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3D-QSAR and Molecular Docking Studies of Quinoline based Pyrrole Derivatives by Crystal Structure of HIV-1 Reverse Transcriptase in Complex with N1-Butyl Pyrimidinedione Non-Nucleoside Inhibitor (PDB: 3LN1)

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KEYWORDS

HIV-1 reverse transcriptase; ADMET; Quinazoline; Molecular docking

ABSTRACT:

Background: The proposed approach summarizes each activity in silico research. The structure-activity correlations and pharmacological effects of compounds containing Quinazoline are examined in this study. Using a variety of computational techniques, in silico studies allow for forecasting structural changes and how they would impact the pharmacological properties as well as the efficiency of these modifications. The computational study of Quinazoline derivatives is the main topic of this article. All compounds' cytotoxicity against HIV-1 reverse transcriptase was assessed, and the outcomes showed that several of them had strong inhibitions.

Materials and Methods: The aim of this study was to investigate PDB Code:3 LAN enzyme inhibitory, and HIV-1 reverse transcriptase activities of a new series of 1H-Quinazoline derivatives, for their possible use as multi-action therapeutic agents. Molecular Design Suite was used to conduct Combi Lab investigations and 3D-QSAR. Pyrex and Biovia software was used for the molecular docking investigation.

Results: Five Derivative's i.e. Derivative's 6; Derivative's 5; Derivative's 10; Derivative's 9 and Derivative's 8 in a library of 10 compounds created using a combinatorial approach demonstrated superior projected biological activity as inflammatory than the dataset's most active molecule. These chemicals exhibited proximal contact with amino acid residues on Crystal structure of HIV-1 reverse transcriptase in complex with N1-butyl pyrimidinedione non-nucleoside inhibitor (PDB: 3LN1) in

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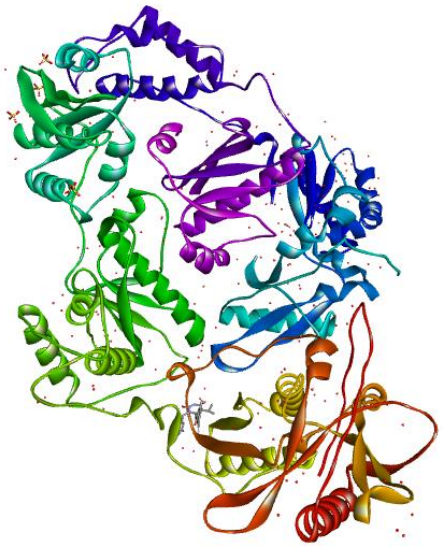
complex with N1-butyl pyrimidinedione non-nucleoside inhibitor such as Phe381, Leu-384, Tyr-385, Trp-387, Phe-518, Gly-526, Met-522, Tyr348, Val-349, Leu-352.

Conclusion: This study determined the structural elements affecting by carefully changing the substituents, ring modifications, and linker groups. The logical creation and optimization of more powerful and selective molecules is made possible by these discoveries. In contrast to the reference ligand, the current study produced more powerful Quinazolines as inhibiting compounds for Crystal structure of HIV-1 reverse transcriptase in complex with N1-butyl pyrimidinedione non-nucleoside inhibitor (PDB: 3LN1) with excellent interaction.

Pictorial Abstract:



INTRODUCTION

The exploration and subsequent synthesis of innovative hybrid molecules, characterized by a multifaceted array of pharmacological activities achievable through the modulation of a diverse spectrum of biochemical pathways, holds considerable promise in the therapeutic intervention of a wide range of pathological conditions, as it is well acknowledged that multifactorial disorders can have multiple origins[1]. Because the hazards of drug-drug interactions are reduced, this approach has distinct advantages over drug combinations or multicomponent medications, notwithstanding the enormous difficulty in designing and optimizing such molecules[2]. The synchronized combining of various advantageous moieties on similar substance, particularly for treatment of particular illness, is one of the promising developments in drug discovery[3]. The exordium for engendering avant-garde compounds exhibiting pleiotropic pharmacological effects resides optimally within the domain of pharmaceutical advantages that mitigate the exigency for polypharmacy, encompassing therapeutic modalities that concurrently attenuate iatrogenic sequelae, abrogate symptomatic manifestations, or potentiate salutary outcomes via adjuvant therapeutic mechanisms[4]. Even if they have a lot of potential for therapeutic use, this is important to assess possibility of adverse consequences. High atomic weight is a common characteristic of dual inhibitors, which may lessen the likelihood of their therapeutic effects. Consequently, while designing dual inhibitors, the safety profiles and pharmacokinetic characteristics must be carefully taken into account[5]. The combination of imidazole with benzene results in the heterocyclic aromatic organic molecule known as Quinazoline. Because of their many effects of this heterocyclic nucleus, i.e., analgesic, anti-tumor, antiviral, and

