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Original Research Article

QSAR and Molecular Docking Studies on Nitro (Triazole/Imidazole)-Based Compounds as Anti-Tubercular Agents

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ABSTRACT

Tuberculosis is a chronic infectious disease which remains one of the leading causes of death worldwide. Scientists are currently engaging both experimental and theoretical methods to seek solution to this deadly disease.

This work is aimed at identifying descriptors that described the anti-*Mycobacterium tuberculosis* H37Rv activity of nitro(triazole/imidazole)-based compounds and reliable quantitative structure activity relationship (QSAR) model were developed using selected descriptors as well as observing non-bonding interactions between studied complexes.

Nineteen molecules comprising 3-nitrotriazole- and nitroimidazole- analogues were studied as anti-tubercular agents against Rv0371c from *Mycobacterium tuberculosis* H37Rv (PDB ID: 2we9) using semi-empirical PM3 method, quantitative structure activity relation (QSAR) studies and Docking approaches. QSAR model was successfully developed, and the studies indicated that four 2D descriptors (nO, ATS3m, ATS6m and ATS7m) were important factors for the observed biological activity. Also, the studied docking studies revealed that all the studied compounds could form a stable complex with the active site of the protein with compound **10** (N-([1,1'-biphenyl]-3-yl)-2-(3-nitro-1H-1,2,4-triazol-1-yl)acetamide) forming the most stable complex. It was observed that the obtained descriptors perfectly described the anti-*Mycobacterium tuberculosis* activity of the studied nitro(triazole/imidazole)-based compounds and the developed QSAR model proved to be reliable by accurately predicting the experimental IC_{50}. Nonbonding interaction between nitro(triazole/imidazole)-based compounds and *Mycobacterium tuberculosis* H37Rv (PDB ID: 2we9) showed that compound **10** with -8.0 kcal/mol have higher tendency to inhibit *Mycobacterium tuberculosis* H37Rv (PDB ID: 2we9) than other studied compounds.

Keywords: nitrotriazole, nitroimidazole, antitubercular activity, Drug Design, QSAR, Molecular Docking.

Introduction

Tuberculosis (TB) is a chronic infectious disease caused by gram-positive bacteria called *Mycobacterium tuberculosis* (Mtb). Mtb frequently attacks the lungs (pulmonary TB) but can also harm other part of the body.[1] TB remains one of the leading causes of death worldwide.[2] According to Burel *et al*., more than 1.2 million TB deaths have been recorded among both young and old globally.[3] Anti-tubercular drugs include isoniazid (INH), rifampicin (RMP), pyrazinamide, ethambutol and streptomycin (SM). Anti-tubercular drugs include isoniazid (INH), rifampicin (RMP), pyrazinamide, ethambutol and streptomycin (SM).

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Present TB treatment takes a long time (6-12 months) and requires the combination of three or four of the aforementioned drugs.[4] However, there is a low cure rate as a result of poor treatment and noncompliance; this has given rise to selection and spread of multidrug-resistant (MDR) and extensively drug-resistant (XDR) TB. These tuberculosis strains have resulted to low cure rates and high mortality rates as a result of difficulties in the treatment,[5,6] and this has called for a need to develop new anti-TB drugs that can effectively treat all form of resistant Mtb strain and also shorten the long period of TB treatment.

The nitrogen-containing heterocyclic compounds either from natural sources or synthetic compounds have attracted the attention of numerous researchers because of their usefulness in various types of applications. Triazoles moiety is one of the most significant five member heterocyclic compounds with three nitrogen and two carbon atoms.[7] Triazole and its various derivatives have been extensively used as antimicrobial, antifungal, antiviral, anti-inflammatory, analgesic, antiepileptic, antihypertensive, antimalarial, antioxidants, antihistaminic, antianxiety, antidepressant, and anti-tubercular agents.[8-10] They are also used as optical corrosion inhibitors, brightening agents, and as additives with a variety of other purposes.

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On the other hand, nitroimidazoles are a promising new class of compounds that have shown significant anti-tubercular activities in different level of clinical trials.[11]

