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MOLECULAR DOCKING STUDIES OF IMIDAZOLE DERIVATIVES AS NEW CLASS OF HIV-1 PROTEASE INHIBITOR

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Abstract:

The human immunodeficiency virus (HIV) infects the immune system that leads to immune deficiency. Acquired immunodeficiency syndrome (AIDS) is defined as the most advanced stages of HIV infection. It is defined by the occurrence of any of more than 20 opportunistic infections or HIV-related cancers. According WHO and UNAIDS estimation, 36.7 million people were living with HIV globally by the end of 2015. 2.1 million People became newly infected, and 1.1 million died of HIV-related causes at the same year. HIV-1 protease plays a vital role in the maturation of virus in order to produce the infectious viral particles. In this study, molecular docking was performed on various imidazole derivatives by Autodock 4.2 into active sites of HIV-1 protease (PDB ID: 4RVI).

Key Words: *Human immunodeficiency virus, HIV-1 Protease, 4RVI, Molecular Docking, Imidazole derivatives.*

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INTRODUCTION:

Drug designing is an inventive and integrated approach involving multiple steps based on the biological knowledge in order to design a new medication. The main aim of drug designing is to develop a drug in which it is having a high degree of chemotherapeutic index. To design, develop and commercialize a drug, it involves a tedious, time consuming and a high cost process. Taking into consideration all this factors, Computer-aided drug design (CADD) technique is being used now days in order to increase the efficiency in designing a drug. Using CADD technique, the three dimensional models of the drugs and their target site can be studied [1].

The rational drug design can be categorize into two broad groups. The first group is in which the desired properties for targets are developed from small molecules, where the functional roles of the cellular process and 3D structural information are already known. In another group, the development of small molecules with specified properties with the target maybe having the known or unknown structural function [2].

The frequently used method in Structural Based Drug Design is molecular docking. Molecular docking has the ability to predict the accuracy of the conformation small-molecule ligands within its appropriate target binding site. Using molecular docking, some tedious molecular events can be investigated such as performing experiment on ligand binding modes and the corresponding intermolecular interaction that stabilize the ligand receptor complex. Through molecular docking, one can quantitatively predict the binding energy based on the affinity of ligand-receptor complex binding. There are two steps involved in identification of binding conformations. The first step is exploration of a large conformational space representing various potential binding modes and the second step is the accurate prediction of the interaction energy associated with each of the predicted binding conformations. Cyclic process is being used by the molecular docking programs to perform such task, in which the ligand conformation is evaluated by a specific scoring function [3].

Acquired immunodeficiency syndrome (AIDS) is one of the ten deadliest diseases in the world as concern with the global community. Human immunodeficiency virus (HIV) was found to be the causative agent in AIDS. HIV is a retrovirus from the genus Lentivirus. Commonly the retroviruses will be enveloped viruses. There are two identical, single stranded RNA molecules found in HIV as genetic material which is located in the center of it. Viral nucleocapsid (NC) protein, or which is known as p24 will be enclosing the genetic material. There are 7 internal proteins. 4 of the internal proteins are structural and the other 3 proteins are enzymatic. The three enzymatic proteins are reverse transcriptase (RT), intergase (IN) and protease (PR). The three enzymatic proteins will be surrounded by the matrix (MA) protein or which is known as p17 and structural protein. The lipoprotein surface found on the HIV structure will be studded by envelope knobs which consist of glycoprotein gp120 and gp41.

Retrovirus become a HIV-1 by fusion between the attachment spikes like viral glycoprotein gp120 which is the surface of envelope protein, gp41 which is the Trans membrane protein and the host cell receptors which are the CD4, chemokine. The two viral RNA genomes and the viral enzymes (Pol proteins) reverse transcriptase (RT), intergase (IN) and protease (PR) are released by uncoating. Double stranded DNA is produced when reverse transcriptase copies the viral RNA. The new viral DNA will be transported in to the host cell nucleus, in which it is integrated into a host cell chromosome as a provirus by viral intergase (IN). When the host cell replicates, the provirus also may be replicated. The RNA for new retrovirus genomes and RNA that encodes the retrovirus capsid (CA), enzymes and envelope protein may be produced, from the transcription of the provirus. Viral proteases process the viral proteins and some of the viral proteins will be moved to the host plasma membrane. The mature retrovirus will leave the host cell, acquiring an envelope and attachment spikes as it buds out. The provirus which replicates at the latent state may produce new retroviruses.CCR5 and CXCR4 are the seven Trans membrane G protein-couples chemokine receptors which act as a core receptor for HIV-entry [4]

Great efforts have been directed towards the development of antiretroviral therapies since the outbreak of AIDS. The antiretroviral therapies mainly target the HIV-1. One of the proteins which are mainly targeted is the HIV-1 Protease (PR). It is one of the important enzymes needed in order for assembly and maturation of the infectious virions HIV [5].

HIV-1 protease does play an important role in the maturation of viral in order to produce the virus particles which are infectious. There are at least 9 distinct sites in which the protease cleaves the precursor of Gag and Gag-Pol polyproteins. From the cleavages, the structural protein matrix, capsid, nucleocaspid, spacer peptides p1,p2 and p6, functional enzymes reverse transcriptase, protease and integrase are being released. By modifying the role of the protease, it will help in deactivating the viral particles and it can aid in reducing the chances of infectivity. Due to this, inhibiting the HIV-1 protease as a target in preventing HIV or AIDS has become common. HIV-1 protease consists of an aspartic protease. The catalytic site of HIV-1 protease is characterized as Asp-Thr-Gly sequence and it is applicable to all the aspartic protease [6].

Imidazole is a planar five-membered ring system. It has three carbon and two nitrogen atom in position 1 and 3. Glyoxaline was the first name given to imidazole [7]. The first synthesis of imidazole was done with glyoxal and ammonia. The amphoteric nature of imidazole allows it is susceptible to electophilic and nucleophilic attack and it function both as acid and base. Imidazole having characteristic such as highly stable to thermal, acid, base, oxidation and reduction conditions. Imidazole is having extensive intramolecular hydrogen bonding [Delia Hernandez Romero et al., 2014]. Imidazole is highly soluble in water and other polar solvents. Since the hydrogen atom can be located on either side of each nitrogen, imidazole exists in two equivalent tautomeric forms. It is an aromatic compound due the presence of sextet of π-electrons. It does also consist of a pair of electrons from the protonated nitrogen atom and one from each of the remaining four atoms of the ring [8].

