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Development of Novel Sulfonamide-Based Pyrazole-Clubbed Pyrazoline Derivatives: Synthesis, Biological Evaluation, and Molecular Docking Study

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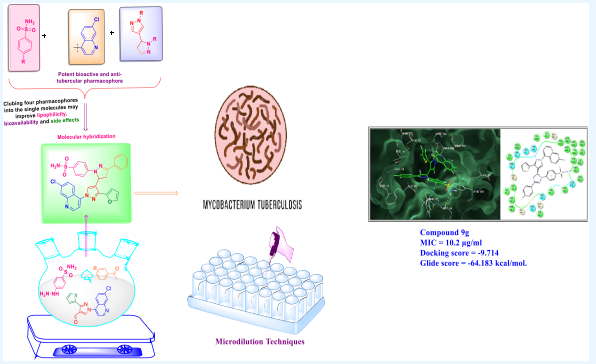
ABSTRACT: To overcome the multidrug-resistant tuberculosis (MDR-TB) problem, we reported the synthesis of novel sulfonamide-based pyrazole-clubbed pyrazoline derivatives (**9a-p**) by reaction of 1-(7-chloroquinolin-4-yl)-3-(thiophene/furan-2-yl)-1*H*-pyrazole-4-carbaldehyde chalcone derivatives (**8a-p**) and 4-hydrazinylbenzenesulfonamide (**2**) in the presence of a catalytic amount of Conc. HCl and ethanol are used as a solvent. Newly synthesized compounds were tested against the *Mycobacterium tuberculosis* H_{37}Rv strain, wherein compounds **9g**, **9h**, **9i**, **9j**, **9m**, and **9n** were found to be the most potent. The structures of the newly synthesized analogues were determined by different spectroscopic techniques like ESI-MS, FT-IR, NMR, and UV methods. Additionally, molecular docking studies of the active site of mycobacterial InhA resulted in well-aggregated elucidations for these compounds with a binding strength in the range of **−9.714** to **−8.647**. Compound 4-(1′-(7-chloroquinolin-4-yl)-5-(4-fluorophenyl)-3′-(thiophen-2-yl)-3,4-dihydro-1′*H*,2*H*-[3,4′-bipyrazol]-2-yl)benzenesulfonamide (**9g**) shows excellent antitubercular activity against M. tuberculosis H_{37}Rv, achieving an MIC of **10.2 μg/mL** and **99%** inhibition with a docking score of **−9.714** and a Glide energy of **−64.183 kcal/mol**. In silico ADMET predictions indicated the drug-likeness of synthesized novel molecules.



INTRODUCTION

Tuberculosis (TB) is caused by the *Mycobacterium tuberculosis* bacteria, which spreads when people who are sick with TB expel bacteria into the air (e.g., by coughing). Tuberculosis is the world's second leading cause of death from a single infectious agent after COVID-19 (novel coronavirus disease), and it has affected almost twice as many deaths as HIV/AIDS. According to the World Health Organization's tuberculosis report for 2023, more than 10 million people were infected worldwide, among which 1.30 million deaths related to *M. tuberculosis* were reported.[1] The combination of three or four drugs comprising isoniazid, rifampicin, and pyrazinamide with or without ethambutol is the most effective treatment currently available, but after some intervals of treatment, bacteria start developing resistance toward the drugs. The treatment of multidrug-resistant tuberculosis continues for the long term, and it is accompanied by challenges, including patient compliance for the full extent of therapy, in addition to the toxicity of prolonged drug treatment. The increase in cases of multidrug-resistant tuberculosis has driven sincere attention toward the development of new antitubercular drugs with novel mechanisms of action.

Scientists have shown continuous interest in innovating novel antitubercular agents that incorporate sulfonamide-based pyrazole combined with pyrazoline moieties in their scaffolds. The pyrazole-clubbed pyrazoline exhibits a wide range of pharmacological activities such as antifungal,[2] antimalarial,[3] antimicrobial,[4] antitubercular,[5,6] and anticancer.[7] Quinolines and their derivatives are found in a wide range of natural products having potent biological activities like anticancer,[8,9] antimalarial,[10,11] antibacterial,[12] antitubercular,[13] antiviral,[14−16] and anti-inflammatory.[17] Despite the fact that sulfonamides remain an ideal scaffold in modern medicinal chemistry for the development of novel biologically active molecules. Around 150 FDA-approved sulfur-containing drugs are available in the market with a wide variety of pharmacological actions. Sulfonamides are a class of medicines used in medicinal chemistry, and they have displayed a wide range of pharmaceutical activities such as antibacterial,[18] anticancer,[19−22] anti-inflammatory,[23] antitubercular,[24,25] and anti-HIV.[26]

To prevent treatment failures and the spread of drug resistance, the World Health Organization presently recommends the utilization of two or more bioactive molecules.