Recent transformation and innovation in the field of computational chemistry has led to the use of diverse methods for the qualitative and quantitative evaluation of substances in almost every field of chemistry.[12] More so, pharmaceutical chemist use *in silico* methods in various aspect of drug design and development and these have increased the chances of success in various stages of drug discovery processes (from target identification, validation, discovery of primary hit and lead compounds to the final stage of lead optimization).[13] Quantitative structure activity relationship (QSAR) and molecular docking are examples of vital computational tools commonly used in drug design and development. QSAR is a technique used to predict and classify biological activity of compounds by utilizing experimental data and molecular structures.[7] QSAR models help in the selection of alternative mechanism of action, project new design methodologies, to determine relevant structural characteristics and to propose new hypotheses for future work. Molecular docking is a structure-based drug design technique use to stimulate the molecular interaction and predict the binding affinity between a small molecule (a ligand) and a protein (receptor).[14] It also helps to explain the fundamental biochemical processes.[15] However QSAR and molecular docking studies have contributed immensely in making drug discovery more efficient, less time consuming, less expensive and prevent a lot of environmental toxicity that would have resulted from numerous experimental processes.[16] In this work, descriptors that described the anti-*Mycobacterium tuberculosis* H37Rv activity of nitro(triazole/imidazole)-based compounds were identified and reliable quantitative structure activity relationship (QSAR) model were developed using selected descriptors obtained from the optimized nitro(triazole/imidazole)-based compounds as well as observing non-bonding interactions between studied compounds and the target (Rv0371c from *Mycobacterium tuberculosis* H37Rv (PDB ID: 2we9)).

Materials and Methods

Collection of dataset

Nineteen molecules comprising 3-nitrotriazole- and nitroimidazole-analogues obtained from literature were investigated in this work.[17] The general structure, IUPAC name and experimental IC_{50} of these compounds are shown in Table 1.

Optimization and docking studies

The studied compounds were optimized using semi-empirical PM3 method via Spartan14 and series of molecular descriptors were obtained for further study.[18] The optimized compounds were further used as ligands for the docking studies. The receptor Mtb H37Rv (PDB code: 2we9) was downloaded from protein data bank.[19] To obtain the desired chain of the receptor, Discovery Studio 4.1 visualizer was used to treat the pdb file by removing water molecules, multiple ligands and non-protein parts. Autodock tool was used to convert the ligands and the receptor to pdbqt format. The spacing was set to be 1.00Å, the grid box centre was (X = 35.929, Y = 27.684, Z = 39.858) and box size (X = 40, Y = 40, Z = 70). The docking process was carried out using AutoDock Vina[20] and the output of docking process analyzed using Biovia Discovery Studio.[20] The binding affinities and the molecular interaction for each complex were observed.

QSAR study

The optimum Model that was used as a tool for predicting reported experimental bioactivities was developed using multiple linear regression method. Four descriptors that could give a good prediction were randomly selected from the calculated molecular parameters and the selected descriptors served as the independent variable and the experimental IC_{50} values were used as the dependent variable. The model was constructed according to the following linear equation.

$IC_{50} = \alpha + \beta_1 X_1 + \beta_2 X_2 + \cdots + \beta_n X_n$ ---------- (1)

Where α and β are constants i.e regression coefficients determined through regression analysis, X_1, X_2.... X_n are quantum chemical indices characteristic of the molecule.

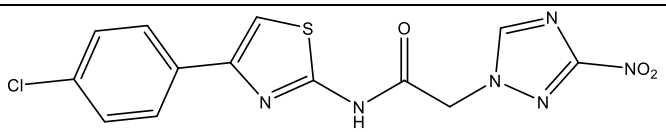
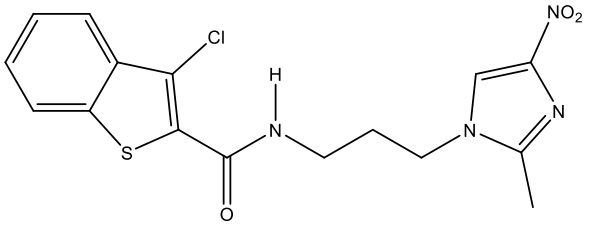
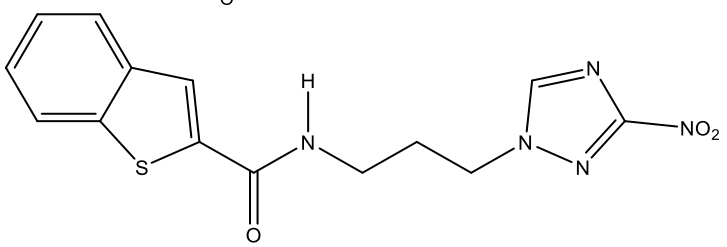
The reliability of the QSAR model was validated by calculating cross Adjusted R^2, (R_a^2) using statistical equations (2)

$R_a^2 = \frac{(N-1)\times R^2 - P}{N-1-P}$ ---------- (2)

$IC_{50} = 58.293983863(\text{nO}) + 0.054509242(\text{ATS3m}) - 0.185735838(\text{ATS6m}) + 0.145505664(\text{ATS7m}) - 279.171300765$ ---------- (3)

R^2= 0.945, Adj R^2= 0.914, F-value = 4.175, P-value ≤0.001, CVR^2 = 0.846

Table 1: IUPAC Name, Chemical Structures of the Studied Compounds

	IUPAC NAME	CHEMICAL STRUCTURE
1	-chloro-N-(4-(3-nitro-1H-1,2,4-triazol-1-yl)butyl)benzo[b]thiophene- 2-carboxamide	
2	3-chloro-N-(3-(2-methyl-4-nitro-1H-imidazol-1-yl)propyl)benzo[b]thio phene-2-carboxamide	
3	3-chloro-N-(3-(3-nitro-1H-1,2,4-triazol-1-yl)propyl)benzo[b]thiophene -2-carboxamide	