Imidazole is having a unique position in heterocyclic chemistry since its derivatives are having a versatile property in in chemistry and pharmacology. The nitrogen containing heterocyclic ring of the imidazole possesses biological and pharmaceutical importance. Natural product such as purine, histamine, histidine and nucleic acid consist of imidazole ring. Since it is having the characteristic of being polar and ionisable aromatic compound, it helps in improving the pharmacokinetics characteristics of the lead molecules and it is used to optimize the solubility and bioavailability parameters of the poorly solouble lead molecules. The imidazole derivatives have a broad spectrum of biological activity such as antibacterial, anticancer, antitubercular, antifungal, analagesic and anti-HIV activities [9].

Imidazole derivatives could interfere with the HIV protein thus inhibit the replication of the retrovirus. Imidazole can easily bind with protein, due to these characteristics; they can bind to the reverse transcriptase site of the HIV-1 and inhibit the replication of the strain [10]. In this study, molecular docking was performed on various imidazole derivatives by Autodock 4.2 into active sites of HIV-1 protease (PDB ID: 4RVI).

MATERIALS AND METHODS:

Preparation of ligand

The ligands which are the nitroimidazole derivatives was chosen and designed. ChemSketch was used to draw the 2D structure of the ligands. MarvinSketch was used to convert the 2D structure of the ligands into the 3D structures and it was later saved in pdb format. The pdb format of the ligands was viewed in USCF Chimera and the energy of the ligands was minimized using USCF Chimera.

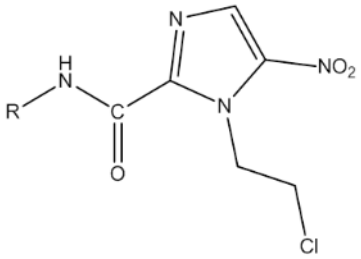
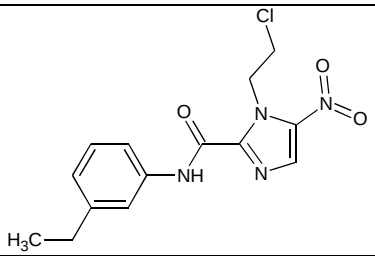
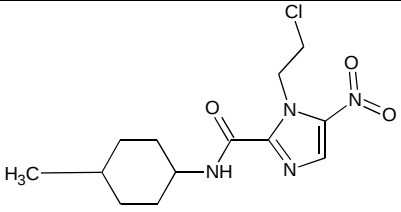
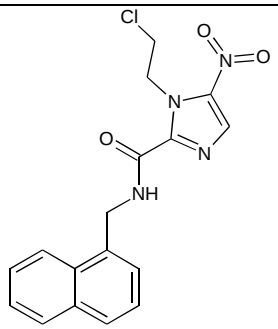
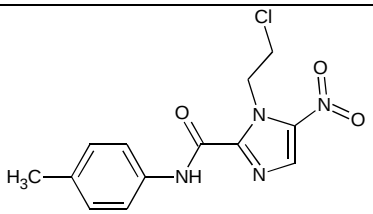
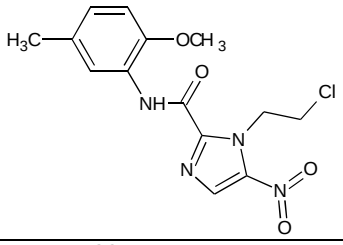
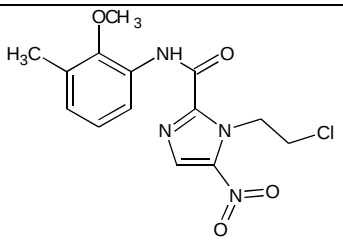
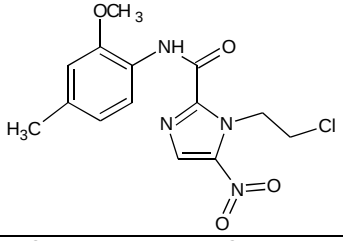
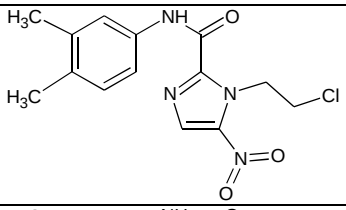
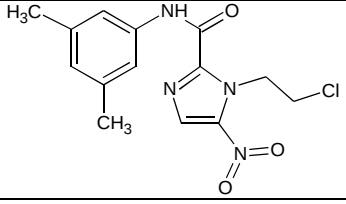
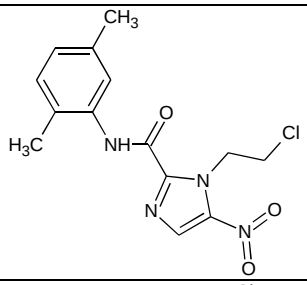
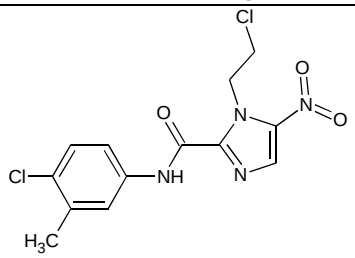
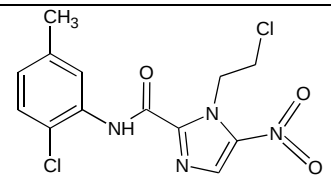
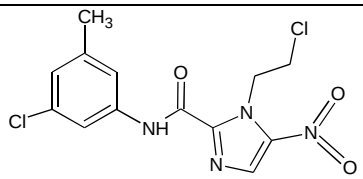
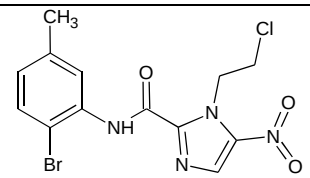
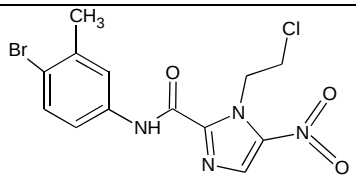
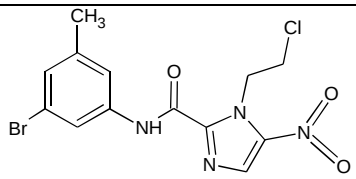
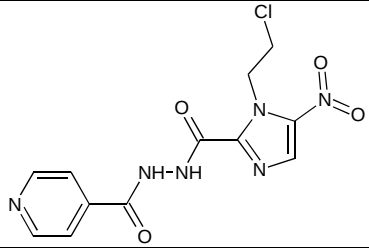