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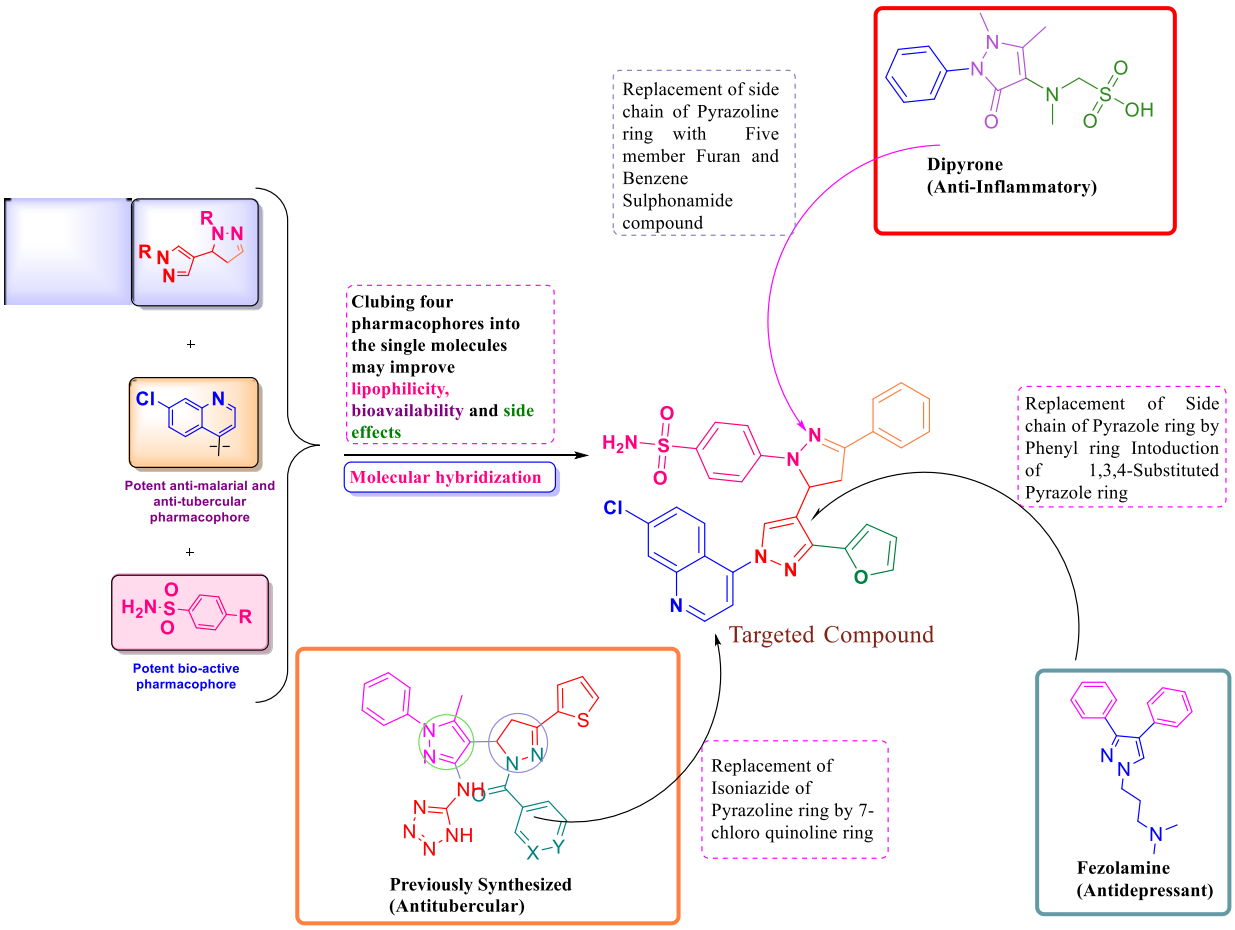

Figure 1. Designing concept and SAR of novel heterocycles (**9a-p**).

Incorporating more than one structurally active component into a single molecule may result in improved activity. Therefore, our focus was on the molecular hybridization concept to develop new structural scaffolds by incorporating active pharmacophores such as pyrazole, pyrazoline, quinoline, and the sulfonamide side chain into a single molecule. This approach aims to improve the antitubercular activity while reducing side effects and enhancing lipophilicity.

The novel sulfonamide-based pyrazole and pyrazoline hybrids described in this study represent a promising avenue for the development of new antitubercular agents, particularly against drug-resistant strains of tuberculosis. By integrating the pharmacophores of fezolamine, an antidepressant, and dipyrone, an anti-inflammatory, we designed a series of compounds (**9a–p**) with enhanced biological activities. Our approach involved carefully considering the structure–activity relationship (SAR) of various pharmacophores during the synthesis of these targeted compounds (Figure 1). Notably, we substituted the side chains of the pyrazoline ring from dipyrone with five-membered furan and benzenesulfonamide groups and modified the pyrazole ring of fezolamine to include a phenyl ring alongside a 1,3,4-substituted pyrazole framework. Additionally, we incorporated isoniazid and tetrazole rings into a previously synthesized compound, replacing them with a 7-chloroquinoline and a benzenesulfonamide moiety. This strategic modification aims to enhance efficacy and reduce the likelihood of resistance, thereby contributing valuable insights to the field of medicinal chemistry in combating tuberculosis.

We previously reported a series of pyrazolylpyrazoline derivatives combined with triazole and tetrazole moieties, demonstrating their in vitro antitubercular efficacy. Notably, one compound (3′-((1*H*-tetrazol-5-yl)amino)-5′-methyl-1′-phenyl-5-(thiophen-2-yl)-3,4-dihydro-1′*H*,2*H*-[3,4′-bipyrazol]-2-yl)(pyridin-3yl)methanone exhibited a minimum inhibitory concentration (MIC) of **12.5 μg/mL**. This active molecule achieved a docking score of **−8.884** and a Glide energy of **−61.144 kcal/mol** when analyzed in the active site of mycobacterial enoyl reductase (InhA).[27] These results highlight the potential for developing new hybrids based on sulfonamide, pyrazole, pyrazoline, and quinoline pharmacophores.

In this study, we present the synthesis of novel 7-chloroquinoline hybrid sulfonamide-based pyrazolylpyrazoline derivatives (**9a–p**) and evaluate their in vitro antitubercular activity. Structural modifications such as substituting triazole and tetrazole rings with thiophene, furan, and chloroquinoline were employed to enhance pharmacological potency. Furthermore, we replaced 2-acetyl isoniazid and thiophene with sulfonamide and substituted phenyl rings. The synthesized compounds demonstrated significant inhibitory effects, with compound 4-(1′-(7-chloroquinolin-4-yl)-5-(4-fluorophenyl)-3′-(thiophen-2-yl)-3,4-dihydro-1′*H*,2*H*-[3,4′-bipyrazol]-2-yl)-benzenesulfonamide (**9g**) showing excellent antitubercular activity against M. tuberculosis $H_{37}Rv$, achieving an MIC of **10.2 μg/mL** and **99%** inhibition rate. The most active compound **9g**, exhibited a docking score of **−9.714** and a Glide energy of **−64.183 kcal/mol**, indicating effective binding within the active site of InhA through a network of bonded and

