Journal of Applied and Natural Science
15(3), 917 - 925 (2023)
ISSN : 0974-9411 (Print), 2231-5209 (Online)
journals.ansfoundation.org

Research Article

Inhibition of *Mycobacterium tuberculosis* MtrA response regulator by anticancer drugs via computational methods

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Article Info
https://doi.org/10.31018/jans.v15i3.4631
Received: April 22, 2023
Revised: July 23, 2023
Accepted: July 29, 2023

How to Cite
Satsangi, A. T. *et al.* (2023). Inhibition of *Mycobacterium tuberculosis* MtrA response regulator by anticancer drugs via computational methods. *Journal of Applied and Natural Science*, 15(3), 917 - 925. https://doi.org/10.31018/jans.v15i3.4631

Abstract
Mycobacterium tuberculosis (MTB) causes TB disease and millions of deaths are reported every year. Drug resistance TB and its complex treatment is a big problem worldwide. The present study aimed to design new and safer antitubercular compounds to tackle this serious threat. The unique drug target is the MtrAB Two-component regulatory system (2CRS) of mycobacteria. MtrAB system consists of MtrB sensor kinase (SK) and MtrA response regulator (RR). This system is essential in MTB and is involved in mycobacteria's proliferation. This important physiological process is operated by the phosphorylation of MtrB and then to MtrA. The phosphorylation mechanism triggers modulation in the expression of MtrA targets genes and helps perform appropriate function. This phenomenon depends on the active and inactive confirmation of MtrA, which involves a ligand (Metal ion complex e.g. Mg2+). In this study, anti-cancerous compounds were selected for the inhibition of MtrA. However, molecular docking exhibited binding affinity ranging from −10.8 to −4.7 kcal/mol, targeting the binding pocket of the selected Tuberculosis–MtrA protein (PDB ID: 5L8X). This energy difference between the native ligand and docked compounds showed that the six molecules: (Risperidone, 2-(benzofuran-2-yl)-6,7-dimethyl-4H-chromen-4-one, (2E)-1-(4-hydroxyphenyl)-3-(quinolin-4-yl)prop-2-en-1-one, Estradiol Cypionate, (2Z)-6-hydroxy-2-(3,4,5-trimethoxybenzylidene)-1-benzofuran-3(2H)-one, (2E)-3-(2,3-dihydro-1,4-benzodioxin-6-yl)-1-(3-hydroxyphenyl)prop-2-en-1-one) mentioned are more potent than the native ligand.These six molecules were first time reported as the inhibitor for MtrA of MtrAB Two-component regulatory system and can be utelize for further study.

Keywords: MtrA, Two-component regulatory system, Anticancer compounds, Molecular docking, Tuberculosis, Drug resistance

INTRODUCTION

Tuberculosis (TB) is an airborne mycobacterial infection that leads to fatal diseases and deaths worldwide. Mycobacterium tuberculosis (MTB) is mainly responsible for TB and primarily affects the lungs (Andersen and Scriba 2019). Approximately 1/3rd of the world is the carrier of this infectious pathogen. Globally ~10.4 million people are detected as new TB patients every year, out of which ~1.4 million die (Umubyeyi *et al*., 2008; Mousavian *et al*., 2022). TB is curable but difficult because it requires doses of multiple antibiotics over a long period of time (Sotgiu et al., 2015). Currently available drugs work efficiently against TB, but their side effects are devastating (Yee *et al*., 2003; Jasmer *et al*., 2002). However, the emergence of drug-resistant tuberculosis and TB-HIV coinfection are serious challenges which have made the patient condition more complicated and the treatment less effective (Bell and Noursadhegi 2018).Innovating new drug targets and drug molecules is extremely needed to tackle the associated problems in eliminating TB in the future (Pandey

