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ORIGINAL ARTICLE **OPEN ACCESS**

In Silico Analysis and Molecular Docking Studies of Anti-HIV Ligand Baurenol Against Mutant Hiv-1 Reverse Transcriptase Protein

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ABSTRACT
AIDS is an infectious disease caused by the Human Immunodeficiency Virus (HIV), which affects approximately 36.7 million people and is characterized by impaired defense cells. HIV requires protease, integrase, and reverse transcriptase, which is all crucial enzymes in the viral reproduction process. Natural materials are increasingly being used in anti-HIV research, with researchers betting on these chemicals in the hopes of developing effective medications with fewer adverse effects. Docking was performed using the PDB crystal structure of a mutant HIV-1 reverse transcriptase protein and a small chemical (Baurenol) from the PubChem database. With ligand, the greatest docking score was -8. VAL90, GLU89, TRP88, and ALA158 are the residues that interact with HIV RT. The results showed that in models, the steric, hydrophobic, and electrostatic fields are important. The conformations of chemicals and critical amino acid residues at the docking pocket of RT protein were revealed using molecular docking. The MD simulation tests also showed that the newly developed compounds might stably bind to the HIV-1 RT.
Keywords: *AIDS, HIV-1 Reverse transcriptase, Baurenol, Molecular docking, Interacting Residues*

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INTRODUCTION

HIV is a ribonucleic acid [RNA] virus that contains a single enzyme, reverse transcriptase, which converts viral RNA into deoxyribonucleic acid [DNA] that can then be integrated into the genome of the infected host cell. HIV has been a global health problem for more than 28 years [1, 2]. Inhibiting viral replication is the most basic method [3, 4]. Many investigations have shown that HIV's viral reverse transcriptase is a multifunctional enzyme that plays an important role in the virus's life cycle, making it an appealing target for drug development [5, 6].

As a result, incorporating computational approaches for the design of new medications is one of the strategies utilized nowadays in modern medical chemistry [7, 8]. It is feasible to execute a virtual screening by assessing some key properties of natural products to obtain the medicine using in silico approaches. If a data collection of known medications is used to do the molecular docking technique, docking-based approaches can be effective for estimating the importance of mutations for HIV-1 resistance [9, 10]. In contrast to structure-property relationship analysis, which requires data on a set of low molecular weight compounds and their impact on a specific protein, molecular docking can be performed if data on at least one complex of protein-ligand [protein-low molecular weight drug] is available. We anticipate that the models and docking information obtained will be useful in the future for NNRTIs and accurate activity estimates for newly developed HIV-1 reverse transcriptase inhibitors.

MATERIALS AND METHODS

Protein preparation

The investigation was based on the X-ray diffraction-based crystal structure of Y188c mutant HIV-1 reverse transcriptase Baurenol with a resolution of 2.60 [11, 12]. The protein was found in the Protein Data Bank (PDB). [PDB ID: 1JLF] [PDB ID: 1JLF] [PDB ID: 1J the discovery studio application [Figure1]

emptied all water particles from all protein structures. Protein was relegated and, at long last, the protein was saved. [13, 14] pdbqt format

Ligand preparation

The two-dimensional structure of Baurenol was converted into a three-dimensional structure using the open Babel organize atom converter and saved in PDB format for Docking compatibility, and the ligand structure was taken from the PubChem database[Figure 2] and optimized with 3D-geometry. Energy is reduced and converted to the ligand. ligand.pdbqt files with PDB entries [15, 16].

Active site prediction

The official location of the protein, or more frequently than not, a stash at the protein's surface, comprises buildups capable of substrate specificity that operate as proton benefactors or acceptors regularly. The key phase in a structure-based sedate plan is distinguishing proof and characterization of official location. Computational and written reports have set the official place apart. The cast distinguishes the changing geographical localization of the protein. To envision the official location, these servers methodically outfit the zone and volume at the plausible dynamic position of each take.

Docking protocol

The receptor lattices were built using 92x110x25 network focuses in XYZ with a network box centered within the run of 18.2716, -15.2718, 27.1045 co-crystallized after the protein and ligand were converted to PDBQT data. The protein and ligand for docking were chosen at that stage, and the Programme was executed. Positional root-mean-square deviation [RMSD] occurrences were grouped and spoken to by the outcome with the most ideal free vitality of official. Biovia discovery studio was used to investigate the protein-ligand interaction. The yields were evaluated using their atomic surfaces and various bands. As PNG records, the yields are spared.

