Electronic Supplementary Information

A combination of docking and cheminformatics approaches for the identification of inhibitors against 4′ Phosphopantetheinyl transferase of *Mycobacterium tuberculosis*

Akshay Rohilla[1], Garima Khare[1*] and Anil K. Tyagi[1, 2*]

[1]Department of Biochemistry, University of Delhi South Campus, Benito Juarez Road, New Delhi 110021, India

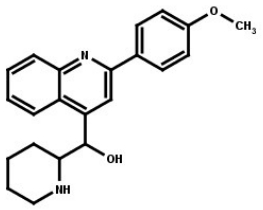
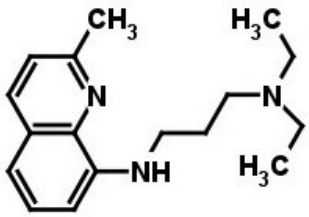
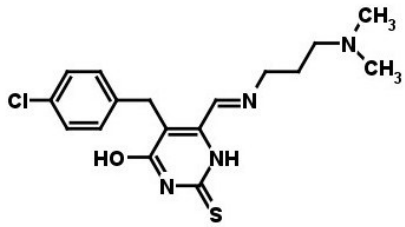
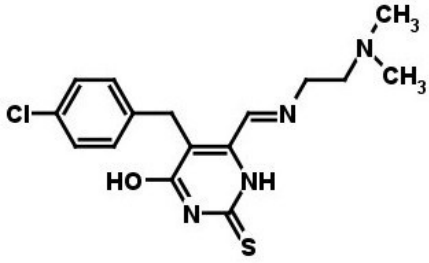
[2]Vice Chancellor, Guru Gobind Singh Indraprastha University, Sector 16-C, Dwarka, New Delhi 110078, India

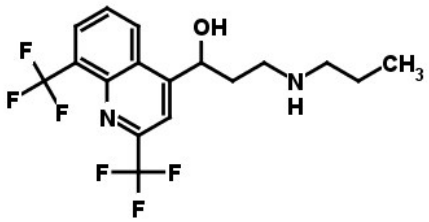
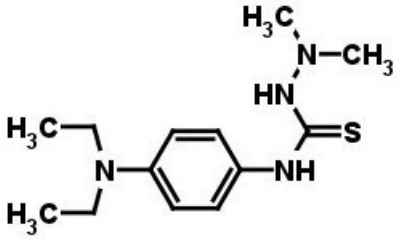
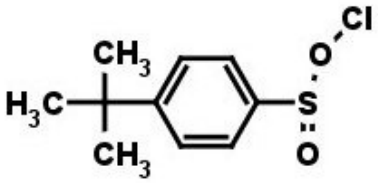
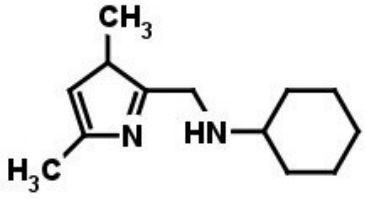
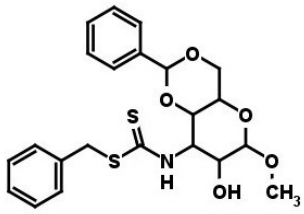
*Corresponding authors:

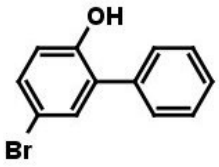
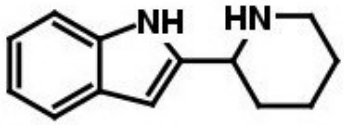
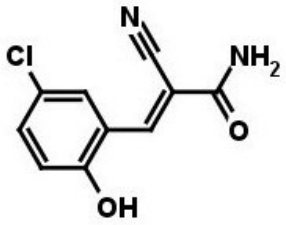
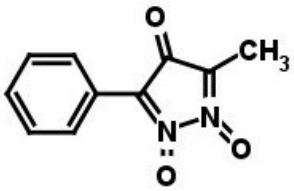
Prof. Anil K. Tyagi: Department of Biochemistry, University of Delhi South Campus, Benito Juarez Road, New Delhi-110021, India. Email: aniltyagi@south.du.ac.in, Tel: 91-11-24110970, Fax: 91-11-24115270

