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Research Article

Molecular Docking and Phamcokinetic Investigation to Design new Antituberclosis Drugs

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Abstract

Tuberculosis remains a critical global health challenge, causing illness and death among millions each year. It is currently ranked as the second leading cause of mortality among communicable diseases worldwide. In this study, a modeling technique was employed to predict the inhibition activity of several prominent compounds previously reported to be effective against Mycobacterium tuberculosis. To achieve this, multiple regression and genetic function approximation (GFA) methods were used to develop predictive models. The resulting model was influenced by several topological descriptors—AATS7s, GATS4v, nHBint3, and RDF90i—which were rigorously tested and validated.In addition, molecular docking studies were conducted to evaluate the interactions between the compounds and the target enzyme, DNA gyrase, using PyRx and Discovery Studio software. The results revealed that compounds 5, 7, 10, 11, 12, 20, 25, 26, 27, and 28 exhibited significant binding affinities, ranging from –6.3 to –16.5 kcal/mol. Notably, compound 12 demonstrated the highest binding affinity at –16.5 kcal/mol.These findings suggest that compound 12 could serve as a promising structural template for the design of new, more effective anti-tuberculosis drugs by medicinal chemists and pharmacists.

Keywords: Anti-tuberculosis, Descriptor, Docking, Interaction, Receptor.

Introduction

The World Health Organization (WHO) has declared tuberculosis (TB) a major global health issue. Although there has been a downward trend in its prevalence and incidence, new cases continue to be reported across all continents, particularly in South-East Asia and Africa. In 2017, WHO reported that approximately 9 million people were infected with TB, resulting in 1.6 million deaths worldwide [1].Commonly recommended anti-tubercular drugs for the treatment of TB include rifampicin, pyrazinamide, para-aminosalicylic acid, and isoniazid [2]. However, studies have shown that many patients fail to respond positively to these treatments due to the emergence of drug-resistant strains of Mycobacterium tuberculosis. Moreover, several of these drugs are associated with adverse side effects [2].As a result, the search for novel anti-tubercular agents with enhanced efficacy and reduced toxicity remains a significant challenge for pharmacists and medicinal chemists [3].One promising target in the development of new TB therapies is DNA gyrase, a type II topoisomerase essential to all bacteria. This enzyme introduces negative supercoils into the bacterial chromosome, helping to relax the positive supercoils generated by translocating RNA polymerase. Its action is crucial for chromosome condensation and proper segregation during cell division [4,5]. DNA gyrase is a tetrameric enzyme composed of two A subunits (GyrA) and two B subunits (GyrB). The GyrA subunits contain the DNA-binding domain, while the GyrB subunits are responsible for ATP hydrolysis, which drives the rapid cleavage and rejoining of DNA strands. Together, GyrA and GyrB facilitate DNA replication, making this enzyme essential for bacterial survival.Given its vital role in DNA replication, DNA gyrase is a promising target for antibacterial agents. Inhibitors that block DNA replication by targeting

either the GyrA subunit (DNA-binding domain) or the GyrB subunit (ATP-binding site) have shown potential as effective therapeutic agents.In the search for such agents, heterocyclic compounds have attracted considerable interest in medicinal chemistry due to their diverse structural features [6]. Among these, triazoles and their analogues have gained particular attention in pharmacological research. Triazole is a five-membered, diunsaturated heterocyclic ring composed of two carbon atoms and three non-adjacent nitrogen atoms. Its unique structure makes it a valuable scaffold in drug development [3,6].Recent studies have highlighted the significance of the triazole nucleus in medicinal chemistry. It has gained widespread attention among pharmacists, biochemists, biologists, and chemists as one of the major bioactive scaffolds in drug design and chemotherapy applications [7]. Triazole derivatives have demonstrated a broad range of pharmacological activities, including analgesic, anti-tubercular [8,9], anti-neoplastic [10], and anti-malarial effects [11]. Notably, triazole compounds have also been identified as some of the most effective molecules against Mycobacterium tuberculosis, making them promising candidates for anti-TB drug development [12].In recent times, advancements in computational chemistry have created new opportunities and challenges in drug discovery. These developments have popularized in silico methods in structure-based drug design, significantly reducing both the cost and time required to screen large virtual libraries of chemical compounds. Among the most widely adopted computational tools are Quantitative Structure–Activity Relationships (QSAR) and molecular docking [2].QSAR is a powerful computational technique that predicts the biological or inhibitory activity of chemical compounds by correlating molecular descriptors with experimental data. It establishes mathematical relationships between chemical structure and biological activity, guiding the design of more effective molecules.Molecular docking, on the other hand, predicts the binding site and binding affinity between a ligand (molecule) and its target receptor. This approach provides crucial insights into ligand-receptor interactions, aiding in the design of potential drug candidates with improved activity against specific targets [2].The initial stage in designing and synthesizing novel anti-tubercular compounds with enhanced efficacy and minimized toxicity involves selecting appropriate computational methods to reduce experimental workload and optimize time efficiency. In this context, computer-aided drug design (CADD) has played a crucial role in the discovery of new drug candidates, particularly in pharmaceutical design, drug metabolism, and medicinal chemistry [13].This computational approach has enabled the optimization of chemical structures with specific, well-defined objectives [14]. Among the most effective techniques within CADD are QSAR modeling and molecular docking .Therefore, this study aims to develop a QSAR model, perform molecular docking simulations, and provide computational insights into the design of novel compounds as potent antagonists targeting the DNA gyrase receptor.