RESULTS AND DISCUSSIONS

Heat atoms such as water molecules and ligand groups found in the protein for our study Y188c mutant HIV-1 reverse transcriptase were deleted and converted to autodock compatibility [PDBQT format] in our docking macromolecule. The energy-reduced for the small molecule Baurenol was 1111.27, and the file was then saved in PDBQT format. The cast discovered and defined the active sites of this protein, and the residues found in these sites were VAL90, GLU89, TRP88, and ALA158. They're also backed up by academic studies. The many protein conformations with each ligand were investigated. Baurenol has the best binding affinity of -8. [Table 1] shows the distances between H-bonds and the H-bond interacting residues. The root means square deviation will be 0 in such conformation. [Table 2] shows 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]. [Figures 3, 4, 5, 6, 7, 8, and 9] show the interactions of protein and ligand [Baurenol]. It can also be seen in many charts, such as the Ramachandran plot [Figure10], the Hydrophobicity plot [Figure11], and some contact plots, such as the CAlpha plot [Figure12], the CBeta plot [Figure13], the Side Chain plot [Figure14], and the H bond plot [Figure15], and Residue plot [Figure16].

The HIV-1 infection causes acquired immunodeficiency syndrome that is a fatal human health-threatening disease [17]. The disease presents a serious health care challenge because each year it affects an increasing number of people [18]. A barrier in the treatment of AIDS is the mutation of HIV, which confers resistance against enzyme inhibitors [which protease, integrase, and reverse transcriptase]. Most of the existing antiretroviral treatments are highly cytotoxic to the affected patients [19]. Therefore, one of the strategies used today in modern medical chemistry is the insertion of computational methods for the planning of new drugs [20]. So Baurenol is an attractive drug for HIV infection.

A human health-threatening condition, acquired immunodeficiency syndrome, is caused by HIV-1 infection [17]. Because the condition affects an increasing number of people each year, it poses a severe health care challenge [18]. The mutation of HIV, which gives resistance to enzyme inhibitors [such as protease, integrase, and reverse transcriptase], is a hurdle in the therapy of AIDS. The majority of currently available antiretroviral medications are highly cytotoxic to patients [19]. As a result, incorporating computational approaches for the planning of new medications is one of the strategies utilized nowadays in modern medical chemistry [20]. As a result, Baurenol is a promising HIV treatment.

Table 1. The molecular docking studies of Baurenol with Y188c mutant HIV-1 Reverse transcriptase

S. No	Compound name	Docking score	H-Bond Interaction	Distance
1	Baurenol	-8	VAL90 GLU89 TRP88 UNK1 ALA158	5.35 2.18 5.17 4.65 4.48

Table 2. Shows the various binding affinity and root mean square deviation [RMSD] Upper and Lower Bound values of Baurenol

Ligand	Binding Affinity	rmsd/ub	rmsd/lb
1jlf_A_baurenol_uff_E=1111.27	-8	0	0
	-7.9	9.337	5.245
	-7.9	9.54	3.357
	-7.8	8.661	4.791
	-7.8	6.564	3.307
	-7.4	8.952	4.746
	-7.3	7.036	3.859
	-7.3	9.957	6.635
	-7.2	27.18	25.031