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et al., 2017). In addition, the most vexatious thing about microbes is their nature of adaptability to the changing environment. The survival of bacterium is maintained by signal transduction system and it is mainly driven by serine-threonine kinases (STPKs) and two-component regulatory systems (2CRSs). However, the ubiquity of 2CRSs in bacteria and their unavailability in humans have made them attractive and safer drug target (Stock *et al.,* 2000). 2CRSs are the key components MTB uses to receive signals from the host environment and appropriately execute the response to adapt, grow and survive in the adverse host environment (Kim & Forst, 2001). Therefore, 2CRSs are preferred as drug targets to combat TB. 2CRS consist of two coupled proteins constituting a pair; a membrane-linked sensor kinase (SK) and its response regulator (RR) in the cytosol (Zahrt and Deretic 2000; Haydel & Clark-Curtiss 2004). MTB genome contains 11 paired 2CRS, while 6 single RR and 2 single SK genes. Out of 11, MtrAB is one of the important 2CRSs, includingMtrB as sensor kinase and MtrA as response regulator protein. It is essential for survival in MTB (Via *et al*., 1996; Zahrt and Deretic, 2000; Haydel *et al*., 2012). MtrAB system plays role in cell division and cell wall maintenance processes.

In general, a sensor kinase receives signal and transfers it to the regulator. This involves binding chemical signals to the extracellular sensor domain, which induces autophosphorylation of SK at a histidine residue conserved in the catalytic core in the cytoplasm (Parkinson and Kofoid 1992). This SK then transfers a phosphoryl group specifically to an aspartate residue conserved in the signal receiver domain of RR. Phosphorylation of the receiver domain turns on the effector domain resulting in the affinity for DNA, which regulates the expression of gene/s in a regulon and modulates transcription (Haydel and Clark-Curtiss 2004).

MTB survival and proliferation involve functions of many MtrA target genes, including DnaA, which is involved in chromosome replication. The modulation in the expression level of MtrAregulon genes depends on its phosphorylation potential (Fol *et al.,* 2006). Crystal structure data of MTB MtrA has defined the role of phosphorylation based on its active and inactive confirmation. The overall structure and function of MtrA depend on the rearrangement of ligand (Metal ion Mg2+ / Ca2+) involving highly conserved aspartate residue (ASP-56) at the active site (Friedland *et al.,* 2007). Several metal complexes (ligands) that have been reported as anticancer compounds also work as potent antibacterial (SubhadeepSen *et al.,* 2022). These findings prompted to screen the anticancer compounds against MTB MtrA via computational biology approach to develop new drugs against drug-resistant TB. The present study could be another stride to combat this fatal disease in future.

MATERIALS AND METHODS

Data collection and selection

The present study collected different MtrA protein structures from RCSB PDB1(https://www.rcsb.org/), such as 5LAA, 5L8X, 3NHZ, 6ZW0, 2GWR, and 6R2Q. Anticancer compounds were retrieved from Super Natural II --a database of natural products (http:// bioinformatics.charite.de/supernatural). One-hundred three anti-cancer compounds collected from PubChem database (https://pubchem.ncbi.nlm.nih. gov/
) in. sdf format for the screening and docking with MtrA3. On the basis of different parameters such as Method, Organisms, Macromolecule, and Unique Ligands, the study chose the 5L8X for this experiment.

Preparation of protein and collected compound

The publication methodology (Yadav *et al*., 2022; Kumar *et al*., 2022) was used for preparing of protein and another processing. However, MtrA protein (5L8X) was opened with UCSF chimera and prepared by removing ligand, ions, solvent , and adding hydrogens atoms and Gasteiger charge to the chain B. Similarly, the ligands were also prepared in UCSF chimera by adding hydrogen atoms and Gasteiger charge.

Binding energy analysis

PyRx (Yadav *et al*., 2022) is a virtual screening programme used in computational drug discovery to check libraries of compounds against possible therapeutic targets. Pharmaceutical Chemists can execute Virtual Screening using PyRx from any platform, and the software supports users at every stage of the procedure, from data preparation through job submission and outcome analysis. PyRx is a useful tool for computer-aided drug design since it has a docking wizard and an intuitive user interface. Additionally, PyRx has extensive visualisation capabilities and chemical spreadsheet-like features that are crucial for structure-based drug creation. PyRx software was used to screen these compounds plugged in with Openbable, pythen, etc. To screen 103 compounds, the study prepared the protein structure at default parameters and minimised them. For screening, we choose a centre of -10.3126; -12.0484; -8.1951 Å and grid size of 21.0349; 16.9052; 34.4485 Å for ligand binding inside the active pocket.

