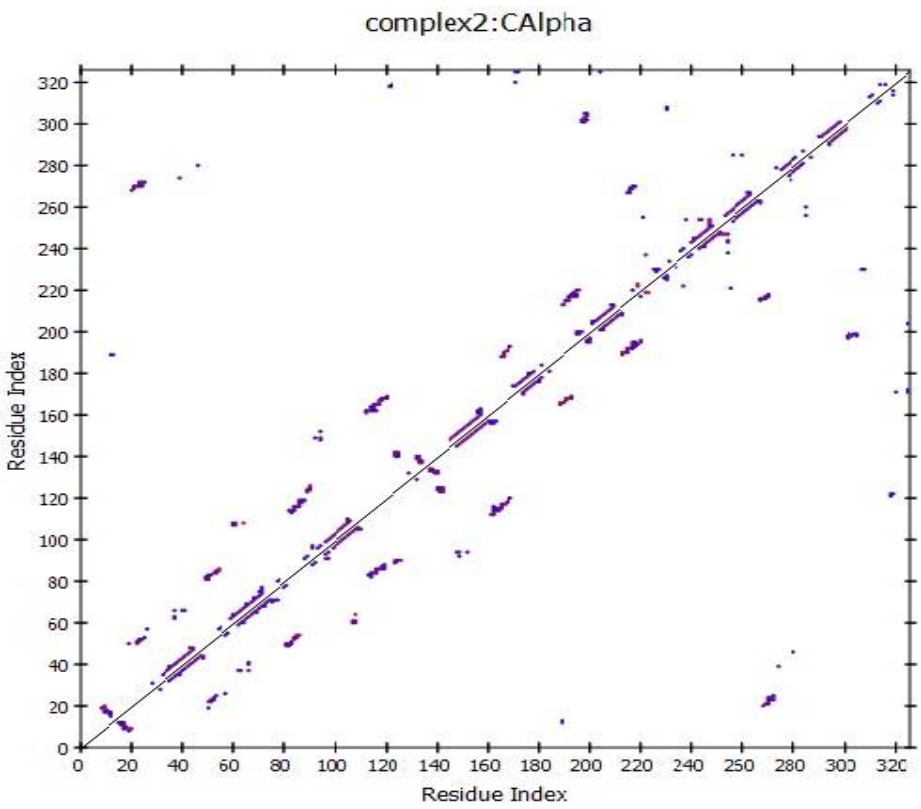

Figure 12 shows the interaction of Gentiobiose and human 3-alpha hydroxysteroid dehydrogenase type 3 in C-Alpha Plot

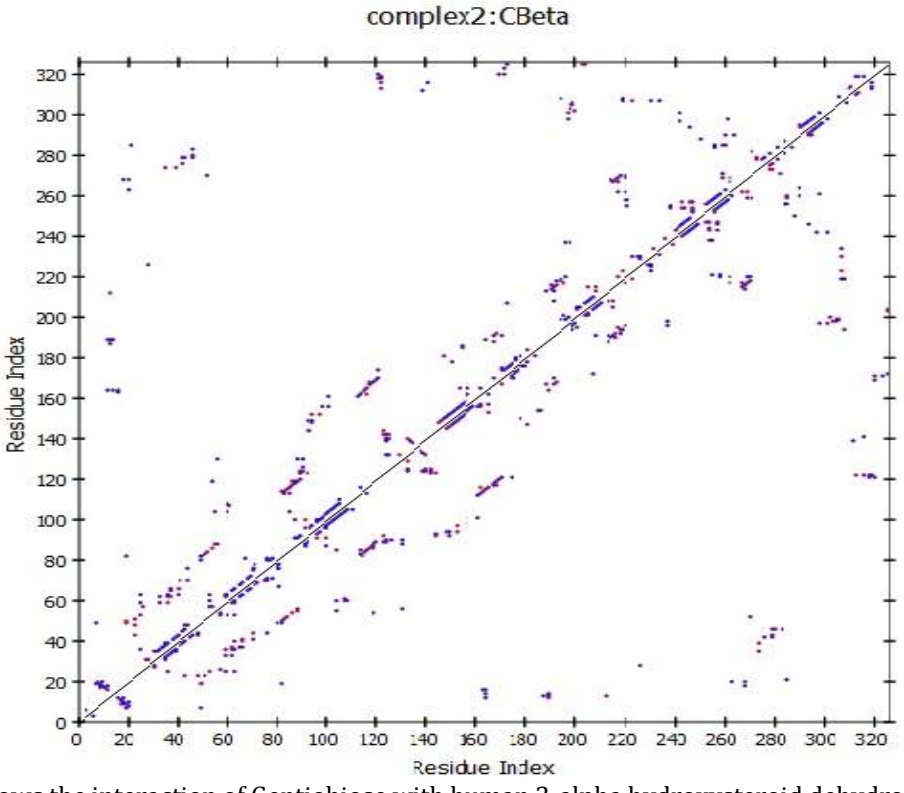

Figure 13 shows the interaction of Gentiobiose with human 3-alpha hydroxysteroid dehydrogenase type 3in C-Beta Plot