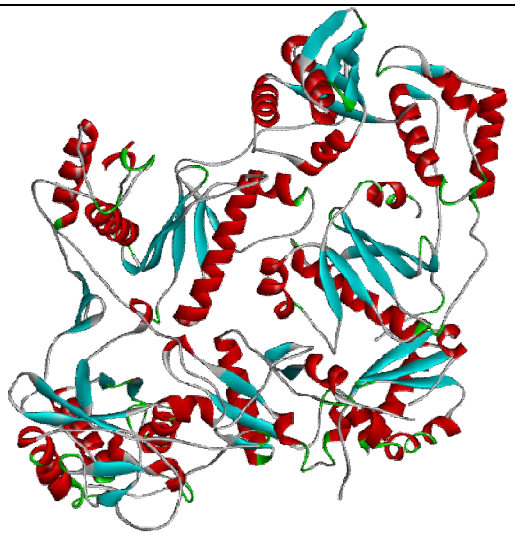


Figure1 3D structure of Y188c mutant HIV-1 Reverse transcriptase

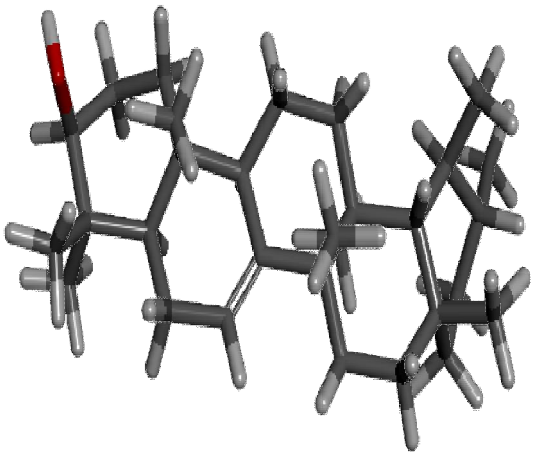


Figure2 3D Structure of Baurenol

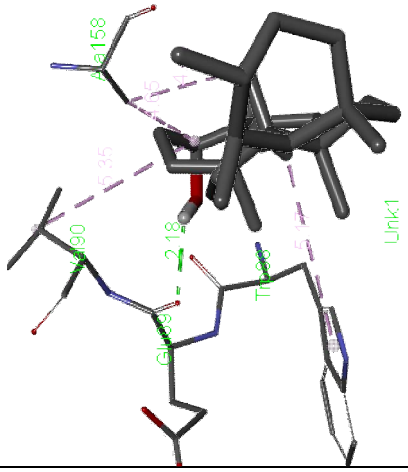


Figure 3 Interaction of Baurenol and Y188c mutant HIV-1 Reverse transcriptase

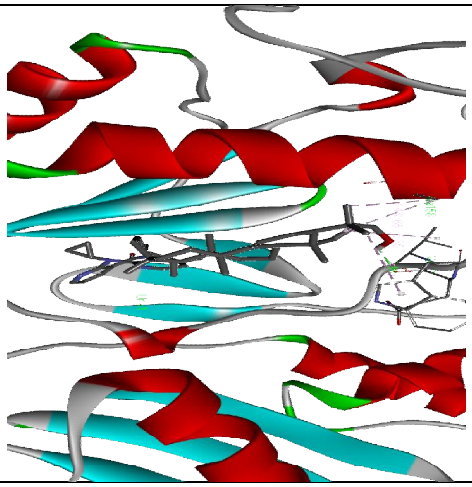
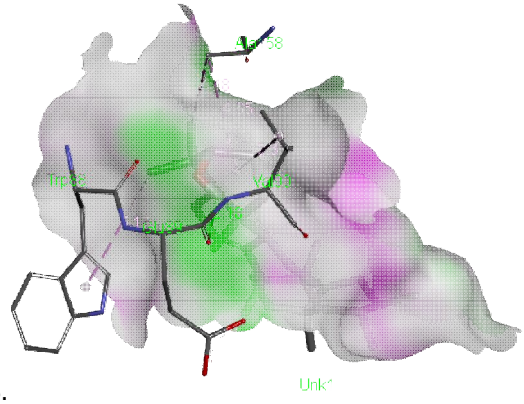


Figure 4 inhibitor of Baurenol with their receptors

5.



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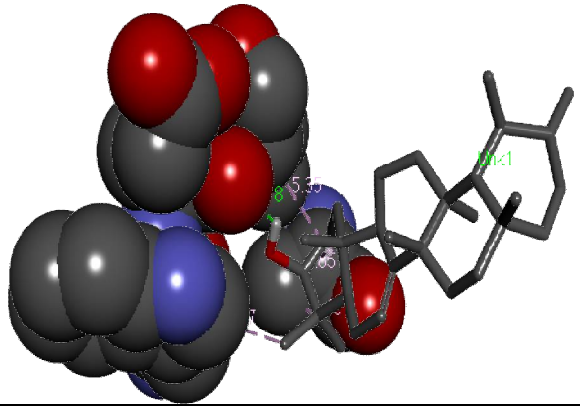
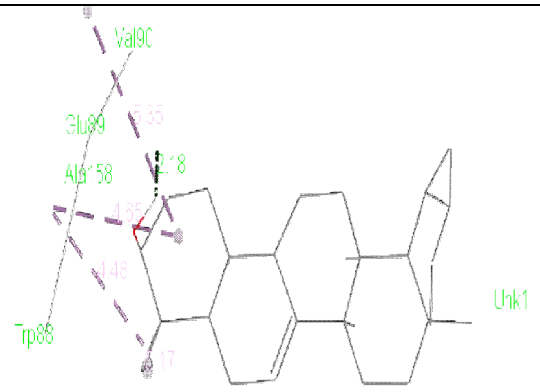


Figure 5&6 Interaction of Baurenol and Y188c mutant HIV-1 Reverse transcriptase with their molecular surfaces

7.