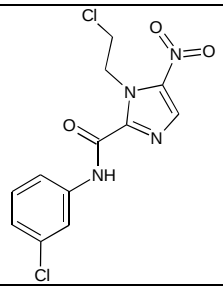
Fig 1: Structure for Imidazole Derivatives

Table 1: List of Ligands

NO	LIGANDS	STRUCTURE	IUPAC NAME
1	1A		1-(2-chloroethyl)-N-(3-ethylphenyl)-5-nitro-1H-imidazole-2-carboxamide
2	2A		1-(2-chloroethyl)-N-(4-methylcyclohexyl)-5-nitro-1H-imidazole-2-carboxamide

3	3A		1-(2-chloroethyl)-N-(naphthalen-1-ylmethyl)-5-nitro-1H-imidazole-2-carboxamide
4	4A		1-(2-chloroethyl)-N-(4-methylphenyl)-5-nitro-1H-imidazole-2-carboxamide
5	5A		1-(2-chloroethyl)-N-(2-methoxy-5-methylphenyl)-5-nitro-1H-imidazole-2-carboxamide
6	6A		1-(2-chloroethyl)-N-(2-methoxy-3-methylphenyl)-5-nitro-1H-imidazole-2-carboxamide
7	7A		1-(2-chloroethyl)-N-(2-methoxy-4-methylphenyl)-5-nitro-1H-imidazole-2-carboxamide
8	8A		1-(2-chloroethyl)-N-(3,4-dimethylphenyl)-5-nitro-1H-imidazole-2-carboxamide
9	9A		1-(2-chloroethyl)-N-(3,5-dimethylphenyl)-5-nitro-1H-imidazole-2-carboxamide

10	10A		1-(2-chloroethyl)-N-(2,5-dimethylphenyl)-5-nitro-1H-imidazole-2-carboxamide
11	11A		1-(2-chloroethyl)-N-(4-chloro-3-methylphenyl)-5-nitro-1H-imidazole-2-carboxamide
12	12A		1-(2-chloroethyl)-N-(2-chloro-5-methylphenyl)-5-nitro-1H-imidazole-2-carboxamide
13	13A		1-(2-chloroethyl)-N-(3-chloro-5-methylphenyl)-5-nitro-1H-imidazole-2-carboxamide
14	14A		N-(2-bromo-5-methylphenyl)-1-(2-chloroethyl)-5-nitro-1H-imidazole-2-carboxamide
15	15A		N-(4-bromo-3-methylphenyl)-1-(2-chloroethyl)-5-nitro-1H-imidazole-2-carboxamide
16	16A		N-(3-bromo-5-methylphenyl)-1-(2-chloroethyl)-5-nitro-1H-imidazole-2-carboxamide
17	17A		N'-{[1-(2-chloroethyl)-5-nitro-1H-imidazol-2-yl]carbonyl}pyridine-4-carbohydrazide

18	18A		1-(2-chloroethyl)-N-(3-chlorophenyl)-5-nitro-1H-imidazole-2-carboxamide

Preparation of protein

The crystal structure of the target protein HIV-1 protease (PDB ID: 4RVI) has been taken from the Protein Data Bank (PDB) database. The crystallized ligand was separated from the target protein by removing the heteroatoms in protein data bank data base and the energy of the protein was minimized by using USCF Chimera. This energy minimized protein was used in our study.

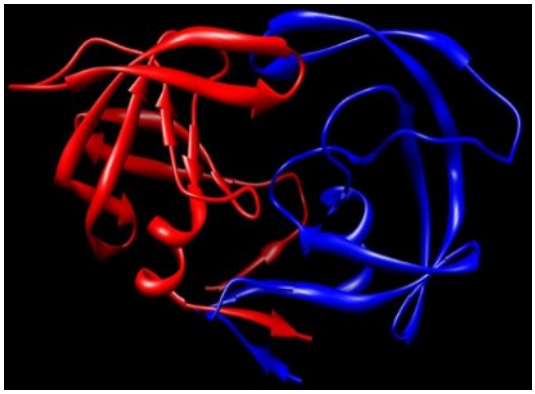


Fig 2: Ribbon Structure of 4RVI (Target Protein)

Molecular docking

In order to find the binding modes of ligands, docking of the ligands with HIV-1 protease was carried out using Autodock 4.2. The "Autodock tools" was used to prepare, run and analyze the docking stimulation. It requires a pre-calculated grid maps, one for each atom type present in the ligand being docked as it states the potential energy arising from the interaction with macromolecule. This grid must surround the region of interest which are the active site in the macromolecule.

In this study, the active site "Asp 25" was selected based on the amino acid residues of the co-crystallized ligand bounded with HIV-1 protease (PDB ID: 4RVI). This would be considered as the best accurate active region as it is solved by experimental cystallographic data.

Docking software Autodock 4.2 program supplied with Autogrid 4.0 and Autodock 4.0 was used to produce grid maps. Lamarkian Genetic Algorithm (LGA) was chosen to search for the best conformers. Maximum of 10 conformers was considered for each docking during the docking process.

RESULTS

TABLE 2: LIGANDS DOCKING RESULT

No	Ligand	Ligand Efficiency	Intermolecular Energy	Van Der Waals Dissolution Energy	Electrostatic Energy	Total Internal energy	Unbound Energy
1	1A	-022	-6.55	-6.77	0.22	-1.03	-1.03
2	2A	-0.23	-6.28	-6.56	0.28	-1.07	-1.07
3	3A	-0.2	-6.88	-7.42	0.54	-1.47	-1.47
4	4A	-0.22	-6.12	-6.33	0.21	-0.96	-0.96
5	5A	-0.23	-6.6	-6.76	0.16	-1.17	-1.17
6	6A	-0.23	-6.55	-6.75	0.19	-1.22	-1.22
7	7A	-0.2	-5.98	-6.18	0.21	-1.14	-1.14
8	8A	-0.21	-6.21	-6.43	0.22	-1.0	-1.0
9	9A	-0.23	-6.64	-6.95	0.31	-0.95	-0.95
10	10A	-0.24	-6.67	-6.29	-0.38	-0.66	-0.66
11	11A	-0.22	-6.37	-6.57	0.2	-1.06	-1.06
12	12A	-0.24	-6.77	-7.12	0.34	-1.1	-1.1
13	13A	-0.23	-6.6	-7.02	0.41	-0.93	-0.93
14	14A	-0.25	-7.07	-7.23	0.16	-1.21	-1.21
15	15A	-0.28	-7.62	-7.74	0.12	-1.08	-1.08
16	16A	-0.22	-6.31	6.52	0.21	-1.04	-1.04
17	17A	-0.16	-5.42	-5.77	0.35	-1.05	-1.05
18	18A	-0.24	-6.46	-6.65	0.19	-1.1	-1.1