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psychoactive properties, they have played a significant role in medicinal chemistry[6]. The intricate biological reaction with viral infections, which is defensive action towards immune cells[7]. In human viral infection, Crystal structure of HIV-1 reverse transcriptase in complex with N1-butyl pyrimidinedione non-nucleoside inhibitor (PDB: 3LN1) contributes to angiogenesis as well as cell division and death. One technique for figuring out how a protein and ligand interact is called molecular docking, and it explains the molecule's orientation, binding interactions, and binding energy[8]. Predicting the shared molecular characteristics those in molecular interactions with biological target and initiate response requires the use of pharmacophore methods[9-10]. The purpose of this investigation was to determine the molecular interactions in Quinazolines analogues and Crystal structure of HIV-1 reverse transcriptase in complex with N1-butyl pyrimidinedione non-nucleoside inhibitor, as well as to screen the synthetic compounds' physicochemical and ADMET characteristics[11]. Additionally, pharmacophore modelling studies were used to examine distinctive traits. Since Quinazoline derivatives reported to have anti-viral features, it is necessary to demonstrate how they work[12]. To ascertain these compounds in silico inhibitory effect, were docked with Crystal structure of HIV-1 reverse transcriptase in complex with N1-butyl pyrimidinedione non-nucleoside inhibitor). As a result, in-silico research helps identify how Quinazolines work to block Crystal structure of HIV-1 reverse transcriptase in complex with N1-butyl pyrimidinedione non-nucleoside inhibitor (PDB: 3LN1) enzymes, which is what gives them their Anti-viral infection properties. HIV-1 Reverse Transcriptase enzyme is a vital defensive mechanism against all forms of physical, chemical, and viral assault[13]. When this mechanism is dysregulated, the body develops pathological conditions, such as organ rejection, autoimmune diseases, and allergies[14]. Needleman and Isakson originally described two cyclooxygenase isoenzymes in 1997. The "Inducible" enzyme, Crystal structure of HIV-1 reverse transcriptase in complex with N1-butyl pyrimidinedione non-nucleoside inhibitor (PDB: 3LN1), causes viral reactions and is triggered by a variety of events. It is currently unclear what the exact roles of a Crystal structure of HIV-1 reverse transcriptase in complex with N1-butyl pyrimidinedione non-nucleoside inhibitor (PDB: 3LN1) isoform that is solely expressed in particular brain and spinal cord areas. Numerous studies have linked Crystal structure of HIV-1 reverse transcriptase in complex with N1-butyl pyrimidinedione non-nucleoside inhibitor (PDB: 3LN1) to a range of viral illnesses gives result, also used in viral infection treatment. In order to mitigate these serious side effects, selective Crystal structure of HIV-1 reverse transcriptase in complex with N1-butyl pyrimidinedione non-nucleoside inhibitor (PDB: 3LN1), inhibitor medications were created. These medications have viral inhibitor property same as non-selective inhibitors, but they also have improved gastric safety profiles. The distinct chemical makeup of Crystal structure of HIV-1 reverse transcriptase in complex with N1-butyl pyrimidinedione non-nucleoside inhibitor (PDB: 3LN1) was associated with their adverse effects. As a result, research for selective anti-viral medications with superior safety profiles than the others anti-viral drugs on the market is still ongoing. In Crystal structure of HIV-1 reverse transcriptase in complex with N1-butyl pyrimidinedione non-nucleoside inhibitor (PDB: 3LN1), activity of inhibition synthesized derivatives were evaluated. Lastly, the synthesized compounds docked into Crystal structure of HIV-1 reverse transcriptase in complex with N1-butyl pyrimidinedione non-nucleoside inhibitor (PDB: 3LN1), site to clarify their possible method of action.

MATERIAL AND METHOD

Molecular Docking and Ligand preparation:

Preceding molecular docking, test compounds of Derivative's 1– Derivative's 10 structures and scheme of Quinazoline were given in Table 1. We optimized by using the semi-empirical approach and the ArgusLab 4.0.1 software program. Getting proteins ready We used a variety of different Crystal structure of HIV-1 reverse transcriptase in complex with N1-butyl pyrimidinedione non-nucleoside inhibitor (PDB: 3LN1), enzyme crystal structures via the RCSB for docking studies. Maestro 11.9 was used for all computational analysis. Software were installed on Dell Inc. 27-inch computer that was on Linux x86_64 as OS and has Intel Core i7-7600U CPU at 3.90 GHz x8 with 16 GB RAM and 1 TB SSD. Drug likeness, physicochemical characteristics, and ADMET of compounds were studied. The PDB supplied Ribbon composition for Crystal structure of HIV-1 reverse transcriptase in complex with N1-butyl pyrimidinedione non-nucleoside inhibitor (PDB: 3LN1). Auto dock

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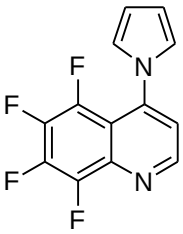
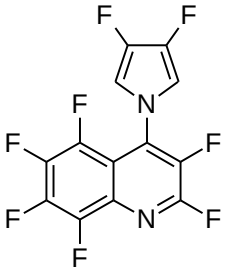
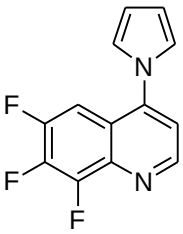
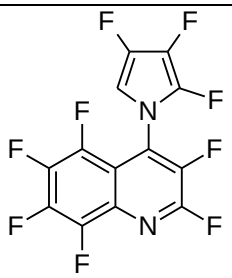
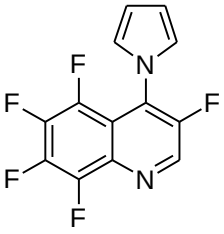
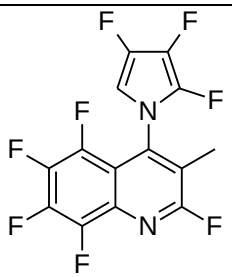
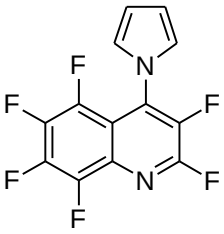
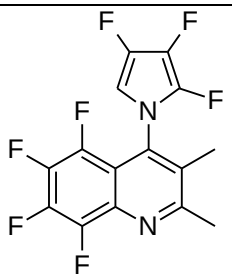
version was 1.5.6. Chain A was chosen. Hydrogen with polarity and Gasteiger charges introduced after water was removed. The compounds' 2D formula was drawn using ChemDraw Ultra 12.0. Avogadro software was used to minimize energy use. Autodock Vina was used to realize the docking process, while Discovery Studio 3.5 was used to visualize the interactions. Crystal structure of HIV-1 reverse transcriptase in complex with N1-butyl pyrimidinedione non-nucleoside inhibitor (PDB: 3LN1) crystal structures were compared to the anticipated conformations of docking data in order to optimize the docking method. Derivatives of designed compound of Quinoline based Pyrrole Derivatives were shown in table 1.