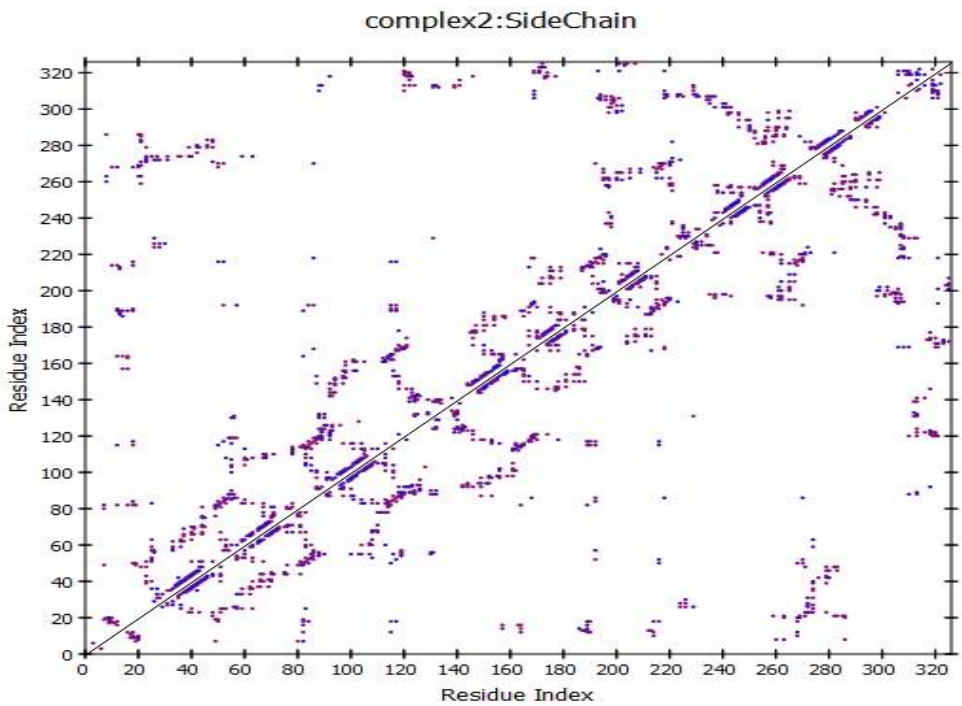

Figure 14 shows the interaction of Gentiobiose with human 3-alpha hydroxysteroid dehydrogenase type 3 in Sidechain Plot

