Journal of Carcinogenesis
Covering Genesis to Therapeutics

Journal of Carcinogenesis, ISSN: 1477-3163
2025; Vol 24: Issue 7s, https://carcinogenesis.com/

Synthesis and Docking Studies of some novel 1, 2, 4-Triazole Derivatives and Their Biological Evaluation

Ms. Jyoti Agarwal[1], Dr. Vandana Sharma[2], Atul Gupta[3]

[1]Ph. D Scholar , Arya College of Pharmacy, Kukas, Jaipur

[2]Professor & Principal, Arya College of Pharmacy, Kukas, Jaipur

[3]Research Scholar , LBS College of Pharmacy, Jaipur

Corresponding Author

Ms. Jyoti Agarwal

Ph. D Scholar , Arya College of Pharmacy, Kukas, Jaipur

ABSTRACT

The present study focuses on the synthesis, characterization, and docking studies of novel 1,2,4-triazole derivatives to explore their potential biological activities. The triazole nucleus, a five-membered heterocyclic compound containing three nitrogen atoms, is known for its broad pharmacological profile, including antimicrobial, antifungal, antiviral, and anticancer properties. In this work, a series of triazole and Schiff base derivatives were synthesized using standard organic synthesis techniques and characterized by TLC, IR, NMR, and mass spectrometry. The synthesized compounds were screened against bacterial strains (S. aureus, B. subtilis, E. coli) and fungal strains (A. niger, C. albicans) using the agar well diffusion method. Several derivatives, particularly 4(g), 5(b), 5(g), and 6(a), showed significant antibacterial activity, while 4(f), 5(f), 6(c), and 6(j) exhibited potent antifungal effects. Docking studies using the HIV-1 reverse transcriptase enzyme (2RK-1) revealed that compounds 4g and 5e exhibited favorable binding interactions, including hydrogen bonding and hydrophobic contacts, supporting their potential as anti-HIV agents. The results suggest that triazole derivatives represent a promising scaffold for developing novel antimicrobial and antiviral agents..

Keywords: *1,2,4-Triazole derivatives; Schiff base; Docking studies; Antibacterial activity; Antifungal activity; HIV-1 reverse transcriptase; Molecular modeling; Heterocyclic compounds; Structure-activity relationship; Drug design*

How to Cite: Ms. Jyoti Agarwal, Dr. Vandana Sharma, Atul Gupta, (20yy) Synthesis and Docking Studies of some novel 1, 2, 4-Triazole Derivatives and Their Biological Evaluation, *Journal of Carcinogenesis*, *Vol.24, No.7s*, 989-1010

1. INTRODUCTION: SYNTHESIS & DOCKING STUDIES

Synthesis of a compound refers to the process of creating that compound through chemical reactions. In medicinal chemistry, this often involves starting with simpler, commercially available chemicals known as starting materials, and then using various chemical reactions to transform them into the desired compound. The goal of synthesis is to produce the target compound in high yield and purity.

Docking studies are computational simulations used to predict how a synthesized compound might interact with a specific biological target, typically a protein. Proteins are important in biological systems and often serve as targets for drug molecules. Docking studies use molecular modeling techniques to predict how a compound fits into the binding site of a protein, how strong the interaction might be, and what specific interactions are formed (e.g., hydrogen bonds, hydrophobic interactions). This information helps researchers understand the potential efficacy and mechanism of action of a compound before it is tested in the laboratory.[1,2,3]

2. COMPOUND INTRODUCTION:

Bladin originally used the term "triazole" in 1885 to refer to the three-membered, heterocyclic, aromatic ring structure with five nitrogen atoms and the chemical formula C2H3N3. Following its discovery, triazole's chemistry evolved considerably and quickly thanks to the development of a number of simple and practical synthetic methods and its adaptable interactions with biological systems. For example, the development of several azole derivatives, such as fluconazole, itraconazole, voriconazole, posaconazole, and efinaconazole, was prompted by the 1944 discovery of azole derivatives' antifungal characteristics. Among other Candida strains, those resistant to fluconazole can be effectively treated with voriconazole and posaconazole. The production of ergosterol is inhibited and the P450-dependent enzyme (CYP 51) is blocked as part

of the well-established mechanism of such antifungal action. The heme iron of the CYP might be able to coordinate with one or more triazole-type ring structures. Numerous triazoles are adaptable, physiologically active substances that are frequently employed as plant retardants and fungicides. However, because triazoles react similarly to azides due to their large number of nitrogen atoms, they are also helpful in bioorthogonal chemistry. Last but not least, triazoles are helpful as coordination molecules despite not usually being haptic ligands due to their abundance of free lone pairs.'

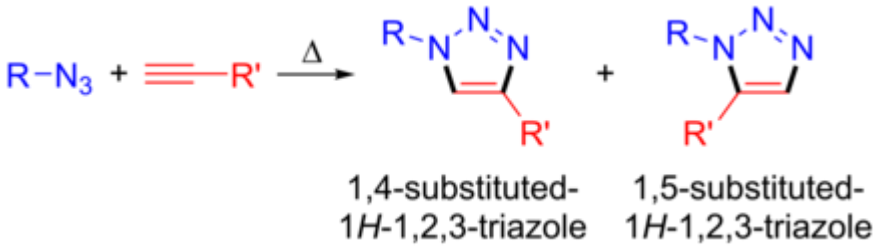
Isomerism:

Triazole isomers come in four different forms, which are often separated into two pairs of tautomers. Three nitrogen atoms are next to each other in 1,2,3-triazoles, whereas one nitrogen atom is separated from the others in 1,2,4-triazoles by an interstitial carbon. There are two tautomers in each group, which vary in the nitrogen that has a hydrogen bond attached to it.

Preparation of Triazoles:

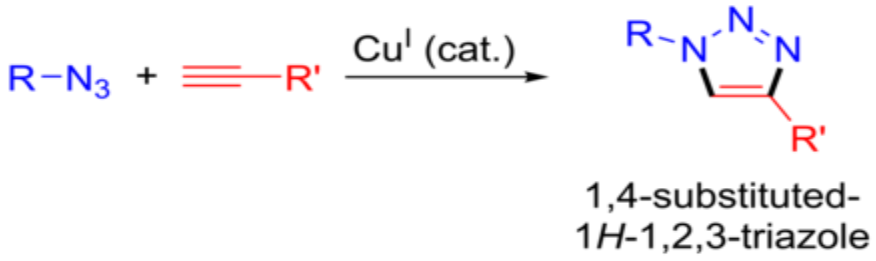
Vicinal triazoles, commonly referred to as 1,2,3-triazoles, are typically made via the (3+2) cycloaddition method. For unsubstituted triazoles, a typical method is the

Huisgen azide-alkyne 1,3-dipolar cycloaddition: An azide and an alkyne react at high temperatures to produce a ring. When the Huisgen approach is employed to make substituted triazoles, it yields a combination of isomers (usually 1,4- and 1,5-disubstituted**).**

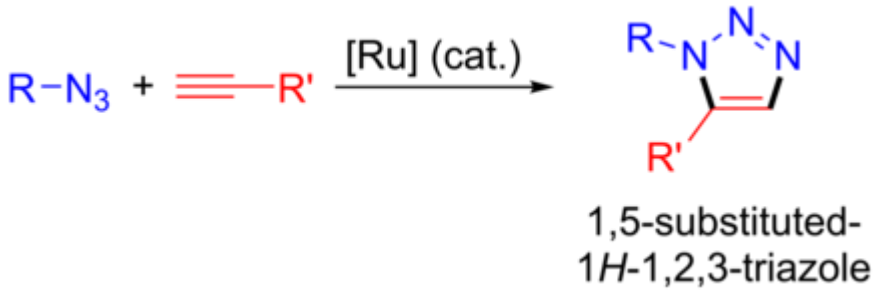


In order to selectively prepare a desired isomer, metal catalysts are employed.

The 1,4-disubstituted 1,2,3-triazole synthesis is aided by the copper (I) salts in the copper-catalyzed azide-alkyne cycloaddition (CuAAC). CuBr (PPh3) is a typical catalyst because it can produce triazoles with a wide range of substituents in solvent or under well-controlled reaction conditions. It is also very resistant to oxidation even at temperatures above freezing. [4,5,6,7,8]



Conversely, ruthenium catalysts (RuAAC) select for 1,5-disubstituted 1,2,3-triazoles



3. AIM & OBJECTIVES OF RESEARCH WORK:

One of the fundamental goals of organic and medicinal chemistry is to develop, synthesize, and produce compounds that therapeutic value, triazole , a heterocuclic compound and its derivatives exhibit broad spectrum of biological activities, e.g. anticonvulsant ,antimicrobial, antiviral, anti-inflammatory ,anti cancer activity etc. In view of the broad spectrum activities

of triazole derivative,it was thought worthwhile to synthesize triazole derivatives and study their biological activities.

The goal of the research was to develop and synthesis novel Schiff's bases and triazole amine derivatives, as well as to analyze their potential biological properties, particularly anti-HIV-1 activity, and to determine their active site on reverse transcriptase enzyme (2RK-1).

4. MATERIALS AND METHODS:

4.1 chemical required:

S. No.	Name	Specifications	Manufacturer
	Methanol	LR Grade	Loba Chemie Ltd.
	2-chloro benzoic acid	LR Grade	Loba Chemie Ltd.
	2,4-dichloro benzoic acid	LR Grade	Loba Chemie Ltd.
	2-Picolinic acid	LR Grade	Loba Chemie Ltd.
	Carbon di sulfide	LR Grade	Loba Chemie Ltd.
	Potassium hydroxide	LR Grade	Loba Chemie Ltd.
	Methyl iodide	LR Grade	Loba Chemie Ltd.
	Ethyl acetate	LR Grade	Loba Chemie Ltd.
	Glacial acetic acid	LR Grade	Loba Chemie Ltd.
	4-Choloro benzoic acid	LR Grade	Loba Chemie Ltd.
	Chloro acetyl chloride	LR Grade	Loba Chemie Ltd.
	Di ethyl amine	LR Grade	Loba Chemie Ltd.
	Ethanol	LR Grade	Loba Chemie Ltd.
	Di propyl amine	LR Grade	Loba Chemie Ltd.
	Di butyl amine	LR Grade	Loba Chemie Ltd.
	Chloroform	LR Grade	Loba Chemie Ltd.
	Diethyl ether	LR Grade	Loba Chemie Ltd.
	Benzene	LR Grade	Loba Chemie Ltd.
	Magnesium sulphate	LR Grade	Loba Chemie Ltd.
	Dimethyl sulphoxide	LR Grade	Loba Chemie Ltd.
	Hydrazine hydrate	LR Grade	Loba Chemie Ltd.
	Dimethyl formamide	LR Grade	Loba Chemie Ltd.
	Morpholine	LR Grade	Loba Chemie Ltd
	Piperidine	LR Grade	Loba Chemie Ltd
	2-pyrrolidinone	LR Grade	Loba Chemie Ltd
	2-methylpiperidine	LR Grade	Loba Chemie Ltd
	4-methyl piperidine	LR Grade	Loba Chemie Ltd
	Pyrrolidine	LR Grade	Loba Chemie Ltd
	diisopropylamine	LR Grade	Loba Chemie Ltd

	MH agar media	-	Hi-Media
	Casitone agar media	-	Hi-Media
	Ampicillin	-	Hindustan Antibiotics Ltd.
	Fluconazole	-	Hindustan Antibiotics Ltd.