Materials and Methods

Preparation of Ligands and Protein

The Protein Databank [https://www.rcsb.org/structure/7VJT] provided the crystal structure of Mycobacterium TB Pks13-TE (Polyketide Synthase 13 - Thioesterase) in pdb format. The ligand used in the study is drawn using a tool called Chemsketch [https://www.acdlabs.com/resources/free-chemistry-software-apps/chemsketch-freeware/]. [15]

Formation of Target Protein

The resolution of the structure of Mycobacterium tuberculosis Pks13-TE (Polyketide Synthase 13-Thioesterase) (PDB ID: 7VJT) is 1.94 A^{o}. The Protein Databank provided it in PDB format. Two chains, A and B, are present in Mycobacterium TB Pks13-TE (Polyketide Synthase 13-Thioesterase). By allocating hydrogen and polarities and computing Gasteiger charges, the protein structures were prepared for docking investigations. Furthermore, the Auto-Dock program (Auto-Doch Vina) was used to transform the protein structures from the pdb format to the pdbqt format [16].

Preparation of Ligand

The software Chemsketch (https://blog.acdlabs.com/acdlabs/rss.xml) was used to design the derivative of dihydroquinoline-1,2,3-triazole, download the file in MOL format, and perform docking tests. The software was used to extract all of the ligand molecules from the single file that contained the drawn molecule. Then, all of the ligand molecules were converted from MOL format to PDB format using open babel and specially written PERL scripts.

Molecular Docking

All of the ligands in the organic chemistry library were used in molecular docking studies against Mycobacterium tuberculosis Pks13-TE (Polyketide Synthase 13-Thioesterase) in order to find potential hit compounds for further drug development research [17]. The docking investigations in the current study were carried out using AutoDock version 4.2. AutoDock uses a Lamarckian Genetic Algorithm (LGA) and is based on a semi-empirical free energy force field. The docking grid was manually made by viewing the protein and encompassed the entire Mycobacterium tuberculosis Pks13-TE (Polyketide Synthase 13-Thioesterase) binding site. [18] The orientation and chemical interactions between the suggested derivatives of dihydroquinoline-1,2,3-triazole and the protein target are determined by molecular docking experiments. The docking studies were aided by the Autodock vina program.

The cavity detection wizard locates the binding sites before importing the planned derivatives for the molecular interaction studies. Mycobacterium tuberculosis Pks13-TE (Polyketide Synthase 13-Thioesterase) ribbon diagram with

the dihydroquinoline-1,2,3-triazole derivatives is displayed in Figure 1. The coordinates for docking the ligand library with 7F9K were X=-8.741, Y=-24.608, and Z= 158.181, whereas the grid dimensions were set to X=40, Y=40, and Z=40. Along with a number of nearby residues, GLN A 1701 was one of the important residues in the binding site [Fig 2].Finally, using a self-written PERL script and all of the ligands from the library, molecular docking was carried out on the target proteins with a particular emphasis on the docking of Mycobacterium tuberculosis Pks13-TE (Polyketide Synthase 13-Thioesterase). In order to find possible ligand molecules appropriate for additional drug design research and to validate the importance of Mycobacterium tuberculosis Pks13-TE (Polyketide Synthase 13-Thioesterase) as a crucial drug target in tuberculosis, the organic molecular library was positioned into the active site of the bacteria. To make it easier to choose candidates with better pharmacokinetic profiles for upcoming wet lab testing, the pharmacokinetic characteristics of the top-ranked compounds were also calculated.

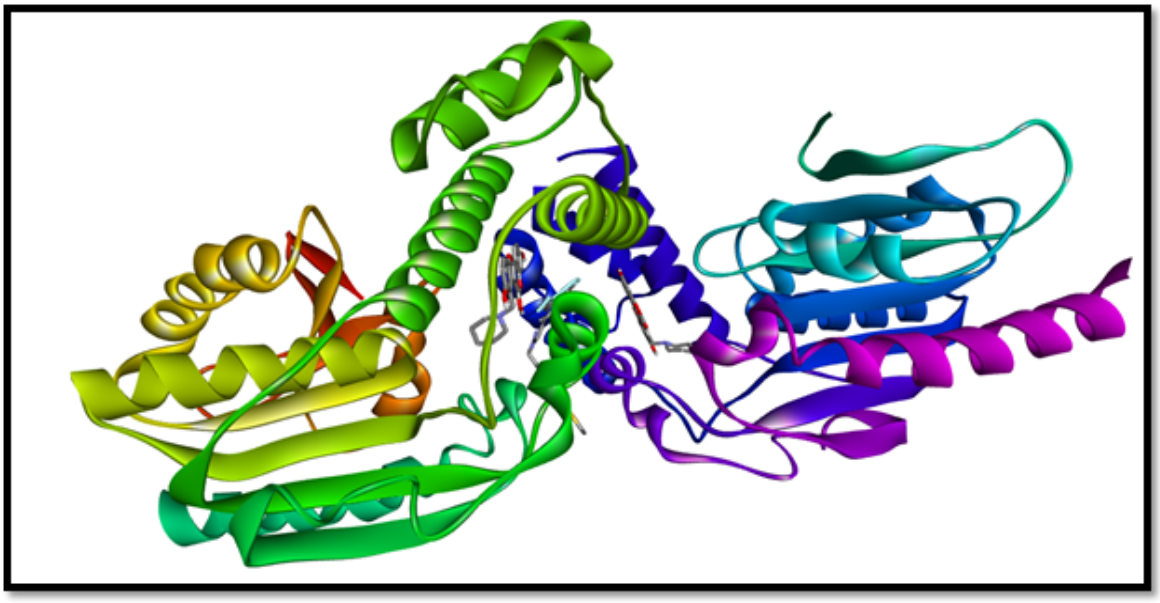


Figure. 1 Mycobacterium tuberculosis Pks13-TE (Polyketide Synthase 13 - Thioesterase) with the dihydroquinoline-1,2,3-triazole derivatives