Table 1: Derivatives of designed compound of Quinoline based Pyrrole Derivatives

Derivative's Code	**Structure**	**Derivative's Code**	**Structure**
Derivative's 1		Derivative's 6	
Derivative's 2		Derivative's 7	
Derivative's 3		Derivative's 8	
Derivative's 4		Derivative's 9	

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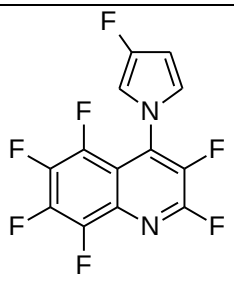
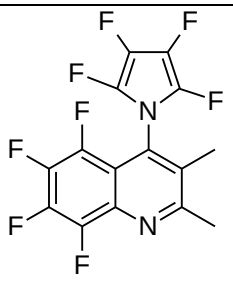
Derivative's 5		Derivative's 10	

RESULTS

Molecular docking and Lipinski's rule of five:

QSAR is one such technique that was covered drug discovery in the above session/chapter. In this above session/chapter will cover the newly developed idea of "drug-likeness" as well as the computer modelling of a number of biological and physicochemical characteristics that are crucial in turning a clinical lead into a commercially available medication. Pharmacologists and medicinal chemists have looked for beneficial drug-like chemical characteristics that produce agents with predictable oral therapeutic effectiveness. Drug development process follows Lipinski's "rule of five" which is computational and experimental method for estimating solubility, permeability. Crystal structure of HIV-1 reverse transcriptase in complex with N1-butyl pyrimidinedione non-nucleoside inhibitor (PDB: 3LN1) enzymes were docked with the drugs, and the molecular interactions between them were examined. Tables number 4 summarize interactions between chemicals with residues of dynamic amino acids, whereas Figure number 5 and 6 display the 2D - 3D conformations for molecular bindings of Derivative's 1– Derivative's 10. Computer-aided molecular design (CAMD) has traditionally concentrated on lead optimization and identification, and several creative techniques have been created to help increase the binding affinities of drug candidates to certain receptors. Those are general guideline which assesses drug-likeness and establishes whether molecule has pharmacological activity. The rule was founded on the finding that the majority of medications that work well when taken orally are tiny, somewhat lipophilic molecules. It is employed in the process of developing new drugs when pharmacologically active lead structures are gradually improved to boost their activity and selectivity while maintaining their drug-like physicochemical characteristics. Bonds rotation; H-bond acceptors; H-bond donors; Lipinski; Ghose; Veber; Egan and Muegge violations were given in Table number 2. ADMET (which stands for absorption, distribution, excretion, and toxicity) characteristics for substances are necessary to create effective oral medications. The toxicity of a ligand is thought to be required to ligand as function to effective discovery tool, and Qik-Prop produces physically relevant descriptions. The Ligprep module used for ligand preparation utilized in investigation. The protein preparation wizard utilized for protein preparation. The PDB data bank provided the X-ray crystal structures of Crystal structure of HIV-1 reverse transcriptase in complex with N1-butyl pyrimidinedione non-nucleoside inhibitor (PDB: 3LN1), The grid generated using Receptor Grid Generation Wizard. Receptor Grid Generation Wizard were given in Fig.4 Glide XP coupled the ligand with the protein, and the interactions were seen. Based on the optimal ligand-protein interaction, the scoring function assigns points. The extra-precision mode was used to assess the docking positions. The program detects steric conflicts, metal-ligation interactions, hydrophobic interactions, and hydrogen bonding. Every substance has a molecular weight between 400 and 500, which is less than 500. The compounds' computed log P values fall between 3.56-5.35. The substances being studied have donors of hydrogen bonds.

