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Antimycobacterial potential of novel hydrazone derivatives

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Molecular docking of 1 to 51 compounds has been performed in Small-Molecule Drug Discovery Suite of Schrödinger. Fifty one compounds have been targeted on 2NSD and 2X22 involved in tuberculosis activity. Aryloxy moiety on refluxing with chloroethyl acetate in the presence of potassium carbonate and acetone has yielded ethyl aryloxy acetate (A), which have been reacted with hydrazine hydrate to produce aryloxyacetyl hydrazine (B), which on treatment with aromatic aldehydes or ketones yield hydrazones (C). The novel series of compounds have been elucidated on the basis of spectral studies and screened for antimycobacterial activity. The compounds are significantly sensitive at concentration 50 and 100 µg/mL. Compound 11 shows sensitivity at 25 µg/mL. The antibacterial activity is strongly connected with the position of the substituent on aromatic aldehyde or ketones in relation to the hydrazide skeleton.

Keyword: Hydrazone, molecular docking, antimycobacterial activity

In hydrazone, the nitrogen is attached to hydrogen; these Hydrazone are stable enough for isolation[1]. However in some cases, especially with simple R group, they rapidly decompose or polymerizes unless there is at least one aryl group on nitrogen or the carbon[2]. When there is an aryl group the compound are quite stable and these compound called as Schiff bases and the reaction is best way to prepare them. The reaction is straightforward and proceeds in high yield[3].

Tuberculosis (TB) is a deadly disease caused by mycobacterium of the "tuberculosis complex", including primarily *Mycobacterium tuberculosis* as well as *Mycobacterium bovis* and *Mycobacterium africanum*[4].

Drug discovery and development could be a complicated, time intense and a rich method[5]. It becomes still more expensive when the safety, efficacy and other issues are raised. In silicoapproach of drug design, computational approach plays a significant role in all stages of drug development from the initial lead design to final stage clinical development[6].

M. tuberculosis contains mycolic acids that are unusually long chain α-alkyl β-hydroxy fatty acids of 60–90 carbons[7]. The antitubercular (anti-TB) drugs such as isoniazid[8] and ethionamide[9] have shown to target the synthesis of these mycolic acids, which are the central constituents of mycobacterial cell wall.

The chemistry of these derivatives has been the fascinating field of investigation in medicinal chemistry, they have been found to exhibit enhanced biological profile. Hydrazone are known to exhibit wide variety of biological activities. They are used as antibacterial agent, anti-tubercular agents, analgesic, anti-inflammatory agent, antiviral agents, antifungal agent, muscle relaxants and antihistamines, *etc*[10-13].

The enzymatic acetylation of isoniazid by N-acetyltransferase (NAT) represents a major metabolic pathway for isoniazid in humans, so blocking acetylation *via* chemical modification of the hydrazine unit with a functional group, while preserving potent antimycobacterial action, has the potential to counterbalance the known side effects of INH, improve clinical outcomes and reduce the emergence of acquired isoniazid resistance in patients. Subsequently, numerous studies have pointed out the importance of developing novel hydrazones as promising anti-tubercular agents.

Materials and Methods

Molecular Docking

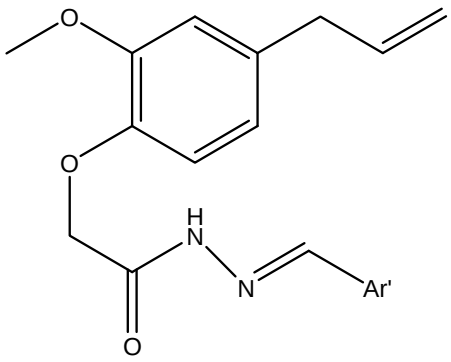
All fifty one compounds (Table I) were docked in Small-Molecule Drug Discovery Suite of Schrödinger. All these compounds were targeted on seven enzymes such as 2NSD and 2X22 involved in tuberculosis activity. The generated lower energy conformers of all ligands were docked into generated

grid of active site of enzymes by XP precision of docking inside Glide-v7.4 [14, 15].

Synthesis

The reactions were carried out in oven-dried glassware (120°C) under an atmospheric condition unless as indicated otherwise. Chemicals and related solvents were of Merck Chemicals Co and purchased from Gurudatta Chemical Distributor, Satara. Analytical thin layer chromatography (TLC) was performed on percolated plates and purifications were