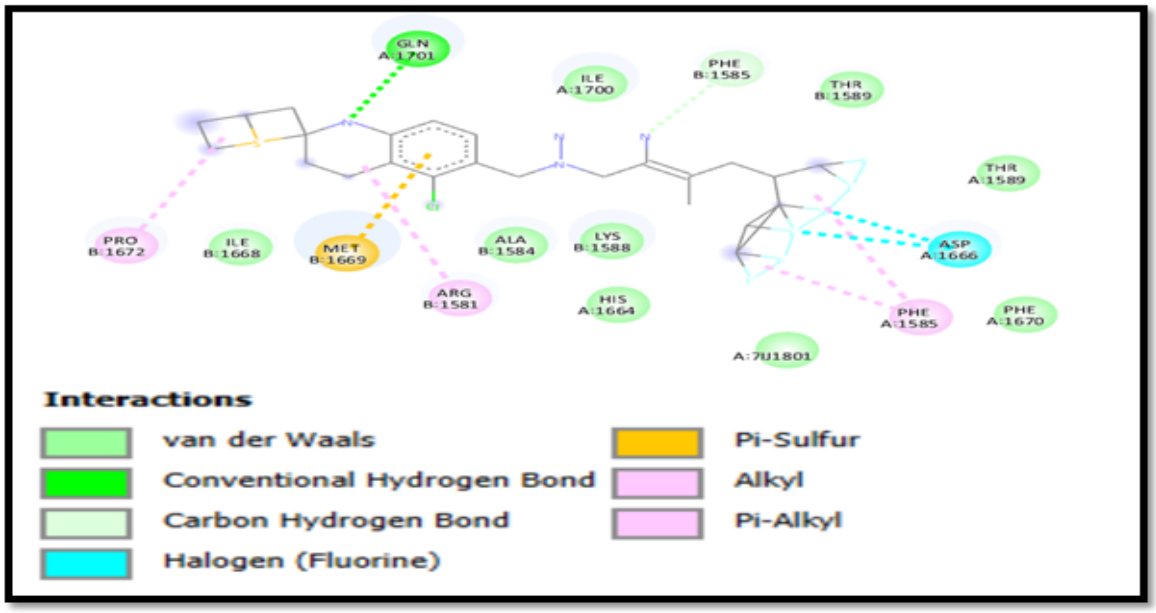
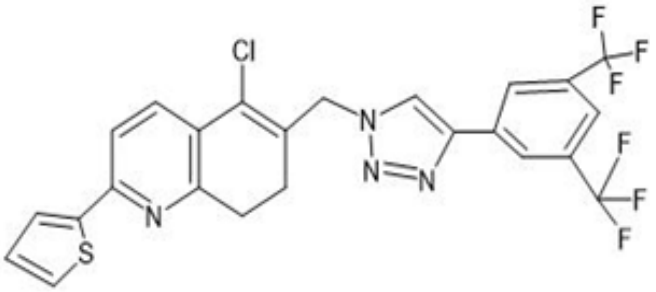
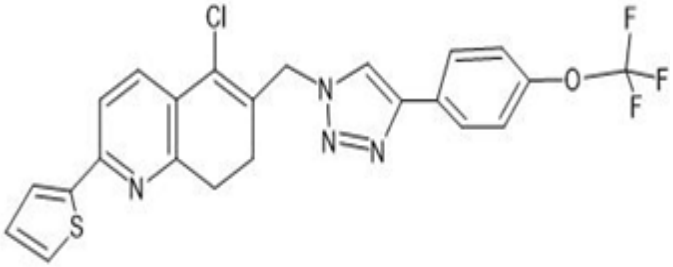
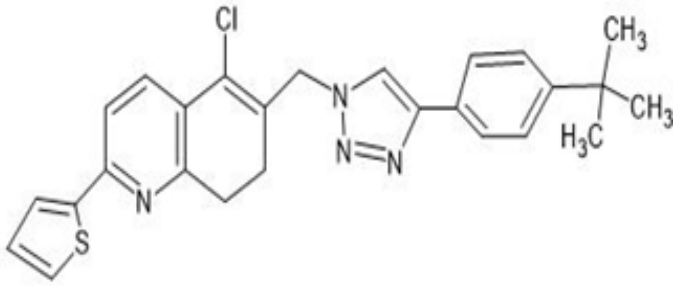
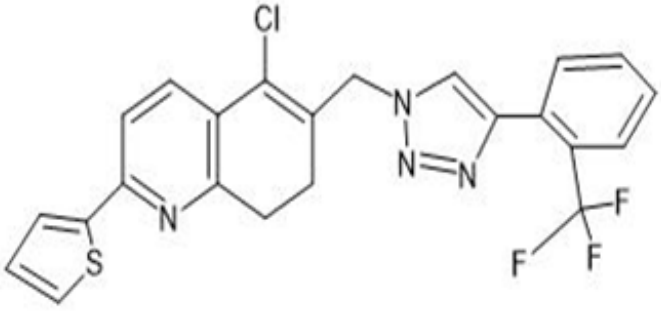
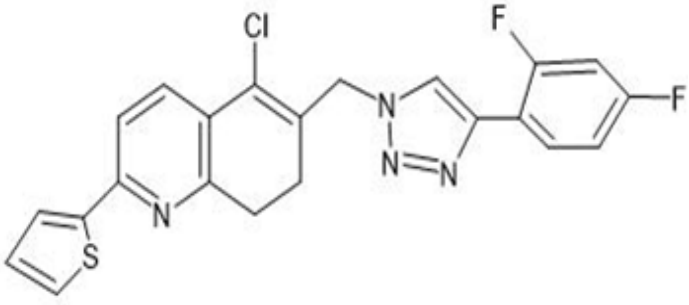


Figure. 2. Showing Interaction of ligand R1 with Residues

S.No.	Structure
R1.	
R2.	
R3.	
R4.	
R5.	