Table 3: Interacting Residues, Hydrogen Bond and Its Distance, Binding Energy of Ligands and Their Inhibition Constant

No	Ligands	Interacting Residues		Hydrogen Bond	Hydrogen Bond Distance (Å)	Binding Energy (kJ/mol)	Inhibition Constant
1	1A	ALA 28 ASP 29 GLY 48 GLY 49	ILE 50 A ILE 50 B ILE 84 VAL 32	pro: B: ILE 50: HN	2.205	-4.76	325.08µM
2	2A	GLY 27 ILE 50 A ILE 50 B LEU 23	PRO 81 THR 82 A THR 82 B	pro: B: ILE 50: HN	1.964	-4.79	307.5µM
3	3A	ASP 25 A ASP 25 B GLY 27 GLY 49 A GLY 49 B	ILE 50 A ILE 50 B ILE 84 LEU 23 THR 82	pro: A: ILE 50: HN	1.854	-5.09	185.01µM
4	4A	ILE 50 A ILE 50 B	THR 82 A THR 82 B	pro: A: ILE 50: HN pro: B: ILE 50: HN	2.226 2.087	-4.62	407.72µM
5	5A	ALA 28 ASP 29 GLY 48 GLY 49 A	GLY 49 B ILE 50 A ILE 50 B	pro: B: ASP 29: HN pro: B: ILE 50: HN	2.15 2.008	-5.1	181.51µM
6	6A	ASP 29 GLY 27 GLY 48	ILE 50 PRO 81	pro: B: ASP 29: HN	2.11	-5.06	194.58µM
7	7A	ALA 28 GLY 27 ILE 50 A	ILE 50 B ILE 84	pro: B: ILE 50: HN	2.205	-4.48	516.58µM
8	8A	ALA 28 ASP 29 GLY 27	ILE 50 ILE 84 THR 82	pro: B: ASP 29: HN pro: B: ILE 50: HN	2.167 2.152	-4.72	344.93µM
9	9A	ILE 50 A ILE 50 B ILE 84	THR 80 THR 82	pro: A: ILE 50: HN pro: B: ILE 50: HN	2.118 1.959	-5.15	168.52µM
10	10A	ALA 28 ARG 8 ASP 29 GLY 27 GLY 48 GLY 49 A	GLY 49 B ILE 50 A ILE 50 B ILE 84 LEU 23 THR 82	pro: A: ILE 50: HN pro: A: ILE 50: HN	1.794 1.73	-5.18	160.17µM
11	11A	ALA 28 A ALA 28 B ASP 29 A ASP 29 B GLY 27	ILE 50 A ILE 50 B ILE 84 A ILE 84 B VAL 32	pro: B: ASP 29: HN pro: B: ILE 50: HN	2.115 2.03	-4.88	264.49µM
12	12A	ILE 50 A ILE 50 B ILE 84	THR 80 THR 82	pro: A: ILE 50: HN pro: B: ILE 50: HN	2.054 1.858	-5.28	134.22µM

13	13A	GLY 49 ILE 50 A ILE 50 B LEU 23	PRO 81 THR 80 THR 82	pro: A: ILE 50: HN pro: B: ILE 50: HN	2.137 2.123	-5.11	178.93µM
14	14A	ALA 28 ASP 29 GLY 48 GLY 49 A	GLY 49 B ILE 50 A ILE 50 B	pro: B: ASP 29: HN pro: B: ILE 50: HN pro: A: ILE 50: HN	2.166 2.089 2.145	-5.58	81.47µM
15	15A	ALA 28 ASP 25 A ASP 25 B ASP 29 ASP 30 GLY 27	GLY 48 GLY 49 A GLY 49 B ILE 50 A ILE 50 B ILE 84	pro: A: ASP 29: HN	1.901	-6.12	32.41µM
16	16A	ILE 50 A ILE 50 B	ILE 84 PRO 81	pro: B: ILE 50:HN	1.834	-4.82	292.4µM
17	17A	ALA 28 A ALA 28 B ASP 29 A ASP 29 B GLY 27	ILE 50 ILE 84 A ILE 84 B VAL 32	pro: B: ASP 29:HN	1.93	-3.63	2.19mM
18	18A	ALA 28 ASP 29 GLY 48	GLY 49 ILE 50 A ILE 50 B	pro: A: ILE 50: HN pro: B: ILE 50: HN	2.183 1.96	-4.97	226.6µM