4.2 Test microorganisms:

S. No.	Microorganism	Code	Purchase from
	Bacillus subtilis	MTCC-441	**Institute of microbial technology, sector 39-A, Chandigarh, India**
	Staphylococcus aureus	MTCC-442	
	Escherichia coli	MTCC-443	
	Candida albicans	MTCC-227	
	Aspergillus niger	MTCC-282	

4.3 Instruments used:

S.No.	Name	Model	Manufacturer
1.	F.T.I.R Spectrophotometer	IR affinity-1	Shimadzu
2.	Mass spectrometer	Jeol SX-102	Shimadzu
3.	NMR spectrometer	Bruker-300	-

4.4 Glassware's used:

S. No.	Name	Model	Manufacturer
	Beakers	100 ml, 250 ml, 500 ml, 1000 ml	Borosil(R)
	RBF	250 ml,500 ml and 1000 ml	Borosil(R)
	Conical flask	250 ml	Borosil(R)
	Volumetric flask	10 ml, 25 ml and 100 ml	Borosil(R)
	Funnel	100 mm. (diameter)	Borosil(R)
	Pipettes	1,2 and 5 ml	Borosil(R)
	Test tubes	10 ml	Borosil(R)

Reflux condenser	200 mm (Length)	Borosil(R)
Distillation unit	1.5 L/H (output capacity)	Borosil(R)
Petri Dishes	12cm (diameter)	Borosil(R)
Measuring cylinder	5 ml,10ml and 50 ml	Borosil(R)
Appendrop Tube	2 ml	Borosil(R)
Micropippete	100µL	Borosil(R)

4.5. METHODS

(A) Thin layer chromatography of compounds

On glass plates covered with silica gel G, substances were analyzed using thin layer chromatography. Using a standard spreader, the adsorbent silica gel G was applied on 20 × 5 cm TLC plates that had been cleaned beforehand to a thickness of around 0.3 mm. To activate, the plates were put in a hot air oven set at 105°C for 30 minutes. On the active plate, the compound solution was placed at a point approximately 2 cm above the lower edge. The mobile stages were chosen through a process of trial and error.Exposure to iodine vapor allowed the dots to become visible.[9,10]

(B) Elemental analysis (Qualitative)

Qualitative tests for elemental detection; nitrogen, sulphur and halogens in compounds were performed by using Lassaigne's sodium fusion test.[11]

(C) Solubility of intermediates and products in different solvents

The intermediates and end products were dissolved using a variety of solvents, including water, ethanol, chloroform, methanol, acetone, dimethyl formamide (DMF), and dimethyl sulphoxide (DMSO). Ten milligrams of every chemical were weighed, and then 10 milliliters of each separate solvent were put to a 100 milliliter beaker. The results were then noted.

(D) Determination of melting point range

The open capillary technique, which uses the melting point equipment, was used to estimate the uncorrected melting point ranges of the goods. Compounds were inserted into a sealed capillary from one end. The thermometer was then added to the capillary caverns that were created for them. Melting point range was defined as the temperature range between the compound's beginning melting point and full melting point..

(E) IR spectral analysis:

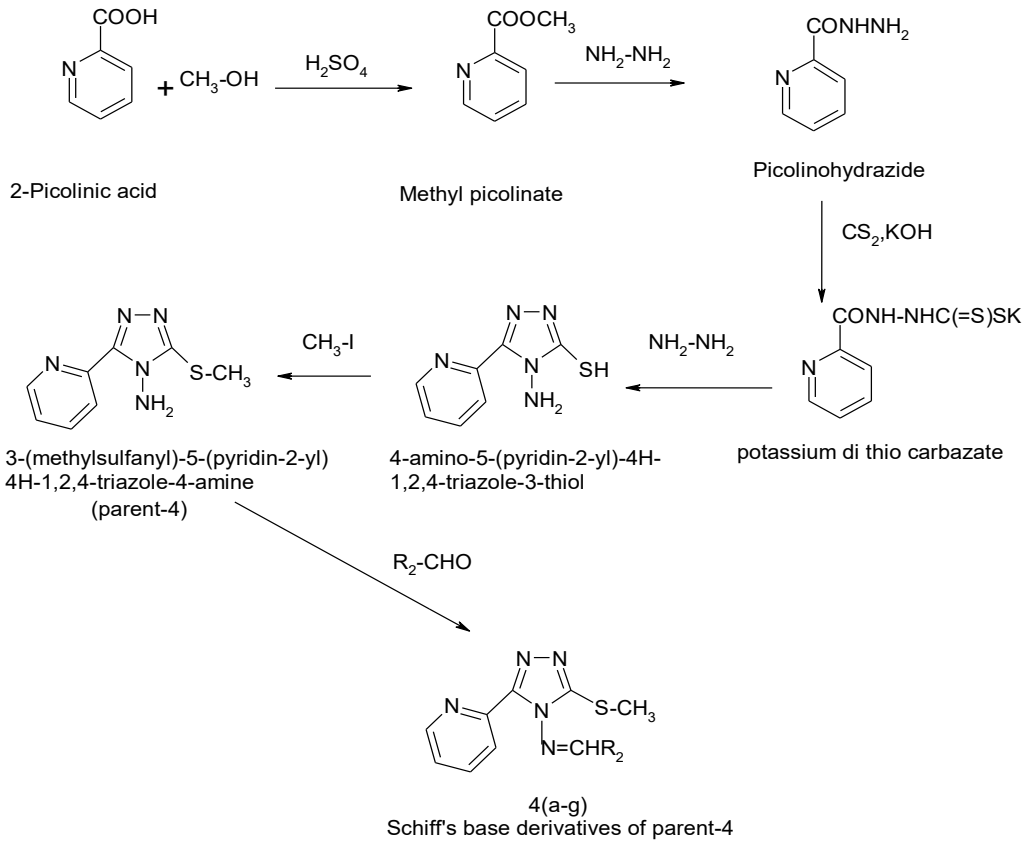
The IR spectra of compounds in KBr pellets were recorded using a Shimadzu IR spectrophotometer. Potassium bromide pellets were produced using 200 mg of dehydrated 1 mg of chemical was added to the potassium bromide and well mixed in the mortar. The mixture is put in an evacuated die and exposed to a pressure of 10-15 Torr. A translucent disk was created, which was then put in a pellet holder and scanned using IR.[12]

(F) Molecular weight determination method

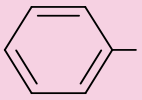
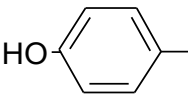
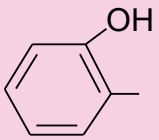
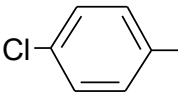
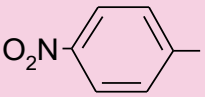
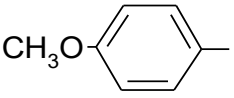
Molecular weight was determined by Rast's method (freezing point depression method) using naphthalene as solvent. Naphthalene was taken in a boiling tube (weight of naphthalene was about 4 times of the solute weight) tied with a thermometer and dipped in to a beaker containing water. Naphthalene was melted completely by heating the beaker on a water bath. Naphthalene was taken out in a wide mouth container and determined the freezing point by cooling. The freezing pint for naphthalene was noted down as $T_1{}^0C$. Now known weight of solute (compound whose weight had to be determined) was taken and mixed with naphthalene and both were meted together. By using the same procedure freezing point for naphthalene-solute mixture as $T_2{}^0C$ was determined. A second addition of 0.2 gram of solute was made and the freezing point was again noted as before to serve as a duplicate determination. [13]

5. SYNTHETIC SCHEMES

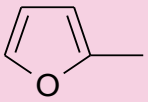
5.1 Scheme-1 Starting with 2-Picolinic acid:



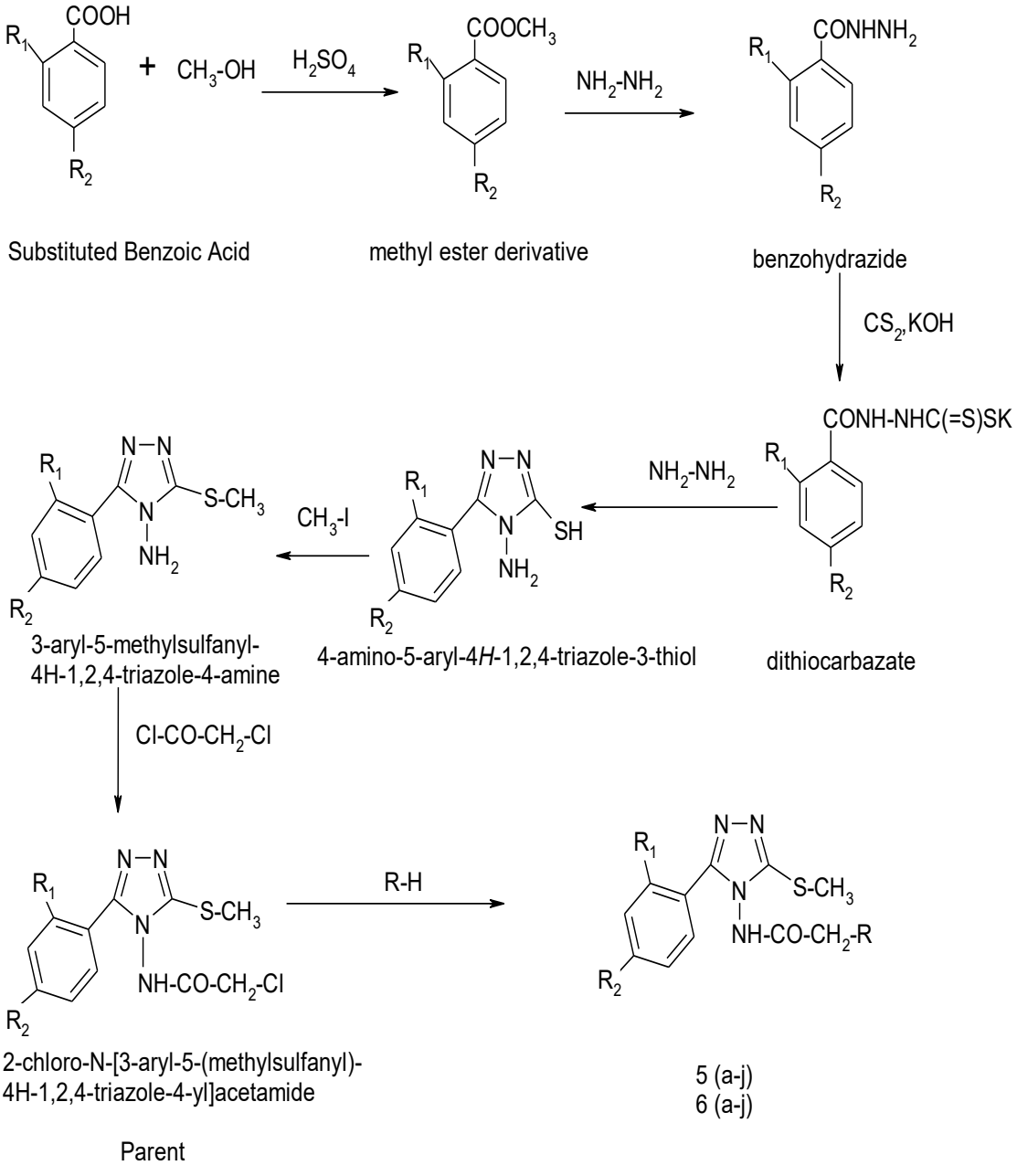
5.1.1 Synthesized compounds in scheme:

S. No.	Compound code	R_2
	4a	
	4b	
	4c	
	4d	
	4e	
	4f	

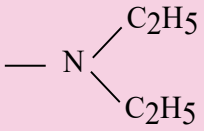
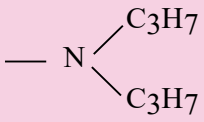
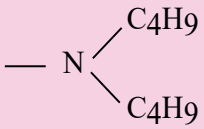
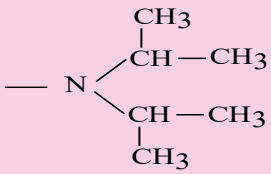
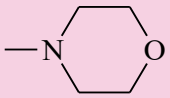
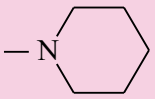
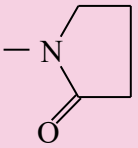
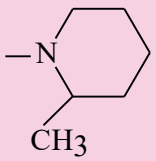
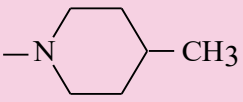
4g

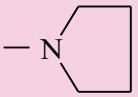
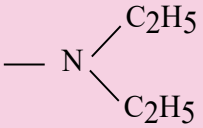
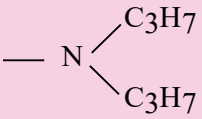
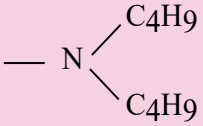
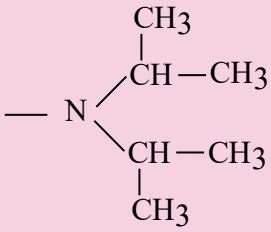
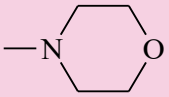
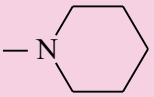
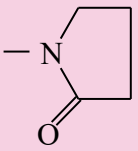
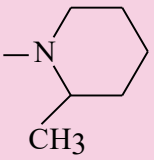
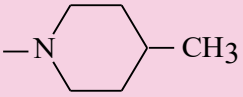


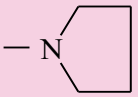
5.2 Scheme-2: Synthesis of parent-5 & 6 and their amines derivatives



5.2.1 Synthesized compounds in scheme-2

S. No.	Compound code	R_1	R_2	R
8.	5(a)	Cl	H	
9.	5(b)	Cl	H	
10.	5(c)	Cl	H	
11.	5(d)	Cl	H	
12.	5(e)	Cl	H	
13.	5(f)	Cl	H	
14.	5(g)	Cl	H	
15.	5(h)	Cl	H	
16.	5(i)	Cl	H	

17	5(j)	Cl	H	
18.	6(a)	Cl	Cl	
19.	6(b)	Cl	Cl	
20.	6(c)	Cl	Cl	
21.	6(d)	Cl	Cl	
22.	6(e)	Cl	Cl	
23.	6(f)	Cl	Cl	
24.	6(g)	Cl	Cl	
25.	6(h)	Cl	Cl	
26.	6(i)	Cl	Cl	

27	6(j)	Cl	Cl	

6. RESULT DISCUSSION:

Results of Antibacterial Activity of compounds

Table: 6.1. Zone of inhibition (diameter in mm) of synthesized compounds

Zone of inhibition by agar well diffusion (diameter in mm)									
Compound Code	***S.aureous***			***B.subtilis***			***E.coli***		
	125	***250***	***500***	***125***	***250***	***500***	***125***	***250***	***500***
	µg/100 µL			µg/100µL			µg/100µL		
4(a)	-	-	12	-	-	14	12	14	18
4(b)	-	14	16	-	12	14	-	-	12
4(c)	-	10	12	-	-	-	-	-	12
4(d)	13	16	20	-	12	15	-	-	13
4(e)	-	-	13	-	-	13	14	17	19
4(f)	-	15	16	-	-	11	-	-	-
4(g)	-	13	15	-	11	15	-	-	12
5(a)	-	-	14	-	-	12	-	-	13
5(b)	-	14	18	-	12	14	-	10	12

Zone of inhibition by agar well diffusion (diameter in mm)									
Bacteria	***S.aureous***			***B.subtilis***			***E.coli***		
C.code	125	250	500	125	250	500	125	250	500
5(c)	-	-	12	-	15	19	-	12	14
5(d)	-	12	15	12	17	20	-	-	12
5(e)	-	-	12	-	10	12	-	12	14
5(f)	-	-	10	-	-	12	-	12	14
5(g)	13	15	19	10	13	17	-	-	12
5(h)	-	-	12	-	-	14	12	14	18

5(i)	-	14	16	-	12	14	-	-	12
5(j)	-	10	12	-	-	-	-	-	12
6(a)	12	15	19	-	13	15	-	-	13
6(b)	-	-	13	-	-	13	14	17	19
6 (c)	-	15	16	-	-	11	-	-	-
6(d)	-	14	18	-	11	15	-	-	12
6(e)	12	15	19	-	13	15	-	-	13
6(f)	-	-	13	-	-	13	14	17	19
6(g)	-	15	16	-	-	11	-	-	-
6(h)	-	14	18	-	11	15	-	-	12
6(i)	-	-	12	-	15	19	-	12	14
6(j)	-	12	15	12	17	20	-	-	12
Control(-)	-	-	-	-	-	-	-	-	-
Ampicillin	19	25	35	15	19	24	11	14	18

(–), indicates there was no observed zone of inhibition

Results of Antifungal Activity

Table: 6.2 Zone of inhibition (diameter in mm) of Synthesized compounds

Zone of inhibition by agar well diffusion(diameter in mm)						
CompoundCode	***Aspergillus niger***			***Candida albicans***		
	125	***250***	***500***	***125***	***250***	***500***
	µg/100µL	µg/100µL	µg/100µL	µg/100µL	µg/100 µL	µg/100µL
Zone of inhibition by agar well diffusion(diameter in mm)						
Fungal strain	***Aspergillus niger***			***Candida albicans***		
C.code	**125**	**250**	**500**	**125**	**250**	**500**
4(a)	-	-	12	-	12	14
4(b)	-	12	14	-	-	13
4(c)	-	-	11	13	17	19
4(d)	-	-	11	-	-	13
4(e)	11	14	16	-	-	10
4(f)	12	15	18		-	12

4(g)	11	13	15	-	11	14
5(a)	-	-	13	-	13	15
5(b)	-	-	12	-	14	16
5(c)	-	-	10	13	15	18
5(d)	-	-	11	-	-	13
5(e)	-	-	11	-	-	13
5(f)	12	14	18	-	-	12
5(g)	-	-	11	-	12	14
5(h)	-	11	13	-	-	10
5(i)	-	12	14	-	-	12
5(j)	-	12	14	12	15	19
6(a)	-	-	10	-	-	10
6(b)	-	13	16	-	-	12
6 (c)	13	16	19	-	12	14
6(d)	-	-	13	-	-	11
6(e)	-	-	12	-	12	14
6(f)	-	12	14	-	-	13
6(g)	-	-	11	-	-	13
6(h)	-	-	11	-	-	12
6(i)	11	14	16	-	-	10
6(j)	12	15	18		-	12
Control	-	-	-	-	-	-
Fluconazole	22	28	36	24	30	38

(–), indicates there was no observed zone of inhibition

Docking

DOCKING: IN SILICO APPROACH

Docking process is started by using demo version of GRIP batch docking in Biopredicta Module of V-life science is used for docking. Docking process is started by using :

2RK-I : Crystal Structure of HIV-1 Reverse Transcriptase (RT) in Complex with a triazole derived NNRTI

Molecular Design Suite 3.5 – Biopredicta Module

Model Development:

Step 1. Generation of 2D-Structure of 4g and 5e:

The structures of the said molecules were designed using Chem Draw Ultra 11.0. Saved the same with the extension .*mol.

Step 2. Conversion into 3D- Form of the Biopredicta Module

The molecules were imported in the Molecular design suite and saved as .mol2 file.