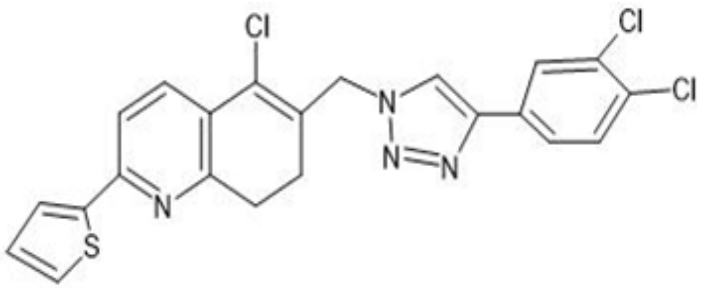
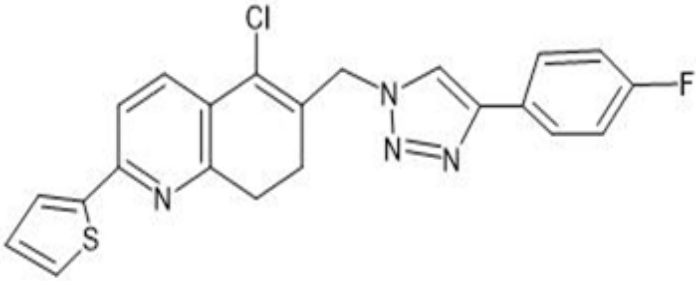
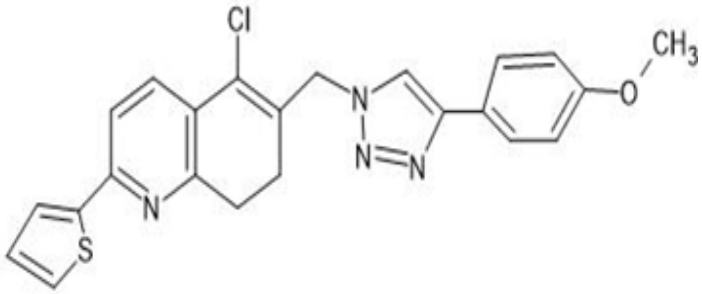
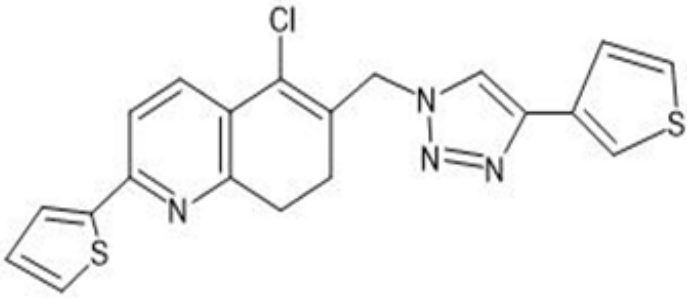
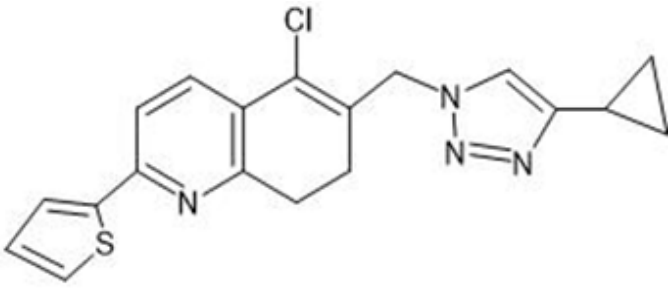
R6.	
R7.	
R8.	
R9.	
R10.	

Table1 Structures of the designed derivatives of dihydroquinoline-1,2,3-triazole

Drug-likeness and ADME Prediction

The pharmacokinetic characteristics and drug-likeness of the proposed derivatives were analyzed using the Swiss ADME program available online (http://www.swissadme.ch). The assessment of drug-likeness for the compounds was conducted following Lipinski's rule of five. This suggestion aims to set foundational standards for the drug-likeness of new molecular entities [19]. According to the rule of five, molecules should not exceed five hydrogen bond donors, have more than ten hydrogen bond acceptors, possess a logP (iLogP) greater than five, or have a molecular weight surpassing 500. Indicators of poor absorption included various traits, such as a low count of rotatable bonds (nRotb) and a topological polar surface area (TPSA) of less than 140 Å² [20]. The pharmacokinetic factors assessed encompass molar refractivity (MR), the logarithm of skin permeability (logKp), the ability to penetrate the blood-brain barrier (BBB), status as a substrate for permeability glycoprotein (Pgp), and gastrointestinal (GI) absorption.

Analysis of Docking

All of the ligands underwent molecular docking, which was considered successful because every ligand was positioned inside the receptor's active site. For additional examination, the ten molecules with the highest estimated free energy of binding (EFEB) scores were chosen. The protein-ligand complexes of these high-scoring molecules were examined for interactions, the orientation of the docked compounds, and the interacting residues in the active site were noted. The ten molecules that were selected had EFEB values ranging from -11.2 to -8.2. [Table 2]. The top-scoring molecule, A1, is interacting significantly with all of the GLN A:1701 residues in the binding cavity [Figure 2]. [First Table 2]. GLN:1633 and A2, the molecule with the second-highest EFEB score, establish hydrogen bonds [Table 2].