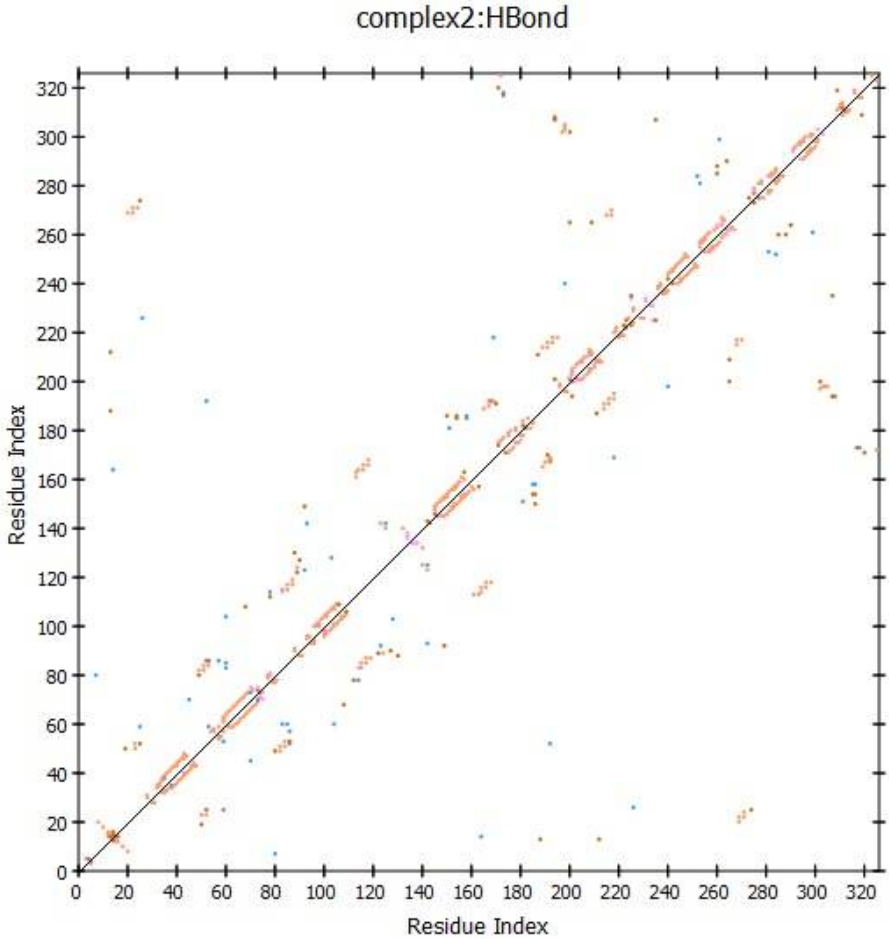

Figure 15 shows the interaction of Gentiobiose with human 3-alpha hydroxysteroid dehydrogenase type 3 in H-bond Plot

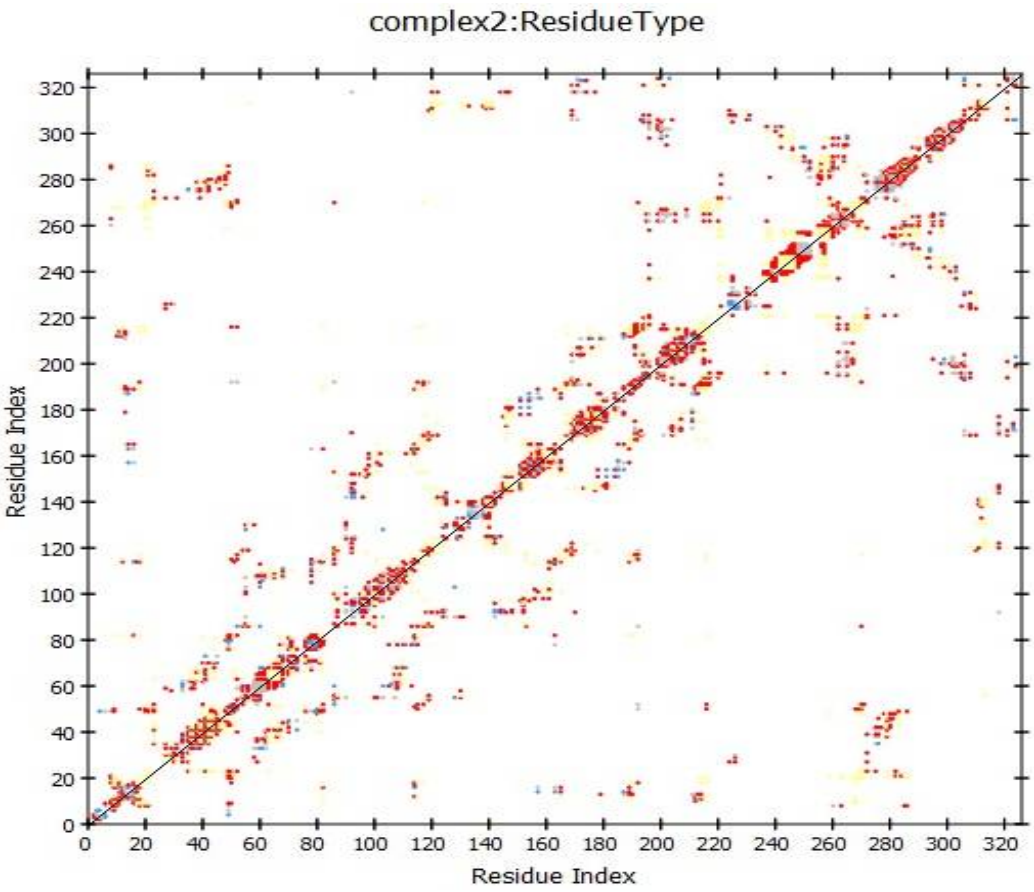

Figure 16 shows the interaction of Gentiobiose with human 3-alpha hydroxysteroid dehydrogenase type 3 in Residue Plot

CONCLUSION

Various medications were utilised to treat breast cancer, the most malignant illness that affects women. Human 3-alpha hydroxysteroid dehydrogenase type 3 and Gentiobiose were used in computational studies. -8 is the greatest binding score. MET2846, IIE2873, GLU2828, PRO2825, UNK1, and ASN2881 would be the interacting residues in the pocket atoms. The receptor-ligand interactions in other plots, such as hydrophobicity plots and side-chain plots, were also investigated. As a result, Gentiobiose is a promising medication for the treatment of breast cancer.

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