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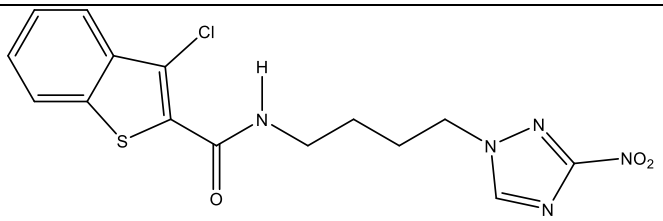
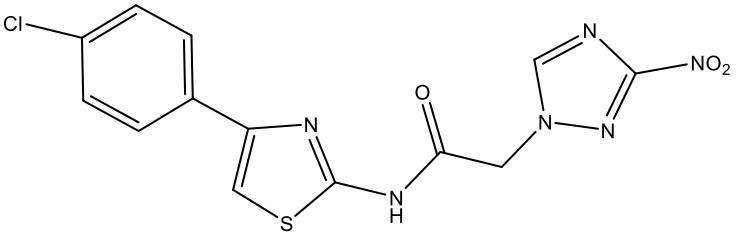
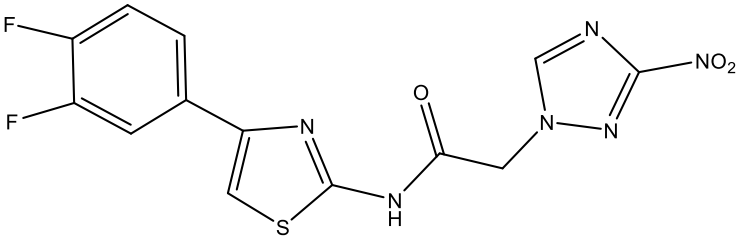
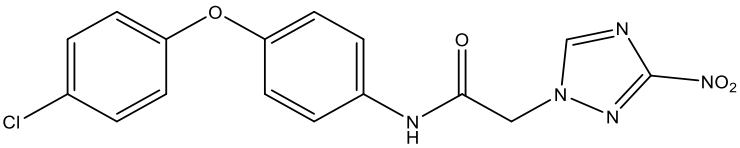
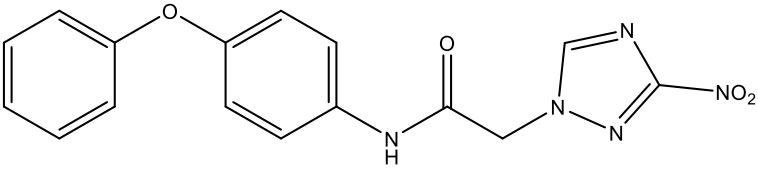
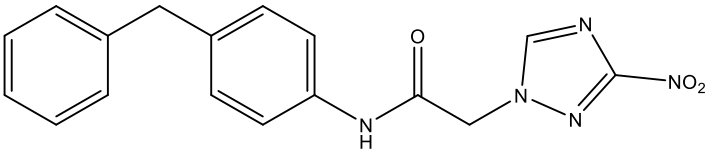
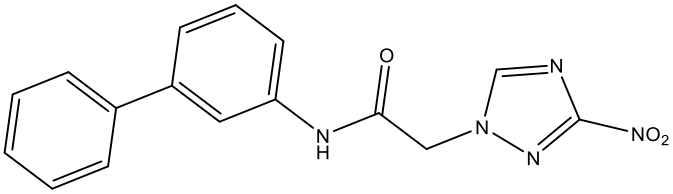
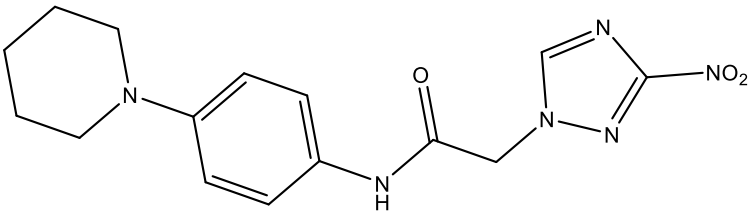
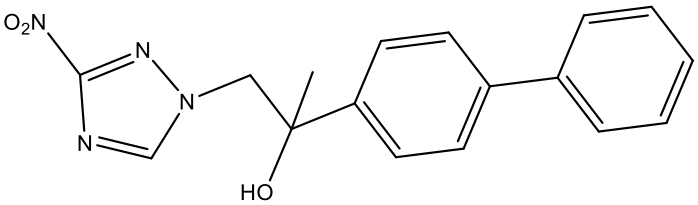
4	N-(4-(3-nitro-1H-1,2,4-triazol-1-yl)butyl)benzo[d]thiazole-2-carboxam - ide	
5	N-(4-(4-chlorophenyl)thiazol-2-yl)-2-(3-nitro-1H-1,2,4-triazol-1-yl)acetam - ide	
6	N-(4-(3,4-difluorophenyl)thiazol-2-yl)-2-(3-nitro-1H-1,2,4-triazol-1-yl)acetamide	
7	N-(4-(4-chlorophenoxy)phenyl)-2-(3-nitro-1H-1,2,4-triazol-1-yl)acetamide	
8	2-(3-nitro-1H-1,2,4-triazol-1-yl)-N-(4-phenoxyphenyl)acetamide	
9	N-(4-benzylphenyl)-2-(3-nitro-1H-1,2,4-triazol-1-yl)acetamide	
10	N-([1,1'-biphenyl]-3-yl)-2-(3-nitro-1H-1,2,4-triazol-1-yl)acetamide	
11	2-(3-nitro-1H-1,2,4-triazol-1-yl)-N-(4-(piperidin-1-yl)phenyl)acetamide	
12	2-([1,1'-biphenyl]-4-yl)-1-(3-nitro-1H-1,2,4-triazol-1-yl)propan-2-ol	