Docking efficacy analysis

UCSF Chimera is a molecular visualization program developed by the University of California, San Francisco (UCSF). It was used to visualize and analyse 3D molecular structures. Chimera provided tools for 3D structure visualization, analysis, and manipulation. It can be used to view volumetric data, such as electron density maps, and to visualize and animate atomic-level protein, nucleic acid, and small molecule struc-

Table 1. Binding energy of anticancer compounds at zero RMSD and RMSF value via Structure-based virtual screening using PyRx

Compound name	PubChem ID	Binding	RMSD/UB	RMSD/LB
2-(benzofuran-2-yl)-6,7-dimethyl-4H-chromen-4-one	740749	-10.8	0	0
risperidone	5073	-10.7	0	0
(2E)-1-(4-hydroxyphenyl)-3-(quinolin-4-yl)prop-2-en-1-one	16408384	-9.7	0	0
(2Z)-6-hydroxy-2-(3,4,5-trimethoxybenzylidene)-1-benzofuran-3(2H)-one	907815	-9.7	0	0
Estradiol Cypionate	9403	-9.7	0	0
4'-Chloro-6-fluoroflavone	930090	-9.5	0	0
Loracarbef	5284585	-9.5	0	0
(E)-3-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-1-(3-hydroxyphenyl)prop-2-en-1-one	6215176	-9.5	0	0
Iloperidone	71360	-9.4	0	0
Bendroflumethiazide	2315	-9.3	0	0
Sitagliptin	4369359	-9.3	0	0
2-(3,4-dimethoxyphenyl)-6-fluorochromen-4-one	803329	-9.2	0	0
Tectochrysin	5281954	-9.2	0	0
4'-Hydroxy-2,4-dimethoxychalcone	5729232	-9.1	0	0
2-(2-fluorophenyl)-7-methoxychromen-4-one	929915	-9.1	0	0
Naftifine	47641	-9.1	0	0
7-methoxyisoflavone	638006	-9	0	0
3-(4-chlorophenyl)-2-oxochromen-7-yl acetate	1383010	-8.9	0	0
(Z)-6-methoxy-2-(3,4,5-trimethoxybenzylidene) benzofuran-3(2H)-one	1754693	-8.9	0	0
2-(2,4-dichlorophenyl)-7-methoxy-4H-chromen-4-one	930509	-8.9	0	0
Protokylol	4969	-8.9	0	0
3-(4-methoxyphenyl)-7-(2-(4-(4-methoxyphenyl) piperazin-1-yl)ethoxy)-4H-chromen-4-one	17584963	-8.9	0	0
3-(2-methoxyphenoxy)-7-[(3-methoxyphenyl)methoxy] chromen-4-one	1760139	-8.9	0	0
7-Hydroxy-5-methoxy-2-phenyl-chromen-4-one	5490127	-8.8	0	0
4',6-DICHLOROFLAVONE	688871	-8.8	0	0
3-(4-methoxyphenyl)-4-methyl-2-oxo-2H-chromen-7-yl 2-methylpropanoate	7198328	-8.8	0	0
Lobeline	101616	-8.8	0	0
5-methoxy-4-oxo-2-phenyl-4H-chromen-7-yl dimethylcarbamate	16408080	-8.7	0	0
5-hydroxy-4-oxo-2-phenyl-4H-chromen-7-yl dimethylcarbamate	16408727	-8.7	0	0
(3-aminophenyl)(3,4-dimethoxyphenyl)methanone	10563087	-8.6	0	0
prop-2-en-1-yl 2-{[3-(4-chlorophenyl)-4-methyl-2-oxo-2H-chromen-7-yl]oxy}acetate	7198309	-8.6	0	0
4-methyl-2-oxo-3-phenylchromen-7-yl propanoate	7198318	-8.6	0	0
3-(4-methoxyphenyl)-2-oxo-2H-chromen-7-yl isobutyrate	7198327	-8.6	0	0
Diclorofeno	3037	-8.6	0	0
(2E)-3-(2,4-dimethoxyphenyl)-1-(2-hydroxy-5-methylphenyl)prop-2-en-1-one	6080111	-8.6	0	0
6-chloro-2-(3,4-dimethoxyphenyl)-4H-chromen-4-one	803883	-8.5	0	0
2-(4-chlorophenyl)-6-methoxy-4H-chromen-4-one	877751	-8.5	0	0
Perflubron	9873	-8.5	0	0
3-(3,4-dimethoxyphenyl)-2-oxo-2H-chromen-7-yl 2-	7198329	-8.4	0	0
5,7-Dimethoxyflavone	88881	-8.4	0	0
(Z)-3-oxo-2-(3,4,5-trimethoxybenzylidene)-2,3-dihydrobenzofuran-6-yl 3-methoxybenzoate	1762231	-8.4	0	0

Contd…….