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Table 2: In silico ADMET (Absorption, Distribution, Metabolism, Excretion, and Toxicity) and Calculations of Lipinski's rule of Five and Druglikeness

Molecule	GI absorption	BBB permeant	Pgp substrate	CYP1A2 inhibitor	CYP2C19 inhibitor	CYP2C9 inhibitor	CYP2D6 inhibitor	CYP3A4 inhibitor	log Kp (cm/s)	Lipinski #violations	Ghose #violations	Veber #violations	Egan #violations	Muegge #violations	Bioavailability Score	TPSA
1	High	Yes	Yes	No	Yes	No	No	No	-5.63	0	0	0	0	0	0.55	17.82
2	High	Yes	Yes	Yes	Yes	No	No	Yes	-5.8	0	0	0	0	0	0.55	17.82
3	High	Yes	Yes	Yes	Yes	No	No	Yes	-5.76	0	0	0	0	0	0.55	17.82
4	High	Yes	Yes	Yes	Yes	No	No	Yes	-5.59	0	0	0	0	0	0.55	17.82
5	High	Yes	Yes	Yes	Yes	No	No	No	-5.62	0	0	0	0	0	0.55	17.82
6	High	No	Yes	No	Yes	No	No	No	-5.43	1	1	0	1	0	0.55	17.82
7	Low	No	Yes	No	Yes	No	No	No	-5.23	1	1	0	1	0	0.55	17.82
8	Low	No	Yes	No	Yes	No	No	No	-5.06	1	1	0	1	0	0.55	17.82
9	Low	No	Yes	No	Yes	No	No	No	-5.27	1	1	0	1	0	0.55	17.82

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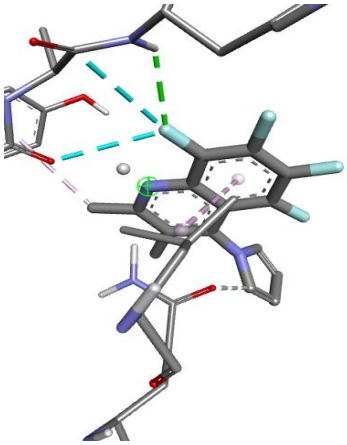
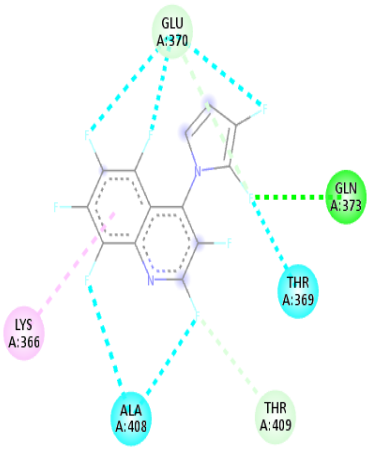
10	Low	No	Yes	No	Yes	No	No	No	-5.23	1	1	0	1	0	0.55	17.82

IN SILICO ADMET

Molecular modelling utilizes quantum techniques to evaluate possibility of interaction, including cytochrome P450s, which has role in ADME processes. QSAR techniques is commonly used for data modelling of Derivative's 1– Derivative's 10. These look for relationships between a collection of chemical and structural molecules likes GI absorption; BBB permeant; Pgp substrate; CYP1A2 inhibitor; CYP2C19 inhibitor; CYP2C9 inhibitor; CYP2D6 inhibitor; and CYP3A4 inhibitor in question and certain property using statistical methods. Choosing appropriate mathematical method, appropriate chemical descriptors for ADMET endpoint, sizable enough collection of data pertaining with same endpoint for model validation are all essential components of effective prediction models for ADMET parameters. Good ADMET property prediction techniques are becoming more and more necessary to achieve two main goals. In order to lower the risk, novel compounds libraries should be designed first. Secondly, screening and testing should be optimized by focusing on the most promising compounds. Predicting characteristics like oral absorption, bioavailability, BBB penetration, clearance, and Vd (for frequency) which give information about dosage quantity and frequency is our goal. Molecular modelling and data modelling are the two categories of computational techniques that are employed. Recent developments in the prediction of ADME-related physicochemical qualities (like lipophilicity), ADME properties (like absorption), and toxicity problems (like drug–drug interactions) are discussed in this article see Table number 2. During the next ten years or so, automated medium and HTS in-vitro tests will be employed.

Table 3: Docking Poses 2D and 3D:

Compound Code	2D Images	3D Images
Derivative's 1		

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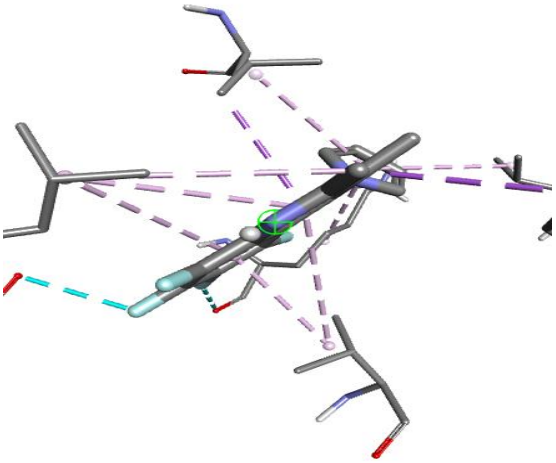
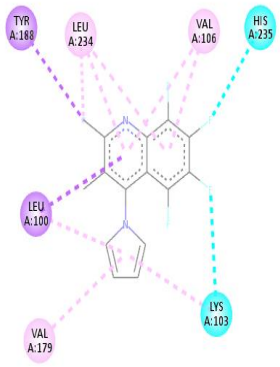
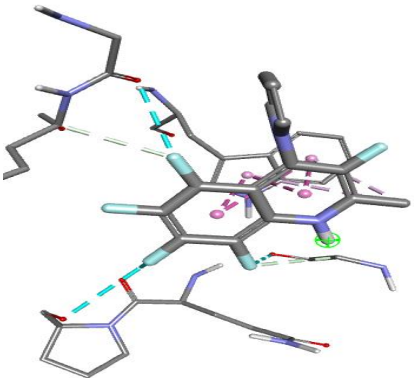
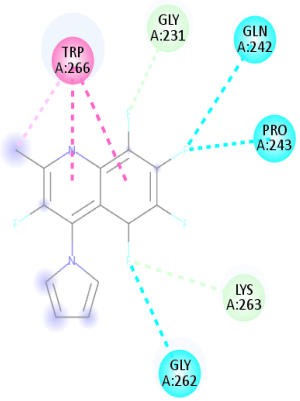
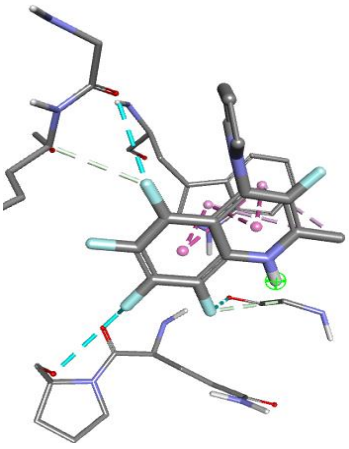
Derivative's 2		
Derivative's 3		
Derivative's 4		