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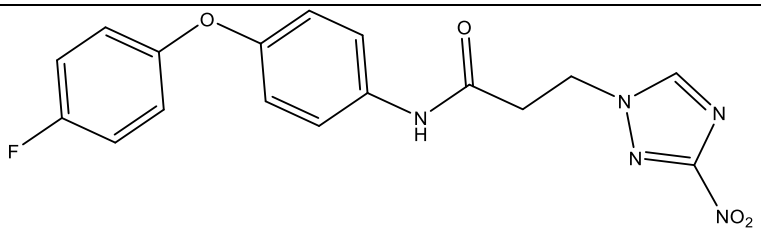
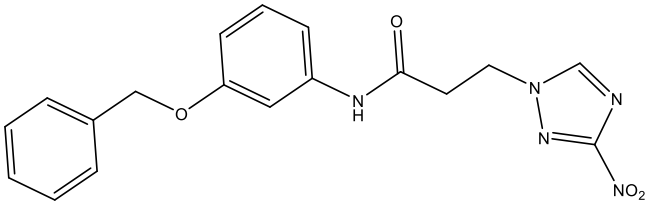
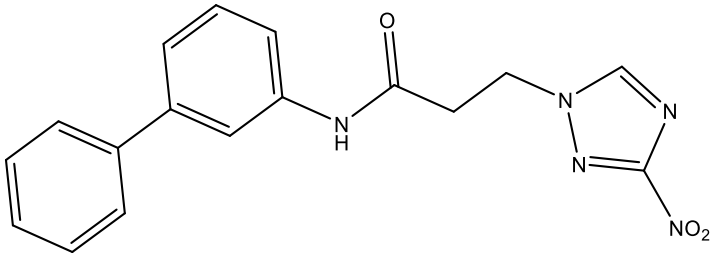
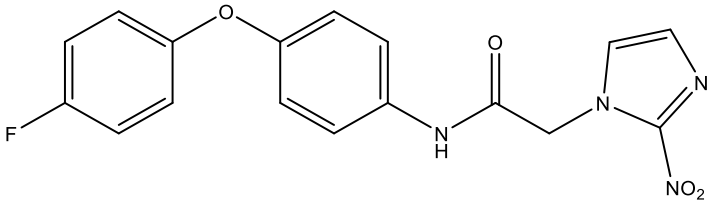
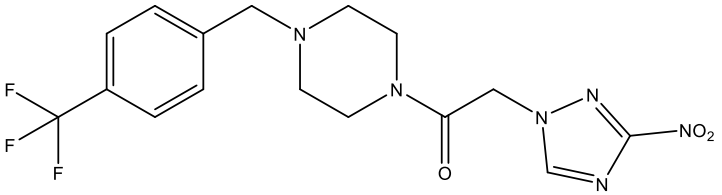
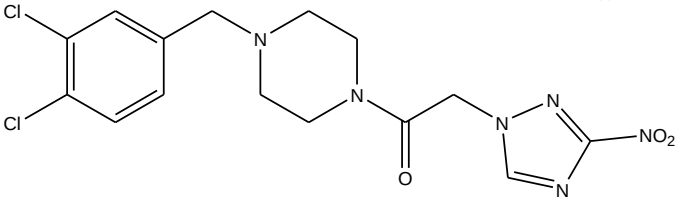
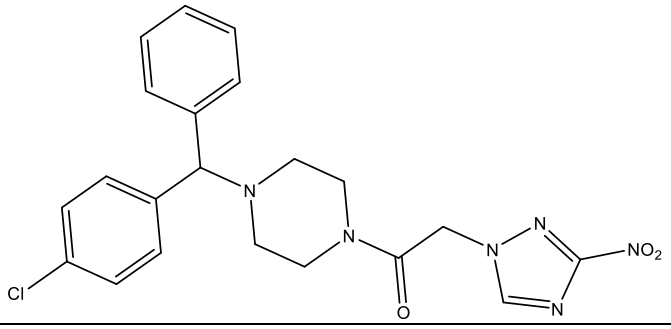
13	N-(4-(4-fluorophenoxy)phenyl)-3-(3-nitro-1H-1,2,4-triazol-1-yl)propanam – ide	
14	N-(3-(benzyloxy)phenyl)-3-(3-nitro-1H-1,2,4-triazol-1-yl)propanamidec	
15	N-([1,1'-biphenyl]-3-yl)-3-(3-nitro-1H-1,2,4-triazol-1-yl)propanamide	
16	N-(4-(4-fluorophenoxy)phenyl)-2-(2-nitro-1H-imidazol-1-yl)acetamide	
17	2-(3-nitro-1H-1,2,4-triazol-1-yl)-1-(4-(4-(trifluoromethyl)benzyl)piperazin-1-yl)ethan-1-one	
18	1-(4-(3,4-dichlorobenzyl)piperazin-1-yl)-2-(3-nitro-1H-1,2,4-triazol-1-yl)ethan-1-one	
19	1-(4-((4-chlorophenyl)(phenyl)methyl)piperazin-1-yl)-2-(3-nitro-1H-1,2,4-triazol-1-yl)ethan-1-one	