Table I — List of compounds screening for molecular docking



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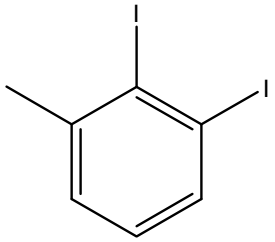
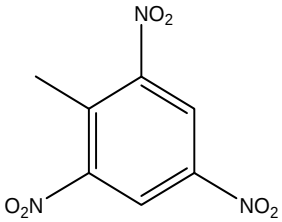
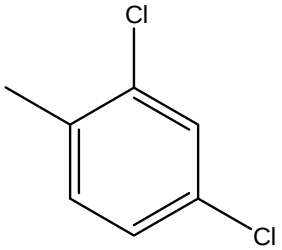
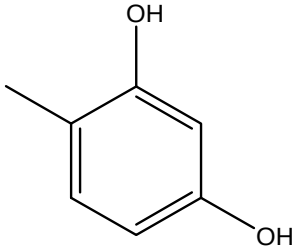
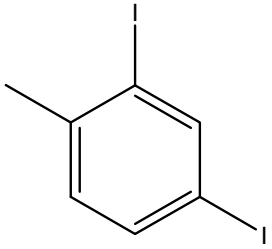
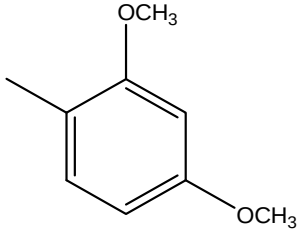
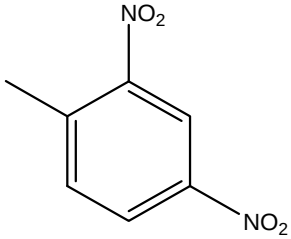
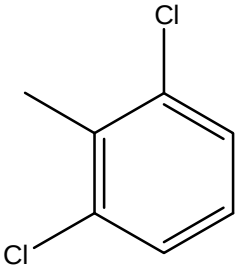
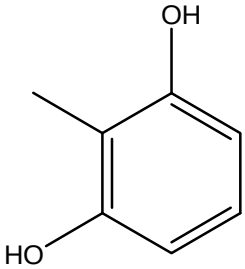
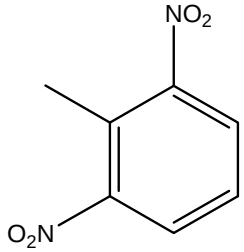
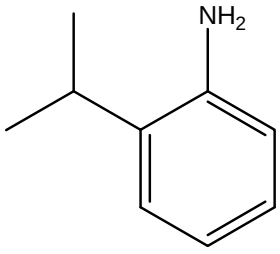
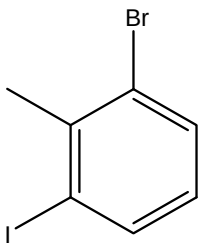
1		2		3	
4		5		6	
7		8		9	
10		11		12	

(*Contd.*)

Table I — List of compounds screening for molecular docking (Contd.)