8.

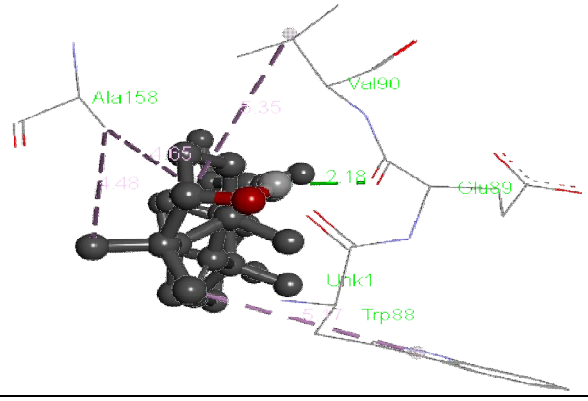


Figure 7&8 shows the interaction of Baurenol and Y188c mutant HIV-1 Reverse transcriptase with their bonds

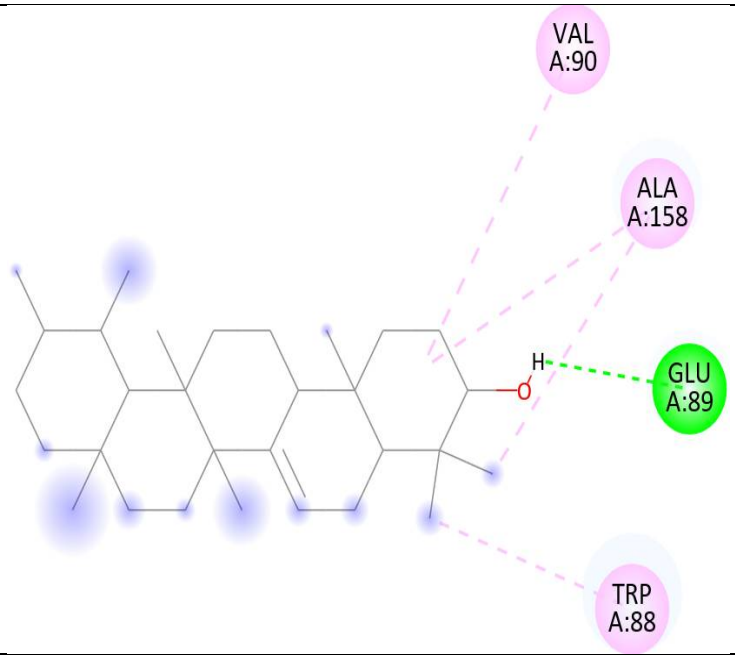


Figure 9 shows the 2D diagram of the interaction of Baurenol and Y188c mutant HIV-1 Reverse transcriptase with their bonds