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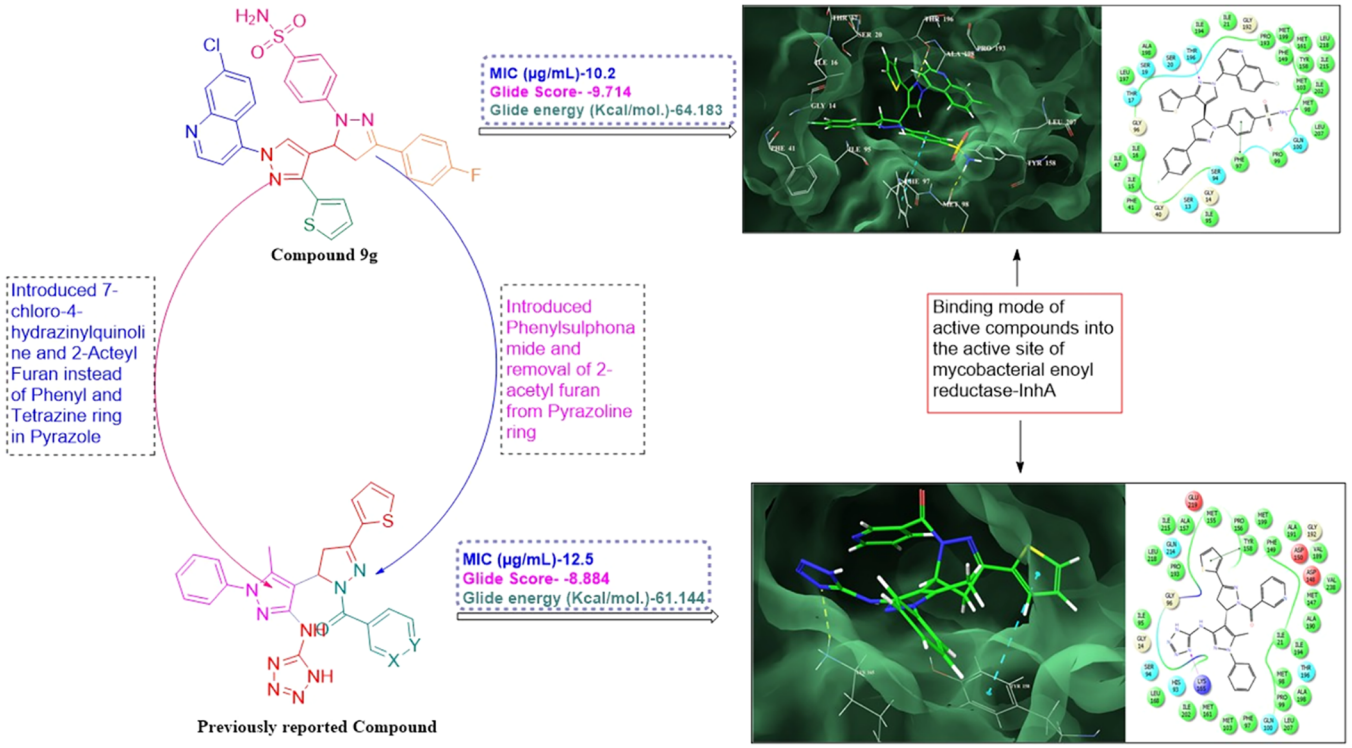

Figure 2. Comparison and structural modifications in our previous study based on pyrazole−pyrazoline hybrids with the reported work.

Scheme 1. Synthesis of Novel Sulfonamide-Based Pyrazole-Clubbed Pyrazoline Derivatives (9a-p)

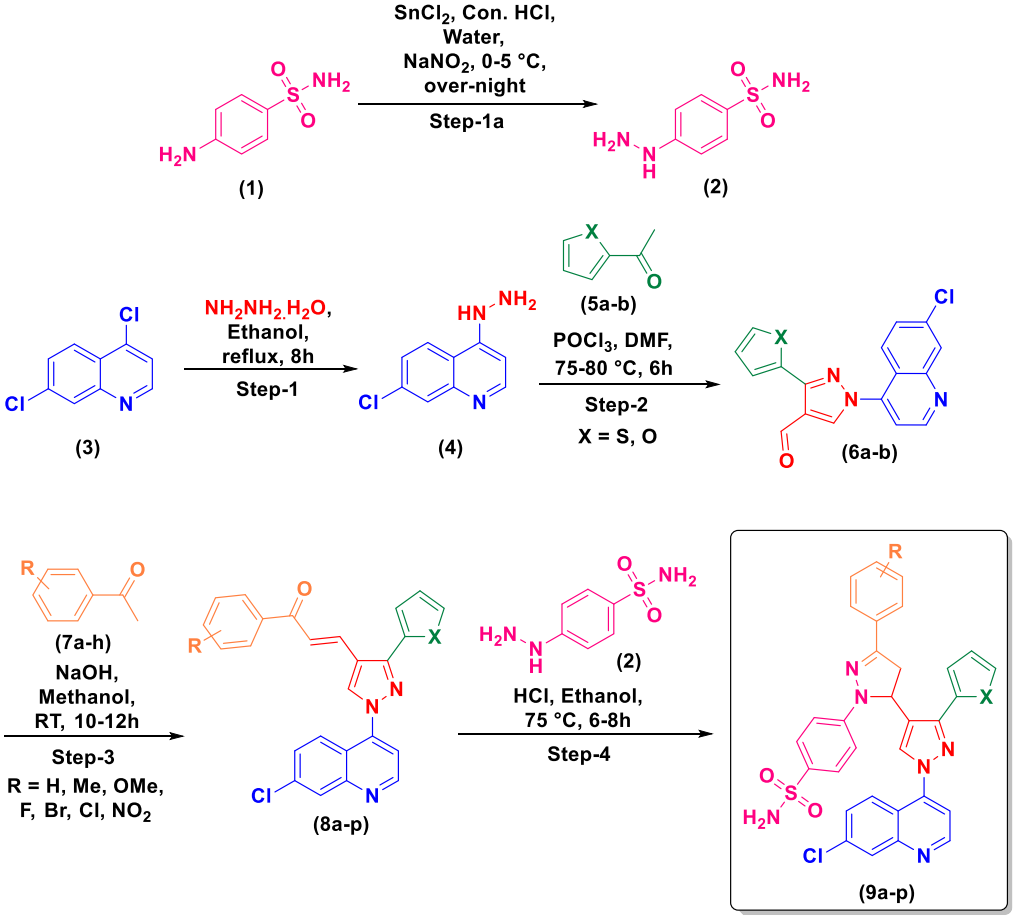

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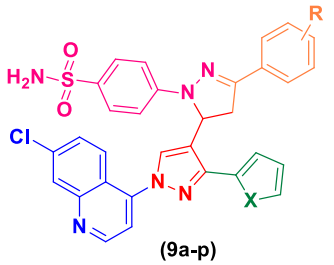
Table 1. Synthesis of Novel Sulfonamide-Based Pyrazole-Clubbed Pyrazoline Derivatives (9a-p)



(9a-p)

Comp.Code	R	X	Yield (%)	Reaction Time (h)
9a	H	S	81	3
9b	H	O	83	2
9c	4-CH_3	S	79	3
9d	4-CH_3	O	81	3
9e	4-OCH_3	S	78	4
9f	4-OCH_3	O	86	3
9g	4-F	S	82	3
9h	4-F	O	84	4
9i	4-Br	S	82	4
9j	4-Br	O	79	3
9k	4-Cl	S	82	3
9l	4-Cl	O	83	3
9m	4-OH	S	78	2
9n	4-OH	O	80	3
9o	4-NO_2	S	85	4
9p	4-NO_2	O	84	4

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nonbonded interactions, surpassing the previously synthesized compound.