Step 3. Labeling of the Molecules:

4g and 5e molecules were checked out for their 3D-labelling and shown in Figure 1,2

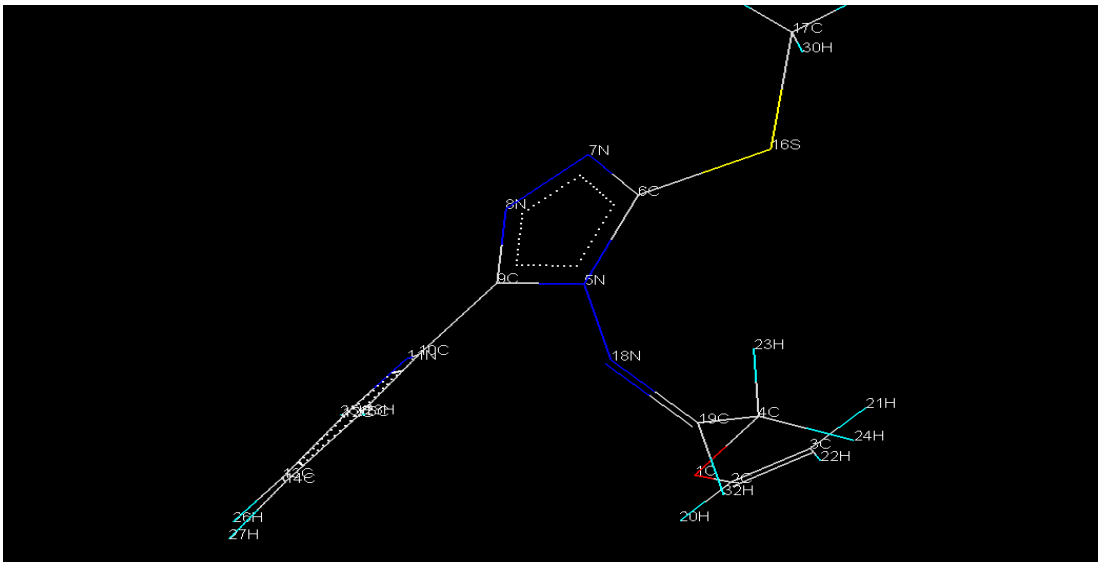


Figure: 1 labeled Structure of Compound 4g

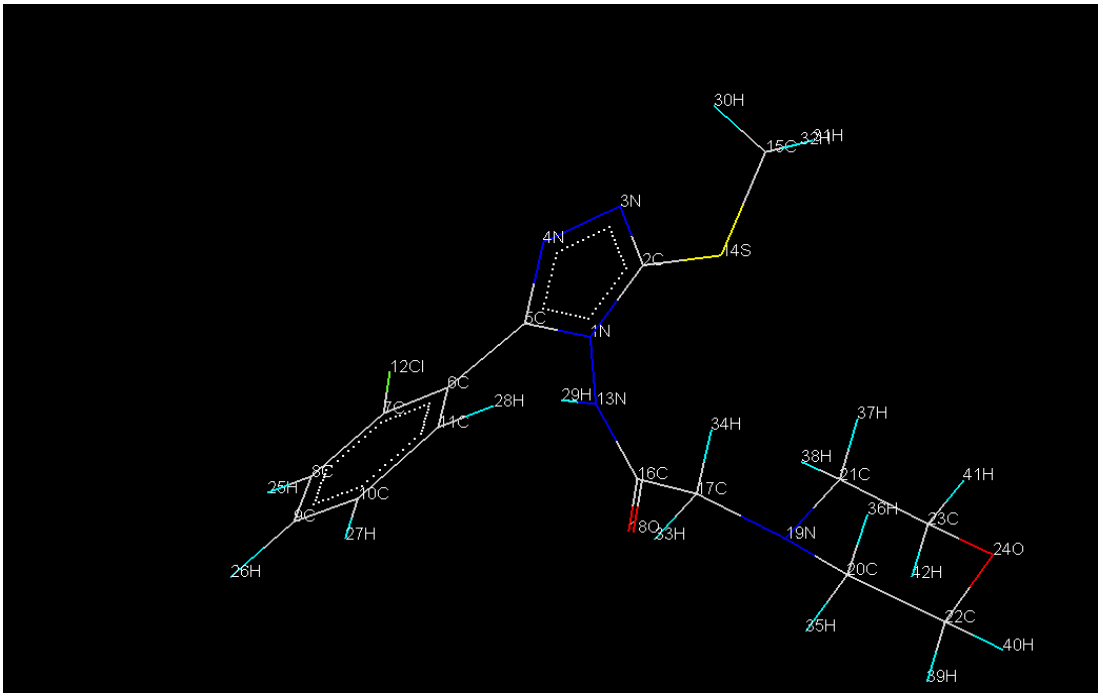


Figure: 2 Labeled Structure of Compound 5e

Step 4: Energy Minimization

The compounds individually subjected to the energy minimization using Merck molecular force field until each compound possesses the minimum energy.

Step 5: Generation of Conformers

Rotatable bonds in any molecule will be responsible for possibilities of various conformers with different energies. Using systemic and monte carlo method along with the selection of the important rotatable bonds, various conformers were generated. Five conformers from each molecule with minimum energies were selected (Least energy conformers are the stable ones)[Shown in Figure3 and 4].

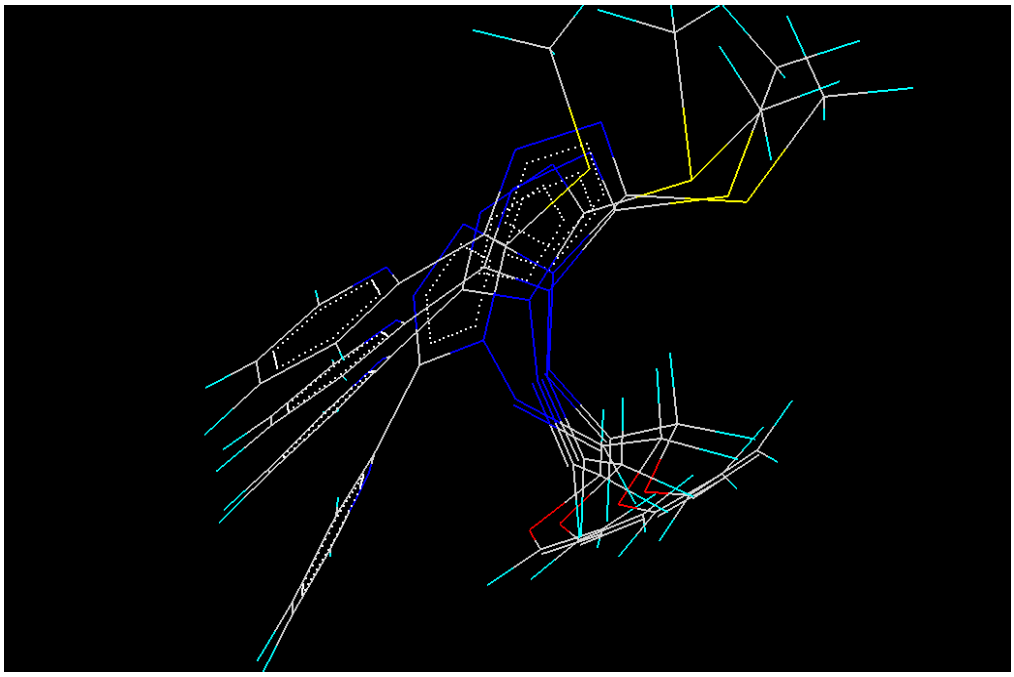


Figure :3 Alignment of Best five conformers of Compound 4g

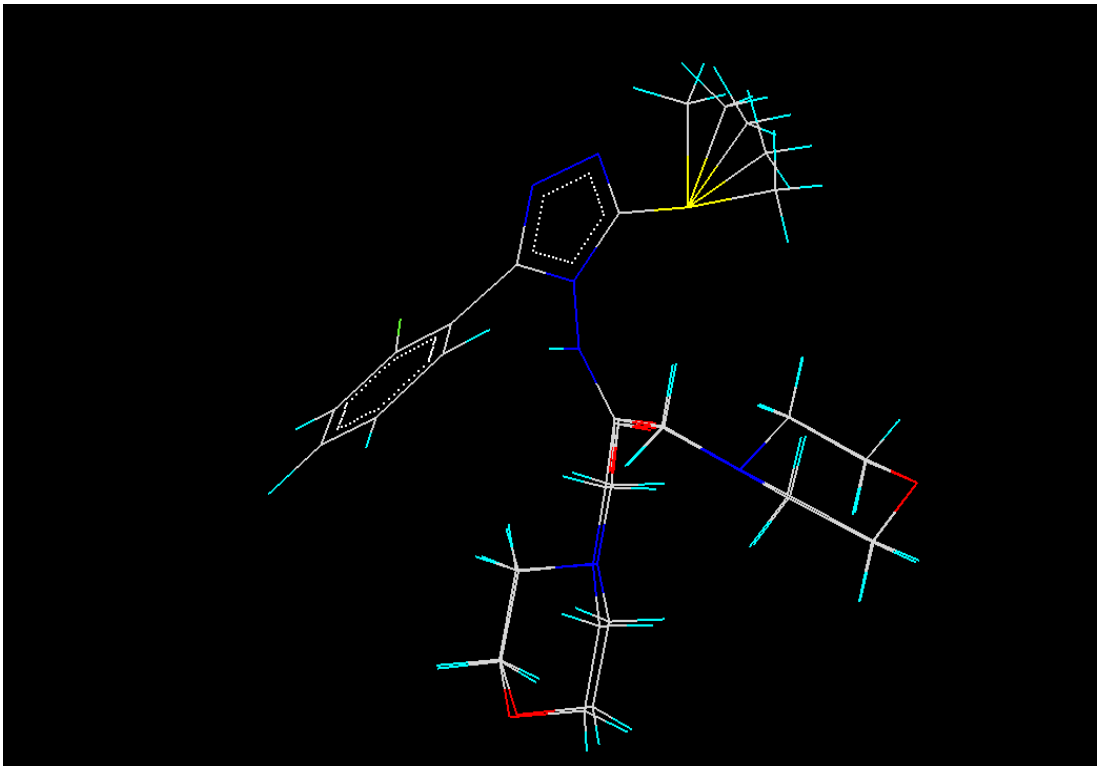


Figure : 4 Alignment of Best five conformers of Compound 5e

Step 6: Collecting the 2RK-I

The structure of Human reverse transcriptase enzyme along with co-crystallization of standard 1,2,4-Triazole were taken from the protein data bank with an extension .pdb[Shown in Figure 5 and 6].