S.No.	Binding affinity ((kcal/mol)	Hydrogen Bonding	Hydrophobic interaction
R1.	-6.7	Tyr226, His225, Thr227, Lys188, Lys297	9
R2.	-6.7	Tyr226, Lys188, Ala293, Lys297, Gly191, His225, Thr227,	10
R3.	-6.6	Lys213, Thr215, Ser219, Thr223	9
R4.	-6.4	Val196, Ala222, Glu192	5
R5.	-6.3	Ile229, His225, Asp228, Thr227, Ser230	4
R6.	-6.2	Met281, Ala277,Leu261, Lys266, Val272, lys280	8
R7.	-6.2	Val235, Lys213, Thr215, Ser219, Thr227	8
R8.	-6.2	Ala277, Val196, Glu192	5
R9.	-6.2	Lys213, Val235, Thr215, Ser219, Thr223	7
R10.	-6.2	Met281, Ala277, Leu261, Gly262, Lys266, Val272, Lys280	7

Table 2: Binding affinity of selected potential molecules

Molecular parameters

In comparison to larger molecules, drug molecules with molecular weights near 500 Da are more readily transported, dispersed, and absorbed.[21] The physicochemical properties were assessed, indicating that the molecular weight of each selected molecule was under 500 Da, with the exception of the R1 ligand. Each molecule presented in [Table 3] demonstrated a log P value of less than 5, as illustrated in [Table 3]. Furthermore, all chosen molecules possessed fewer than 5 hydrogen bond donors and fewer than 10 hydrogen bond acceptors, as detailed in [Table 3].

Drug-likeness and ADME prediction

Chemical compounds and prospective pharmaceuticals are evaluated for drug-likeness according to the Lipinski rule of five (Ro5). Chemicals intended for pharmaceutical use should possess a molecular weight (MW) of under 500 g/mol, a logarithm of the partition coefficient (logP) of less than 5, fewer than five hydrogen bond donors (HBDs), and fewer than ten hydrogen bond acceptors (HBAs), in accordance with Lipinski's Ro5. [22] Additionally, it has been found that pharmacological flexibility and permeability correlate with a topological polar surface area (TPSA) of no more than 140

Å² and a maximum of 10 rotatable bonds (RotB), respectively. Compounds that fulfill these criteria have demonstrated improved bioavailability and pharmacokinetic properties.[23-26]

Low molecular weight (MW) molecules are lightweight and easily penetrate cell membranes. Low molecular weight (MW500) chemicals are more effectively absorbed when taken orally [27], whereas compounds with MW >500Da are absorbed through a different pathway, usually via the membrane [28]. It was found that all data [Table 3] were below 500 Da Except R1 ligand . The implicit logP (IlogP) allows a specific molecule to dissolve in both solvents while preserving its neutrality and indicates the octanol/water partition coefficients of that molecule in two immiscible solvents. Initially, it was utilized for pharmacological and medicinal studies. IlogP aids in drug interactions with their biological targets [29] and is essential for the absorption of medications in the oral cavity [27]. Octanol's combined hydrophilic and lipophilic qualities were thought to make it an excellent mimic of the features of phospholipid membranes [30]. Lipinski's rule of five indicated that the expected IlogP values (Table 3) were below five (3.68-4.28). As a result, the generated derivatives ought to have high absorption levels. Any heteroatom with at least one bound hydrogen atom is a hydrogen bond acceptor. The sum of these heteroatoms (N and O atoms) should be less than 10 ac, according to the Lipinski rule of five [27].

The H-bond acceptors for the chosen compounds ranged from 3 to 9, as [Table 3] demonstrates, which is lower than the highest limit that Ro5 anticipated. The following is the H-bond donor (HBD) count: Any heteroatom with a formal positive charge, including the oxygens linked to it, is a hydrogen bond donor, except for pyrrole, nitrogen, halogens, sulfur, heterochromatic oxygen, and higher oxidation states of nitrogen, phosphorus, and sulfur. According to the Ro5, the total number of hydrogen bond donors (the sum of the OH and NH groups) should be less than or equal to five. As can be seen in [Table 3], every HBD value that was acquired was less than 5.

Both HBA and HBD were deemed significant because of their capacity to prevent oral absorption and their ability to cooperate with other substances and macromolecules [27].

The total polar atoms (oxygen, nitrogen, and their related hydrogens) on a molecule's surface are called its TPSA, and they are calculated by adding up all of the polar components [31]. Predicting drug transport attributes such intestinal absorption [32] and BBB penetration is the aim of the TPSA. In medicinal chemistry, TPSA has become well-known for virtual screening and ADME property prediction [33]. Good blood-brain barrier penetration is indicated when the quantitative value of TPSA is less than 60 Å2 [34]. It was discovered that the TPSA values of the suggested derivatives (Table 3) varied between 71.84-100.08 Å2.

S.No.	MW	iLOGP	#Rotatablebonds	#H-bondacceptors	#H-bonddonors	Lipinski#violations	TPSA
R1	540.91	4.28	6	9	0	2	71.84
R2	488.91	4.12	6	7	0	0	81.07
R3	410.94	3.9	4	3	0	0	100.08
R4	472.91	3.98	5	6	0	1	71.84
R5	440.9	3.79	4	5	0	1	71.84
R6	473.81	4.17	4	3	0	1	71.84
R7	422.91	4.04	4	4	0	0	71.84
R8	434.94	4.08	5	4	0	0	81.07
R9	410.94	3.9	4	3	0	0	100.08
R10	368.88	3.68	4	3	0	0	71.84

Table 3: Lipinski's and Veber parameters of the designed derivatives of dihydroquinoline-1,2,3-triazole

Because the results are below 140Å2, this indicates that intestinal absorption is good. However, because the TPSA values are higher than 60Å2, the BBB assessment indicates that the recommended derivatives do not successfully cross the blood-brain barrier (Table 4). The total number of rotatable bonds (RBN) is the sum of all the bonds that can freely spin around themselves. These non-ring single bonds are joined by a non-terminal heavy atom, or non-hydrogen. Oral availability of compounds with less than 10 rotatable bonds has been observed [35]. The proposed compounds exhibited a high oral bioavailability, as evidenced by the fact that their number of rotatable bonds was less than five Except R1 and R2 ligands.