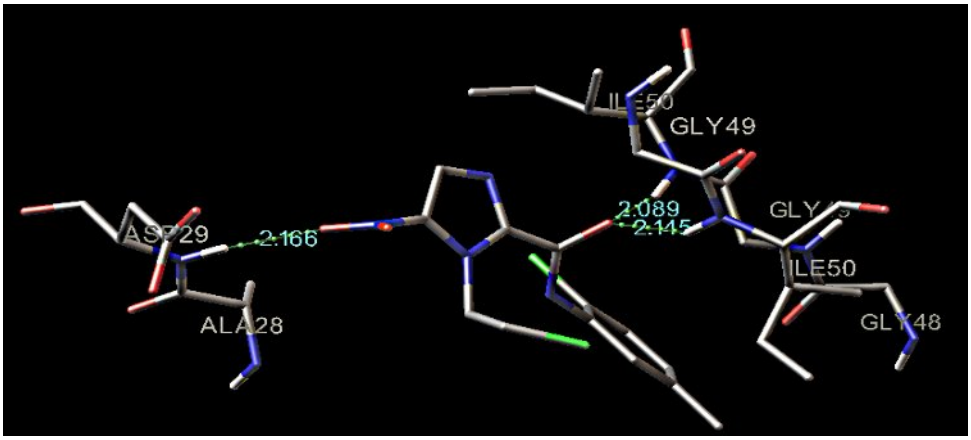


Fig 3: Interacting Residues of Ligand 14A with HIV-1 Protease

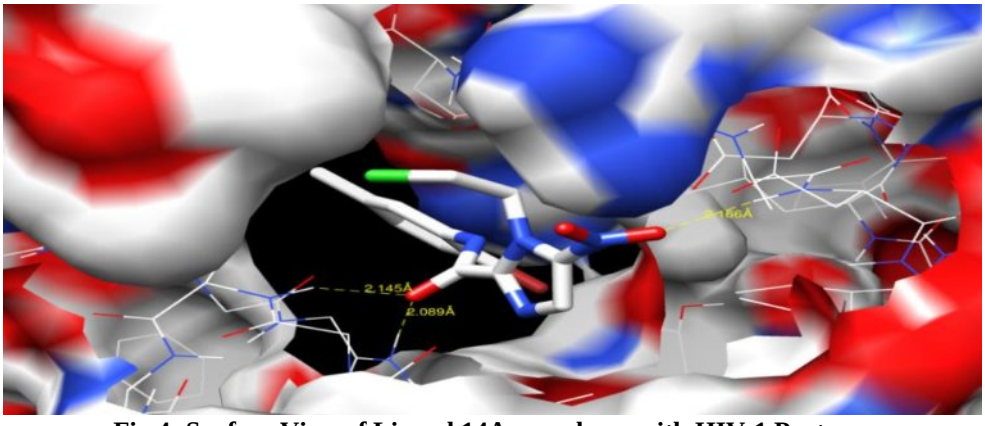


Fig 4: Surface View of Ligand 14A complexes with HIV-1 Protease

Ligand 14A was docked with HIV-1 Protease. The docking result shows that the binding energy of ligand 14A with HIV-1 protease to be -5.58 kJ/mol. The ligand efficiency is found to be -0.25, and the Van der Waals dissolution energy is -7.23. The intermolecular energy of the ligand shows -7.07 with a total energy of -1.21. The inhibition constant was found to be 81.47 µM. There are seven Van der Waals interacting residues formed from docking result of Ligand 14A with HIV-1 protease; it includes ALA 28, ASP 29, GLY 48, GLY 49 A, GLY 49 B, ILE 50 A and ILE 50 B. Ligand 14A exhibited 3 hydrogen bonds. The first hydrogen was found to be interacting with amino acid ASP 29. The hydrogen bond is found to be formed between amine functional group of the HIV-1 protease and "O" atom in ligand with a bond distance of 2.166 Å. The other two hydrogen bonds were found to be interacting with amino acid ILE 50 in the binding region. The hydrogen bonds are found to be formed between amine functional group of the HIV-1 protease and "O" atom in ligand with the bond distance of 2.089 Å and 2.145 Å, respectively.