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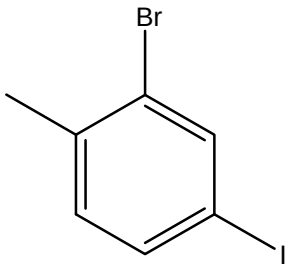
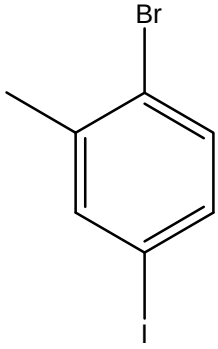
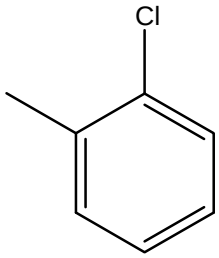
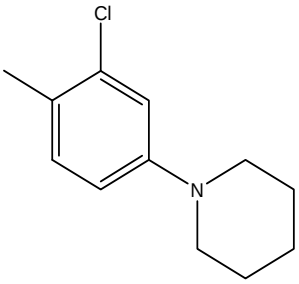
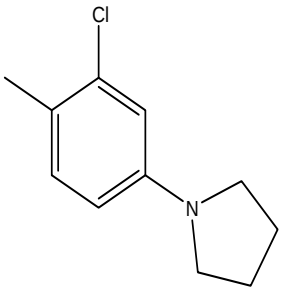
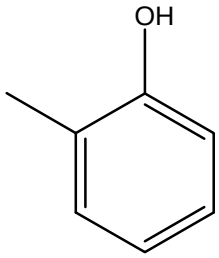
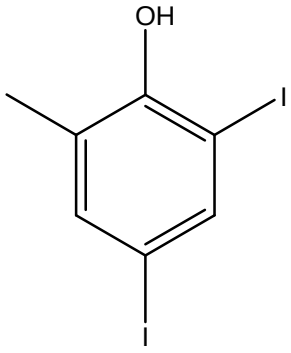
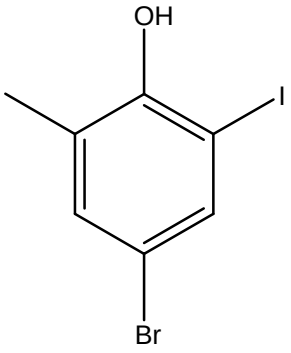
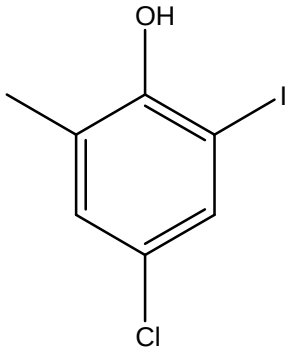
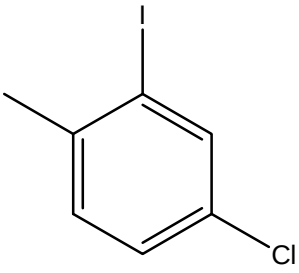
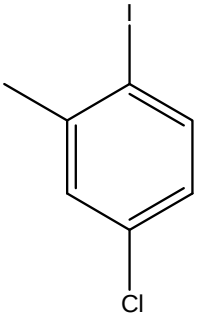
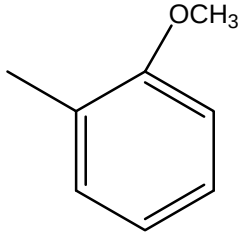
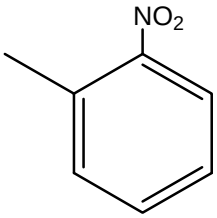
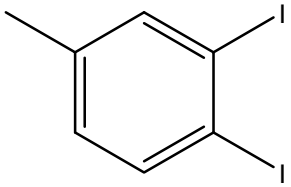
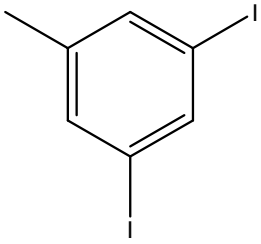
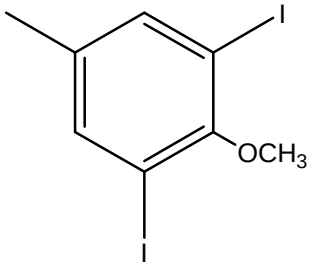
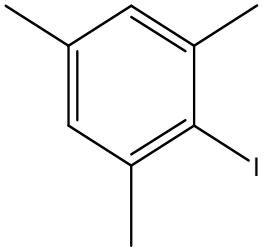
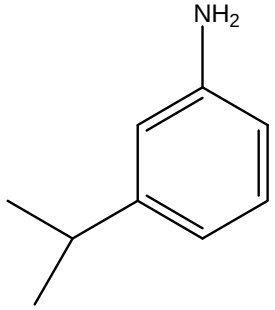
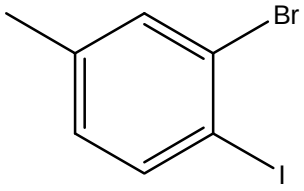
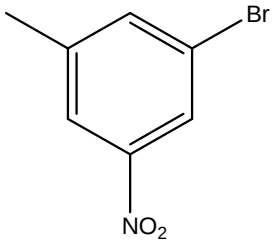
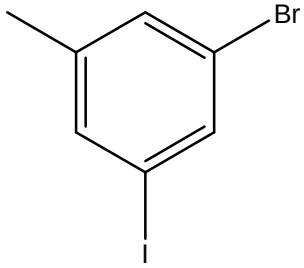
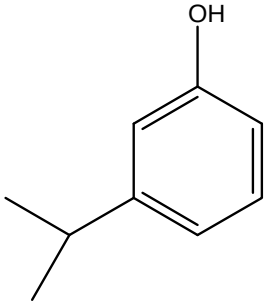
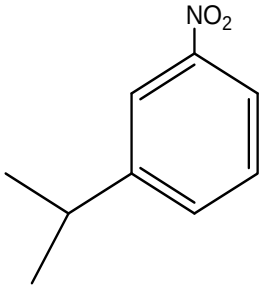
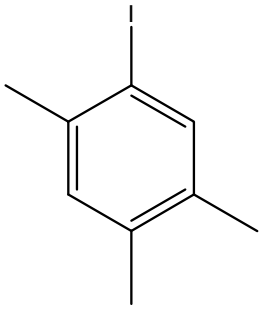
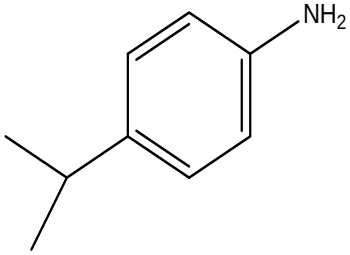
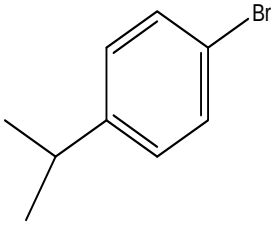
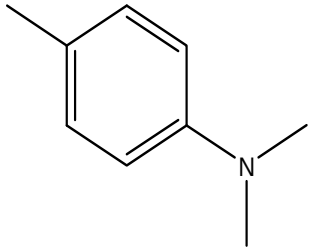
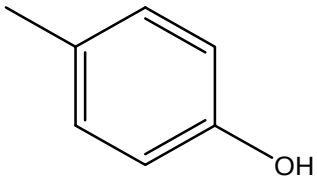
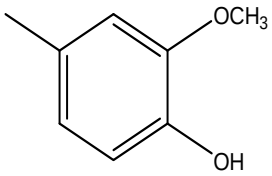
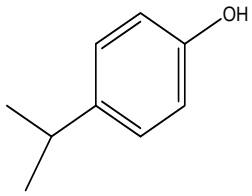
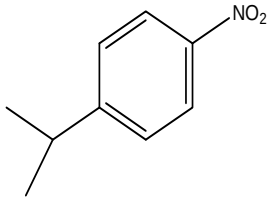
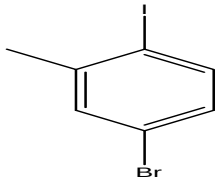
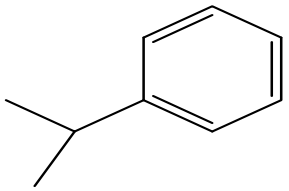
13		14		15	
16		17		18	
19		20		21	
22		23		24	
25		26		27	