Additionally, pharmacokinetic and toxicity predictions were conducted to assess the ADME properties and safety profiles of these new molecules. Figure 2 illustrates the structural modifications and provides a comparative analysis of the biological activity and molecular docking results.

RESULTS AND DISCUSSION

Chemistry. The route for the synthesis of novel sulfonamide-based pyrazole-clubbed pyrazoline derivatives (**9a-p**) is presented in Scheme 1.

The starting compound 4-hydrazinylbenzenesulfonamide (**2**) was prepared through a diazotization reaction of sulfanilamide with $NaNO_2$ and HCl, followed by reduction using $SnCl_2$ and HCl, yielding 76%. On the other hand, 7-chloro-4-hydrazinyl-quinoline (**4**) was synthesized by reacting 4,7-dichloroquinoline (**3**) with hydrazine hydrate in ethanol under reflux conditions for 8 h, yielding 84%. 1-(7-Chloroquinolin-4-yl)-3-(thiophen-2-yl)-1*H*-pyrazole-4-carbaldehyde (**6a**) and 1-(7-chloroquinolin-4-yl)-3-(furan-2-yl)-1*H*-pyrazole-4-carbaldehyde (**6b**) were prepared with yields ranging from 72% to 82% by reacting derivative (4) with 2-acetyl thiophene (**5a**) or 2-acetyl furan (**5b**) in the presence of DMF and $POCl_3$ at temperatures between 75 and 80 °C for 5 h. Subsequently, chalcone derivatives 1-(7-chloroquinolin-4-yl)-3-(thiophene/furan-2-yl)-1*H*-pyrazole-4-carbaldehyde (**8a-p**) were synthesized by reacting derivatives (**6a-b**) with substituted acetophenones (**7a-h**) in the presence of sodium hydroxide in methanol at room temperature for 10−12 h. Further derivatives (**8a-p**) reacted with derivatives (**2**) in the presence of a catalytic amount of conc. HCl and ethanol as a solvent at 75 °C for 6−8 h. The resulting reaction mixture was poured into an ice mixture and neutralized with a $NaHCO_3$ solution. The precipitate was filtered, vacuum-dried, and crystallized in an ethanol-chloroform combination (1:0.25) and dried in a hot air oven at 60 °C. The desired compounds (**9a-p**) were obtained with good yields ranging from 78 to 86% and excellent purity.

The structures of newly synthesized compounds (**9a−p**) were elucidated by elemental analysis, mass spectra, FT-IR, ^{1}H NMR, and ^{13}C NMR techniques, and thin-layer chromatography (TLC) was used to confirm the purity of the synthesized compound. For all of the newly synthesized compounds (**9a-p**), FT-IR displayed characteristic absorption band at 3350−3310 cm^{-1} due to -NH stretching, absorption bands at 3064−3023 cm^{-1} due to aromatic C−H stretching, and C═N stretching absorption band observed in between of 1587 and 1620 cm^{-1}.^{1}H NMR spectrum of derivatives (**6a-b**) displayed proton of −CHO groups near 9.7−10.3 ppm and protons of aryl ring at 6.8−8.5 ppm. CH_2 (methylene) protons of the pyrazoline ring resonated as a pair of doublets of doublets (dd) at 3.20−3.28 ppm (H_a) and 3.77−3.90 ppm (H_b), respectively. Due to vicinal coupling with the two magnetically nonequivalent protons of the methylene group at the fourth position in the pyrazoline ring, −CH (H_x) proton appeared as a doublet of doublets between 5.94 and 6.22 ppm. All aromatic protons (Ar−H) were detected within the range of 6.20 to 8.23 ppm in the NMR spectra. The ^{13}C NMR spectra of the targeted compounds (**9a−p**) exhibited a signal around 55.4 to 56.1 ppm, confirming the presence of the methylene group (C_4), which indicates the successful formation of the pyrazoline ring in these compounds. Additionally, a signal in the range of 150 to 155 ppm was observed, corresponding to the neighboring carbon of the quinoline ring (−C═N−). Furthermore, the ESI-MS spectra revealed that the derivatives (**9a−p**) displayed a characteristic $[M+1]^+$ ion peak, providing additional support for the structural integrity of the synthesized compounds. The reaction time and (%) yield results are represented in Table 1.

Biological Evaluation. *In Vitro Antitubercular Activity.* All synthesized analogues (9a−p) were assessed for their in vitro antitubercular activity against the H37Rv strain by Lowenstein−Jensen slope technique with a slight modification.[28] The newly synthesized compounds exhibit good to excellent antitubercular activity against the H_{37}RV strains compared with the standard drugs isoniazid and rifampicin. The results are characterized in Table 2.

Table 2. In Vitro Antitubercular Activity of Compounds (9a−p) against *M. tuberculosis* H_{37}Rv Strain

compound no.	% inhibition, MIC (μg/mL)	compound no.	% inhibition, MIC (μg/mL)
9a	75	**9j**	**96 (62.5)**
9b	72	**9k**	94
9c	70	**9l**	88
9d	76	**9m**	**99(12.5)**
9e	57	**9n**	**96 (62.5)**
9f	55	**9o**	88
9g	**99 (10.2)**	**9p**	86
9h	**98 (25)**	**Rifampicin**	**98 (40)**
9i	**98 (25)**	**Isoniazid**	**99 (0.20)**

The assessment of the synthesized compounds revealed that analogues **9g**, **9h**, **9i**, **9j**, **9m**, and **9n** exhibited remarkable antitubercular activity, achieving inhibition rates of **99**, **98**, **98**, **96**, **99**, and **96%** at a minimum inhibitory concentration (MIC) of 250 μg/mL, respectively. Notably, compound **9g** (**MIC = 10.2 μg/mL**) and compound **9m** (**MIC = 12.5 μg/mL**) emerged as the most potent candidates, demonstrating superior activity compared to rifampicin (**MIC = 40 μg/mL**) against *M. tuberculosis*, with both compounds exhibiting a **99%** inhibition rate. Additionally, compounds **9h** and **9i** with MIC values of 25 **μg/mL** also displayed significant antitubercular efficacy, achieving **98%** inhibition. The remaining derivatives exhibited moderate to good activity.

Encouragingly, compounds **9g**, **9h**, **9i**, and **9m** present opportunities for further optimization to enhance their potency against the H_{37}Rv strain. In comparison, the other derivatives were less effective than the standard antitubercular agents isoniazid and rifampicin. A graphical representation of the antitubercular activity for the newly synthesized compounds is illustrated in Figure 3.