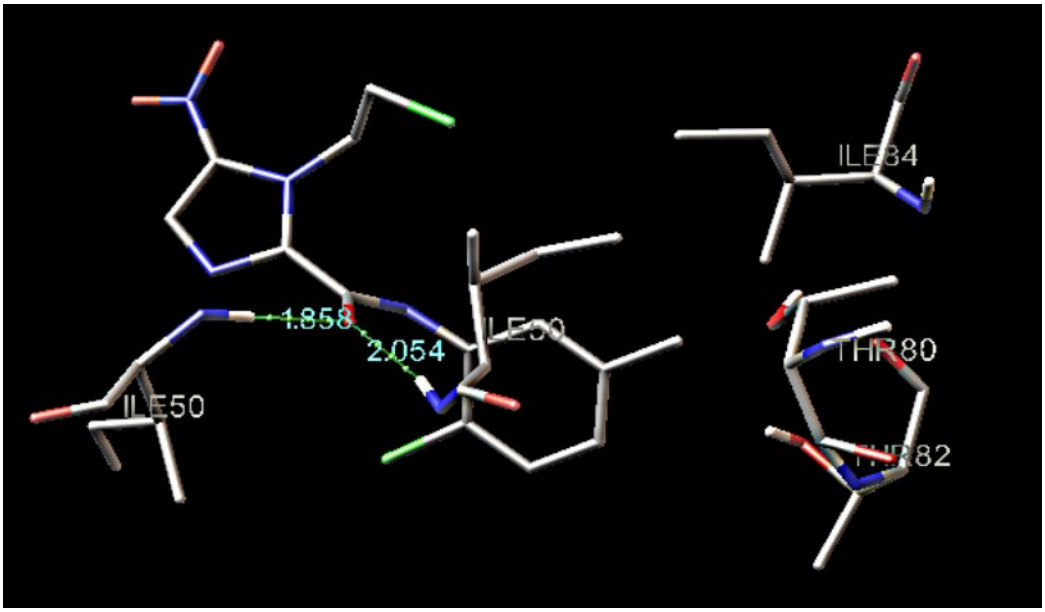


Fig 5: Interacting Residues of Ligand 12A with HIV-1 Protease

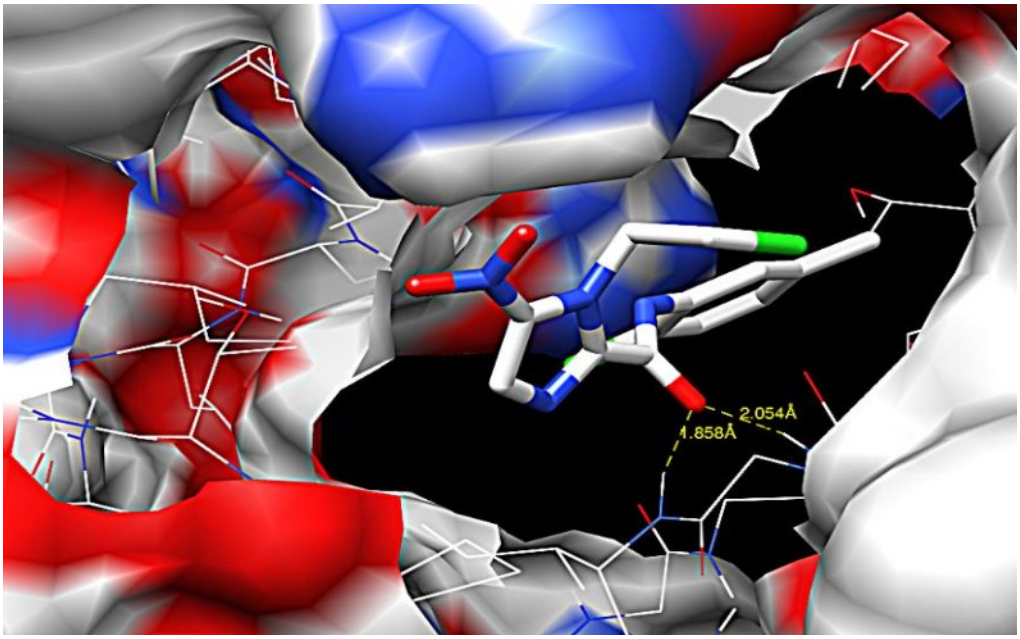


Fig 6: Surface View of Ligand 12A complexed with HIV-1 Protease

Ligand 12A was docked with HIV-1 Protease. The docking result shows that the binding energy of ligand 12A with HIV-1 protease to be -5.28 kJ/mol. The ligand efficiency is found to be -0.24 and the Van der Waals dissolution energy is -7.12. The intermolecular energy of the ligand shows -6.77 with a total energy of -1.1. The inhibition constant was found to be 134.22 µM. There are five Van der Waals interacting residues formed from docking result of Ligand 12A with HIV-1 protease, which includes ILE 50 A, ILE 50 B, ILE 84, THR 80 and THR 82. Ligand 12A exhibited 2 hydrogen bonds. Both the hydrogen bond was found to be interacting with amino acid ILE 50 in the binding region. The hydrogen bonds are found to be formed between amine functional group of the HIV-1 Protease and "O" atom in ligand with the bond distance of 1.858 Å and 2.054 Å, respectively.

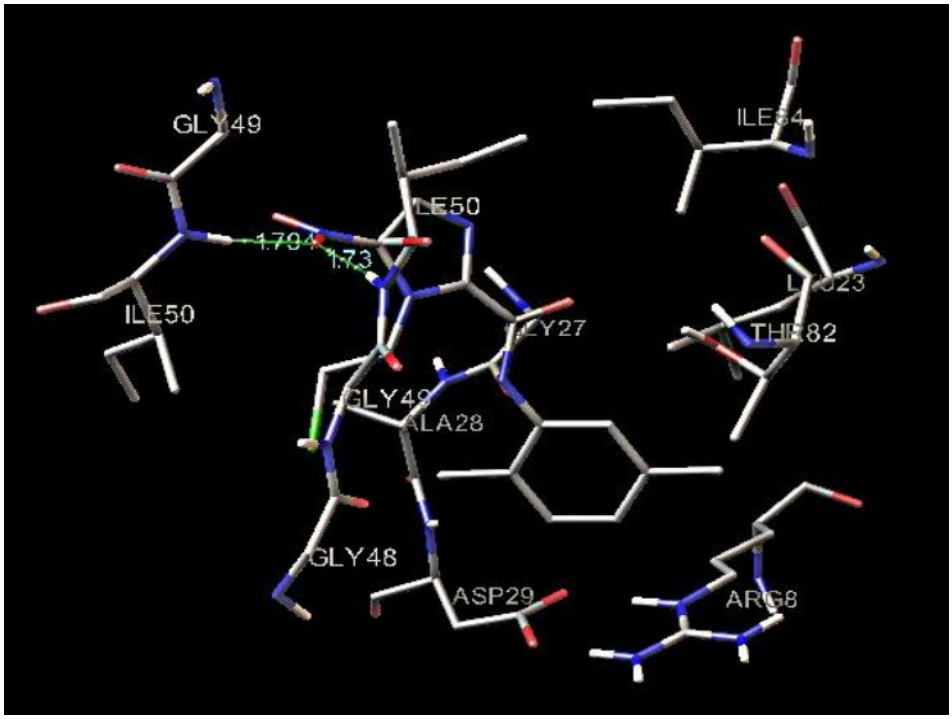


Fig 7: Interacting Residues of Ligand 10A with HIV-1 Protease

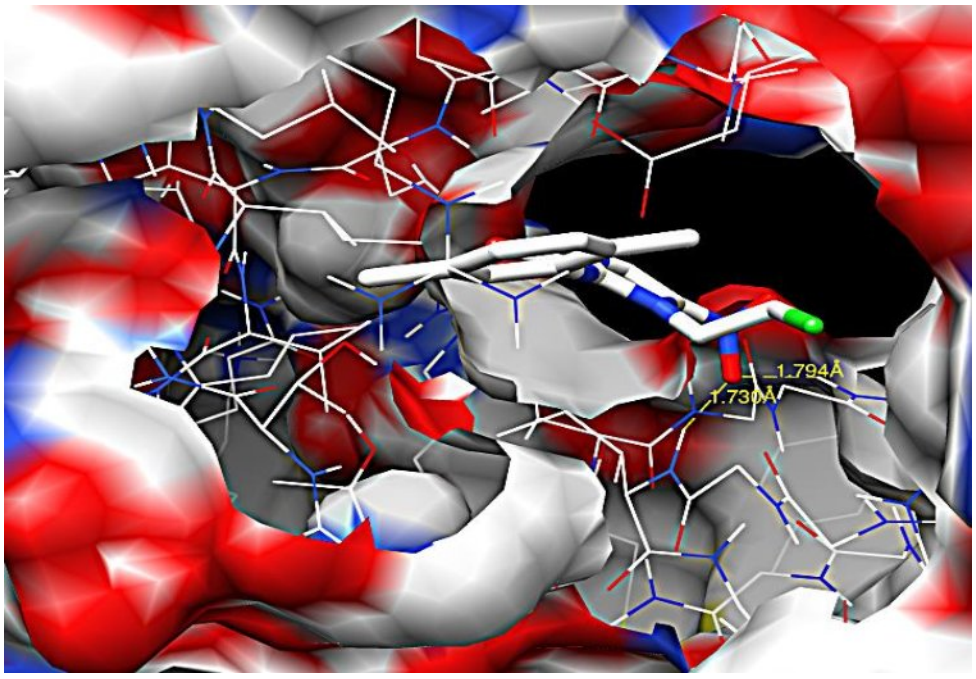


Fig 8: Surface View of Ligand 10Acomplexed with HIV-1 Protease

Ligand 10A was docked with HIV-1 Protease. The docking result shows that the binding energy of ligand 10A with HIV-1 protease to be -5.18 kJ/mol. The ligand efficiency is found to be -0.24 and the Van der Waals dissolution energy is -6.29. The intermolecular energy of the ligand shows -6.67 with a total energy of -0.66. The inhibition constant was found to be 160.17 µM. There are 12 Van der Waals interacting residues formed from docking result of Ligand 10A with HIV-1 protease, it includes ALA 28, ARG 8, ASP 29, GLY 27, GLY 48, GLY 49 A, GLY 49 B, ILE 50 A, ILE 50 B, ILE 84, LEU 23 and THR 82 . Ligand 10A exhibited 2 hydrogen bonds. Both the hydrogen bond was found to be interacting with amino acid ILE 50 in the active site. Both hydrogen bonds are found to be formed between amine functional group of the HIV-1 Protease and oxygen in ligand with bond distance of 1.794 Å and 1.73 Å, respectively.