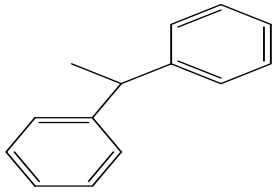
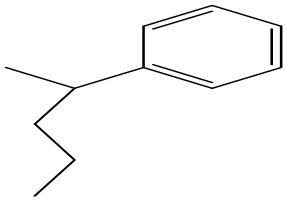
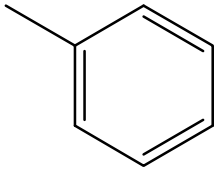
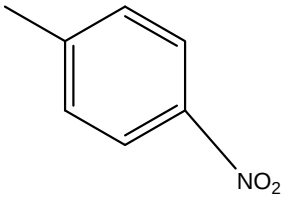
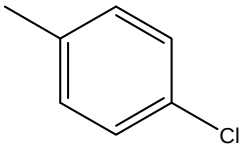
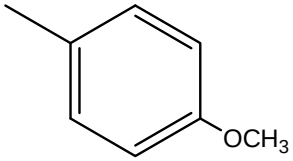
(*Contd.*)

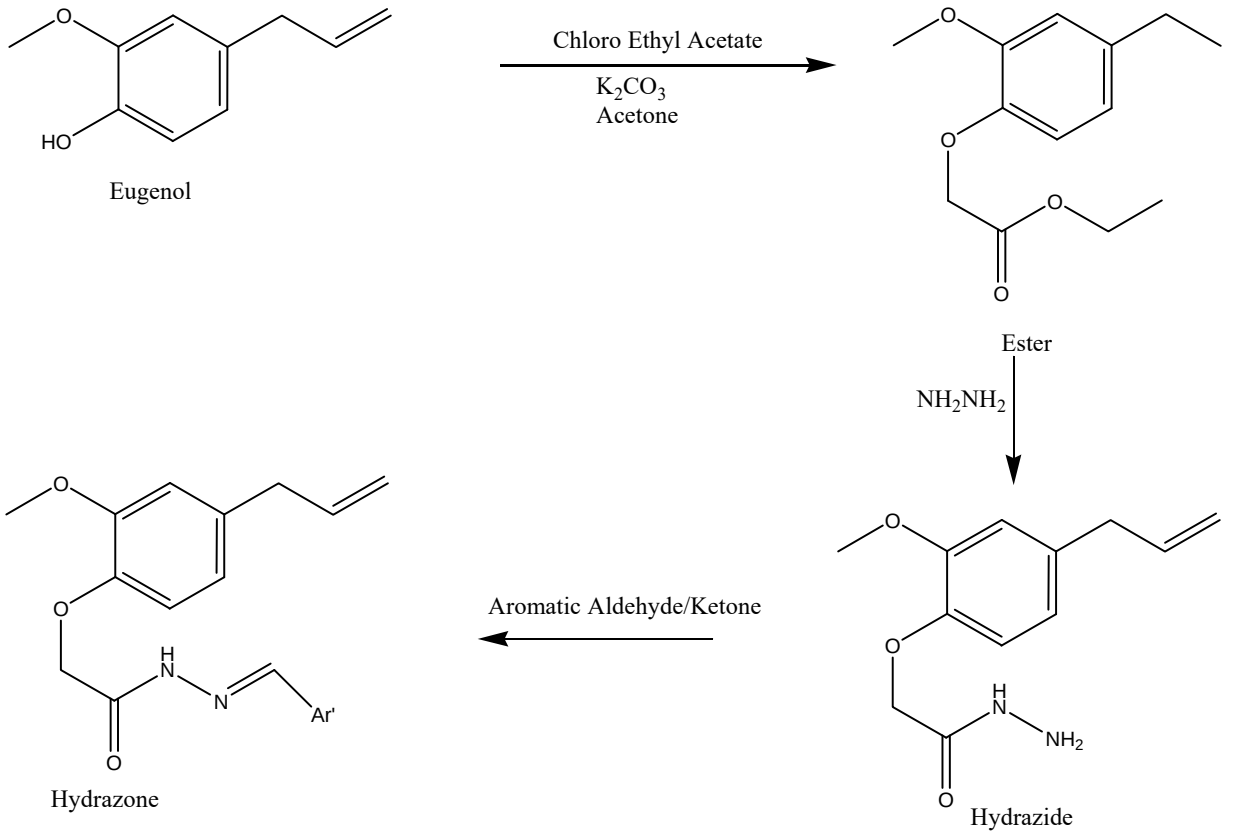
Table I — List of compounds screening for molecular docking (Contd.)

Compd	Ar'	Compd	Ar'	Compd	Ar'
28		29		30	
31		32		33	
34		35		36	
37		38		39	
40		41		42	
43		44		45	

(*Contd.*)

Table I — List of compounds screening for molecular docking (Contd.)

Compd	Ar'	Compd	Ar'	Compd	Ar'
46		47		48	
49		50		51	



Scheme I

done for all ten synthesized compound by column chromatography.

The physical data such as melting points were determined in open capillary tubes. IR spectra were recorded on Shimadzu, MIRacle-10, IRAffinity-1, H NMR spectra on Agilent, VNMRS 400 using $CDCl_3$ solvent and mass spectra on Agilent, 6103 quadrapole LCMS.

Ethyl aryloxy acetate (A): A mixture of eugenol (0.1 mol), ethyl chloro acetate (0.1 mol) and anhydrous potassium carbonate (0.15 mol) in dried acetone was refluxed for 12 h. Resultant mixture was distilled off and poured on to ice-cold water and stirred. Residue was extracted with ether and the extract was dried over anhydrous sodium sulphate and was purified under reduced pressure to yield compound A.