The pharmacokinetic properties of the designed compounds that are investigated in the insilico ADME studies include molar refractivity (MR), log of skin permeability (log Kp), blood-brain barrier (BBB) penetration, permeability glycoprotein (Pgp) substrate, gastrointestinal (GI) absorption, and cytochrome P450 (CYP450) enzymes: CYP1A2, CYP2C9, and CYP2C19 inhibitors. The reciprocal of a mole of a sub-

stance's volume is called molar refractivity (MR). A material's total polarizability per mole is associated with its molar refractivity. Molar refractivity data can be used to determine the electronic polarizability of certain ions in solution [36].

The results of the refractive index can be used to describe molecular interactions in solution. The molar reactivity value should fall between 40 and 130 for the best oral bioavailability and absorption [37]. Adequate intestinal absorption and oral bioavailability are demonstrated by acceptable molar refractivity values in conjunction with the number of rotatable bonds [38]. The target compound's MR values range from 101.73 to 124.72 m3/mol. This implies that the recommended substances have adequate intestinal absorption and oral bioavailability. Permeability is crucial to the development of therapeutics because it predicts metabolite absorption, distribution, metabolism, and excretion (ADME).

The ability of molecules to penetrate the outer layer of the skin is measured by skin permeability (Kp) [39]. Assessments of a compound's biological absorption through the skin are included in the Kp, which has been used as a source of data for threat assessment on the skin [40]. The log Kp values of all the generated compounds were determined to be within the permissible range of -6.29 to -5.26 (Table 4) [41]. The blood-brain barrier (BBB) is a microvascular endothelial layer of cells that envelops the central nervous system (CNS).

The BBB functions as a structural and chemical barrier that prevents many medications from accessing the brain, making the use of recently produced medications to treat brain illnesses or other conditions related to the brain pointless. It has been demonstrated that certain possible therapeutic chemicals present a significant obstacle to treatment research for illnesses of the central nervous system if there is little or no BBB penetration [42–43]. None of our proposed derivatives possessed BBB permeability, according to the results of the BBB permeability test (Table 4).

S.No.	MR	logKp(cm/s)	Glabsorption	BBBpermeant	Pgpsubstrate	CYP1A2inhibitor	CYP2C1Ginhibitor	CYP2CGinhibitor
R1	124.71	-5.31	Low	No	Yes	Yes	No	No
R2	121.38	-5.41	Low	No	Yes	Yes	No	Yes
R3	112.58	-6	High	No	Yes	Yes	Yes	Yes
R4	119.7	-5.53	Low	No	Yes	Yes	No	Yes
R5	114.62	-5.82	Low	No	Yes	Yes	Yes	Yes
R6	124.72	-5.26	Low	No	Yes	Yes	Yes	Yes
R7	114.66	-5.78	High	No	Yes	Yes	Yes	Yes
R8	121.19	-5.94	High	No	Yes	Yes	Yes	Yes
R9	112.58	-6	High	No	Yes	Yes	Yes	Yes
R10	101.73	-6.29	High	No	Yes	Yes	No	Yes

CYP2C19 inhibitors absorption, blood-brainbarrier (BBB) penetration, Molar refractivity (MR), gastrointestinal (GI), cytochrome P450 (CYP450) enzymes:CYP1A2,CYP2C9, permeabilityglycoprotein (Pgp)substrate and log of skin permeability (logKp)

Table 4 Pharmacokinetics properties of the designed derivatives of dihydroquinoline-1,2,3-triazole

Conclusion

SwissADME, Autodock vina, and Mgl Tool were used to do the pharmacokinetics and docking studies of the ten (10) substituted derivatives of dihydroquinoline-1,2,3-triazole. It is a digitally new study of a selected molecule that supports green chemistry because no environmentally hazardous components were created. Since none of the drugs violated Lipinski's rule of five, their pharmacokinetic characteristics are sound. The compound's activity could be attributed to the hydrogen bond and other hydrophobic interactions within the molecule. The derivatives may be used to treat tuberculosis because of their remarkable pharmacokinetic properties.

Authors' Declaration Statements

Ethics Approval and Consent to Participate

Not applicable (as no human or animal subject was used in the investigation)

Competing Interests

Not declared.