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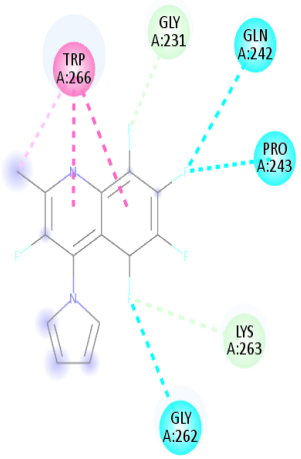
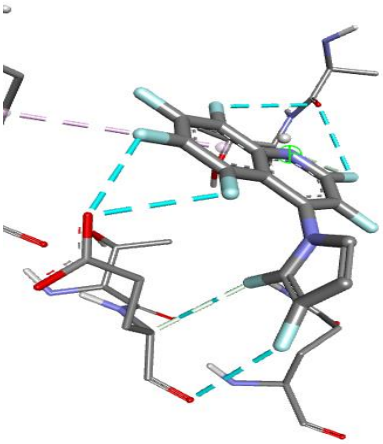
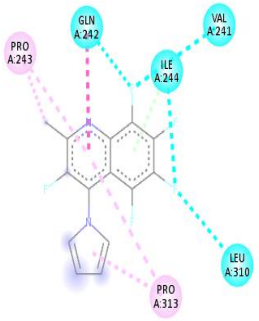
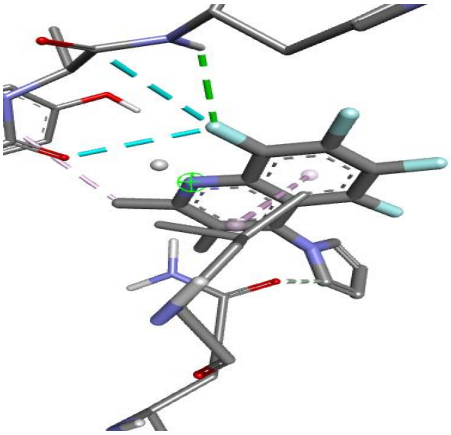
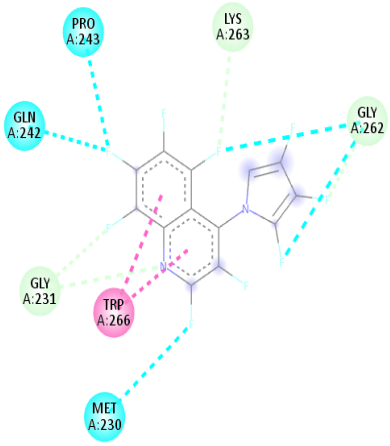
		
Derivative's 5		
Derivative's 6		

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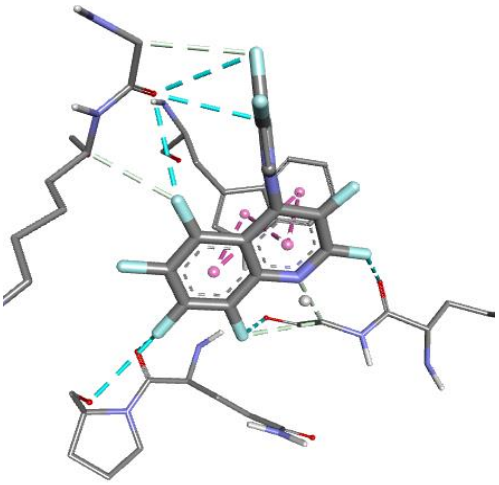
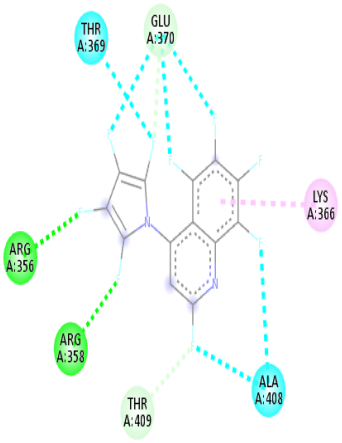
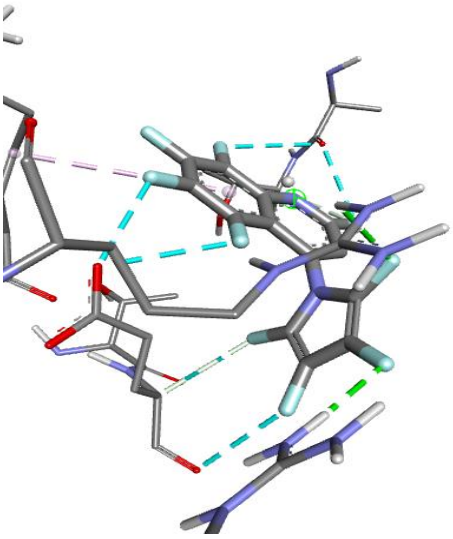
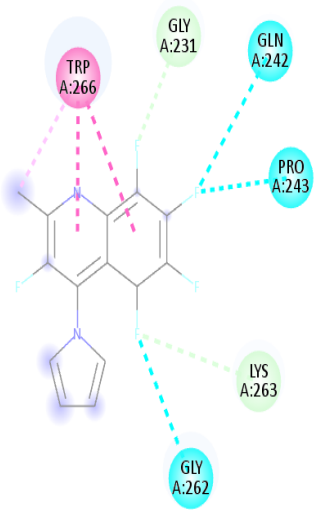
Derivative's 7		
Derivative's 8		
Derivative's 9		