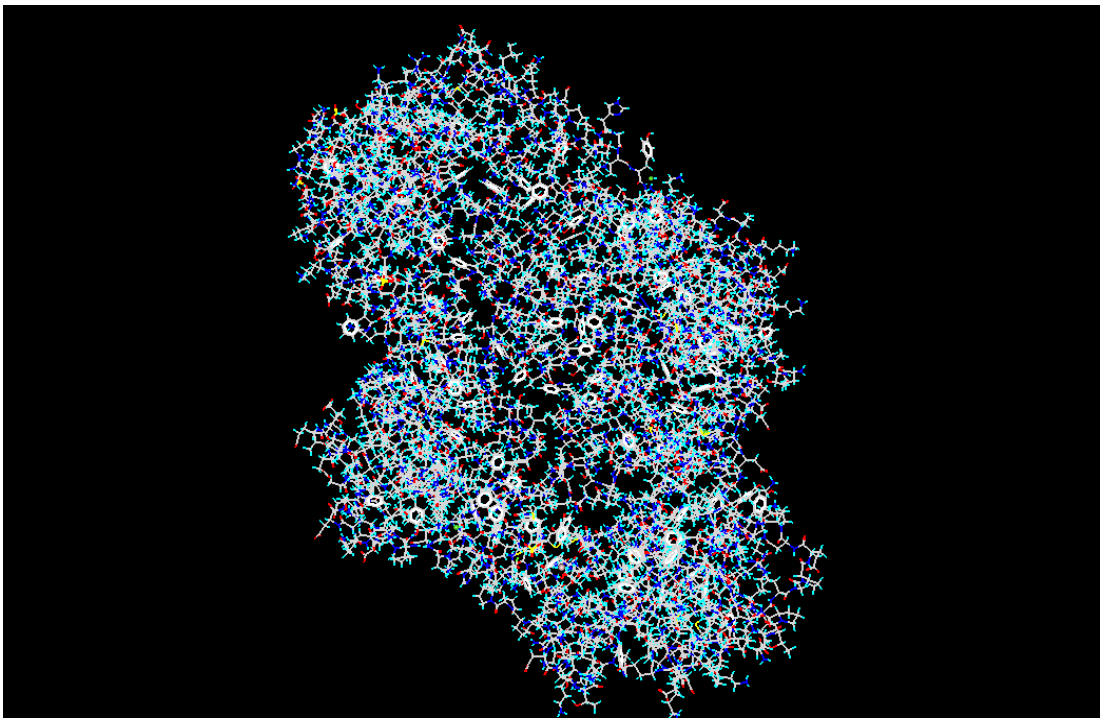


Figure: 5 Crystal Structure of 2RK-I (Cocrystallization of Triazole with Reverse Transcriptase Enzyme)

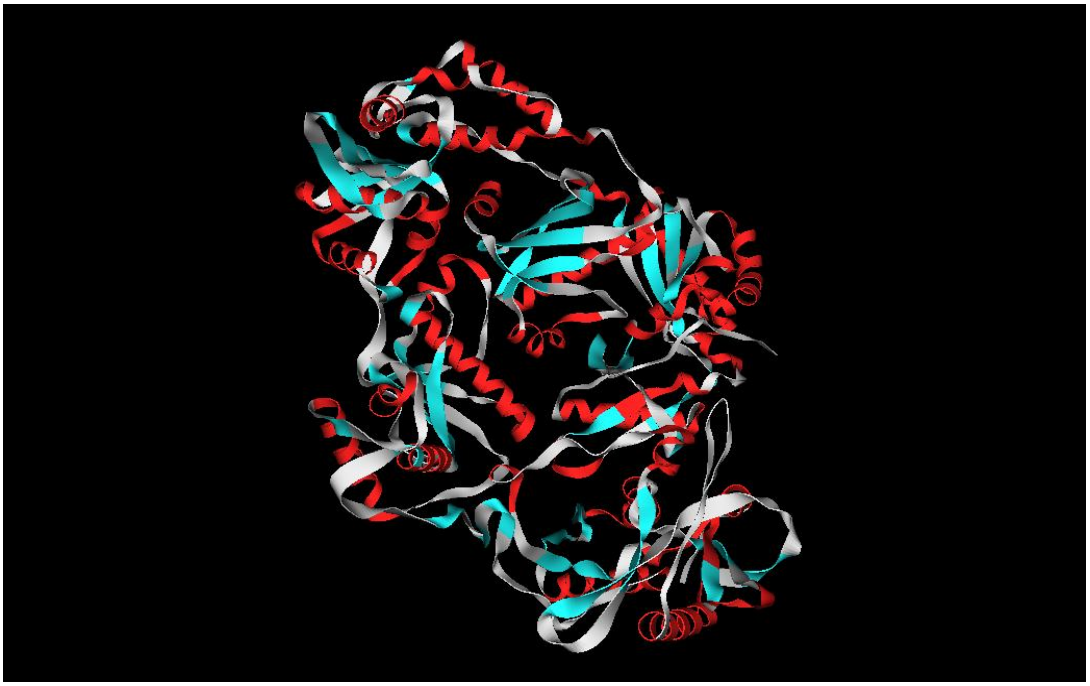


Figure : 6 Tertiary structure of 2RK-I

Step 7: Extraction of Reference Ligand from 2RK-I:

Using the standard procedure, the reference ligand was isolated from the protein and saved as Reference Ligand [Shown in Figure 7]

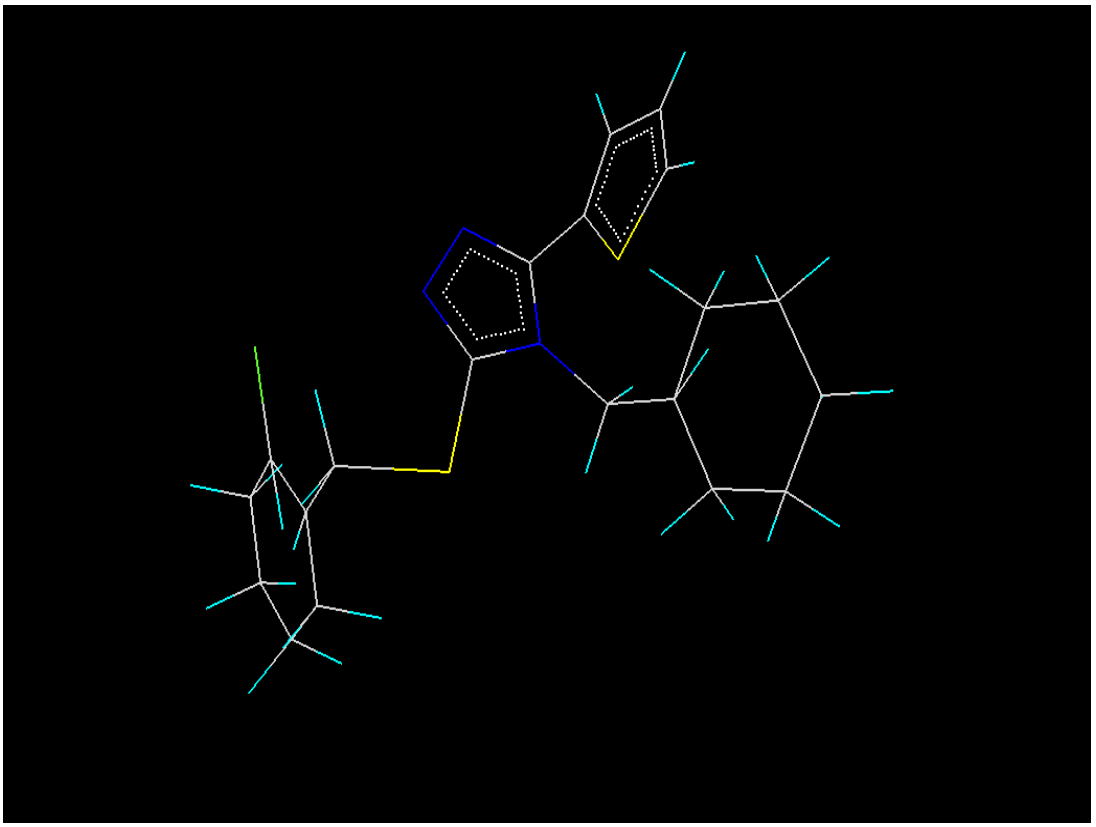


Figure : 7 Standard/Reference Ligand isolated from Co-crystallized Protein 2RK-I

Step 8: Docking Using Robust GRIP Technique

The following steps are required to be done.

Selected aporeceptor after extraction of reference ligand from 2RK-I.

Selected the Best Conformers.

Generated the empty folder with a name output.

Selected the reference ligand.

Selected parameters as exhaustive, no. of placements as 30 and then started docking.

Docking results

After careful observation, it was observed that the reference ligand molecule is having hydrogen bonding, hydrophobic interactions and vanderwaal interactions with the amino acids of the active site present on the 2RK-I.

The H-bonding of reference ligand is with the lysine present at 103 position (Figure 8). Hydrophobic interactions of reference ligand are with proline, tyrosine181A, tyrosine188A, lysine103A , serine105A , valine106A , histidine , leucine , tryptophan (Figure 9). Vanderwaal interactions of reference ligand are with proline, tyrosine, glutamine, valine, Isoleucine, tryptophan, phenylalanine, leucine, serine, glycine (Figure10).