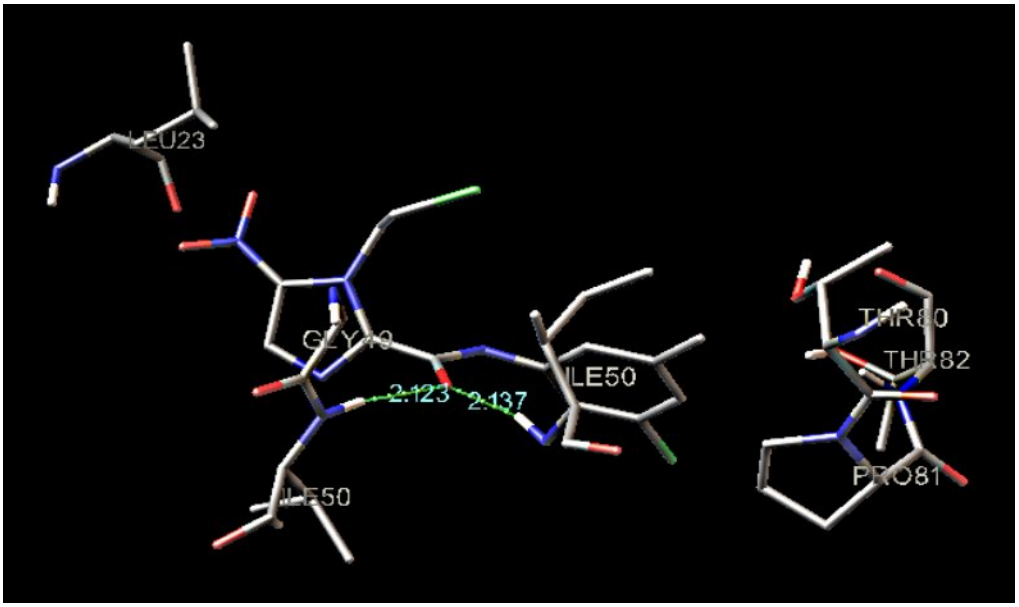


Fig 9: Interacting Residues of Ligand 13A with HIV-1 Protease

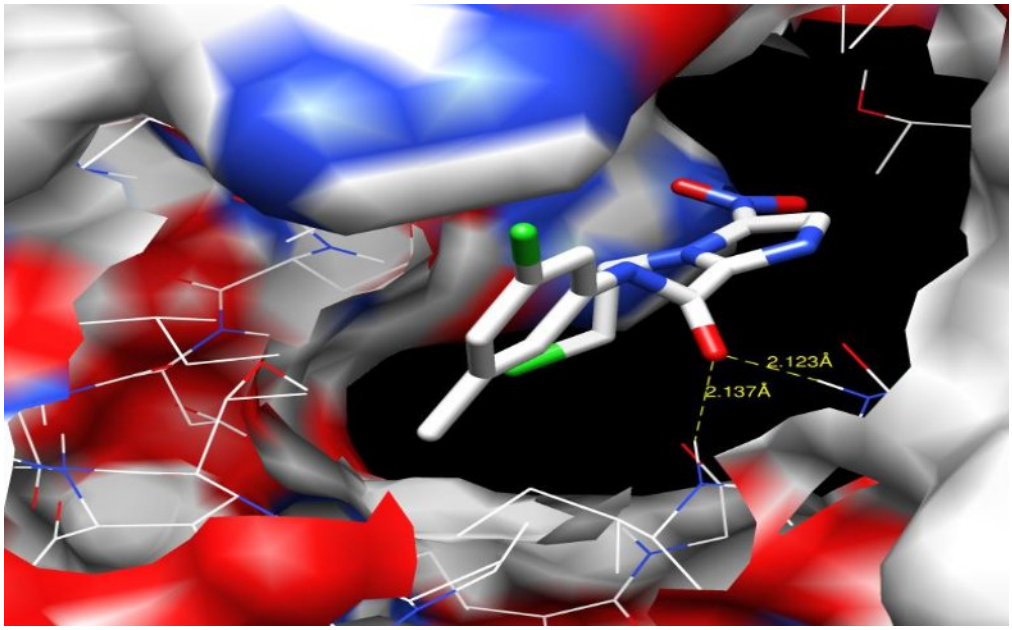


Fig 10: Surface View of Ligand 13Acomplexed with HIV-1 Protease

Ligand 13A was docked with HIV-1 Protease. The docking result shows that the binding energy of ligand 13A with HIV-1 protease to be -5.11 kJ/mol. The ligand efficiency is found to be -0.23 and the Van der Waals dissolution energy is -7.02. The intermolecular energy of the ligand shows -6.6 with a total energy of -0.93. The inhibition constant was found to be 178.93 µM. There are 7 Van der Waals interacting residues formed from docking result of Ligand 13A with HIV-1 protease; it includes GLY 49, ILE 50 A, ILE 50 B, LEU 23, PRO 81, THR 80 and THR 82. Ligand 13A exhibited 2 hydrogen bonds. Both the hydrogen bonds are found to be interacted with amino acid "ILE 50" in the binding region. The hydrogen bonds are found to be formed between amine functional group of the HIV-1 Protease and "O" atom in ligand with the bond distance of 2.123 Å and 2.137 Å, respectively.