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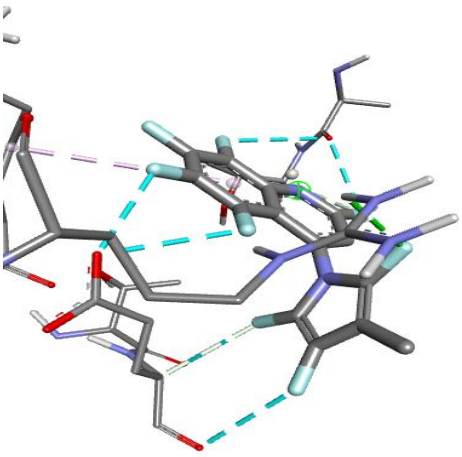
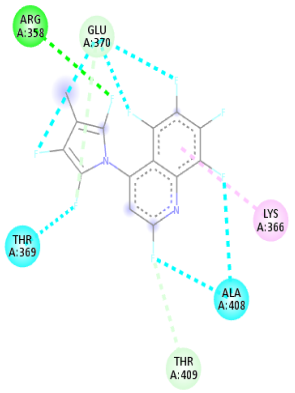
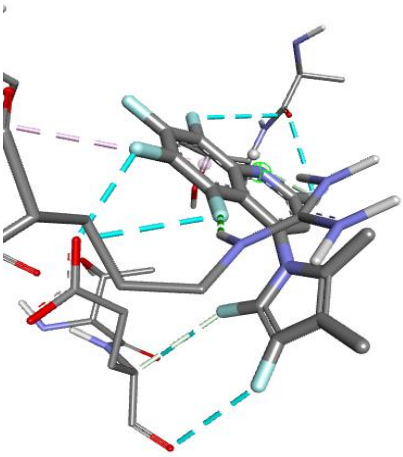
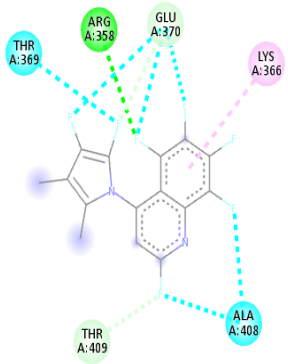
		
Derivative's 10		

DISCUSSION

Analogues with best interactions and far from zero auto dock score determined as best conformation. All of the "compounds had molecular weights less than 500," according to data warrior results, suggesting that they will bind action site. To have a good in vivo response, pharmacodynamics and pharmacokinetic characteristics must be balanced. Further details on medication dose and regimen are also provided by ADMET. According to "Lipinski's rule of five", an oral medication is selected if its molecular weight is < 500, hydrogen bond donors is less than five, hydrogen bond acceptors is less than ten, and log P value less than five. Oral bioavailability depends on molecular flexibility, which is shown by the number of rotatable bonds. Additionally, as TPSA is indirectly related to percentage absorption, it suggested that used as 3D descriptor in number of hydrogen bonding groups. All drugs had LogP below 5, which indicates excellent penetration and absorption across cell membranes. Table 1 provides various derivatives of Quinazoline which specifics on the "binding energies and hydrogen bonds" of Derivative's 1– Derivative's 10. Furthermore, the dock score values of all the produced compounds ranged from 9.5 and 8.5 kcal/mol, suggesting their binding energies lower to Quinazoline, which has "binding energy" of 9.5 kcal/mol. Interactions towards