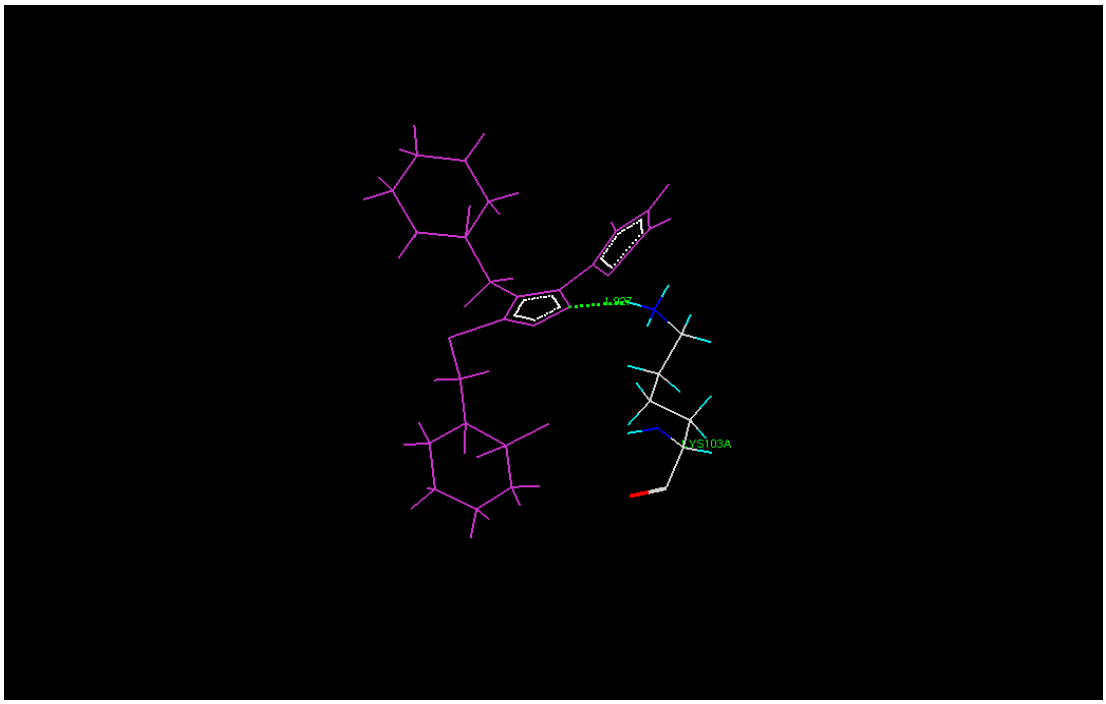


Figure : 8 H Bonding Interaction of Reference Ligand with The amino acid present on the active site of 2RK-I

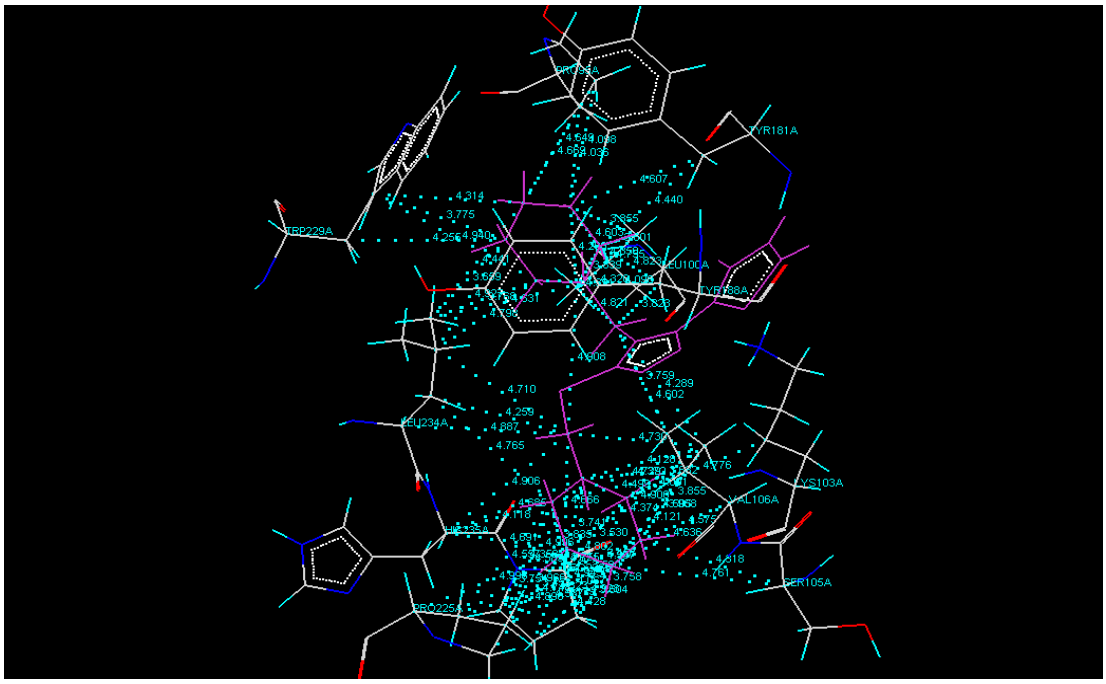


Figure: 9 Hydrophobic interactions of Reference Ligand with the amino acids at the active site of 2RK-I

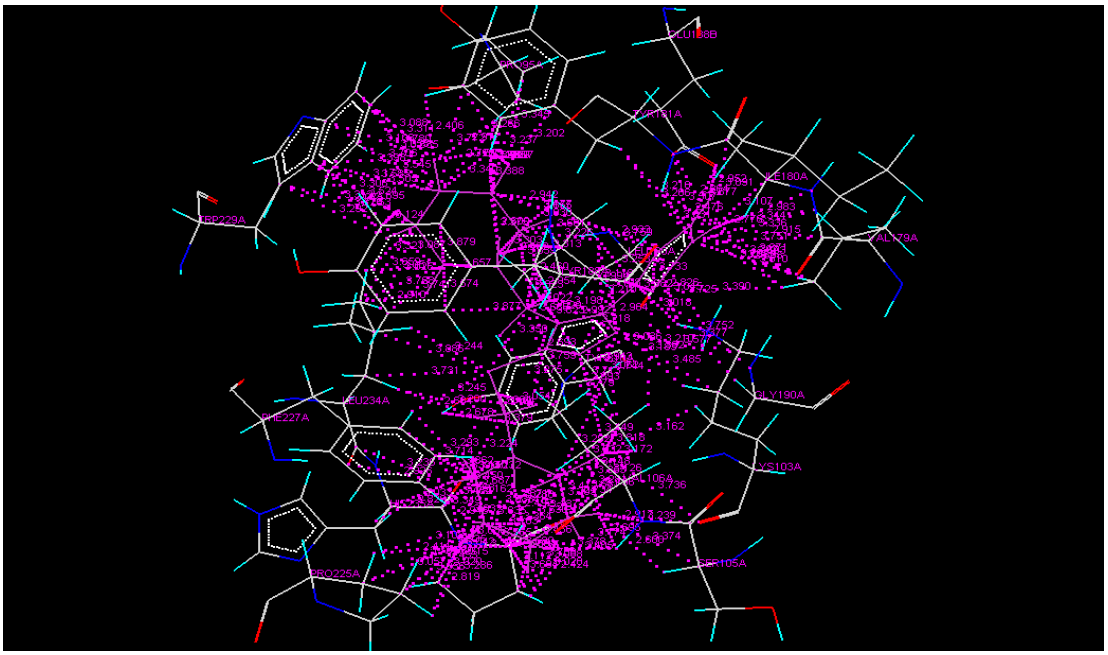


Figure: 10 Vander Waal Interactions of Reference Ligand with the amino acids at the active site of 2RK-I

Compound 4g have hydrophobic, pi-staking and vanderwaal interactions with the amino acids present on the active site of the reverse transcriptase 2RK-I.

Hydrophobic interactions of 4g molecule are with Leucine, Lysine, Glycine, Valine, Serine,Proline (Figure 11). Pi-staking of 4g molecule are with Tyrosine188 and Pheylalanine 227 (Figure 12). Vander waal interactions of 4g molecule are with leucine, tyrosine, valine, phenylalanine, serine, proline, lysine, glycine (Figure 13).

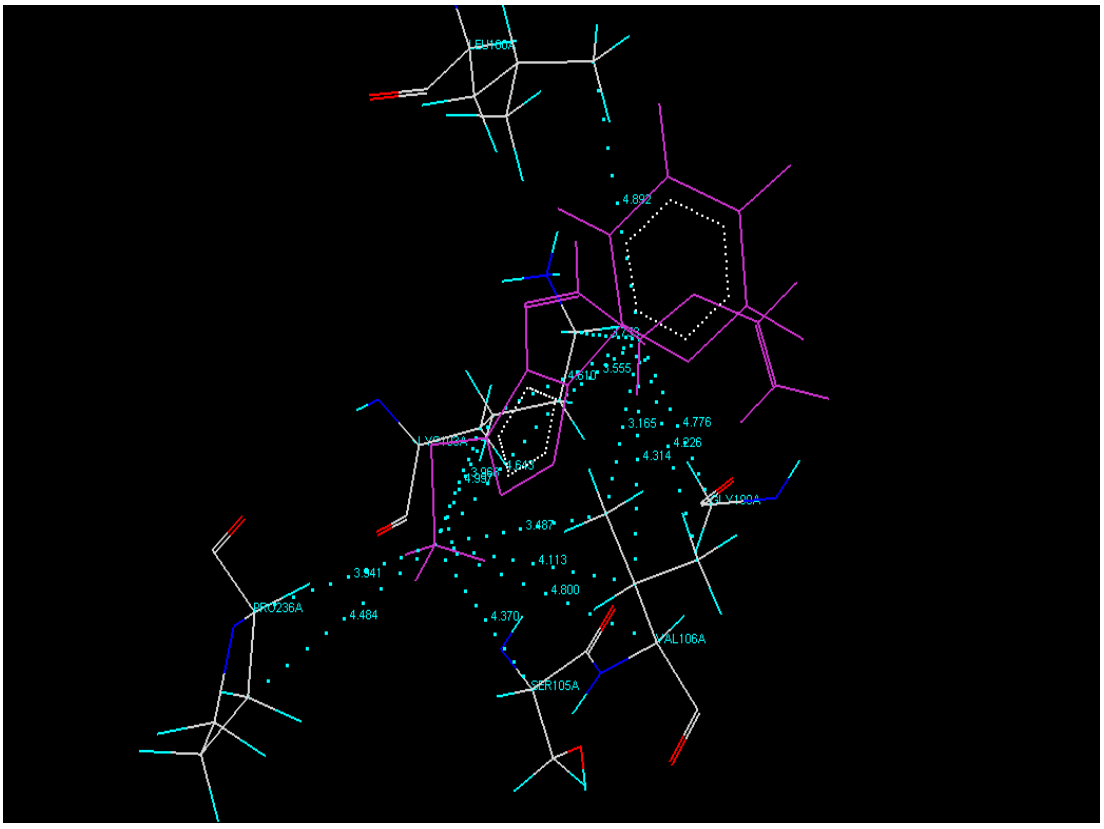


Figure: 11 Hydrophobic Interactions of 4g molecule with amino acids at the active site of 2RK-I