Ethylaryloxy acetyl hydrazine (B): A mixture of compound A (0.05 mol) and hydrazine hydrate (0.075 mol) in ethanol was refluxed for 4 h and after

distilling off the solvent the residue was recrystallized from methanol to yield compound B.

Hydrazone (C): A mixture of compound B (0.01 mol) and aromatic aldehyde (0.01 mol) or ketone was refluxed for 2h using acetic acid. Crystals formed were washed with ice-cold water, dried and recrystallized from methanol to yield compound (Scheme I)

Anti-tubercular activity

The synthesized compounds were evaluated for anti-tubercular activity against standard strain H37RV. The method used was microplateAlamar Blue assay (MABA). Being a non-toxic method, it has several advantages such as thermal stability of the reagent, and good correlation with BACTEC radiometric method. The final drug concentrations tested were 100 to 0.2 µg/mL. Plates were covered and sealed with parafilm and incubated at 37ºC for five days. After addition of Alamar Blue reagent and incubating for 24 hrs, the results were observed. A blue color in the well was interpreted as no bacterial growth, and pink color was scored as growth.

Results and Discussion

Molecular docking

The Insilco study of all fifty one compounds was performed in Small-Molecule Drug Discovery Suite of Schrödinger. The compounds 4, 5, 11, 18, 30, 34, 35, 37, 38, 42, 43, 44, 45, 46 and 47 having good docking score and predicted interaction with enzymes. The docking result of novel hydrazone demonstrated that the binding energies were in therange of -6.097 kcal/molto -10.393 kcal/mol, with the minimum binding energy of -10.393kcal/mol (Table II). The

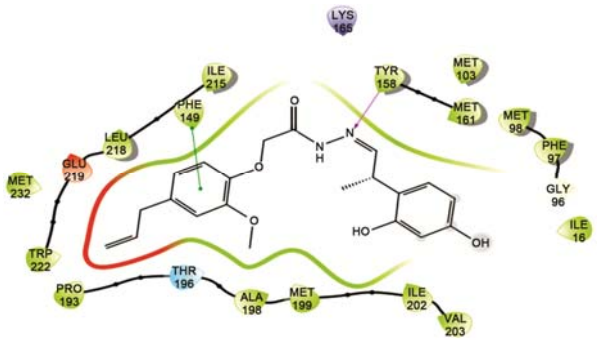


Figure 1 — Orientation of compound 4 with 2NSD enzyme

Table II — Docking score of compounds

Title	XP GScore	Title	XP GScore	Title	XP GScore	Title	XP GScore
	2NSD				2X22		
Isoniazide	-3.682			Isoniazide	-5.451		
1	-8.747	27	-7.37	1	-5.959	27	--
2	-6.847	28	-8.101	2	-4.009	28	-7.486
3	--	29	-6.097	3	-8.007	29	-2.37
4	-10.393	30	-9.021	4	-8.426	30	-7.769
5	-7.919	31	-7.804	5	-6.09	31	-6.092
6	-7.247	32	-6.384	6	--	32	-4.919
7	-7.179	33	-6.955	7	-6.67	33	-6.071
8	-8.387	34	-10.13	8	-5.981	34	-7.448
9	-8.525	35	-9.813	9	-7.538	35	--
10	-7.099	36	-6.538	10	--	36	-6.226
11	-9.5	37	-9.632	11	-7.726	37	-9.092
12	-6.942	38	-9.587	12	-4.965	38	-7.932
13	-8.921	39	-6.818	13	--	39	-5.289
14	-8.216	40	-6.921	14	-8.073	40	-7.674
15	-7.428	41	-6.98	15	-6.721	41	--
16	-7.815	42	-9.747	16	-2.124	42	-8.527
17	-7.266	43	-9.256	17	-6.04	43	-6.551
18	-7.632	44	-8.898	18	-6.625	44	-5.356
19	-7.681	45	-9.049	19	-5.954	45	-6.262
20	-7.466	46	-9.593	20	-4.423	46	-7.758
21	-6.799	47	-9.485	21	-7.037	47	-7.556
22	-7.005	48	-6.469	22	-5.353	48	-4.896
23	-7.867	49	-8.072	23	--	49	-5.725
24	-7.883	50	-6.338	24	-4.742	50	-6.666
25	-8.657	51	-6.175	25	-6.098	51	-4.293
26	-8.15			26	-4.74		

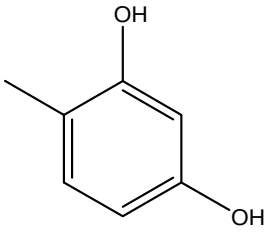
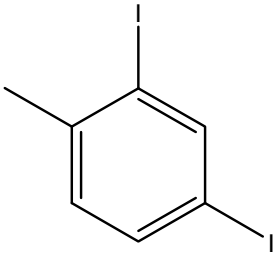
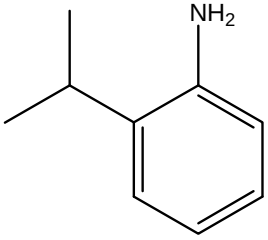
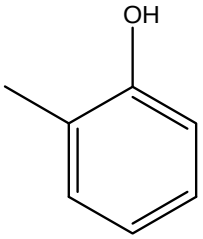
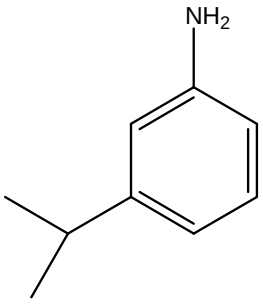
Note-: Sign ‘ -- ’ indicate compound does not show any Gscore.

molecules were then tested for structure analysis by the visualization tool. The entire compounds protein-ligand complex showed H - bond with the active site residue TYR 158 and PHE 149 (Figure 1).