Molecular Docking Study. The enoyl acyl carrier protein reductase (ENR) from *M. tuberculosis* is one of the crucial enzymes donating in type II fatty acid biosynthesis, which is a fundamental component of the bacterial cell wall.[29] Inhibition of InhA disrupts the integrity of the mycobacterial cell wall and thus qualifies it as the promising target of novel antimycobacterial drugs.[29] Results of the docking study showed that all of the pyrazolylpyrazoline derivatives (**9g**, **9h**, **9i**, **9j**, **9m**, and **9n**) could bind to the active site of InhA with good docking scores in the range of **−9.714 to −8.647** (Table 3).

In order to identify the most significantly interacting residues and the type of thermodynamic interactions that govern the binding of these molecules, a detailed analysis of the per-residue interactions for one of the most active analogue **9g** is elaborated

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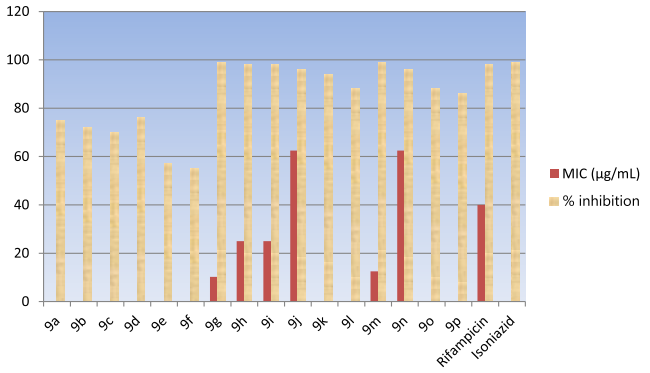

Figure 3. Graphical representation of the antitubercular activity of compounds (**9a-p**).

in the next section. The lowest energy docked conformation of **9g** (Glide score: −9.714 and Glide binding energy: −64.183 kcal/mol) (Figure 3) showed that the observed potency is due to the extensive van der Waals interactions observed with Leu207(−1.669 kcal/mol), Ile202(−1.198 kcal/mol), Met103-(−2.194 kcal/mol), Gln100(−2.274 kcal/mol), Pro99(−1.084 kcal/mol), Met98(−1.507 kcal/mol), Phe97(−4.211 kcal/mol), Gly96(−2.906 kcal/mol), Ile95(−2.018 kcal/mol), Ser94(−1.034 kcal/mol), Phe41(−1.735 kcal/mol), Ile16-(−4.132 kcal/mol), Ile15(−1.146 kcal/mol), and Gly14-(−1.402 kcal/mol) residues through 5-(4-fluorophenyl)-3,4-dihydro-pyrazol-2-yl)benzenesulfonamide portion while (7-chloroquinolin-4-yl)-2-(thiophenyl)-pyrazole portion exhibited similar type of interactions with Met199(−4.727 kcal/mol), Ala198(−2.648 kcal/mol), Leu197(−1.51 kcal/mol), Thr196-(−3.648 kcal/mol), Ile194(−2.671 kcal/mol), Pro193(−1.4 kcal/mol), Tyr158(−2.242 kcal/mol), Phe149(−1.929 kcal/mol), Ile21(−1.392 kcal/mol), Ser20(−1.905 kcal/mol), and Thr17(−1.245 kcal/mol) residues lining the active site. The higher binding affinity portrayed by **9g** can also be attributed to favorable electrostatic interactions observed with Thr196-(−1.099 kcal/mol), Arg195(−1.063 kcal/mol), Gln100(−1.053 kcal/mol), and Met98(−2.517 kcal/mol) residues. Along with these nonbonded interactions, **9g** and **9m** were also found to be engaged in significant hydrogen bonding interactions with Thr196(2.282 Å), Met98(1.842 Å) and Thr196(2.65 Å), Met98(1.805 Å), respectively, and residues with pyrazolyl nitrogen (−N−) and sulfonamide group (NH_2), respectively (Figures 4 and 5). Furthermore, the compound also exhibited a close pi−pi stacking interaction with Phe97 (3.135 Å) and Phe97 (2.295 Å) through the phenyl ring. Such bonded (hydrogen bonding and pi-sacking) interactions serve as anchors to guide the 3D orientation of a ligand into the active site and further facilitate the van der Waals and electrostatic interactions.

In Silico Pharmacokinetic/Toxicity Predictions. In silico ADME (absorption, distribution, metabolism, and excretion) and toxicity predictions for the pyrazolylpyrazoline derivatives (9g, 9h, 9i, 9j, 9m, and 9n) were conducted by using the QikProp module from Schrodinger software. This tool compares a compound's molecular properties with those of 95% of approved drugs, providing insights into its pharmacokinetic behavior while also identifying 30 types of reactive functional groups that could lead to false positives in high-throughput screening. The analysis also evaluates the compounds against Lipinski's Rule of Five, a key set of criteria for drug-likeness, with all derivatives meeting the following conditions: molecular weight (molecular weight) less than 650, log Po/w between −2 and 6.5, and QPlogS greater than −7. Furthermore, the QPlogBB parameter, which predicts the potential to cross the blood-brain barrier (BBB), showed favorable results, indicating good central nervous system penetration. The QPPMDCK value, which estimates permeability through MDCK (Madin-Darby canine kidney) cells, a model for the BBB, suggested a high cell permeability. Additionally, the QPPCaco parameter, predicting intestinal absorption, remained below 500 nm/s, which is a desirable trait for drug candidates. All of these properties suggest that the pyrazolylpyrazoline derivatives possess suitable ADME characteristics, making them promising candidates for further optimization in drug development (Table 4).[30]

CONCLUSIONS

We have synthesized novel bioactive compounds (**9a-p**), which are 7-chloroquinoline hybrid sulfonamide-based pyrazolylpyrazoline derivatives, to overcome drug-resistance problems associated with first- and second-line tubercular drugs. Most of the newly synthesized analogues demonstrated high purity and good yield. The inclusion of electron-withdrawing and electron-donating groups in compounds **9g**, **9h**, **9i**, **9j**, **9m**, and **9n** resulted in marvelous antitubercular activity. The compounds exhibit favorable binding within the active site of InhA. These in silico findings, validated by in vitro antitubercular outcomes, laid the groundwork for further exploration of structure-based drug design strategies aimed at identifying potent leads with enhanced selectivity. The outstanding antitubercular activity of compound 4-(1′-(7-chloroquinolin-4-yl)-5-(4-fluorophenyl)-3′-(thiophen-2-yl)-3,4-dihydro-1′*H*,2*H*-[3,4′-bipyrazol]-2-yl)benzenesulfonamide (**9g**) attributed to the fusion of pyrazole and pyrazoline rings with chloroquinoline, sulfonamide, 2-acetyl thiophene, and fluorophenyl ring, and a high docking score encouraged us to develop new antitubercular drugs.