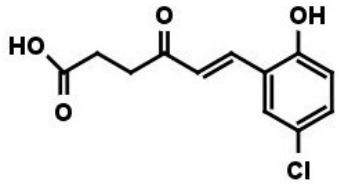
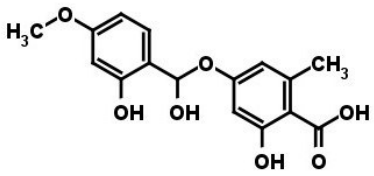
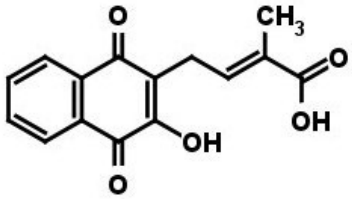
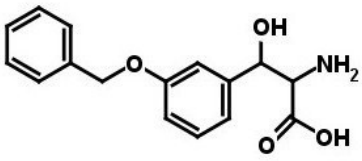
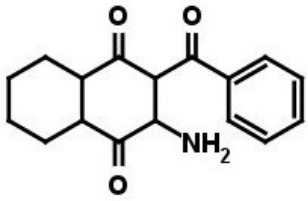
Dr. Garima Khare: Department of Biochemistry, University of Delhi South Campus, Benito Juarez Road, New Delhi-110021, India. Email: garima1822@yahoo.co.in, Tel: 91-11-24115209, Fax: 91-11-24115270

Table 1. Details of the molecules belonging to P-series that exhibited inhibition more than 20% against the PptT activity including 2-Dimensional structures, Docking scores and IC_{50} values.

S. No.	P-series	NCI ID	2-D Structure	Docking score	Docking Site	IC_{50} (µg/ml)
1	P-4	23925	 [2-(4-methoxyphenyl)quinolin-4-yl]-piperidin-2-yl methanol	-6.23	Autodock Site 1 (AS1)	68.2±3.98
2	P-52	53979	 N,N – diethyl –N`-(2-methyl quinolin-8-yl)propane-1, 3-diamine	8.21	Schrodinger Site 1 (S1)	2.27±1.38
3	P-61	153785	 5-4-chlorobenzyl)-6-[-{[3-(dimethylamino) propyl]imino}methyl]-2-thioxo-2,3-dihydropyrimidin-4(1H)-one	-7.61	Schrodinger Site 1 (S1)	10.13±1.47
4	P-62	153786	 5-4-chlorobenzyl)-6-[-{[2-(dimethylamino)ethyl]imino}methyl]-2-thioxo-2,3-dihydropyrimidin-4(1H)-one	-8.52	Schrodinger Site 1 (S1)	5.84±1.53

5	P-70	305817	 **1-[2, 8-bis (trifluoromethyl)quinolin-4-yl]-3-(propylamino)propan-1-ol**	-7.76	Schrodinger Site 1 (S1)	7.9±1.4
6	P-81	659178	 **N-[4-(diethylamino) phenyl]-2,2-dimethylhydrazinecarbothioamide**	-7.21	Schrodinger Site 1 (S1)	6.6±1.32
7	P-86	8544	 **1-tert-butyl-4-[(chlorooxy) sulfinyl] benzene**	-8.86	Autodock Site 2 (AS2)	2.66±1.1
8	P-94	47908	 **N-[(3, 5-dimethyl-1H-pyrrol-2-yl) methyl] cyclohexanamine**	-7.37	Autodock Site 2 (AS2)	22±1.83
9	P-95	48602	 **Methyl 4, 6-O-benzylidene-3-{[(benzylsulfanyl) carbonothioyl]amino}-3-deoxyhexopyranoside**	-8.35	Autodock Site 2 (AS2)	8.74±1.25

10	P-102	95701	 **5-bromobiphenyl-2-ol**	-8.07	Autodock Site 2 (AS2)	43.1±1.41
11	P-103	112665	 **2-(piperidin-2-yl)-1H-indole**	-8.03	Autodock Site 2 (AS2)	26±1.34
12	P-110	138367	 **2-(3, 5-dichloro-2-hydroxybenzylidene) hydrazinecarboxiimidamide**	-9.07	Autodock Site 2 (AS2)	8.55±2.16
13	P-114	201529	 **3-(5-chloro-2-hydroxyphenyl)-2-cyanoprop-2-enamide**	-8.63	Autodock Site 2 (AS2)	18.85±1.62
14	P-116	208696	 **3-methyl-5-phenyl-4H-pyrazol-4-one 1, 2-dioxide**	-7.9	Autodock Site 2 (AS2)	12.8±1.44