Results and Discussion

Molecular descriptors

The calculated descriptors obtained from the optimized compounds were highest occupied molecular orbital energy (E_{HOMO}), lowest unoccupied molecular orbital energy (E_{LUMO}), dipole moment (DM), molecular weight (MW), volume, Ovality, polarizability, log P, hydrogen bond donor (HBD), hydrogen bond acceptor (HBA) (Table 2). According to Oyebamiji *et al*., the role played by E_{HOMO} and E_{LUMO} in revealing essential facts about excitation properties of drug-like compounds cannot be overemphasized.[22] Higher E_{HOMO} value showed the compound with better ability to donate electron to neighboring compound and the better the capacity of drug-like compound to inhibit receptor; thus, 2-(3-nitro-1*H*-1,2,4-triazol-1-yl)-N-(4-(piperidin-1-

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Table 2: The calculated molecular descriptors for the studied compounds

	E_{HOMO} (eV)	E_{LUMO} (eV)	DM (Debye)	MW (amu)	OVA	POL	LOG P	HBD	HBA
1	-9.03	-0.86	6.12	407.88	1.63	69.64	1.69	1	9
2	-8.78	-1.29	3.52	406.89	1.64	70.75	1.37	1	7
3	-9.21	-1.02	8.10	331.36	1.55	64.17	0.59	1	9
4	-9.76	-0.89	6.73	374.43	1.63	68.01	2.31	1	9
5	-9.34	-1.49	9.09	364.77	1.54	64.36	1.30	1	10
6	-9.61	-1.61	8.90	366.31	1.55	64.11	0.36	0	8
7	-9.23	-1.07	6.47	373.76	1.58	66.65	-0.32	1	8
8	-9.46	-0.82	9.69	339.31	1.54	65.34	-0.18	1	8
9	-9.41	-1.07	6.00	337.34	1.57	66.26	1.30	1	7
10	-9.49	-1.09	6.85	321.30	1.53	64.49	0.63	1	7
11	-8.51	-1.01	6.73	330.35	1.55	65.61	0.23	1	8
12	-9.58	-0.76	9.59	324.34	1.52	65.36	2.16	1	6
13	-9.21	-0.94	5.79	371.33	1.59	67.41	-0.42	1	8
14	-9.28	-0.89	7.74	367.37	1.62	68.50	0.56	1	8
15	-9.32	-0.91	6.76	337.34	1.56	66.22	1.17	1	7
16	-8.99	-1.33	4.67	356.31	1.53	66.51	-0.51	1	7
17	-9.84	-1.02	6.69	398.34	1.60	68.12	-0.38	0	8
18	-9.35	-0.96	7.13	399.23	1.59	78.89	-1.26	0	8
19	-9.42	-0.94	6.30	440.89	1.63	73.28	-0.21	0	8

yl)phenyl)acetamide (compound **11**) with -8.51eV is expected to inhibit better than other studied compounds. More so, the ability of drug-like compound to receive electron from nearby compounds explains the role of E_{LUMO} in drug design; therefore, N-(4-(3,4-difluorophenyl)thiazol-2-yl)-2-(3-nitro-1H-1,2,4-triazol-1-yl)acetamide (Compound **6**) with -1.61eV is expected to inhibit better than other studied compounds.