Table 3. Molecular Docking of Novel Compounds in the Active Site of MTB Enoyl Reductase (InhA)

comp. code	% inhibition	MIC (μg/mL)	glide score	glide energy (kcal/mol.)	H-bonding (Å)	Pi−Pi stacking (Å)
9g	99	10.2	−9.714	−64.183	Thr196(2.282), Met98(1.842)	Phe97(3.135)
9h	98	25	−9.226	−62.739	Thr196(2.151), Met98(1.839)	
9i	98	25	−9.217	−62.654	Thr196(2.191), Met98(1.842)	Phe97(3.084)
9j	96	62.5	−8.647	−60.026	Thr196(2.312), Met98(1.845)	
9m	99	12.5	−9.710	−64.123	Thr196(2.265), Met98(1.805)	Phe97(2.995)
9n	96	62.5	−8.744	−61.684	Thr196(2.254), Met98(1.838)	
rifampicin	98	40				
isoniazid	99	0.20				

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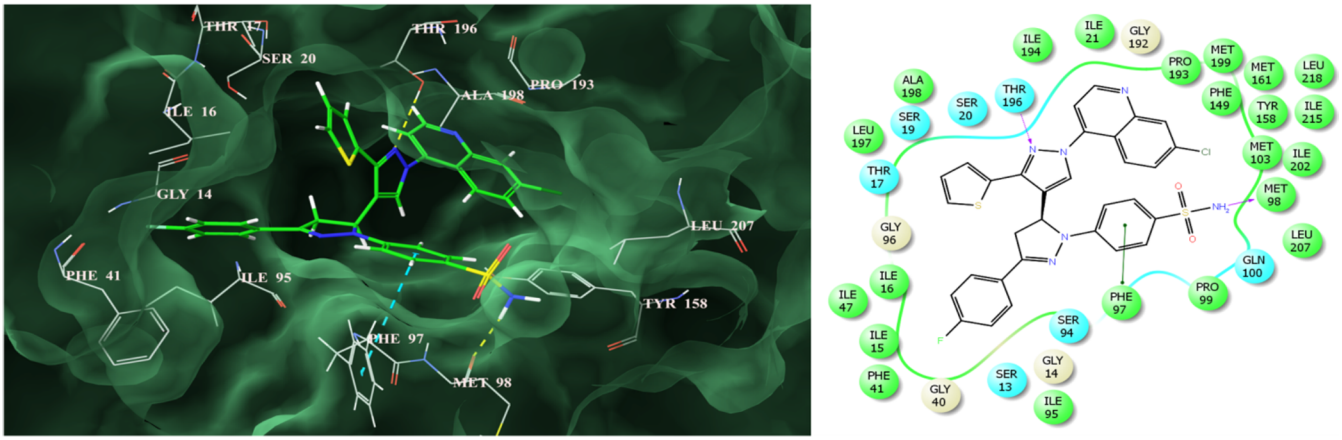

Figure 4. Binding mode and interactions of **9g** into the active site of mycobacterial InhA (on the right side: the pink lines represent the hydrogen bonding, and the green line represents the pi−pi stacking interactions).

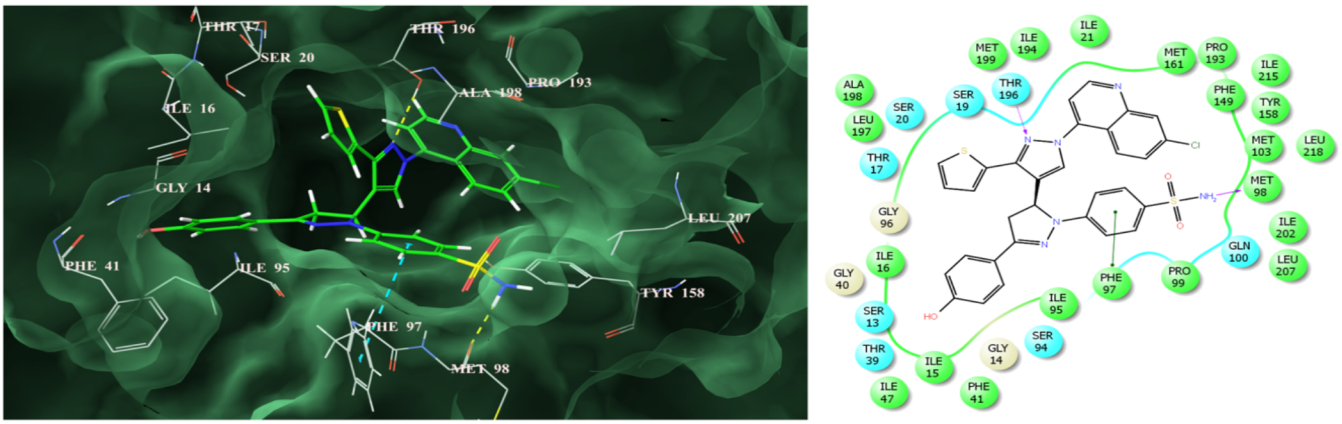

Figure 5. Binding mode and interactions of **9m** into the active site of mycobacterial InhA (on the right side: the pink lines represent the hydrogen bonding, and the green line represents the pi−pi stacking interactions).

EXPERIMENTAL SECTION

A detailed process for the development of novel 7-chloroquinoline hybrid sulfonamide-based pyrazolylpyrazoline derivatives (**9a-p**) is given as below.

Preparation of 4-Hydrazineylbenzenesulfonamide (2). 50 mL of concentrated HCl solution was added into a 3-neck RBF and cooled it at 0−5 °C. Sulfanilamide (**1**) (0.1 mol) and 100 g of ice were added to the RBF and agitated for a few minutes. Then, the sodium nitrite solution (0.1 mol. in 10 mL of water) was added dropwise for 30 min and stirred for another 30 min at 0−5 °C. Under vigorous stirring, this cold diazonium salt solution was added to a well-cooled solution of SnCl2 (50 g) in 75 mL of concentrated HCl and kept overnight in an icebox. Then, it was filtered to obtain a white solid (**2**) with a yield of 76%.

Preparation of 7-Chloro-4-hydrazinylquinoline (4). A mixture of 4,7-dichloroquinoline (**3**) (0.10 mol) and hydrazine hydrate (0.15 mol) in 80 mL of absolute ethanol was refluxed for 8 h. TLC was used to monitor the reaction, with ethanol/acetone (1:1) as the mobile phase. The resulting reaction mixture should be cooled before filtering. The product was recrystallized from ethanol to obtain yellow crystals (**4**) with a yield of 84%.