Table 1. Contd…….

2-(3,4-dimethoxybenzamido)-4,5,6,7-tetrahydrobenzo[b] thiophene-3-carboxamide	1048845	-8.3	0	0
3-(3,4-dimethoxyphenyl)-7-[2-[(2R,6S)-2,6-dimethylmorpholin-4-yl]ethoxy]chromen-4-one	25823942	-8.3	0	0
formononetin	5280378	-8.3	0	0
7-methoxy-3-(4-methoxyphenyl)-2H-chromen-2-one	688973	-8.3	0	0
prop-2-en-1-yl 2-{[3-(4-methoxyphenyl)-4-methyl-2-oxo-2H-chromen-7-yl]oxy}acetate	7198310	-8.3	0	0
4-methyl-7-(2-oxopropoxy)-3-phenylchromen-2-one	7198312	-8.3	0	0
4',7-Dimethoxyisoflavone	136419	-8.2	0	0
(Z)-6-((3-methoxybenzyl)oxy)-2-(3,4,5-trimethoxybenzylidene)benzofuran-3(2H)-one	1781741	-8.2	0	0
(2E)-1-(2,4-dimethoxyphenyl)-3-(2,5-dimethoxyphenyl)	5332328	-8.2	0	0
3-(4-chlorophenyl)-5,7-dihydroxy-4H-chromen-4-one	5398360	-8.2	0	0
(2E)-3-(2,4-dimethoxyphenyl)-1-(2,5-dimethoxyphenyl)	5908100	-8.2	0	0
7-methoxy-3-(4-methoxyphenoxy)-2-methyl-4H-chromen	890010	-8.2	0	0
methyl 2-{[3-(4-methoxyphenyl)-2-oxo-2H-chromen-7-	1424927	-8.2	0	0
3-(4-chlorophenyl)-7-hydroxy-4H-chromen-4-one	5346977	-8.1	0	0
7-hydroxy-3-(4-methoxyphenyl)-8-(morpholinomethyl)-	6059482	-8.1	0	0
7-ethoxy-3-(4-methoxyphenoxy)-2-methyl-4H-chromen-4	908652	-8	0	0
Bexarotene	82146	-8	0	0
(Z)-2-(3,4-dimethoxybenzylidene)-3-oxo-2,3-	1762339	-7.9	0	0
ethyl 5-[(2-methylprop-2-en-1-yl)oxy]-2-phenyl-1-benzofuran-3-carboxylate	702018	-7.9	0	0
Novo-depigman	7638	-7.9	0	0
7-hydroxy-2'-methoxyisoflavone	5397276	-7.9	0	0
lignostilbene	5280698	-7.8	0	0
7-hydroxy-3-(2-methoxyphenoxy)-2-methyl-4H-chromen-	5411134	-7.8	0	0
3-methoxybenzo[c]chromen-6-one	682195	-7.8	0	0
3,5-dimethoxy-N-[5-(2-methylpropyl)-1,3,4-thiadiazol-2-	697534	-7.8	0	0
2-(2-chlorophenyl)-6-methoxy-4H-chromen-4-one	776402	-7.8	0	0
7-ethoxy-3-(2-methoxyphenoxy)-2-methyl-4H-chromen-4	908720	-7.8	0	0
7-methoxy-3-(3-methoxyphenoxy)-2-methyl-4H-chromen	908476	-7.7	0	0
3-(2,5-dimethoxyphenyl)-7-methoxy-4-methyl-2H-	4965671	-7.6	0	0
7-hydroxy-3-(4-methoxyphenyl)-2,8-dimethyl-4H-	5662803	-7.6	0	0
3,4,2',5'-tetramethoxychalcone	5939551	-7.6	0	0
Hetacillin	443387	-7.6	0	0
4H-1-Benzopyran-4-one, 6-bromo-2-(2-methoxyphenyl)-	930701	-7.6	0	0
3-(2,4-dimethoxyphenyl)-7-methoxy-2H-chromen-2-one	4839447	-7.5	0	0
ethyl 5-hydroxy-2-(4-methoxyphenyl)-1-benzofuran-3-	803446	-7.5	0	0
3-(2,5-dimethoxyphenyl)-7-hydroxy-4-methyl-2H-	6217099	-7.4	0	0
ethyl 5-ethoxy-2-(4-methoxyphenyl)-1-benzofuran-3-	948066	-7.4	0	0
Lisdexamfetamine	11597698	-7.4	0	0
3-(2,4-dimethoxyphenyl)-7-hydroxy-4-methylchromen-2-	6217342	-7.3	0	0
Oxazepam	4616	-7.3	0	0
3-(2,4-dimethoxyphenyl)-7-hydroxy-2H-chromen-2-one	6217072	-7.1	0	0
3-(2-ethoxyphenoxy)-7-hydroxy-2-methyl-4H-chromen-4	5417199	-6.9	0	0
1-Phenylurea	6145	-6.9	0	0
Quinizarin	6688	-6.9	0	0
Famotidine	5702160	-6.8	0	0
3-(2-methoxyphenoxy)-2-methyl-4-oxo-4H-chromen-7-yl	1749225	-6.7	0	0
Acetovanillone	2214	-6.6	0	0
Demeclocycline	54680690	-6.6	0	0