Synthesis

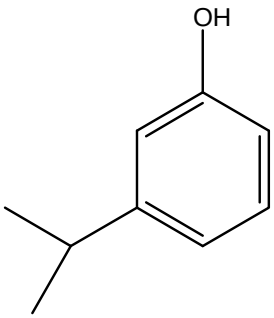
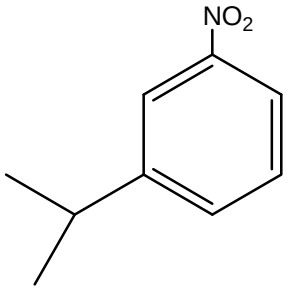
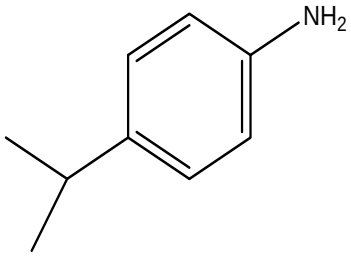
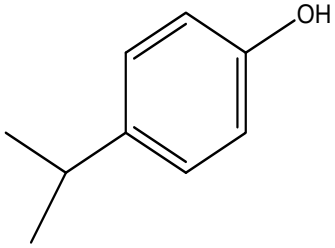
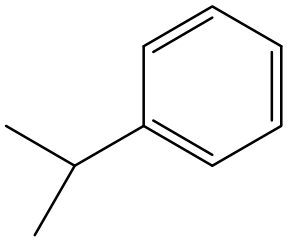
Ten hydrazone derivatives compound no. 4, 5, 11, 18, 30, 34, 35, 37, 42 and 45were selected on the basis of their in silico results. The derivatives were synthesis by condensation of arylhydrazide with various aromatic aldehyde or ketone using ethanol. Physical data of all synthesized compounds are shown in Table III and characterization data mentioned in Table IV.

Table III — Physical characteristics of synthesized compounds

Compd	Ar'	Mol. Formula	Mol. Weight	m.p. (°C)	Yield (%)
4		$C_{21}H_{24}N_2O_5$	384.19	220-221	73.08
5		$C_{19}H_{18}I_2N_2O_3$	576.18	235-236	62.00
11		$C_{21}H_{25}N_3O_3$	367.44	191-192	72.03
18		$C_{19}H_{20}N_2O_4$	340.37	229-230	75.00
30		$C_{21}H_{25}N_3O_3$	367.44	190-191	59.15

(*Contd.*)

Table III — Physical characteristics of synthesized compounds (*Cont*d.)

Compd	Ar'	Mol. Formula	Mol. Weight	m.p. (°C)	Yield (%)
34		$C_{21}H_{24}N_2O_4$	368.43	217-218	74.08
35		$C_{21}H_{23}N_3O_5$	397.42	235-236	60.08
37		$C_{21}H_{25}N_3O_3$	367.44	190-191	72.03
42		$C_{21}H_{24}N_2O_4$	368.43	219-220	76.90
45		$C_{21}H_{24}N_2O_3$	352.43	184-185	65.55

In the IR spectra, all derivatives of hydrazone had a characteristic band inthe region 1700-1650 cm^{-1} due to the C=O stretching vibration. The N-H stretchingvibration of the compounds found a band at 3400-3150 cm^{-1}. Thestretching bands for C=C and C=N groups were observed at 1610-1490 cm^{-1}. Ingeneral the IR stretching frequencies for –OH groups varied for the compounds 4, 18, 34 and 42 inthe region 3200-3650 cm^{-1}.In the 1H NMR spectra of all the compounds, the aromatic andaliphatic protons were observed at the expected ppm scale. Aromatic protons wereobserved at

about δ 6.15-7.78. Because hydrazoneshas some characteristic peak such as –OH, -N-H, -CH=N-N protons were observed as couples of peaks at δ 4.90-5.10, δ 7.10-6.90, δ 3.35-2.53 respectively.

Antimycobacterial activity

The compounds were evaluated *in vitro* for antimycobacterial activity against *M. tuberculosis* H37Rv using microplatealamar blue assay (MABA)