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Crystal structure of HIV-1 reverse transcriptase in complex with N1-butyl pyrimidinedione non-nucleoside inhibitor (PDB: 3LN1) revealed that they have anti-viral properties. A:ARG356: HH22;A:ARG358:HH21;A:GLU370N;A:THR409;A:THR369;A:GLU37;A:GLU370;A:ARG358:HH21;A:GLU370;A:LYS263;A:GLY231;A:GLN242;A:PRO243;A:GLY262;A:TRP266;A:TRP266;A:TRP266;A:TRP266; A:TRP266 were active amino acids in Crystal structure of HIV-1 reverse transcriptase in complex with N1-butyl pyrimidinedione non-nucleoside inhibitor (PDB: 3LN1). Derivative's 5 and Derivative's 6 demonstrated Pi-Pi stacking to A:LYS263; A:GLY231;A:GLN242; A:PRO243;A:GLY262; A:TRP266;A:TRP266; A:TRP266;A:TRP266; A:TRP266 via the Quinazoline and H-bond with Ser-530 via nitrogen of the Quinazoline ring. Derivative's 10 demonstrated Pi-Pi stacking with Tyr385 via the Quinazoline ring and hydrogen bonding with Ser530. Derivative's 10 demonstrated Pi-Pi stacking with A:ARG356: HH22;A:ARG358:HH21; A:GLU370N; A:THR409; A:THR369; A:GLU37; A:GLU370; A:ARG358:HH21; A:GLU370 via benzene ring and H-bond with Met-522 via nitrogen. Comparing the 10 Quinazoline derivatives to the standard drug, Derivative's 10 and Derivative's 9 had a satisfactory docking score of -8.572 kcal/mol. A: ARG356:HH22; A: ARG358:HH21; A: GLU370N; A: THR409; A:THR369; A:GLU37; A:GLU370; A:ARG358:HH21; A:GLU370, were active amino acids in the enzyme Crystal structure of HIV-1 reverse transcriptase in complex with N1-butyl pyrimidinedione non-nucleoside inhibitor (PDB: 3LN1) enzymes. Derivative's 5 demonstrated H-Bond with A: THR409; A: THR369;A:GLU370;A:GLU370;A:GLU370;A:ALA408;A:ALA408;A:LYS366 via benzene. Derivative's 10 demonstrated Pi-cation interaction to A:GLY231;A:GLY262;A:LYS263;A:MET230;A:GLY231;A:GLN242;A:PRO243;A:GLY262;A:GLY262;A:GLY262;A:TRP266 via Quinazoline and Pi-pi stacking with Tyr-385 and Trp-387 via benzene. Derivative's 9 demonstrated H-bond with A: ARG356:HH22; A: ARG358:HH21;A:GLU370N;A:THR409;A:THR369;A:GLU37;A:GLU370;A:ARG358:HH21;A:GLU370: and Ser-530 via Quinazoline and Pi-Pi stacking with Tyr-385. Comparing 16 Quinazoline derivatives to the standard drug (-10.099 kcal/mol), Derivative's 5, Derivative's 6, Derivative's 5, Derivative's 9 and Derivative's 10 showed elevated docking scores, from -9.25 to -9.51 kcal/mol (Table 5). Compound Derivative's 5's binding affinity score with Crystal structure of HIV-1 reverse transcriptase in complex with N1-butyl pyrimidinedione non-nucleoside inhibitor (PDB: 3LN1)is -56.79 kcal/mol, whereas compound Derivative's 6 binding score with Crystal structure of HIV-1 reverse transcriptase in complex with N1-butyl pyrimidinedione non-nucleoside inhibitor (PDB: 3LN1) is -60.27 kcal/mol. Late-stage drug attrition may now be decreased and the most promising compounds can be found using in silico ADME screens. They should thus have high oral absorption; nevertheless, this quality cannot be used to explain variances in bioactivity. Additionally, the compounds' oral absorption percentage ranged from 70.69 to 73.87%, indicating high ADME. Their TPSA values were 101.3 and 104.80 A2 (140 A2), respectively, and rotatable bonds ranged in 7 to 8 (<10). It is generally accepted that a molecule that is soluble in water and satisfies Lipinski's and Veber's criteria is said to possess both lipophilicity and hydrophilicity. Interactions towards Crystal structure of HIV-1 reverse transcriptase in complex with N1-butyl pyrimidinedione non-nucleoside inhibitor (PDB: 3LN1) enzymes revealed that they have anti-viral properties. A:GLY231;A:GLY262;A:LYS263;A:MET230;A:GLY231;A:GLN242;A:PRO243;A:GLY262;A:GLY262;A:GLY262;A:TRP266 were active amino acids in Crystal structure of HIV-1 reverse transcriptase in complex with N1-butyl pyrimidinedione non-nucleoside inhibitor (PDB: 3LN1)enzymes. Derivative's 9 demonstrated Pi-cation interaction to A:PRO243; A: GLY262; A:TRP266; A:TRP266; A:TRP266; A:TRP266; A:TRP266; A:TRP266 via Quinazoline and Pi-pi stacking with Tyr-385 and Trp-387 via benzene. Derivative's 10 demonstrated H-bond with A: LYS263; A: GLY231; A: GLN242; A:PRO243; A: GLY262; A: TRP266; A: TRP266; A:TRP266; A:TRP266; A:TRP266 via Quinazoline and Pi-Pi stacking with Tyr-385. Comparing 10 Quinazoline derivatives to the standard drugs (-10.099 kcal/mol), Late-stage drug attrition may now be decreased and the most promising compounds can be found using in silico ADME screens. To have a good in vivo response, pharmacodynamics and pharmacokinetic characteristics must be balanced. Further details on medication dose and regimen are also provided by ADMET.

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Table 4: The active amino residues, bond length, bond category, bond type, ligand energies, and docking scores.