Preparation of 1-(7-Chloroquinolin-4-yl)-3-(thiophen-2-yl)-1*H*-pyrazole-4-carbaldehyde (6a) and 1-(7-Chloroquinolin-4-yl)-3-(furan-2-yl)-1*H*-pyrazole-4-carbaldehyde (6b). In a 100 mL 3-neck RBF, cooled POCl3 (0.075 mol) was added dropwise through a dropping funnel to previously cooled DMF (0.075 mol at 0−5 °C) and stirred for 15 min. A solution of hydrazine (**4**) (0.025 mol.) and either 2-acetyl thiophene (**5a**) or 2-acetyl furan (**5b**) (0.025 mol.) in DMF was added dropwise into the DMF-POCl3 mixture. The mixture was then warmed to room temperature and heated at 75−80 °C for 5 h. The completion of the reaction was monitored with the help of TLC. After the reaction was complete, the mixture was cooled to room temperature and basified with a saturated solution of $NaHCO_3$. The precipitate of compounds (**6a-b**) was filtered, thoroughly washed with distilled water, dried, and crystallized in ethanol. The synthesized compound was confirmed by ESI-MS and used as such for the next step without further purification.

General Process for the Synthesis of Novel 7-Chloroquinoline Hybrid Sulfonamide-Based Pyrazolylpyrazoline Derivatives (9a−p). Newly synthesized chalcones (**8a-p**) (0.001 mol.) and 4-hydrazinylbenzenesulfonamide (**2**) (0.0025 mol.) were dissolved in a mixture of 35 mL of ethanol and 0.5 mL of HCl. The mixture was rapidly agitated at 75 °C for 6−8 h, and the reaction's completion was monitored by TLC. After the reaction was completed, the reaction liquid was cooled to room temperature before being quenched by pouring it over crushed ice. To obtain the precipitated product, the ice mixture was neutralized with a $NaHCO_3$ solution. The precipitate was filtered, vacuum-dried, and crystallized in an ethanol/chloro-

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ACS Omega 2025, 10, 7120−7130

Table 4. Predicted ADME Parameters of the Pyrazolylpyrazoline Derivative Using QikProp

comp.	CNS	mol_MW	donorHB	acceptHB	QPlogPo/w	QPlogS	QPlogHERG	QPPCaco	QPlogBB	QPPMDCK	QPlogKp	percent human oral absor.	PSA	rule of five violation
9g	−2	629.125	2	8	6.59	−9.987	−7.911	244.564	−1.123	723.122	−2.561	82.362	101.967	2
9h	−2	613.065	2	8	6.154	−9.048	−7.515	268.684	−1.036	546.438	−2.489	80.539	106.588	2
9i	−2	690.031	2	8	6.923	−10.473	−7.956	244.568	−1.079	1060.621	−2.597	84.312	101.967	2
9j	−2	673.97	2	8	6.405	−9.965	−8.013	219.167	−1.208	640.731	−2.639	80.427	110.918	2
9m	−2	627.134	3	8	5.585	−9.295	−7.906	74.196	−1.929	110.153	−3.487	67.209	124.502	2
9n	−2	611.073	3	9	5.129	−8.549	−7.691	75.266	−1.9	76.079	−3.457	64.647	133.031	2

form combination (1:0.25). All of the synthesized derivatives (**9a-p**) were characterized using various spectroscopic techniques, and the characterization data for all of the synthesized compounds (**9a-p**) are listed below.

Characterization of 4-(1′-(7-Chloroquinolin-4-yl)-5-phenyl-3′-(thiophen-2-yl)-3,4-dihydro-1′*H*,2*H*-[3,4′-bipyrazol]-2-yl)benzenesulfonamide (9a). Yield 81%, mp 226−228 °C; IR (KBr) λ_{max}:3351 (N−H stretching), 3320 (N−H stretching), 3063 (Ar−CH stretching), 2925 (C−H aliphatic stretching), 1610 (C═C stretching), 1599 (C═N), 1170 (O═S═O); ^{1}H NMR (DMSO-d6, 400 MHz): 3.81 (dd, 1H, J = 20 Hz, −CH_2 group), 3.86 (dd, 1H, J = 20 Hz, −CH_2 group), 5.15 (dd, 1H, J = 12 Hz, −CH group), 6.20−8.06 (m, 18H, Ar−H), 8.19 (m, 2H, Ar-SO_2NH_2);^{13}C NMR (DMSO-d^6, 100 MHz):43.4, 56.0, 115.2, 115.4, 115.8, 120.2, 120.8, 121.6, 121.7, 123.2, 124.2, 125.9, 127.0, 127.2, 128.2, 128.3, 128.5, 129.4, 130.8, 131.9, 133.3, 135.0, 148.8, 150.0, 152.2; ESI-MS:m/z = 612.2 (M^+); anal. Calcd for $C_{31}H_{23}ClN_6O_2S_2$: C, 60.93, H, 3.79; N, 13.75%; found: C, 60.97; H, 3.81; N, 13.77%.

Characterization of 4-(1′-(7-Chloroquinolin-4-yl)-3′-(furan-2-yl)-5-phenyl-3,4-dihydro-1′*H*,2*H*-[3,4′-bipyrazol]-2-yl)benzenesulfonamide (9b). Yield 82%, mp 227−229 °C; IR (KBr) λ_{max}:3352 (N−H stretching), 3322 (N−H stretching), 3041 (Ar−CH stretching), 2925 (C−H aliphatic stretching), 1611 (C═C stretching), 1599 (C═N), 760 1172 (O═S═O); ^{1}H NMR (DMSO-d6, 400 MHz): 3.80 (dd, 1H, J = 19 Hz, −CH_2 group), 3.84 (dd, 1H, J = 20 Hz, −CH_2 group), 5.15 (dd, 1H, J = 12 Hz, −CH group), 6.22−8.08 (m, 18H, Ar−H), 8.20 (m, 2H, Ar-SO_2NH_2)^{13}C NMR (DMSO-d^6, 100 MHz): 43.5, 56.1, 115.2, 115.5, 115.8, 120.2, 120.8, 121.6, 121.7, 123.2, 124.2, 125.9, 127.0, 127.2, 128.2, 128.3, 128.5, 129.4, 130.8, 131.9, 133.3, 135.0, 148.8, 150.0, 152.3; ESI-MS: m/z = 595.1 (M^+); anal. Calcd for $C_{31}H_{23}ClN_6O_3S$: C, 62.57, H, 3.90; N, 14.12%; found: C, 62.62, H, 3.94; N, 14.18%.