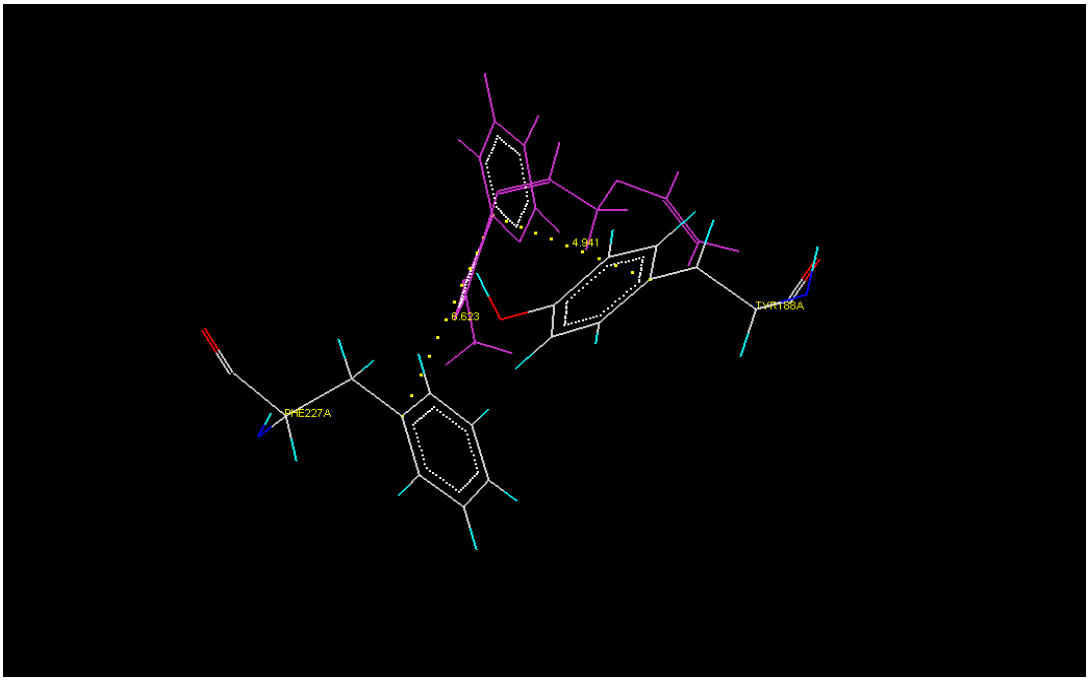


Figure: 12 Pi-staking interactions of 4g molecule with amino acids at the active site of 2RK-I

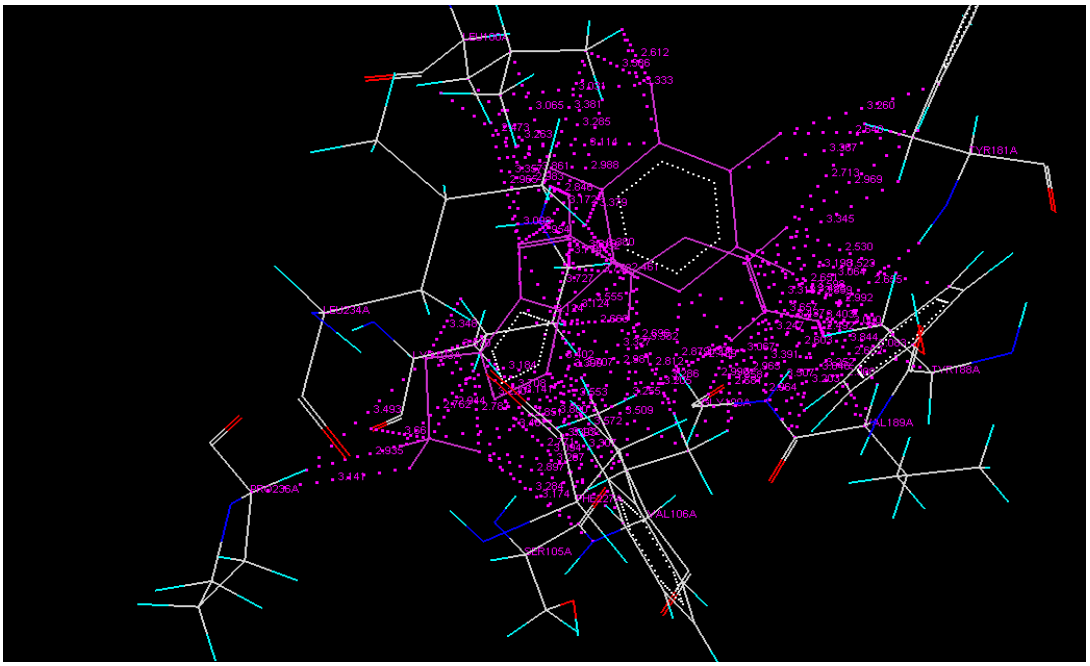


Figure: 13 Vander waal Interactions of 4g molecule with amino acids at the active site of 2RK-I

Compound 5e have hydrogen, hydrophobic, pi-staking and vanderwaal interactions with the amino acids present on the active site of the reverse transcriptase 2RK-I.

The hydrogen bonding of 5e molecule are with tyrosine181 and lysine 103 (Figure 14). Hydrophobic interactions of 5e molecule are with tryptophan, leucine, tyrosine, isoleucine, valine, glycine (Figure 15). Pi-staking of 5e molecule is with phenylalanine 227 (Figure 16). Vander waal interactions of 5e molecule are with tryptophan, leucine, phenylalanine, histidine, proline, valine, serine, glycine, isoleucine, tyrosine, lysine (Figure 17).

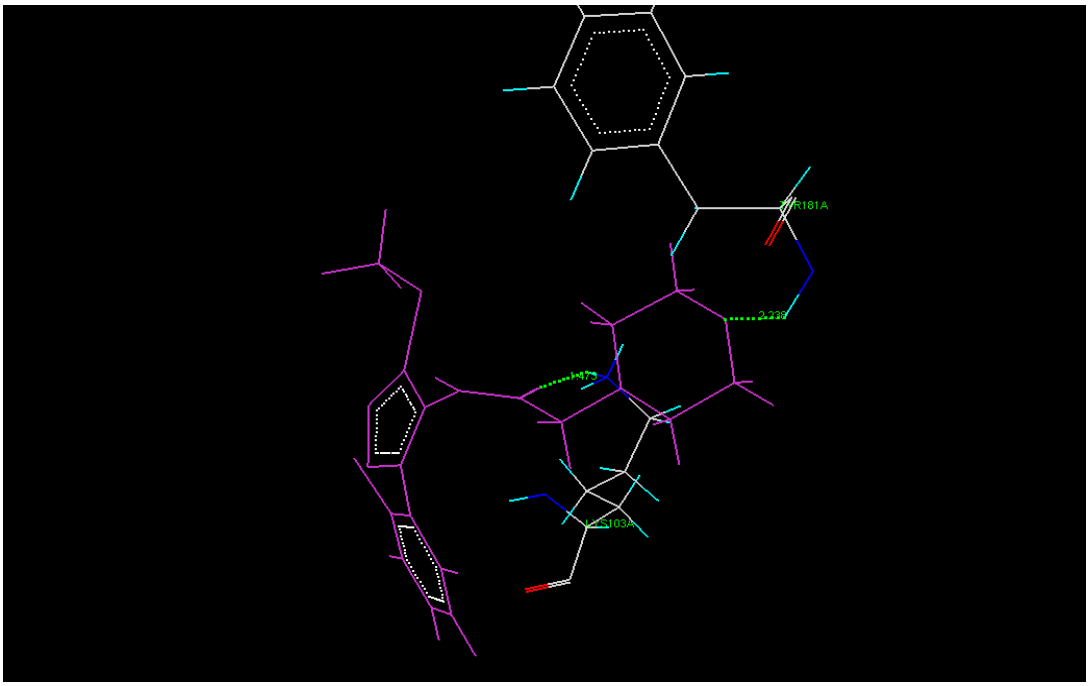


Figure: 14 Hydrogen Bonding of 5e Molecule with the amino acids at the active site of 2RK-I

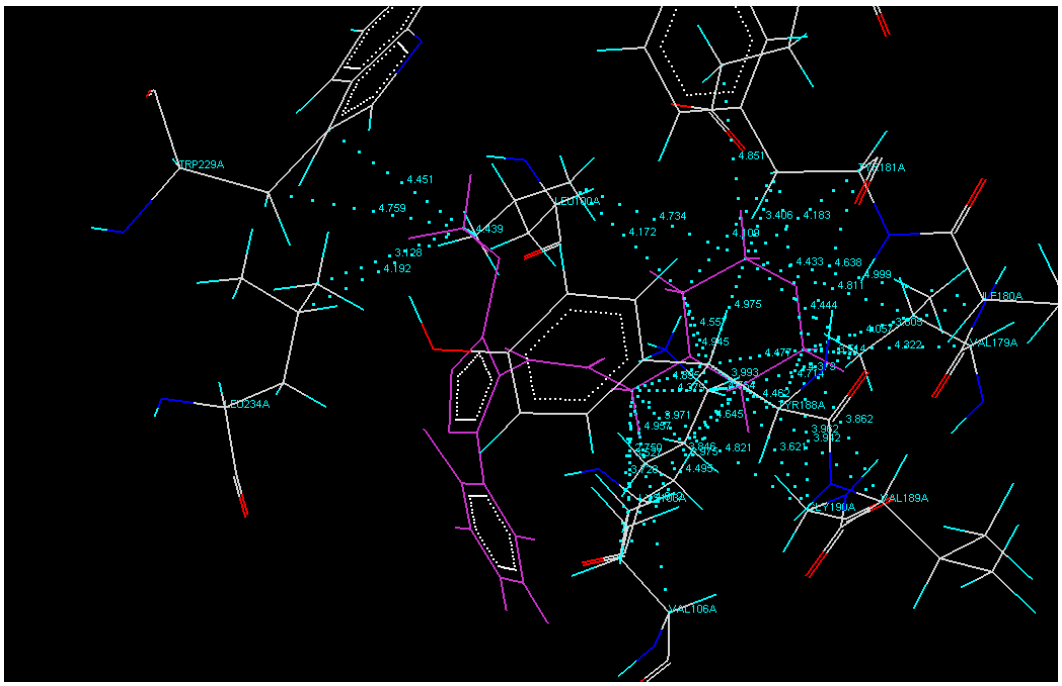


Figure: 15Hydrophobic Interactions of 5e Molecule with the amino acids at the active site of 2RK-I