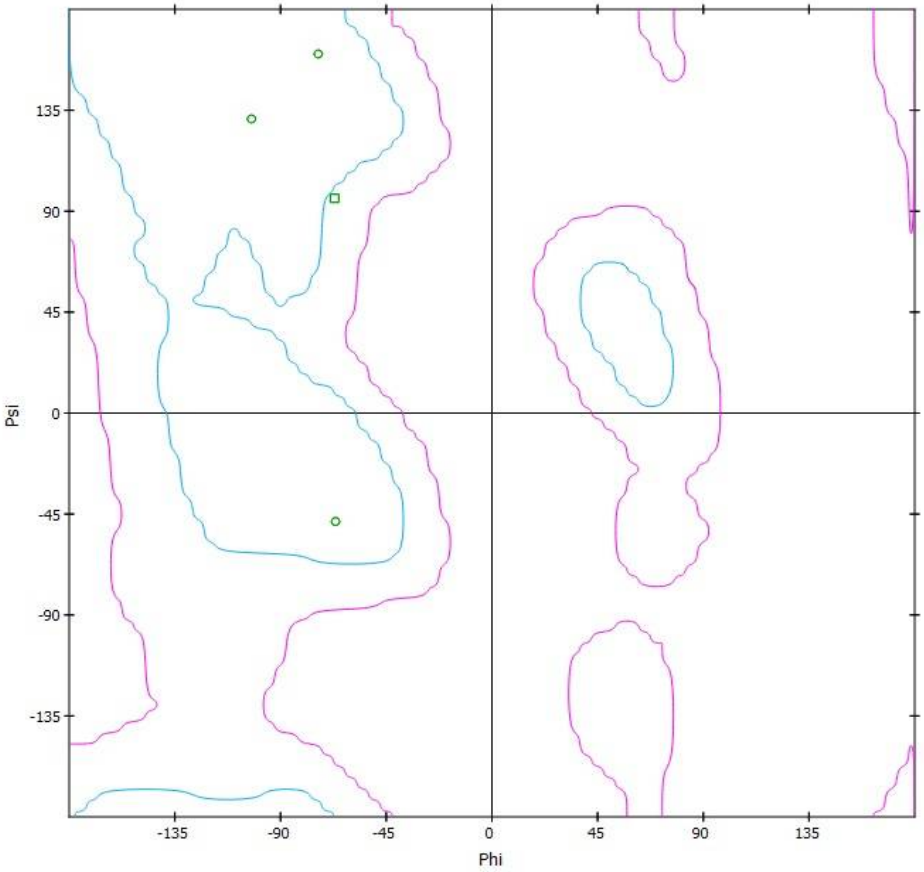


Figure 10 shows the interaction of Baurenol and Y188c mutant HIV-1 Reverse transcriptase in Ramachandran Plot

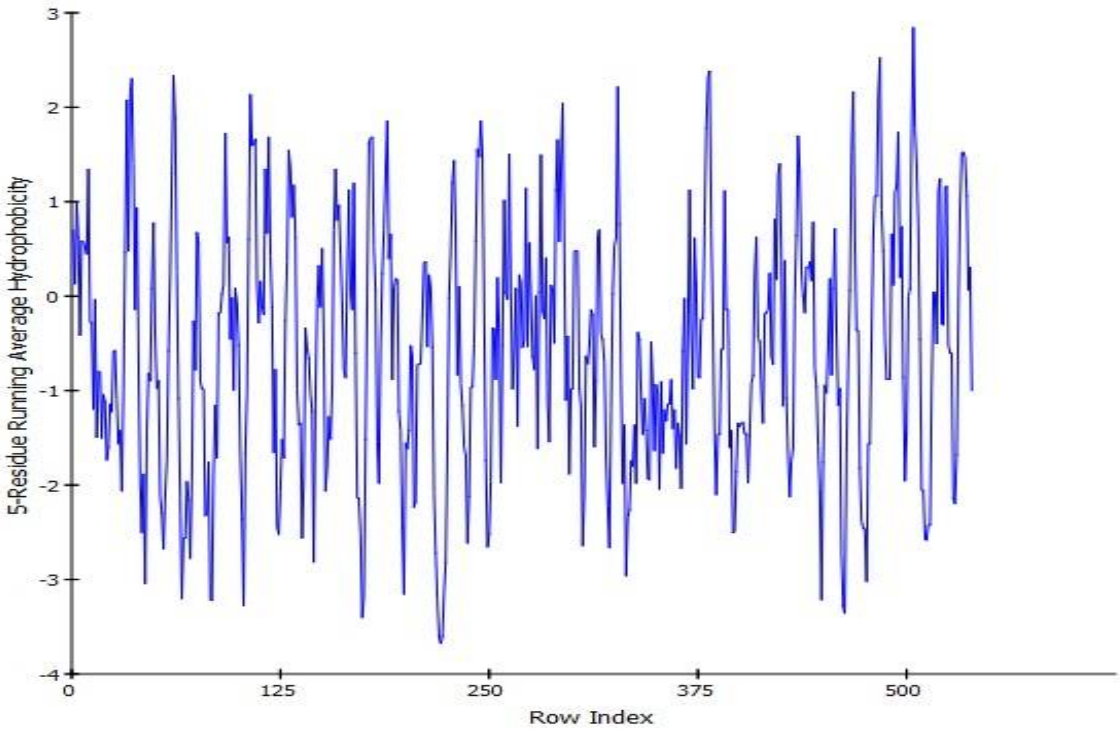


Figure 11 shows the interaction of Baurenol and Y188c mutant HIV-1 Reverse transcriptase in Hydrophobicity Plot