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Refrences

1. W.H. Organization, others, tuberculosis fact sheet (No. 104. 2000. Site Accessed Www Who Intmediacentrefactsheetswho104enindex Html. (2016).
2. Adeniji, Shola Elijah, Sani Uba, and Adamu Uzairu. "Multi-linear regression model, molecular binding interactions and ligand-based design of some prominent compounds against Mycobacterium tuberculosis." Network Modeling Analysis in *Health Informatics and Bioinformatics* 9, no. 1 (2020): 8.
3. Adeniji, Shola Elijah, David Ebuka Arthur, Mustapha Abdullahi, and Abdurrashid Haruna. "Quantitative structure–activity relationship model, molecular docking simulation and computational design of some novel compounds against DNA gyrase receptor." *Chemistry Africa* 3, no. 2 (2020): 391-408.
4. James CW. DNA entanglement and the action of the DNA Topoisomerases. NY: Cold pring Harbor Laboratory Press, Cold Spring Harbor; 2009. p. 245.
5. Huang, You-Yi, Jiao-Yu Deng, Jing Gu, Zhi-Ping Zhang, Anthony Maxwell, Li-Jun Bi, Yuan-Yuan Chen, Ya-Feng Zhou, Zi-Niu Yu, and Xian-En Zhang. "The key DNA-binding residues in the C-terminal domain of Mycobacterium tuberculosis DNA gyrase A subunit (GyrA)." *Nucleic acids research* 34, no. 19 (2006): 5650-5659.
6. Zhang, Ying, Katrin Post-Martens, and Steven Denkin. "New drug candidates and therapeutic targets for tuberculosis therapy." *Drug discovery today* 11, no. 1-2 (2006): 21-27.
7. Adeniji, Shola Elijah, and Olajumoke Bosede Adalumo. "Computational modeling and ligand-based design of some novel hypothetical compound as prominent inhibitors against Mycobacterium tuberculosis." *Future Journal of Pharmaceutical Sciences* 6, no. 1 (2020): 15.
8. https://patents.justia.com/patent/8865910.
9. Hafez, Hend N., Hebat-Allah Abbas, and Abdel-Rahman El-Gazzar. "Synthesis and evaluation of analgesic, anti-inflammatory and ulcerogenic activities of some triazolo-and 2-pyrazolyl-pyrido [2, 3-d]-pyrimidines." *Acta Pharm* 58, no. 4 (2008): 359-378.
10. Guan, Li-Ping, Qing-Hao Jin, Guan-Rong Tian, Kyu-Yun Chai, and Zhe-Shan Quan. "Synthesis of some quinoline-2 (1H)-one and 1, 2, 4-triazolo [4, 3-a] quinoline derivatives as potent anticonvulsants." *J Pharm Pharm Sci* 10, no. 3 (2007): 254-62.
11. Gujjar, Ramesh, Alka Marwaha, Farah El Mazouni, John White, Karen L. White, Sharon Creason, David M. Shackleford et al. "Identification of a metabolically stable triazolopyrimidine-based dihydroorotate dehydrogenase inhibitor with antimalarial activity in mice." *Journal of medicinal chemistry* 52, no. 7 (2009): 1864-1872.
12. Patel, Navin B., Imran H. Khan, and Smita D. Rajani. "Pharmacological evaluation and characterizations of newly synthesized 1, 2, 4-triazoles." *European journal of medicinal chemistry* 45, no. 9 (2010): 4293-4299.
13. Viegas-Junior, Claudio, Amanda Danuello, Vanderlan da Silva Bolzani, Eliezer J. Barreiro, and Carlos Alberto Manssour Fraga. "Molecular hybridization: a useful tool in the design of new drug prototypes." *Current medicinal chemistry* 14, no. 17 (2007): 1829-1852.
14. Oliveira Pedrosa, Michelle D., Rayssa Marques Duarte da Cruz, Jessika de Oliveira Viana, Ricardo Olimpio de Moura, Hamilton Mitsugu Ishiki, Jose Maria Barbosa Filho, Margareth FFM Diniz, Marcus Tullius Scotti, Luciana Scotti, and Francisco Jaime Bezerra Mendonca. "Hybrid compounds as direct multitarget ligands: a review." *Current topics in medicinal chemistry* 17, no. 9 (2017): 1044-1079.
15. Nguyen, William, Madeline G. Dans, Iain Currie, Jon Kyle Awalt, Brodie L. Bailey, Chris Lumb, Anna Ngo et al. "7-N-Substituted-3-oxadiazole Quinolones with Potent Antimalarial Activity Target the Cytochrome bc 1 Complex." *ACS Infectious Diseases* 9, no. 3 (2023): 668-691.
16. O. Trott, A. J. Olson, AutoDock Vina: improving the speed and accuracy of docking with a new scoring function, efficient optimization and multithreading, *Journal of Computational Chemistry* 31 (2010),455-461, DOI 10.1002/jcc.21334
17. Guleria, Vandana, Tarun Pal, Bhanu Sharma, Shweta Chauhan, and Varun Jaiswal. "Pharmacokinetic and molecular docking studies to design antimalarial compounds targeting Actin I." *International journal of health sciences* 15, no. 6 (2021): 4.
18. Kalliokoski, Tuomo, Heikki S. Salo, Maija Lahtela-Kakkonen, and Antti Poso. "The effect of ligand-based tautomer and protomer prediction on structure-based virtual screening." *Journal of Chemical Information and Modeling* 49, no. 12 (2009): 2742-2748.
19. Lipinski, Christopher A. "Drug-like properties and the causes of poor solubility and poor permeability." *Journal of pharmacological and toxicological methods* 44, no. 1 (2000): 235-249.
20. Veber, Daniel F., Stephen R. Johnson, Hung-Yuan Cheng, Brian R. Smith, Keith W. Ward, and Kenneth D. Kopple. "Molecular properties that influence the oral bioavailability of drug candidates." *Journal of medicinal chemistry* 45, no. 12 (2002): 2615-2623.
21. Srimai, Vuppala, Macha Ramesh, Konda Satya Parameshwar, and Tigulla Parthasarathy. "Computer-aided design of selective Cytochrome P450 inhibitors and docking studies of alkyl resorcinol derivatives." *Medicinal Chemistry Research* 22, no. 11 (2013): 5314-5323.
22. Athar, Mohd, Alfred Ndeme Sona, Boris Davy Bekono, and Fidele Ntie-Kang. "Fundamental physical and chemical concepts behind “drug-likeness” and “natural product-likeness”." *Physical Sciences Reviews* 4, no. 12 (2019).