Contd…….

Table 1. Contd…….

Doxepin	667477	-6.6	0	0
fumarate	5460307	-6.5	0	0
Trimethoprim	5578	-6.4	0	0
Tamoxifen	2733526	-6.4	0	0
Adipic acid	196	-6.1	0	0
Isobarbaloin	14989	-6.1	0	0
Enflurane	3226	-5.7	0	0
Isoleucine	6306	-5.6	0	0
Rapacuronium	5311399	-5.6	0	0
Temsirolimus	6918289	-4.9	0	0
Ecothiopateiodide	10547	-4.8	0	0

tures. In addition, Chimera was used for measuring distances, angles, and other properties of molecular structures. It also offers surface and mesh visualization features, and tools for comparing structures and creating high-quality images for publication. UCSf Chimera plugin with Autodockvina was used for docking purposes.

Lead compound ADMET analysis

ADME stands for Absorption, Distribution, Metabolism, and Excretion. It is a term used to describe the properties of a compound that determine its pharmacokinetic profile. ADME testing is critical for pharmaceutical development, as it helps to determine the suitability of a compound as a drug. It looks at how quickly and in what form a compound is absorbed into the body, how long it stays in the body, how it is distributed throughout the body, and how it is metabolized and excreted. ADME testing helps to identify drug candidates that are safe for clinical trials and will have the desired therapeutic effect. SwissADME (http://www.swissadme.ch/) was the server, which was used for the detection of compounds properties by adding their canonical smiles.

RESULTS AND DISCUSSION

Structure-Based Virtual Screening

The anticancer products reported in the supernatural-II a data base of natural products (http://bioinformatics.charite.de/supernatural) (Banerjee et al., 2015) shows the top conformations inside the active pocket of the targeted protein exhibited binding affinity ranging from −10.8 to −4.7 kcal/mol, targeting the binding pocket of the selected Tuberculosis–MtrA protein. Thus, the top docked poses of the first ten compounds—PubChem ID, 740749, 5073, 16408384, 907815, 6215176, 930090, 5284585, 6215176, 71360, and 2315—with significant binding scores (> −9 kcal/mol) were considered for the redocking (Table 1) analysis to find drug-likeness properties and the ideal docking conformation, respectively, in the selected binding pocket of the bacterial protein.

Molecular contact analysis

Using AutoDockVina, ten potential anti-cancer compounds were selected from the virtual screening: PubChem IDs 740749, 5073, 16408384, 907815, 9403, 6215176, 930090, 5284585, 6215176, 71360, and 2315. Following that, for each natural compound, the docked poses with the highest negative docking energy values corresponding to zero RMSD values were considered for further computational analysis. In this study, 5073 (PubChem ID) compound docked with Tuberculosis-MtrA had the highest docking energy (-10.8 kcal/mol), while Tuberculosis-MtrA -2315 docked complex had the lowest docking scores (-8.8 kcal/mol) (Table 2) when compared to reference compounds (PubChem ID 92824) D-Malic acid (-5.4 kcal/mol) (Table 3). Furthermore, when compared to the reference docked complexes, a significant number of intermolecular interactions were observed in the docked complexes, including hydrogen bond formation, π- π stacking, π-cation, hydrophobic, polar, negative, positive, glycine, and salt bridge interactions. As a result, the calculated docking scores and intermolecular contact profiling between the docked anti-cancer compounds and Tuberculosis-MtrA indicate that the docked complexes are stable.