Dipole moment is a measure of the net molecular polarity played a crucial role in non-bonding interactions between ligand and receptor.[23] As reported by Oyewole *et al*.,[24] unpredictable properties of drug-like molecules may occur as a result of very large dipole moment value; thus, all the studied compounds is expected to have strong non-bonded connections *Mycobacterium tuberculosis* H37Rv.

More so, the calculated lipophilicity (Log P) shows the dissolving strength of ligand in lipophilic media. Also, increasing and decreasing value of calculated lipophilicity (Log P) defines the level of penetrability of phamacophore in several biological membranes.[25] Hence, difficulties may be encountered in oral absorption of any developed drug with Log P value of greater than 5; thus, the calculated Log P of the all the studied compounds showed the efficiency of studied compounds.

Furthermore, the studied compounds were subjected to Lipinski rule of five (MW ≤ 500 amu, LogP ≤ 5, HDB≤ 5 and HBA ≤ 10) in order to investigate the drug-likeness of the molecules under study. It was observed that all the studied compounds have the ability to act as drug (Table 2).

QSAR analysis

The studied compounds were divided in to two sets (Training set (60%) and Test set (40%)) via Kennard stone algorithm approach via Dataset Division GUI 1.2 software.[26] The training set comprise of twelve (12) compounds in which the selected descriptors from these compounds were used to develop efficient QSAR model and the test set which comprise of seven (7) compounds were used to ascertain the reliability of the develop model. As shown in Table 3, the predicted IC_{50} were observed to be correlated to the experimental IC_{50} for the training set.

Table 3: Observed and Predicted IC_{50} for the studied compounds

	Experimental IC_{50}	Predicted IC_{50}
1	4.0	1.1
2	175.0	172.1
3	107.0	106.6
4*	4.9	0.9
5*	34.2	-56.0
6*	27.0	20.6
7*	51.0	67.3
8*	65.0	102.5
9	30.0	23.3
10	27.0	30.3
11*	29.0	195.5
12	55.0	61.3
13*	22.0	153.8
14	1.7	13.2
15*	3.6	135.7
16	44.0	27.2
17	25.0	35.9
18	5.9	27.4
19	38.0	19.9

**denotes Test set*

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More so, the developed QSAR model reported in equation 3 was used to predict correlation coefficient (IC_{50}) for the test set and the predicted IC_{50} were reported in Table 3. The predicted IC_{50} shown in Table 3 showed that the developed QSAR model was predictive and efficient, and this was also confirmed through calculated correlation coefficient (R^2) as well as calculated adjusted correlation coefficient (Adj R^2). As reported by Adegoke *et al.*, 2020, any developed QSAR model with $R^2 \geq 0.5$, Adj $R^2 \geq 0.6$ and $CVR^2 \geq 0.5$ is considered to be predictive; thus, as shown in Table 4, the developed QSAR model is proved to be predictive and efficient in predicting biological activity of the studied compounds.[27]

Docking and scoring

In this work, the employed docking method was validated by re-docking the native ligand into the active site of Mtb H37Rv (PDB ID: **2we9**) in order to observe the resemblance between the re-docked ligand with the best conformation to the posture of the native molecule (Figure 1). Therefore, the observed similarity and the root mean square deviation (RMSD) between the re-docked native molecule and the native ligand were nearer to 1; hence, this proved the dependability of the molecular docking method used. The calculated binding affinity for nitro(triazole/imidazole)-based compounds were -6.3 kcal/mol, -6.7 kcal/mol, -7.1 kcal/mol, -6.2 kcal/mol, -7.5 kcal/mol, -7.0 kcal/mol, -7.2 kcal/mol, -7.4 kcal/mol, -6.7 kcal/mol, -8.0 kcal/mol, -6.6 kcal/mol, -7.3 kcal/mol, -7.3 kcal/mol, -7.3 kcal/mol, -7.5 kcal/mol, -6.5 kcal/mol, -7.2 kcal/mol, -7.9 kcal/mol, -6.0 kcal/mol for compound **1- 19**. As shown in Table 4, it was observed that compound **10** with -8.0 kcal/mol possess the highest tendency to inhibit Mtb H37Rv (PDB ID: **2we9**) than other studied compounds (Figure 2). Also, series of residues were observed to be involved in the interaction between nitro(triazole/imidazole)-based compounds and Mtb H37Rv (PDB ID: **2we9**) and were reported in Table 4. As shown in Table 4, all the studied compounds were observed to be more potent than the standard compound used in this work. Also, the correlation between the observed IC_{50}, predicted IC_{50} and binding affinity were shown in Figure 3.