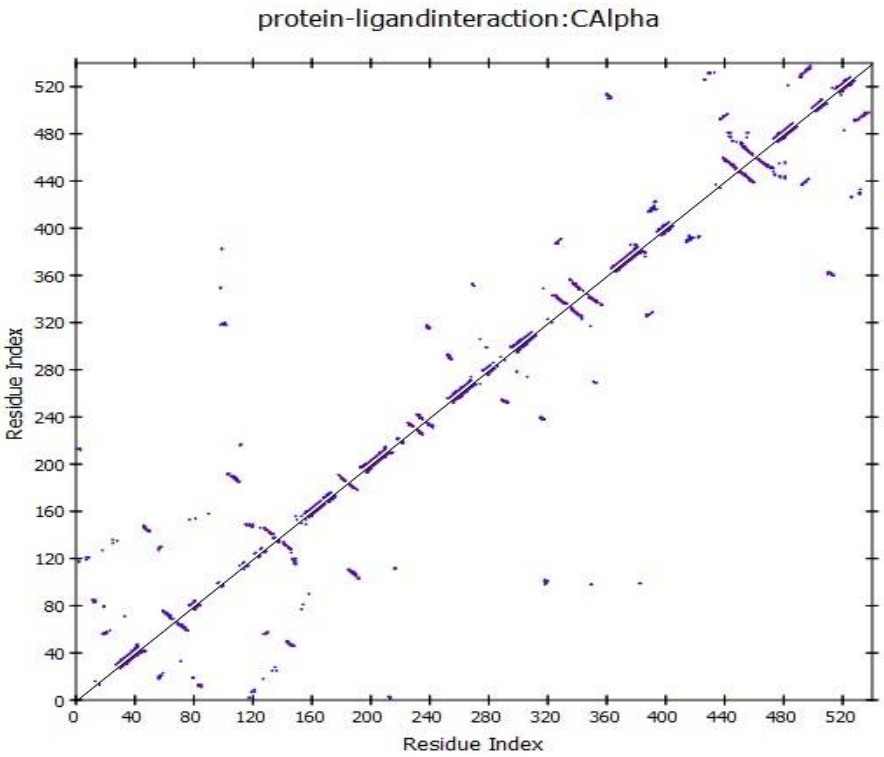


Figure 12 shows the interaction of Baurenol and Y188c mutant HIV-1 Reverse transcriptase in C-alpha Plot

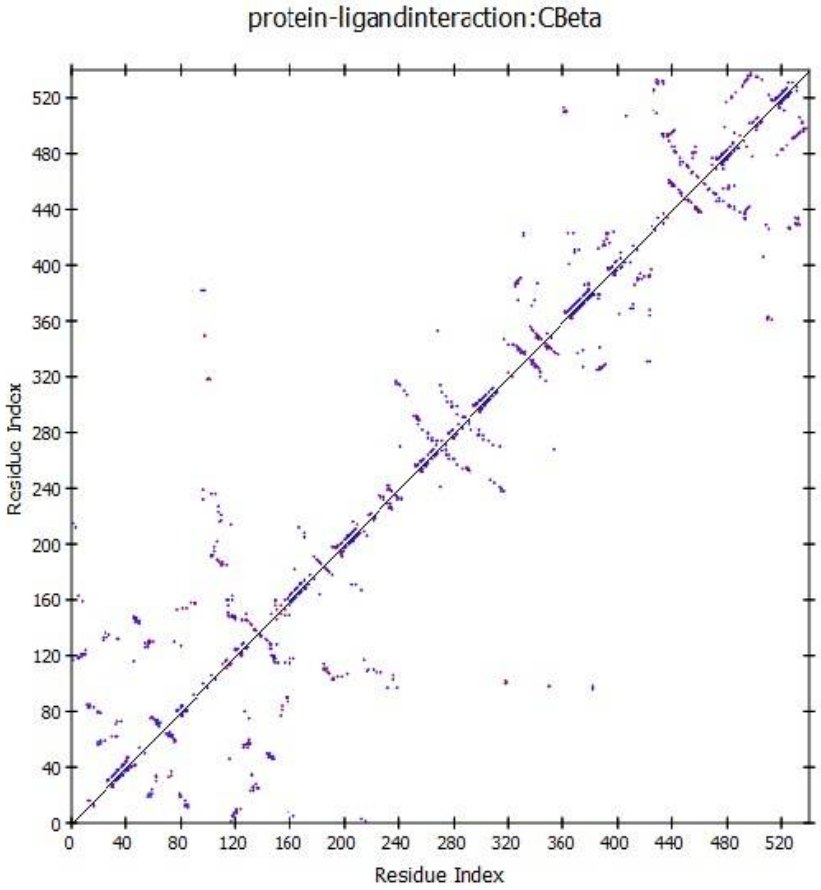


Figure 13 shows the interaction of Baurenol and Y188c mutant HIV-1 Reverse transcriptase in C-Beta Plot