Lead compounds ADMET analysis

The SwissADME online server (http://www.swissadme.ch) was used to understand the properties of the selected compounds related to pharmacokinetics and drug likeliness, such as absorption, distribution, metabolism, and excretion (ADME). Because bioavailability is an important factor in determining whether a drug is a promising therapeutic, several parameters were observed during the ADME analysis, including blood-brain barrier (BBB), permeability, number of hydrogen bond acceptors, number of hydrogen bond donors, aromatic heavy atoms, GI absorption, TPSA and Lipinski violation activities (Table 4).

Table 2. 2D and 3D presentation of complexes (protein-ligand) showed hydrogen bond, hydrophobic bond - stacking, - cation, hydrophobic, polar, negative, positive, glycine, and salt bridge interactions of compounds showing binding energy more than -8.5 Kcal/mol

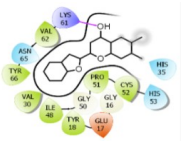
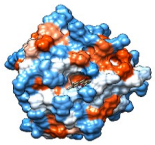
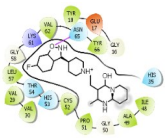
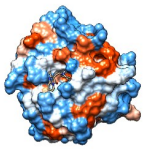
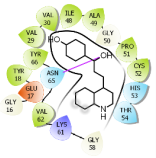
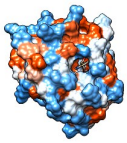
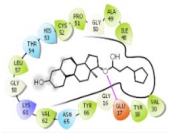
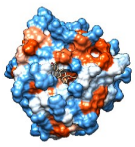
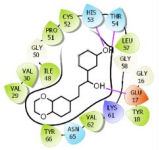
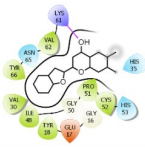
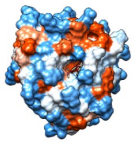
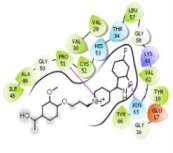
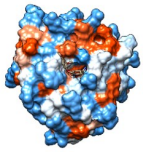
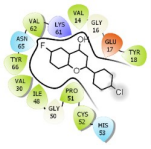
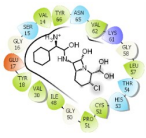
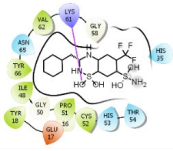
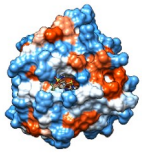
PubChem CID	Binding Energy Kcal/Mol	2D molecular interactions	3Dmolecular interactions
740749	**-10.7**		
5073	**-10.7**		
16408384	**-9.8**		
9403	**-9.7**		
6215176	**-9.7**		
907815	**-9.7**		
71360	**-9.5**		
930090	**-9.4**		
5284585	**-8.8**		
2315	**-8.5**		

Table 3. Ligand orientation and amino acid residues under 3.5Å radius of active pocket of Tuberculosis–MtrA