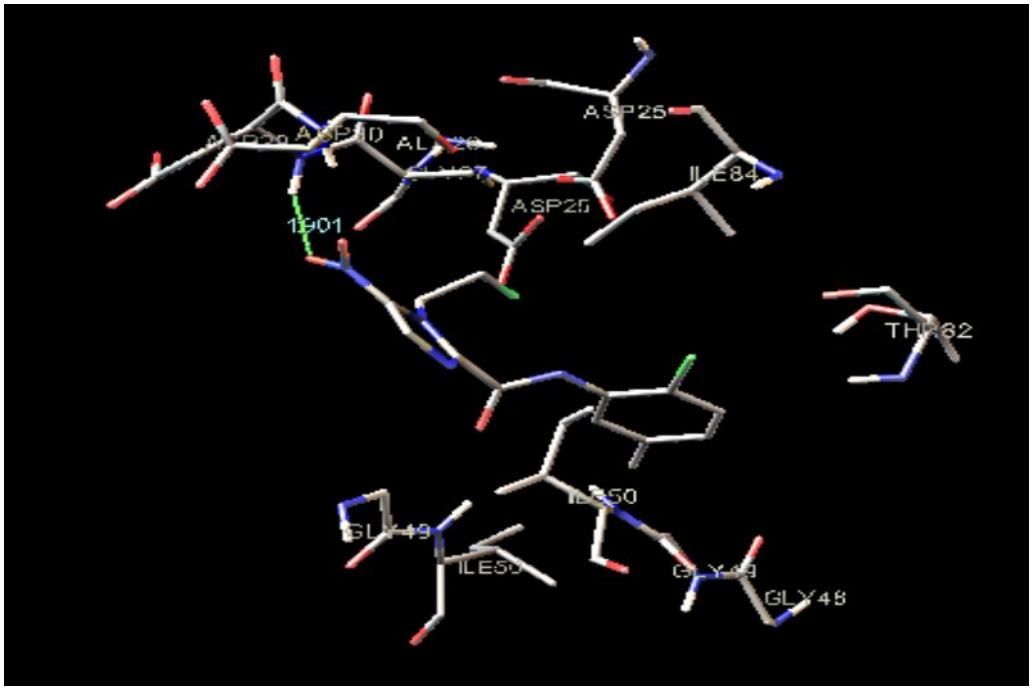


Fig 11: Interacting Residues of Ligand 15A with HIV-1 Protease

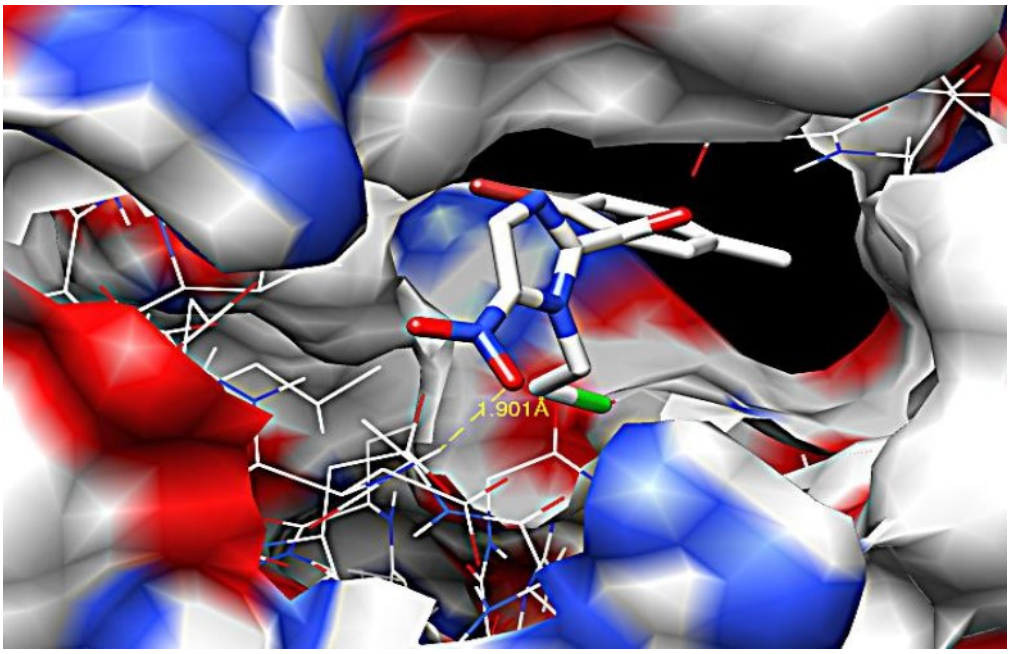


Fig 12: Surface View of Ligand 15Acomplexed with HIV-1 Protease

Ligand 15A was docked with HIV-1 Protease. The docking result shows that the binding energy of

ligand 15A with HIV-1 protease to be -6.12 kJ/mol. The ligand efficiency is found to be -0.28 and the Van der Waals dissolution energy is -7.74. The intermolecular energy of the ligand shows -7.62 with a total energy of -1.08. The inhibition constant was found to be 32.41 µM. There are twelve Van der Waals interacting residues formed from docking result of Ligand 15A with HIV-1 protease, which includes ALA 28, ASP 25 A, ASP 25 B, ASP 29, ASP 30, GLY 27, GLY 48, GLY 49 A, GLY 49 B, ILE 50 A, ILE 50 B and ILE 84. Ligand 15A exhibits single hydrogen bond. The hydrogen is found to be interacted with amino acid "ASP 29". The hydrogen bond is found to be formed between amine functional group of the HIV-1 Protease and "O" atom in ligand with a bond distance of 1.901 Å.

DISCUSSION:

In the current study eighteen nitro-imidazole derivatives was chosen as the ligand, and the docking study was performed with HIV-1 Protease protein as a target receptor in this study. It was done in order to identify the potential leads of HIV-1 protease inhibitor based on the analysis of good binding energy, formation of hydrogen bonds, distances of hydrogen bonds and the Van Der Waals interacting residues of ligand with docked protein. AutoDock 4.2 docking program with Lamarckian genetic algorithm was used to achieve the aim of this study. The HIV-1 Protease protein was extracted from the Protein Data Bank (PDB ID: 4RVI)

Out of the 18 compounds, 5 compounds show the highest binding energy. Ligand 15A and 14A exhibit the maximum binding energy which are found to be -6.12 kJ/mol with ligand efficiency of -0.28 and -5.58 kJ/mol with ligand efficiency of -0.25 respectively. Maximum number of the ligand which was docked show the existence of hydrogen bonding with the amino acid residues ASP29 and ILE50. There were 3 hydrogen bonds formed from ligand 15A and it was found to be formed with 2 residues, ASP29 and ILE50 of HIV-1 Protease protein.

CONCLUSION:

Molecular docking is one of the safest and easiest tools used in order to investigate the property of the molecules using a three-dimensional structure. In this study, molecular docking was conducted in a series of selected imidazole derivatives with HIV-1 protease (PDB ID: 4RVI). All the selected imidazole derivatives show a good binding energy and also a good inhibition constant. This study provides us the theoretical framework to rationally design nitro-imidazole derivatives as HIV-1 protease inhibitors.

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