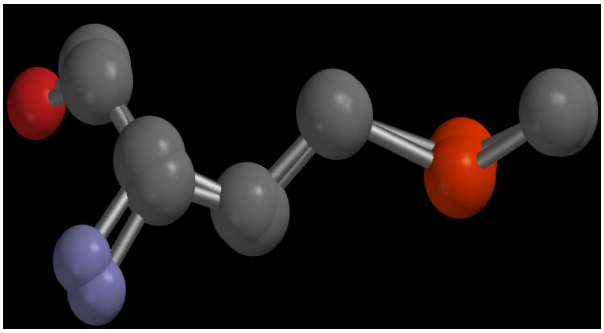

Figure 1: Overlay of native drug-like compounds over re-docked drug compound

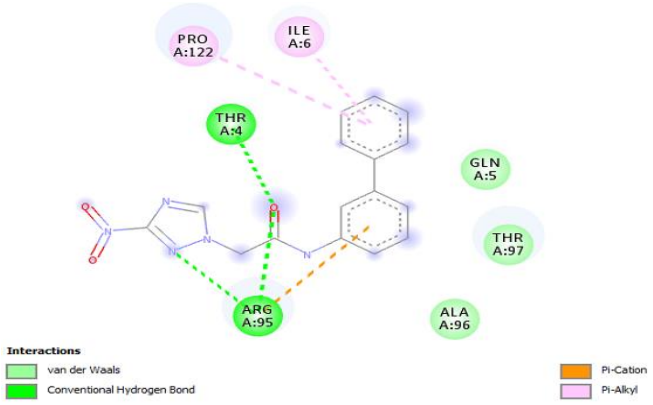

Figure 2: Binding interactions between compound 10 with receptor

Table 4: Interactions between Ligands and **2we9** receptor

	Binding Affinity (kcal/mol)	Residues involved in the interactions with 2we9
1	-6.3	(i) VAL-109 (ii) PRO-111, LIG: O (iii) ASP-30 (iv) THR-31 (v) ALA-36, LIG: N and O (vi) ASP-39 (vii) ARG-29 (viii) GLN-43 (ix) VAL-40 (x) PRO-107 (xi) ALA-110 (xii) VAL-197 (xiii) GLN-108
2	-6.7	(i) GLN-108 (ii) VAL-195 (iii) ARG-29, LIG: O (iv)TYR-28 (v) PRO-111 (vi) THR-31 (vii) ASP-30 (viii) ASP-39 (ix) GLN-43 (x) ALA-36(xi) VAL-40 (xii) PRO-107 (xiii) VAL-109 (xiv) ALA-110
3	-7.1	(i) THR-31 (ii) ASP-39 (iii)) ARG-29, LIG: O (iv) PRO-111 (v)VAL-109 (vi) ALA-110 (vii) VAL-195 (viii) GLN-108 (ix) PRO-107, LIG: H(x) TYR-28 (xi) VAL-40(xii) ALA-36 (xiii) ASP-30
4	-6.2	(i) THR-97 (ii) ARG-95, LIG: N and O (iii) THR-31, LIG: O (iv) GLN-5 (v) ALA-96)
5	-7.5	(i) VAL-100(ii)ILE-118 (iii)TRP-140 (iv)PRO-122 (v)ILE-6 (vi)THR-97 (vii)GLN-5, LIG: N (viii) ARG-95, LIG: O (ix)THR-4, LIG: N
6	-7.0	(i) ALA-96, LIG: F(ii) THR-97(iii) GLN-5, LIG: F (iv)ARG-95, LIG: F and N (v)THR-4
7	-7.2	(i) THR-113(ii)VAL-174 (iii)TYR-131 (iv)ALA-110 (v) VAL-109 (vi)GLN-108 (vii) VAL-195 (viii) GLN108 (ix) GLN-43(x) TRY-28 (ix)VAL-40 (xi)PRO -107(xii) ASP-39 (xiii) ALA-36(xiii) THR-31(xiv) ASP-30 (xv) ASP-175(xvi) PRO-111(xvii) ARG-29, LIG: N(xviii)
8	-7.4	(i) TYR-131 (ii)VAL-174 (iii) THR-113 (iv) ASP-175(v) ALA-110(vi)TYR-28 (vii) PRO-107 (viii)GLN-43 (ix)ASP-39 (x) ALA-36 (xi) PRO-111 (xii) VAL-40 (xiii) ARG-29, LIG: O (xiv)VAL-195(xv)GLN108 (xvi)VAL-109
9	-6.7	(i)ARG-143 (ii)THR-97 (iii)ALA-96 (iv)GLN-5 (v)THR-4 (vi) ARG-95, LIG: O (vii) PRO-94