15	P-137	80978	 **6-(5-chloro-2-hydroxyphenyl)-4-oxohex-5-enoic acid**	-12.38	Schrodinger Site 2 (S2)	1.22±1.38
16	138	81164	 **Evernic acid**	-6.9	Schrodinger Site 2 (S2)	18.3±2.4
17	147	114808	 **4-(3-hydroxy-1, 4 –dioxo-1, 4-dihydronaphthalen-2-yl)-2-methyl but-2-enoic acid**	-9.6	Schrodinger Site 2 (S2)	1.42±1.9
18	177	18762	 **2-amino-3-[3-(benzyloxy) phenyl]-3-hydroxy propanoic acid**	-8.78	Autodock Site 3 (AS3)	3.6±1.45
19	P-183	52238	 **2-amino-3-(phenyl carbonyl) octahydronaphthalene-1, 4-dione**	-9.19	Autodock Site 3 (AS3)	1.172±1.33

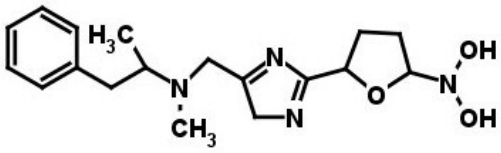
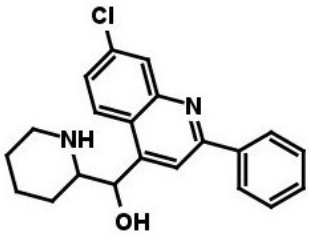
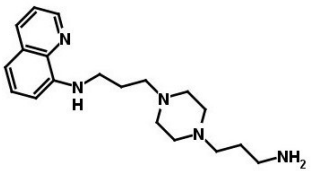
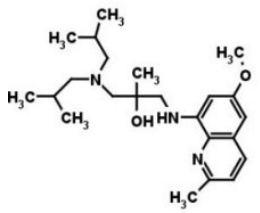
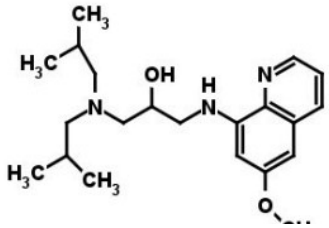
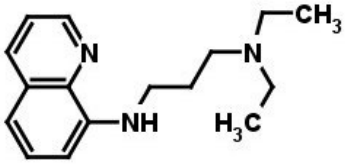
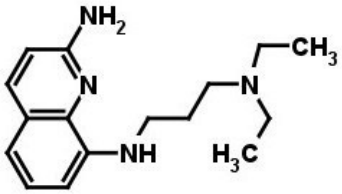
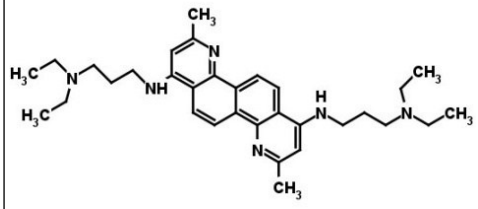
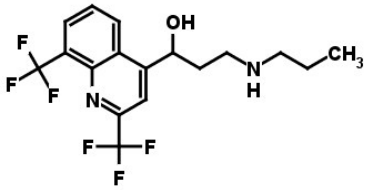
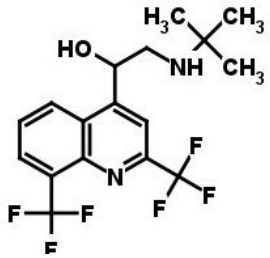
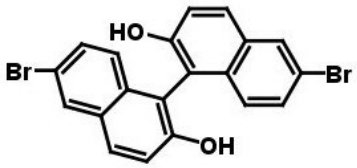
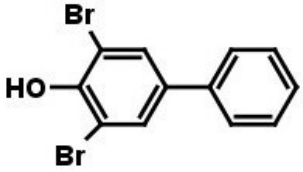
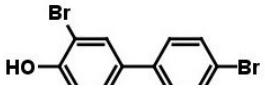
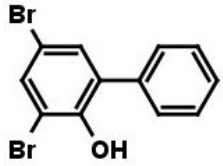
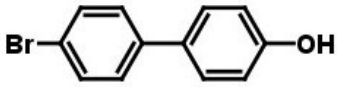
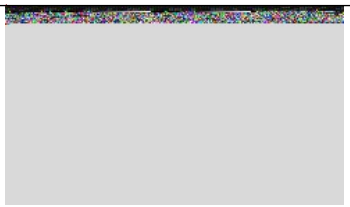
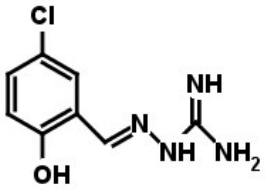
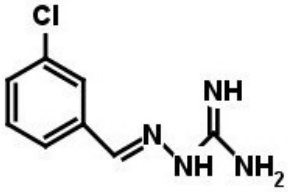
20	P-215	665278	 **N-methyl-N-{[3-(5-nitrotetrahydrofuran-2-yl)-1,2,4-oxadiazol-5-yl]methyl}-1-phenylpropan-2-amine**	-7.35	Autodock Site 3 (AS3)	7.7±1.16