Table IV — IR, ^{1}H NMR and Mass data of synthesized compounds

Compd -C No.	IR, ^{1}H NMR and Mass data
4	IR: 3288, 2945, 1653 for CO of CONH, 1568, 1506, 1352, 1273, 1213, 1157, 840, 561 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.75 (t, CH_3), 6.40 (s, CH), 3.20 (d, CH_2), 6.51 (s, CH), 6.54 (s, CH), 4.21 (d, CH_2), 3.07 (d, CH_2), 8.1 (s, NH), 8.6 (s, N=CH), 3.0 (s, CH), 1.2 (t, CH_3), 6.78 (s, CH), 6.24 (s, CH), 6.15 (s, CH), 5.1 (s, OH), 4.9 (s, OH), 6.34 (s, H); MS: *m/z* 384.1
5	IR: 3660, 2943, 2806, 1674 for CO of CONH, 1595, 1544, 1273, 1041, 842, 758, 636, 574 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.73 (t, CH_3), 6.40 (s, CH), 3.20 (d, CH_2), 6.51 (s, CH), 6.54 (s, CH), 4.20 (d, CH_2), 3.07 (d, CH_2), 8.1 (s, NH), 8.60 (s, N=CH), 7.2 (s, CH), 7.2 (s, CH), 7.7 (s, CH), 8.15 (s, CH), 6.34 (s, H); MS: *m/z* 575.4
11	IR: 3460, 3361, 3221, 3041, 2993, 1658 for CO of CONH, 1625, 1589, 1490, 1448, 1317, 1226, 964, 869, 771, 678 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.72 (t, CH_3), 6.40 (s, CH), 3.25 (d, CH_2), 6.51 (s, CH), 6.54 (s, CH), 4.25 (d, CH_2), 3.07 (d, CH_2), 8.2 (s, NH), 8.8 (s, N=CH), 3.0 (s, CH), 6.87 (s, CH), 6.57 (s, CH), 6.83 (s, CH), 4.0 (d NH_2), 6.33 (s, H); MS: *m/z* 367.3
18	IR: 3431, 3211, 3045, 3016, 1653 for CO of CONH, 1573, 1504, 1467, 1292, 1251, 1157, 1056, 819, 682, 516 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.75 (t, CH_3), 6.40 (s, CH), 3.22 (d, CH_2), 6.51 (s, CH), 6.54 (s, CH), 4.18 (d, CH_2), 3.07 (d, CH_2), 8.1 (s, NH), 8.6 (s, N=CH), 7.4 (s, CH), 6.8 (s, CH), 7.1 (s, CH), 6.8 (s, CH), 5.0 (s, OH), 6.33 (s, H); MS: *m/z* 339.1
30	IR: 3460, 3361, 3221, 1658 for CO of CONH, 1625, 1589, 1448, 1317, 1282, 1226, 869, 771, 678, 576 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.71 (t, CH_3), 6.40 (s, CH), 3.25 (d, CH_2), 6.51 (s, CH), 6.54 (s, CH), 4.24 (d, CH_2), 3.07 (d, CH_2),8.1 (s,NH), 8.6 (s, N=CH), 3.0 (s, CH), 1.2 (t, CH_3) 6.48 (s, CH), 6.96 (s, CH), 6.28 (s, CH), 4.0 (d NH_2), 6.34 (s, H); MS: *m/z* 366.3
34	IR: 3419, 3223, 3089, 2900, 2806, 1651 for CO of CONH, 1570, 1502, 1371, 1055, 815, 675, 514 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.73 (t, CH_3), 6.40 (s, CH), 3.20 (d, CH_2), 6.51 (s, CH), 6.54 (s, CH), 4.24 (d, CH_2), 3.07 (d, CH_2) 8.1 (s,NH), 8.6 (s, N=CH), 3.0 (s, CH), 1.2 (t, CH_3), 6.68 (s, CH), 7.04 (s, CH), 6.55 (s, CH), 5.2 (s, OH), 6.33 (s, H); MS: *m/z* 367.2
35	IR: 3089, 1680 for CO of CONH, 1608, 1519, 1419, 1342, 1242, 1101, 968, 910, 665, 582, 534 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.75 (t, CH_3), 6.40 (s, CH), 3.20 (d, CH_2), 6.51 (s, CH), 6.54 (s, CH), 4.24 (d, CH_2), 3.07 (d, CH_2),8.1 (s,NH), 8.6 (s, N=CH), 3.0 (s, CH), 1.2 (t, CH_3), 7.51 (s, CH), 7.47 (s, CH), 8.01 (s, CH), 6.34 (s, H); MS: *m/z* 396.2
37	IR: 3288, 3251, 3180, 3109, 1660 for CO of CONH, 1589, 1523, 1475, 815, 732 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.74 (t, CH_3), 6.40 (s, CH), 3.22 (d, CH_2), 6.51 (s, CH), 6.54 (s, CH), 4.23 (d, CH_2), 3.07 (d, CH_2),8.1 (s,NH), 8.6 (s, N=CH), 3.0 (s, CH), 1.2 (t, CH_3) 6.87 (s, CH), 6.41 (s, CH), 6.41 (s, CH), 4.2 (d NH_2), 6.32 (s, H); MS: *m/z* 366.1
42	IR: 3288, 2945, 1653 for CO of CONH, 1568, 1506, 1352, 1273, 1213, 1157, 1066, 840, 665, 561 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.73 (t, CH_3), 6.40 (s, CH), 3.22 (d, CH_2), 6.51 (s, CH), 6.54 (s, CH), 4.24 (d, CH_2), 3.07 (d, CH_2),8.1 (s, NH), 8.6 (s, N=CH), 3.0 (s, CH), 1.2 (t, CH_3), 6.78 (s, CH), 6.95 (s, CH), 6.68 (s, CH), 5.0 (s, OH), 6.34 (s, H); MS: *m/z* 366.8
45	IR: 3192, 3018, 2837, 1680 for CO of CONH, 1556, 1278, 1145, 1055, 810, 673, 514 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.73 (t, CH_3), 6.40 (s, CH), 3.22 (d, CH_2), 6.51 (s, CH), 6.54 (s, CH), 4.23 (d, CH_2), 3.07 (d, CH_2), 8.1 (s,NH), 8.6 (s, N=CH), 3.0 (s, CH), 1.2 (t, CH_3), 7.12 (s, CH), 7.21 (s, CH), 7.08 (s, CH), 6.34 (s, H); MS: *m/z* 351.2