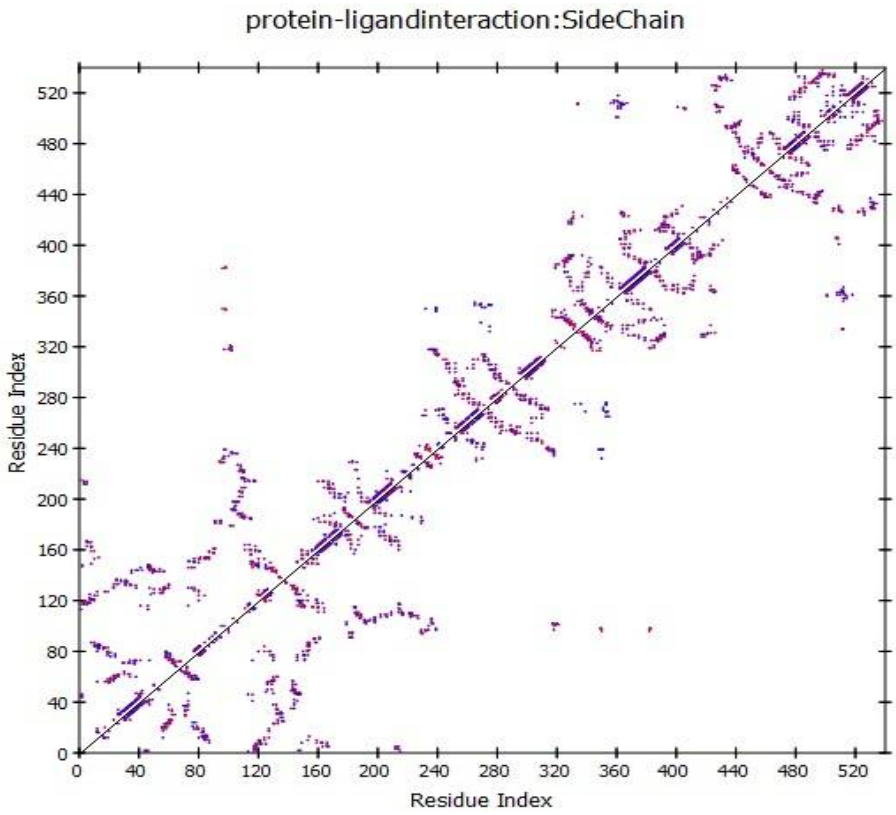


Figure 14 shows the interaction of Baurenol and Y188c mutant HIV-1 Reverse transcriptase in Sidechain Plot