23. Veber, Daniel F., Stephen R. Johnson, Hung-Yuan Cheng, Brian R. Smith, Keith W. Ward, and Kenneth D. Kopple. "Molecular properties that influence the oral bioavailability of drug candidates." *Journal of medicinal chemistry* 45, no. 12 (2002): 2615-2623.
24. Ali, Imran, Sofi Danish Mukhtar, Ming Fa Hsieh, Zeid A. Alothman, and Abdulrahman Alwarthan. "Facile synthesis of indole heterocyclic compounds based micellar nano anti-cancer drugs." *RSC advances* 8, no. 66 (2018): 37905-37914.
25. Chagas, Caroline Manto, Sara Moss, and Laleh Alisaraie. "Drug metabolites and their effects on the development of adverse reactions: Revisiting Lipinski's Rule of Five." *International journal of pharmaceutics* 549, no. 1-2 (2018): 133-149.
26. Huang, Han, Chen-Liang Chu, Lin Chen, and Dong Shui. "Evaluation of potential inhibitors of squalene synthase based on virtual screening and in vitro studies." *Computational Biology and Chemistry* 80 (2019): 390-397.
27. Lipinski, Christopher A. "Lead-and drug-like compounds: the rule-of-five revolution." Drug discovery today: *Technologies* 1, no. 4 (2004): 337-341.
28. Tan, Derek S. "Current progress in natural product-like libraries for discovery screening." Combinatorial chemistry & high throughput screening 7, no. 7 (2004): 631-643.
29. Gleeson, M. Paul, Anne Hersey, Dino Montanari, and John Overington. "Probing the links between in vitro potency, ADMET and physicochemical parameters." *Nature reviews Drug discovery* 10, no. 3 (2011): 197-208.
30. Liu, Xiangli, Bernard Testa, and Alfred Fahr. "Lipophilicity and its relationship with passive drug permeation." *Pharmaceutical research* 28, no. 5 (2011): 962-977.
31. Ertl, Peter, Bernhard Rohde, and Paul Selzer. "Fast calculation of molecular polar surface area as a sum of fragment-based contributions and its application to the prediction of drug transport properties." *Journal of medicinal chemistry* 43, no. 20 (2000): 3714-3717.
32. Li, Shoufeng, Handan He, Lakshman J. Parthiban, Hequn Yin, and Abu TM Serajuddin. "IV-IVC considerations in the development of immediate-release oral dosage form." *Journal of pharmaceutical sciences* 94, no. 7 (2005): 1396-1417.
33. Strazielle, Nathalie, and Jean-François Ghersi-Egea. "Factors affecting delivery of antiviral drugs to the brain." *Reviews in medical virology* 15, no. 2 (2005): 105-133.
34. Prasanna, Sivaprakasam, and Robert J. Doerksen. "Topological polar surface area: a useful descriptor in 2D-QSAR." *Current medicinal chemistry* 16, no. 1 (2009): 21-41.
35. Maximo da Silva, Marciane, Marina Comin, Thiago Santos Duarte, Mary Ann Foglio, João Ernesto De Carvalho, Maria do Carmo Vieira, and Anelise Samara Nazari Formagio. "Synthesis, antiproliferative activity and molecular properties predictions of galloyl derivatives." Molecules 20, no. 4 (2015): 5360-5373.
36. Veber, Daniel F., Stephen R. Johnson, Hung-Yuan Cheng, Brian R. Smith, Keith W. Ward, and Kenneth D. Kopple. "Molecular properties that influence the oral bioavailability of drug candidates." *Journal of medicinal chemistry* 45, no. 12 (2002): 2615-2623.
37. Deosarkar SD, Pawar MP, Sawale RT, Hardas AR, Kalyankar TM (2015) Solvent effects on molar refraction and polarizability of 4-amino-5-chloro-N-(2 (diethylamino)ethyl)-2 methoxybenzamide hydrochloride hydrate solutions at 300C. *J Chem Pharmaceut Res* 7(5):1107–1110
38. Banik, Ishani, and Mahendra Nath Roy. "Study of solute–solvent interaction of some bio-active solutes prevailing in aqueous ascorbic acid solution." *Journal of Molecular Liquids* 169 (2012): 8-14.
39. Ibrahim, Zakari Ya'U., Adamu Uzairu, Gideon Shallangwa, and Stephen Abechi. "Molecular docking studies, drug-likeness and in-silico ADMET prediction of some novel β-Amino alcohol grafted 1, 4, 5-trisubstituted 1, 2, 3-triazoles derivatives as elevators of p53 protein levels." *Scientific African* 10 (2020): e00570.
40. Chen, Chen-Peng, Heinz W. Ahlers, G. Scott Dotson, Yi-Chun Lin, Wei-Chen Chang, Andrew Maier, and Bernard Gadagbui. "Efficacy of predictive modeling as a scientific criterion in dermal hazard identification for assignment of skin notations." *Regulatory Toxicology and Pharmacology* 61, no. 1 (2011): 63-72.
41. Dotson, G. Scott, Chen-Peng Chen, Bernard Gadagbui, Andrew Maier, Heinz W. Ahlers, and Thomas J. Lentz. "The evolution of skin notations for occupational risk assessment: a new NIOSH strategy." *Regulatory Toxicology and Pharmacology* 61, no. 1 (2011): 53-62.
42. Gaur, Rashmi, Jay Prakash Thakur, Dharmendra K. Yadav, Deepak Singh Kapkoti, Ram Kishor Verma, Namita Gupta, Feroz Khan, Dharmendra Saikia, and Rajendra Singh Bhakuni. "Synthesis, antitubercular activity, and molecular modeling studies of analogues of isoliquiritigenin and liquiritigenin, bioactive components from Glycyrrhiza glabra." *Medicinal Chemistry Research* 24, no. 9 (2015): 3494-3503.
43. Ibrahim, Zakari Ya'U., Adamu Uzairu, Gideon Adamu Shallangwa, and Stephen Eyije Abechi. "Pharmacokinetic predictions and docking studies of substituted aryl amine-based triazolopyrimidine designed inhibitors of Plasmodium falciparum dihydroorotate dehydrogenase (PfDHODH)." *Future Journal of Pharmaceutical Sciences* 7, no. 1 (2021): 133.

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