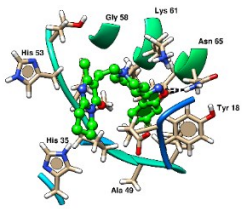
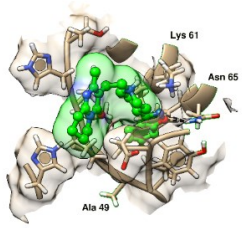
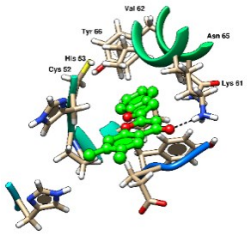
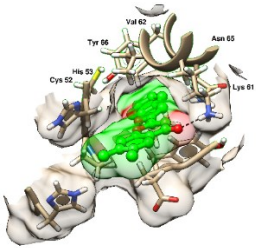
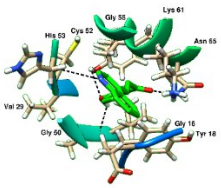
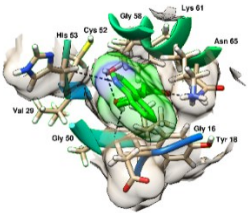
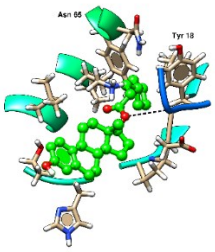
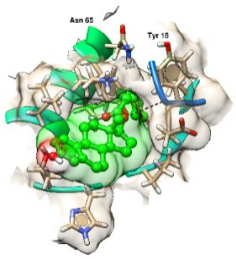
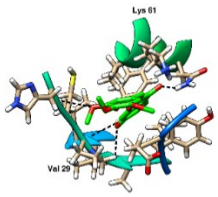
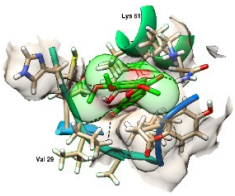
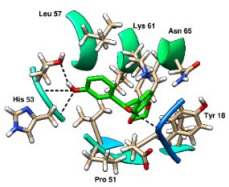
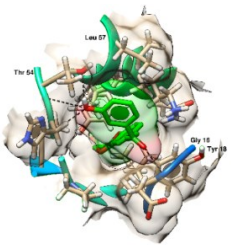
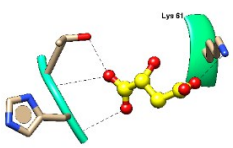
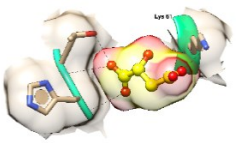
Compound Name	2D interaction under 3.5 Å	3D interaction under 3.5 Å
5073		
740749		
16408384		
9403		
907815		
6215176		
Control		

Table 4. Pharmacokinetics of the top six compounds analysed after docking

PubChem ID	MW	Heavy atoms	Aromatic heavy atoms	Fraction Csp3	Rotatable bonds	H-bond acceptors	H-bond donors	MR	TPSA	GI absorption	BBB permeant	Pgp substrate	Lipinski violations
740749	290.3	22	19	0.11	1	3	0	87.6	43.35	High	Yes	No	0
5073	410.5	30	15	0.52	4	6	0	118	64.16	High	Yes	Yes	0
16408384	275.3	21	16	0	3	3	1	83.6	50.19	High	Yes	No	0
907815	328.3	24	12	0.17	4	6	1	87.3	74.22	High	Yes	No	0
6215176	282.3	21	12	0.12	3	4	1	79.1	55.76	High	Yes	No	0
9403	396.6	29	6	0.73	5	3	1	117	46.53	High	No	No	1

Conclusion

MtrA plays a significant role in the progression of Tuberculosis. The anticancer compounds were docked to find out their potential activity against Tuberculosis bacteria–DNA-binding response regulator Mycobacterium tuberculosis (strain ATCC 25618 / H37Rv) (MtrA) by evaluating their binding affinity against the MtrA gene. Six potent flavonoids were identified through virtual screening, followed by evaluation for ADME. These potent molecules showed good binding energy and multiple bond interactions with the MtrA gene. Also, molecular docking confirmed the valid bond interaction between protein and ligand (Complex) from different orientations. Due to the formation of multiple intermolecular interactions, these complexes can be considered stable. Based on the substantial docking energy (>−10.5 kcal/Mol) and pharmacokinetics analysis, six compounds—PubChem ID 740749, 5073, 16408384, 907815, 9403, 6215176—were considered. The present study concluded (Risperidone, 2-(benzofuran-2-yl)-6,7-dimethyl-4H-chromen-4-one, (2E)-1-(4-hydroxyphenyl)-3-(quinolin-4-yl)prop-2-en-1-one, Estradiol Cypionate, (2Z)-6-hydroxy-2-(3,4,5-trimethoxybenzylidene)-1-benzofuran-3(2H)-one, (2E)-3-(2,3-dihydro-1,4-benzodioxin-6-yl)-1-(3-hydroxyphenyl) prop-2-en-1-one) are the compounds, acceptable inhibitors of the MtrA protein and can be utilized for further studies for developing a potential drug against Tuberculosis.

Conflict of interest

The authors declare that they have no conflict of interest.

ACKNOWLEDGEMENTS

The authors Acknowledge Higher Management of Sharda University, Greater Noida, to provide Seed Grant (SU/SF/2022/18) for completing this study.

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