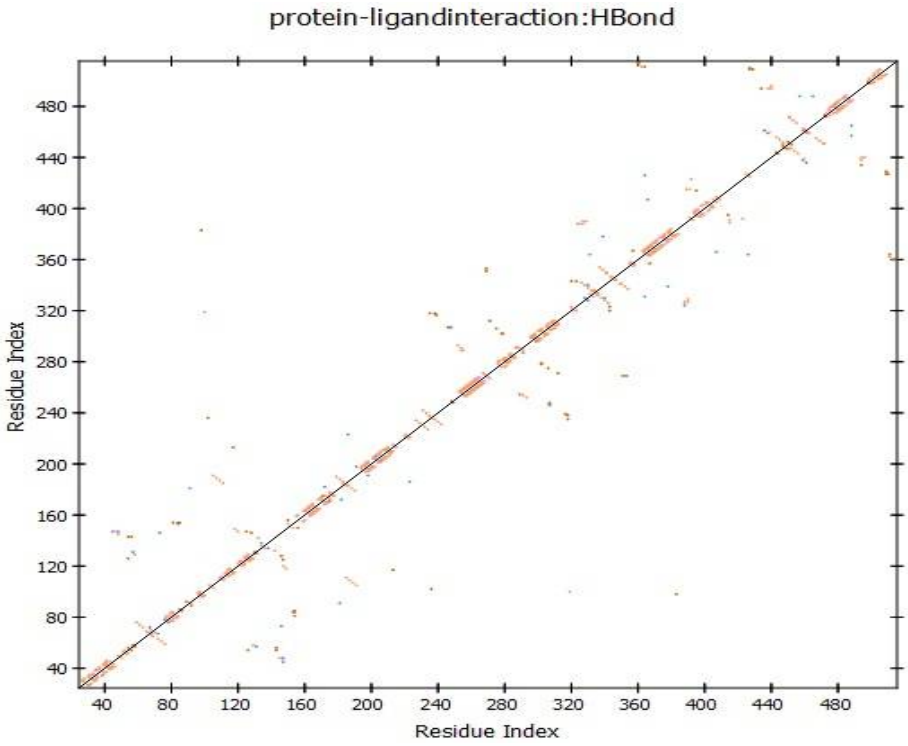


Figure 15 shows the interaction of Baurenol and Y188c mutant HIV-1 Reverse transcriptase in H-bond Plot

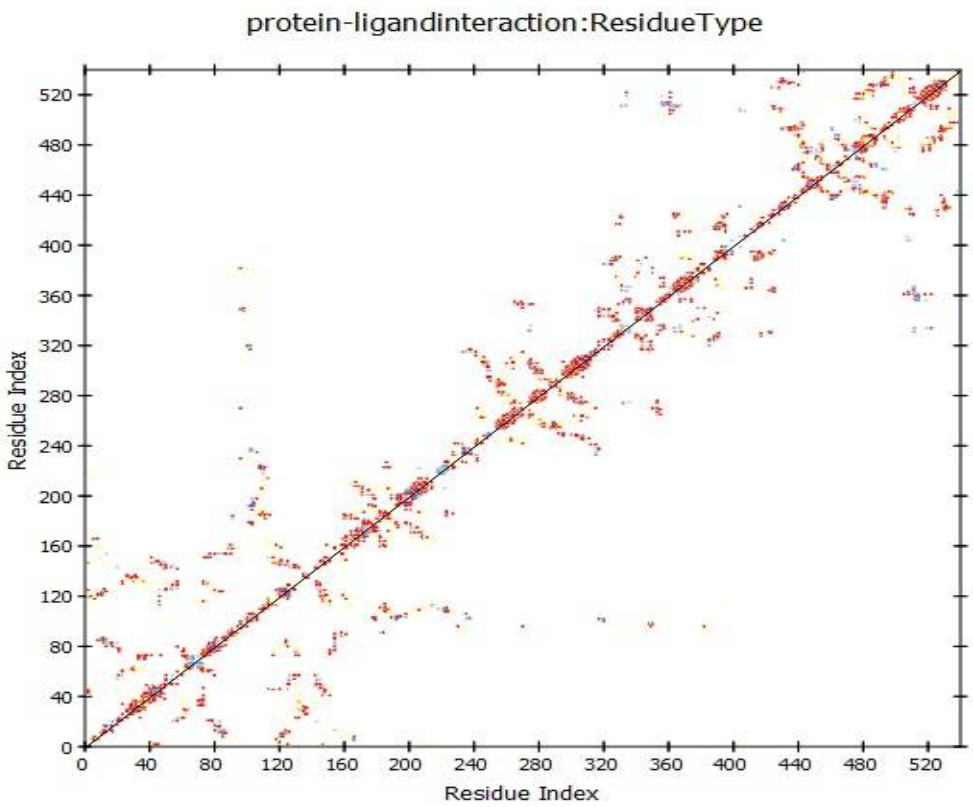


Figure 16 shows the interaction of Baurenol and Y188c mutant HIV-1 Reverse transcriptase in Residue Plot

CONCLUSION

Computational medicinal chemistry studies are being used to search for bioactive with the optimal multi-target interactions for HIV-1. Y188c mutant HIV-1 reverse transcriptase and Baurenol were used to create MD. Those chemicals have the best binding affinity of -8. VAL90, GLU89, TRP88, and ALA158 are some of the most important residues that interact with HIV-1 RT. The tiny chemical is firmly linked to the HIV-1 RT protein of interest. As a result, we anticipate that the tested and developed compounds will be used as lead compounds in innovative HIV-1 NNRTIs.

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