Table V — Antimycobacterial activity of compounds

Sr.No	Sample	100 µg/mL	50 µg/mL	25 µg/mL	12.5 µg/mL	6.25 µg/mL	3.12 µg/mL	1.6 µg/mL	0.8 µg/mL
1	4	S	S	R	R	R	R	R	R
2	5	S	S	R	R	R	R	R	R
3	11	S	S	S	R	R	R	R	R
4	18	S	S	R	R	R	R	R	R
5	30	S	R	R	R	R	R	R	R
6	34	S	S	R	R	R	R	R	R
7	35	S	S	R	R	R	R	R	R
8	37	S	S	R	R	R	R	R	R
9	42	S	S	R	R	R	R	R	R
10	45	S	S	R	R	R	R	R	R
11	Isoniazide	S	S	S	S	R	R	R	R

NOTE: S - Sensitive R- Resistant

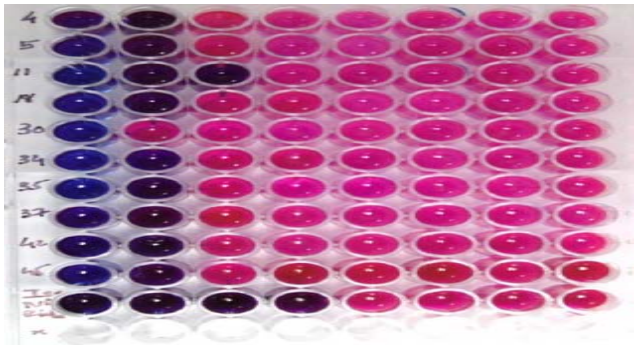


Figure 2 — Microplate Alamar Blue assay (MABA) colour change

method, with Isoniazide as the reference standard. The results expressed in minimum inhibitory concentration (MIC) are listed in Table V and the colour change observed during assay method is shown in Figure 2. The obtained results indicate the biological potential and varying activity depending on the type of substituent on hydrazidenucleus. The most promising seems to be compound no. 11 which show the sensitivity towards bacteria at 25 μg/mL level.

Conclusions

Several new hydrazone derivatives bearing aromatic aldehyde or ketone by there action of aryloxyhydrazide with appropriate aldehyde or ketone or substitutes derivatives of both. The structures of obtained compounds were confirmed by spectroscopic methods. All newly obtained hydrazone derivatives were tested *in vitro* against Mycobacterium strains: M. H37Rv. The antibacterial activity is strongly connected with the position of the substituent on aromatic aldehyde or ketones in relation to the hydrazide skeleton. All synthesized compounds found to be most active against *Mycobacterium tuberculosis*.

The molecular docking studies investigating hydrazone derivatives using the enzyme 2NSD and 2X22 as their potential biological target indicated that the amino, azide, hydroxyl and phenyl nucleus of hydrazone derivatives spacer play an important role in interactions with the active site such as TYR 158, ILE 215, GLU 219, PHE 97 and PHE 149 as the most active amino acid residues.

References

1 J March J, *Advanced Organic Chemistry*, 4th edn (John Willey and Sons, New York), pp.896-897 (1992).

2 Fuloria N K, Shahriar V S & Ali M, *Asian J Chem*, 20 (2008) 4891.

3 Fuloria N K, Shahriar V S & Ali M, *Asian J Chem*, 20 (2008) 6457.

4 Sensi P & Grass I G G, *Burger's Medicinal Chemistry and Drug Discovery*, Vol 2, 5th edn (John Wiley and Sons, New York, NY) pp.575-635 (1996).

5 Pieczonka A M, Aleksandra S, Beata S, Grzegorz M & Paweł S, *Eur J Med Chem*, 64 (2013) 389.

6 Abdel-Wahab F B, Awad A E G & Badria A F, *Eur J Med Chem*,46 (2011) 1505.

7 Takayama K, Wang C & Besra G S, *Clin Microbiol Rev*, 18 (2005) 81.

8 Takayama K, Wang L & David H L, *Antimicrob Agents Chemother*, 2 (1972) 29.

9 Quemard A, Laneelle G & Lacave C, *Antimicrob Agents Chemother*, 36 (1992) 1316.

10 Yatcheria S, Islam A, Dussa N & Bollikolla H, *Indian J Chem*, 54B (2015) 1162.

11 Saidugari S, Rao L, Vidya K, Ram B & Balram B, *Indian J Chem*, 56B (2017) 177.

12 Raja A S, Agarwal A K, Mahajan N, Pandeya S N & Ananthan A, *Indian J Chem*, 49 (2010) 1384.

13 Zheng L W, Wu L L, Zhao B X, Dong W L, Miao J Y, *Bioorg Med Chem*, 17 (2009) 1957.

14 Joshi S D, Dixit S R, Gadag S, Kulkarni V H & Aminabhavi T M, *Res Reports Med Chem*, 6 (2016) 1.

15 Rohane S H & Makwana A G, *Indian J Chem*, 58B (2019) 387.