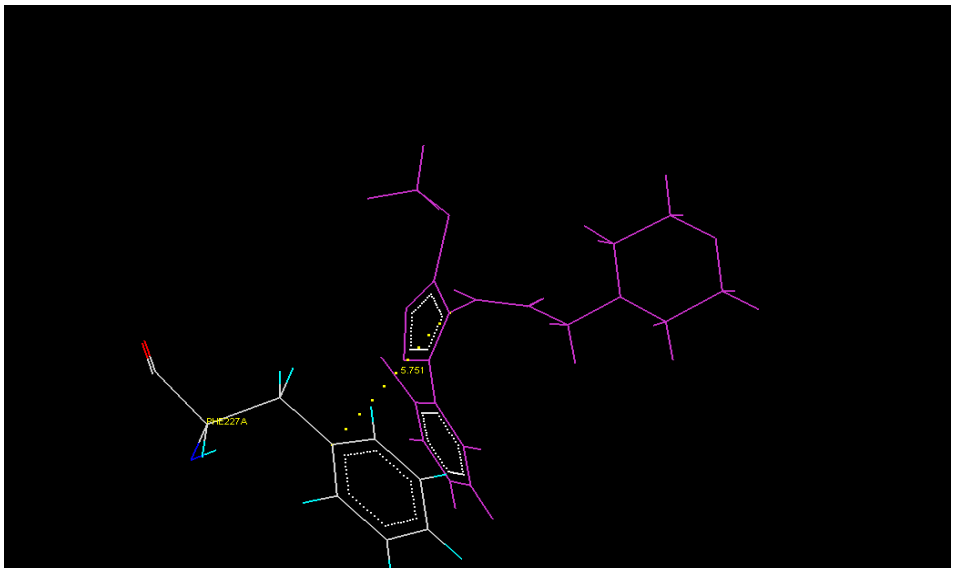


Figure: 16 Pi-staking Interactions of 5e Molecule with the amino acids at the active site of 2RK-I

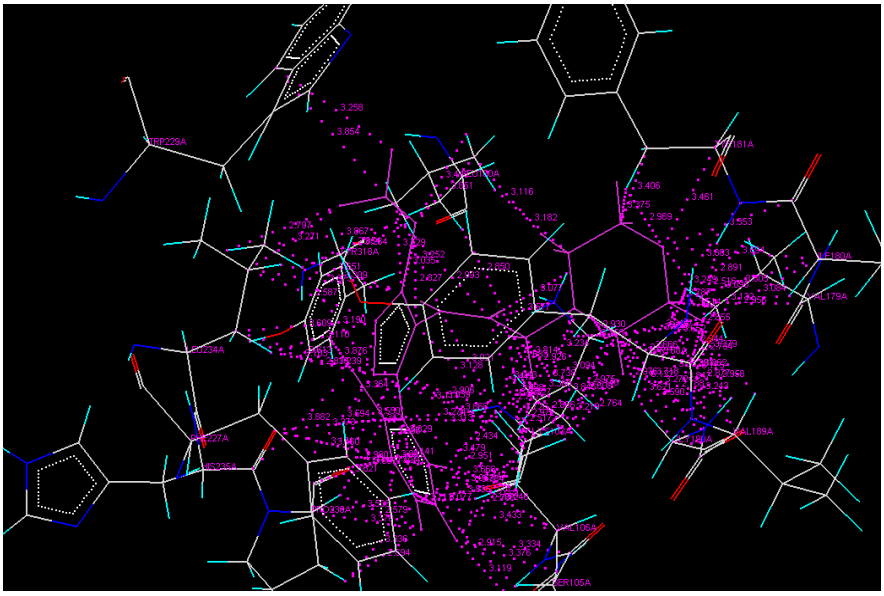


Figure: 17 Vanderwaal Interactions of 5e Molecule with the amino acids at the active site of 2RK-I

Table: 6.3 Dock Score of molecules and Reference ligand

S.No	Molecule	Dock Score
1.	min_4g_C50_P19	-63.190130
2.	min_5e_C1_P16	-44.777277
3	Reference Ligand	-137.058603

7. CONCLUSION

Table 6.1. Preliminary antibacterial studies were conducted on synthesized compounds, by Well Diffusion method. For comparison, Ampicillin was used as standard , procured from Hindustan Antibiotics Pvt..Ltd., Pune.

The findings of the antibacterial screening of compounds were shown in Table 10. Based on these results, it is clear that

the majority of the compounds shown strong inhibitory effect against bacterial species such as S. sureus, B. subtilis, and E. coli. The antibacterial activity of the investigated substances was shown to be dosage dependant. Most chemicals suppressed bacterial growth at doses ranging from 250 µg/mL to 500 µg/mL, with excellent activity at 250 µg/mL. Among the substances examined, 4(g), 5(b), 5(g), and 6(a) had high inhibitory action against B. subtilis and S. aureus. Compounds 5(g), 4(d), 5(i), 6(d), 6(e), and 6(j) exhibited low to moderate efficacy against S. aureus. The results also revealed that compounds 5(c) had modest inhibitory action against B. subtilis. Compounds 4(a), 4(e), 5(h), 6(b), and 6(f) shown strong inhibitory action against E.coli. The results also revealed that compounds 5(a) and 6(c) had lower action against B. subtilis and E. coli. The results also revealed that compounds 5(j) and 6(g) were resistant to B. subtilis. At 125µg/100µL, ampicillin inhibited S. aureus, B. subtilis, and E. coli with zones of 19, 15, and 11 mm, respectively.

Preliminary Antifungal studies were conducted on synthesized compounds, by Well Diffusion method. For comparison, Fluconazole was used as standard , procured from Hindustan Antibiotics Pvt.Ltd., Pune.

Table 6.2 summarizes the invitro Novel antifungal property against two major fungal strains, Aspergillus niger and Candida albicans, was determined using the well diffusion technique. Fluconazole was utilized as a benchmark medication to compare the outcomes.

A significant inhibition of fungal growth (16–30%) was observed at concentrations ranging from 125 µg/100µL to 500 µg/mL for the majority of the synthesized compounds. Compound 4(f), 5(f), 6(c) and 6(j) were found to be very good antifungal agent for A.niger, whereas compound 4(e) and 6(i) showed moderate activity. 4(b), 5(b), 5(i), 6(b), 6(d) and 6(f) showed less activity against A.niger. Compounds 4(c), 5(c) and 5(j) were found to be very good antifungal agent for C.albicans. whereas compound 4(g), 5(a) and 6(e) showed moderate activity 4(a), 5(b), 5(i), 6(b), 6(c) and 6(e) showed less activity against C.albicans. Compounds 4(d), 5(d), 5(e), 6(g) and 6(h) was found to be resistant against A.niger and C.albicans. Fluconazole showed zone of inhibition 22 and 24 mm at 125µg/100µL for A.niger and C.albicans respectively.

REFERENCES

[1] Jakhar, R., Dangi, M., Khichi, A., & Chhillar, A. K. (2020). Relevance of molecular docking studies in drug designing. Current Bioinformatics, 15(4), 270-278.

[2] Yuriev, Elizabeth, and Paul A. Ramsland. "Latest developments in molecular docking: 2010–2011 in review." Journal of Molecular Recognition 26, no. 5 (2013): 215-239.

[3] Morris GM, Lim-Wilby M. Molecular docking. Molecular modeling of proteins. 2008:365-82.

[4] Vora, J. J., Patel, D. R., Bhimani, N. V., & Ajudia, P. V. (2011). Synthesis, characterization and biological evaluation of triazole and fused triazole derivatives. Journal of the Chilean Chemical Society, 56(3), 771-773.

[5] Tang, Hui, Can-Hui Zheng, Xiao-Hui Ren, Jia Liu, Na Liu, Jia-Guo Lv, Ju Zhu, and You-Jun Zhou. "Synthesis and biological evaluation of novel triazole derivatives as antifungal agents." Chinese Chemical Letters 24, no. 3 (2013): 219-222.

[6] Mohsen, Usama. "Biological evaluation of some triazole and triazolothiadiazine derivatives." Marmara Pharmaceutical Journal 16, no. 3 (2012): 229-234.

[7] Shaikh, Mubarak H., Dnyaneshwar D. Subhedar, Laxman Nawale, Dhiman Sarkar, Firoz A. Kalam Khan, Jaiprakash N. Sangshetti, and Bapurao B. Shingate. "1, 2, 3-Triazole derivatives as antitubercular agents: synthesis, biological evaluation and molecular docking study." MedChemComm 6, no. 6 (2015): 1104-1116.

[8] Ali, Abdul Aziz, Dhrubajyoti Gogoi, Amrita K. Chaliha, Alak K. Buragohain, Priyanka Trivedi, Prakash J. Saikia, Praveen S. Gehlot, Arvind Kumar, Vinita Chaturvedi, and Diganta Sarma. "Synthesis and biological evaluation of novel 1, 2, 3-triazole derivatives as anti-tubercular agents." Bioorganic & Medicinal Chemistry Letters 27, no. 16 (2017): 3698-3703.

[9] Bele, Archana A., and Anubha Khale. "An overview on thin layer chromatography." International Journal of Pharmaceutical Sciences and Research 2, no. 2 (2011): 256.

[10] Poole, Colin F. "Thin-layer chromatography: challenges and opportunities." Journal of Chromatography A 1000, no. 1-2 (2003): 963-984.

[11] Jyothsna, S., G. Manjula, Sateesh Suthari, and AS Nageswara Rao. "Qualitative elemental analysis of selected potential anti-asthmatic medicinal plant taxa using EDXRF technique." Heliyon 6, no. 2 (2020).

[12] Dufour, É., 2009. Principles of infrared spectroscopy. Infrared spectroscopy for food quality analysis and control, pp.1-27.

[13] Karol, M. H., Kramarik, J. A., & Ferguson, J. (1995). Methods to assess RAST results in patients exposed to chemical allergens. Allergy, 50(1), 48-54.