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10	-8.0	(i)PRO-122 (ii)THR-4, LIG: O (iii) ILE-6(iv) GLN-5 (v)THR-97 (vi)ALA-96 (vii)ARG-95, LIG: O and N
11	-6.6	(i) THR-(ii) ARG-29 (iii)ASP-39 (iv) ALA-36 (v) PRO-111 (vi) ALA-110 (vii) VAL-195 (viii) GLN-108(ix)VAL-109 (x) PRO-107, LIG: H (xi) TYR-28 (xii) VAL-40 (xiii)GLN-43 (xiv) ASP-30
12	-7.3	(i) THR-97(ii) GLN-5 (iii) ALA-96 (iv)TRP-140 (v) ILE-118 (vi) 1LE-6 (vii) PRO-122(viii)THR-4, LIG: O and N (ix) ARG-95, LIG: O
13	-7.3	(i)ILE-6 (ii) PRO-122 (iii) THR-4 (iv) THR-97 (v) ARG-95, LIG: N and O (vi) ALA-96 (vii) GLN-5, LIG: O (viii) ILE-118 (ix) ASP-119
14	-7.3	(i)ILE-118 (ii)PRO-122 (iii) THR-97 (iv) ALA-96 (v)ARG-95, LIG: H and O (vi) THR-4, LIG: O (vii) GLN-5, LIG: O (viii) ILE-6
15	-7.5	(i)VAL-174 (ii)THR-113 (iii) TYR-131 (iv)PRO-179 (v) VAL-109 (vi)GLN-108 (vii)VAL-195 (viii)PRO-107 (ix)PRO-111 (x)VAL-40 (xi)ASP-39 (xii)ARG-29, LIG: N (xiii)ALA-36 (xiv)THR-31 (xv)GLN-43 (xvi) ALA-110
16	-6.5	(i) ARG-29, LIG: O (ii) SER-194 (iii)GLN-108 (iv)VAL-195 (v)VAL-109 (vi) ALA-110 (vii)PRO-107 (viii)VAL-40 (ix) PRO-111 (x) ASP-39(xi) GLN-43
17	-7.2	(i)ILE-6 (ii)TRP-140 (iii) THR-9, LIG: O and N (iv)GLY-98 (v) PRO-94, LIG: F (vi)ARG-143 (vii)ARG-95, LIG: F (viii)ALA-96 (ix) THR-4 (x) GLN-5 (xi)PRO-122
18	-7.9	(i) ASP-39 (ii) THR-31 (iii) ARG-29, LIG: O (iv) TYR-28, LIG: O (v) GLN-108 (vi)VAL-109 (vii)TYR-131 (viii)ALA-110 (ix) VAL-174 (x)THR-113 (xi)ASP-175 (xii)PRO-107 (xiii)VAL-195 (xiv)VAL-40 (xv) ALA-36 (xvi) GLN-43
19	-6.0	(i) THR-69 (ii) GLY-68 (iii) PHE-46(iv)ASP-47 (v) ALA-44 (vi) ILE-118 (vii)ILE-6 (viii)GLY-45, LIG: O (ix)ARG-115, LIG: O (x) GLN-43(xi) ARG-42 (xii) LEU-49)
Isoniazid	-5.6	

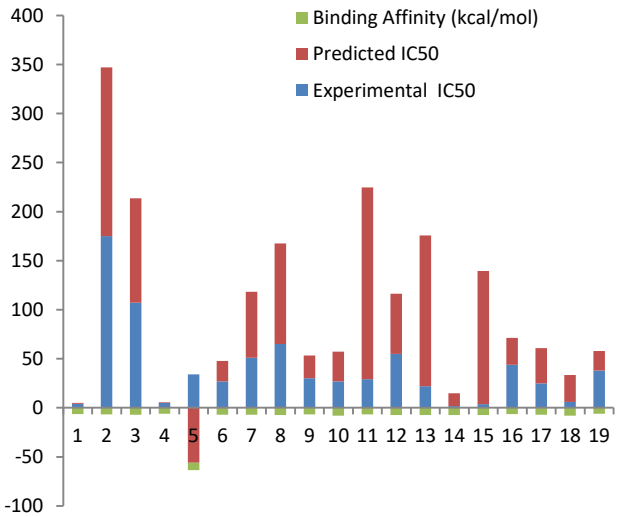

Figure 3: Correlation between observed IC_{50}, predicted IC_{50} and binding affinity

Conclusion

Tuberculosis (TB) is still one of the deadly diseases among human being and despite several efforts put in place by many scientists to curb this disease; its degree of action among humans keeps increasing. In this work, it was observed that the obtained descriptors perfectly described the anti- *Mycobacterium tuberculosis* activity of the studied nitro(triazole/imidazole)-based compounds and the developed QSAR model proved to be reliable by accurately predicting the experimental IC_{50}. Nonbonding interaction between nitro(triazole/imidazole)-based compounds and *Mycobacterium tuberculosis* H37Rv (PDB ID: 2we9) showed that compound **10** with -8.0 kcal/mol have higher tendency to inhibit *Mycobacterium tuberculosis* H37Rv (PDB ID: 2we9) than other studied compounds.

Conflict of Interest

The authors declare no conflict of interest.

Author's Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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