Table 2. The table depicts the details regarding the analogues of various lead molecules which displayed inhibition of PptT activity. These analogues were obtained through structure similarity based approach.

S. No.	PS series	NCI ID	2-Dimensional Structure	IC_{50}	Tanimoto coefficient
Lead Molecule	P-4	23925	 [2-(4-methoxyphenyl)quinolin-4-yl]-piperidin-2-yl methanol	68.4±4	
1	PS-9(Analogue of P-4)	16001	 (7-chloro-2-phenylquinolin-4-yl)(piperidin-2-yl)methanol	64.5±6.2	0.82
Lead Molecule	P-52	53979	 N,N – diethyl –N`-(2-methyl quinolin-8-yl)propane-1, 3-diamine	2.25±1.38	
	Analogues of P-52				
2	PS-4	13040	 N-{3-[4-(3-Aminopropyl)-1-piperazinyl]propyl}-8-quinolamine	0.28±1.27	0.73

3	PS-8	14893	 **1-(Diisobutylamino)-3-[(6-methoxy-2-methyl-8-quinolinyl)amino]-2-methyl-2-propanol**	0.64±1.37	0.71
4	PS-10	29962	 **1-(Diisobutylamino)-3-[(6-methoxy-2-methyl-8-quinolinyl)amino]-2-propanol**	0.6±1.44	.71
5	PS-14	53975	 **N, N-diethyl-N`-(quinolin-8-yl) propane-1,3-diamine**	0.73±1.36	.80
6	PS-15	53976	 **N8-[3-(diethylamino) propyl]quinoline-2,8-diamine**	2.86±1.5	.74
7	PS-40	328398	 **N,N'-Bis[3-(diethylamino)propyl]-3,9-dimethylquinolino[8,7-h] quinoline-1,7-diamine**	0.25±1.4	.70
Lead Molecule	P-70	305817	 **1-[2,8-bis(trifluoromethyl)quinolin-4-yl]-3-(propylamino)propan-1-ol**	7.9±1.4	

	Analogues of P-70				
8	PS-37	305815	 **1-[2, 8-bis(trifluoromethyl) quinolin-4-yl]-2-(tert-butylamino)ethanol**	29.93± 3.23	.79
9	PS-39	305830	 **1-(2, 8-Bis(trifluoromethyl) quinolin-4-yl)-2-piperidin-2-yl)ethanol**	34.5±1 .5	.88
Lead Molecule	P-102	95701	 **5-bromobiphenyl-2-ol**	43.16± 1.41	
10	PS-3	9772	 **6, 6-dibromo-1, 1'-binaphthalelen-2, 2'-diol**	4.12±1 .42	.85
11	PS-13	53508	 **3, 5-dibromobiphenyl-4-ol**	11.14± 1.96	.81
12	PS-24	95696		5±1.98	.77

			 3,4,5-tribromobiphenyl-4-ol		
13	PS-25	95809	 3, 5-dibromobiphenyl-2-ol	18±1.4	.93
14	PS-31	130468	 4`-bromobiphenyl-4-ol	7.12±1.58	.73
Lead Molecule	P-110	138367	 2-(3, 5-dichloro-2-hydroxybenzylidene) hydrazinecarboximidamide	8.55±2.16	
	Analogues of P-110				
15	PS-18	65385	 2-(5-chloro-2-hydroxybenzylidene) hydrazine carboximidamide	66.8±1.53	.96
16	PS-19	67610	 2-(3-chlorobenzylidene) hydrazine carboximidamide	37.6±1.63	.79