Name	Distance	Category	Type	Docking Score
Derivative's 5				
A:LYS263	2.68372	Hydrogen Bond;Halogen	H-Donor;Halogen Acceptor	-9.2
A:GLY231	3.05367	Hydrogen Bond;Halogen	H-Donor;Halogen Acceptor	
A:GLN242	3.64144	Hydrogen Bond;Halogen	H-Donor;Halogen Acceptor	
A:PRO243	3.10072	Halogen	H-Donor;Halogen Acceptor	
A:GLY262	3.20925	Halogen	Pi-Orbitals	
A:TRP266	2.98246	Halogen	Halogen Acceptor	
A:TRP266	3.26362	Halogen	Halogen Acceptor	
A:TRP266	3.47908	Halogen	Halogen Acceptor	
A:TRP266	3.21119 5.32245	Halogen	Halogen Acceptor	
A:TRP266	5.32245	Halogen	Halogen Acceptor	
A:TRP266	2.98246	Hydrophobic	Halogen Acceptor	
Derivative's 8				
A:GLY231	3.16768	Hydrogen Bond;Halogen	H-Donor;Halogen Acceptor	-8.5
A:GLY262	3.36877	Hydrogen Bond;Halogen	H-Donor;Halogen Acceptor	
A:LYS263	3.22901	Halogen	H-Donor;Halogen Acceptor	
A:MET230	3.02892	Halogen	Pi-Orbitals	
A:GLY231	3.42816	Halogen	Halogen Acceptor	
A:GLN242	3.42399	Halogen	Halogen Acceptor	
A:PRO243	3.12308	Halogen	Halogen Acceptor	

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A:GLY262	3.5938	Hydrophobic	Pi-Orbitals	
A:GLY262	3.6142	Hydrophobic	Pi-Orbitals	
A:GLY262	3.96001	Hydrophobic	Pi-Orbitals	
A:TRP266	4.06301	Hydrophobic	Pi-Orbitals	
Derivative's 9				
A:ARG356:HH22 -	2.19424	Conventional Hydrogen Bond;Halogen (Fluorine)	-Donor;Halogen Acceptor	-8.3
A:ARG358:HH21 -	2.72106	Conventional Hydrogen Bond;Halogen (Fluorine)	H-Donor;Halogen Acceptor	
A:GLU370N	3.05127	Carbon Hydrogen Bond;Halogen (Fluorine)	H-Donor;Halogen Acceptor	
A:THR409	3.64844	Carbon Hydrogen Bond;Halogen (Fluorine)	H-Donor;Halogen Acceptor	
A:THR369	3.12689	Halogen (Fluorine)	Halogen Acceptor	
A:GLU37	3.20148	Halogen (Fluorine)	Halogen Acceptor	
A:GLU370	2.96961	Halogen (Fluorine)	Halogen Acceptor	
Derivative's 1				
A:ARG358:HH21 -	3.05326	Hydrogen Bond;Halogen	H-Donor;Halogen Acceptor	-9.0
A:GLU370:	3.15947	Hydrogen Bond;Halogen	H-Donor;Halogen Acceptor	
A:THR409	3.28605	Hydrogen Bond;Halogen	H-Donor;Halogen Acceptor	
A:THR369:		Halogen	Halogen Acceptor	
A:GLU370	2.98008	Halogen	Halogen Acceptor	

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A:GLU370:	3.39019	Halogen	Halogen Acceptor	
A:GLU370:	3.55305	Halogen	Halogen Acceptor	
A:ALA408	3.16144	Halogen	Halogen Acceptor	
A:ALA408:	5.33853	Halogen	Halogen Acceptor	
A:LYS366	3.55035	Halogen	Halogen Acceptor	
Derivative's 10				
A:ARG358:HE -	2.67213	Hydrogen Bond;Halogen	H-Donor;Halogen Acceptor	-9.2
A:GLU370:CA -	3.05	Hydrogen Bond;Halogen	H-Donor;Halogen Acceptor	
A:THR409:CA -	3.44084	Hydrogen Bond;Halogen	H-Donor;Halogen Acceptor	
A:THR369:	3.16615	Halogen	H-Donor;Halogen Acceptor	
A:GLU370:	3.25502	Halogen	Halogen Acceptor	
A:GLU370:OE2 -	2.98927	Halogen	Halogen Acceptor	
A:ALA408	3.55748	Halogen	Halogen Acceptor	
A:LYS366	3.58091	Hydrophobic	Halogen Acceptor	

CONCLUSION

The ligands Derivative's 10 and Derivative's 9 had high docking scores with Crystal structure of HIV-1 reverse transcriptase in complex with N1-butyl pyrimidinedione non-nucleoside inhibitor (PDB: 3LN1) (-9.572 kcal/mol), respectively, out of the 10 Quinazoline derivatives. Furthermore, the pharmacophoric characteristics that underlie their biological action were also disclosed. As a result, these in silico methods have helped identify binding and affinity between Crystal structure of HIV-1 reverse transcriptase in complex with N1-butyl pyrimidinedione non-nucleoside inhibitor (PDB: 3LN1) enzyme & Quinazolines, responsible for anti-viral properties. To ascertain their anti-viral properties, Quinazoline analogues were docked with Crystal structure of HIV-1 reverse transcriptase in complex with N1-butyl pyrimidinedione non-nucleoside inhibitor (PDB: 3LN1) enzymes. All of the compounds' values were discovered to be within the typical range, and Lipinski's rule of five was not broken. Therefore, it is anticipated that the compounds will have a high oral bioavailability.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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ABBREVIATIONS:

Sr.No.	Abbreviation	Full Name
1	mg/kg	Milligram/ kilograms
2	sec	seconds
3	kcal	kilocalorie
4	Mol.Wt	Molecular Weight
5	gm	Gram
6	LEU	Leucine
7	THR	Threonine
8	ALA	Alanine
9	MET	Methionine
10	PHE	Phenylalanine
11	WHO	World health association
12	Log P	partition coefficient

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