Characterization of 4-(1′-(7-Chloroquinolin-4-yl)-3′-(thiophen-2-yl)-5-(*p*-tolyl)-3,4-dihydro-1′*H*,2*H*-[3,4′-bipyrazol]-2-yl)benzenesulfonamide (9c). Yield 79%, mp 232−234 °C; IR (KBr) λ_{max}:3351 (N−H stretching), 3320 (N−H stretching), 3063 (Ar−CH stretching), 2950 (C−H aliphatic stretching), 1611 (C═C stretching), 1599 (C═N), 1167 (O═S═O); ^{1}H NMR (DMSO-d6, 400 MHz):2.10 (s, 3H, −CH_3), 3.81 (dd, 1H, J = 20 Hz, −CH_2 group), 3.86 (dd, 1H, J = 20 Hz, −CH_2 group), 5.10 (dd, 1H, J = 12 Hz, −CH group), 6.20−8.20 (m, 19H, Ar−H & −SO_2NH_2); ^{13}C NMR (DMSO-d^6, 100 MHz): 29.32, 43.4, 56.0, 115.2, 115.4, 115.8, 120.2, 120.8, 121.6, 121.7, 123.2, 124.2, 125.9, 127.0, 127.2, 128.2, 128.3, 128.5, 129.4, 130.8, 131.9, 133.3, 148.8, 150.0, 152.2;ESI-MS:m/z = 625.12(M^+); anal. Calcd for $C_{32}H_{25}ClN_6O_2S_2$: C, 61.48, H, 4.03; N, 13.44%; found: C, 61.49; H, 4.07; N, 13.48%.

Characterization of 4-(1′-(7-Chloroquinolin-4-yl)-3′-(furan-2-yl)-5-(*p*-tolyl)-3,4-dihydro-1′*H*,2*H*-[3,4′-bipyrazol]-2-yl)benzenesulfonamide (9d). Yield 81%, mp 248−250 °C; IR (KBr) λ_{max}:3351 (N−H stretching), 3322 (N−H stretching), 3040 (Ar−CH stretching), 2948 (C−H aliphatic stretching), 1611 (C═C stretching), 1595 (C═N), 1169 (O═S═O); ^{1}H NMR (DMSO-d6, 400 MHz): 2.10 (s, 3H, −CH_3), 3.80 (dd, 1H, J = 20 Hz, −CH_2 group), 3.86 (dd, 1H, J = 20 Hz, −CH_2 group), 5.15 (dd, 1H, J = 16 Hz −CH group), 6.20−8.20 (m, 19H, Ar−H & −SO_2NH_2); ^{13}C NMR (DMSO-d^6, 100 MHz): 29.31, 43.2, 56.0, 115.2, 115.4, 115.8, 120.2, 120.8, 121.6, 121.7, 123.2, 124.2, 125.9, 127.0, 127.2, 128.2, 128.3, 128.5, 129.4, 130.7, 131.9, 133.3, 148.8, 150.0, 152.1;ESI-MS:

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ACS Omega 2025, 10, 7120−7130

m/z = 609.14(M^+); anal. Calcd for $C_{32}H_{25}ClN_6O_3S$: C, 63.10, H, 4.14; N, 13.80%; found: C, 63.12; H, 4.17; N, 13.82%.

Characterization of 4-(1′-(7-Chloroquinolin-4-yl)-5-(4-methoxyphenyl)-3′-(thiophen-2-yl)-3,4-dihydro-1′*H*,2*H*-[3,4′-bipyrazol]-2-yl)benzenesulfonamide (9e). Yield 78%, mp 241−243 °C; IR (KBr) λ_{max}:3351 (N−H stretching), 3320 (N−H stretching), 3063 (Ar−CH stretching), 2949 (C−H aliphatic stretching), 1611 (C=C stretching), 1599 (C=N), 1210 (C−O stretching), 1175 (O=S=O); ^{1}H NMR (DMSO-d^6, 400 MHz): 3.72 (s, 3H, −CH_3), 3.81 (dd, 1H, J = 20 Hz, −CH_2 group), 3.86 (dd, 1H, J = 20 Hz, −CH_2 group), 5.14 (dd, 1H, J = 16 Hz, −CH group), 6.27−8.22 (m, 19H, Ar−H & −SO_2NH_2); ^{13}C NMR (DMSO-d^6, 100 MHz): 39.2, 43.4, 56.0, 115.2, 115.4, 115.8, 120.2, 120.8, 121.6, 121.7, 123.2, 124.2, 125.9, 127.0, 127.2, 128.2, 128.3, 128.5, 129.4, 130.8, 131.9, 133.3, 148.8, 150.0, 151.2;ESI-MS: m/z = 641.2(M^+); anal. Calcd for $C_{32}H_{25}ClN_6O_3S_2$: C, 59.95, H, 3.93; N, 13.11%; found: C, 59.97; H, 3.96; N, 13.12%.

Characterization of 4-(1′-(7-Chloroquinolin-4-yl)-3′-(furan-2-yl)-5-(4-methoxyphenyl)-3,4-dihydro-1′H,2H-[3,4′-bipyrazol]-2-yl)benzenesulfonamide (9f). Yield 86%, mp 253−255 °C; IR (KBr) λ_{max}:3352 (N−H stretching), 3327 (N−H stretching), 3024 (Ar−CH stretching), 2912 (C−H aliphatic stretching), 1610 (C=C stretching), 1590 (C=N), 1178 (O=S=O); ^{1}H NMR (DMSO-d^6, 400 MHz):3.50 (s, 3H, −OCH_3), 3.82 (dd, 1H, J = 20 Hz, −CH_2 group), 3.81 (dd, 1H, J = 20 Hz, −CH_2 group), 5.10 (dd, 1H, J = 16 Hz, −CH group), 6.21−8.18 (m, 19H, Ar−H & −SO_2NH_2); ^{13}C NMR (DMSO-d^6, 100 MHz): 29.3, 43.2, 56.1, 115.2, 115.4, 115.8, 120.2, 120.8, 121.6, 121.7, 123.2, 124.2, 125.9, 127.0, 127.2, 128.2, 128.3, 128.5, 129.4, 130.7, 131.9, 133.3, 148.8, 150.0, 152.1;ESI-MS: m/z = 625.2 (M^+); anal. Calcd for $C_{32}H_{25}ClN_6O_4S$: C, 61.49, H, 4.03; N, 13.44%; found: C, 61.51; H, 4.05; N, 13.45%.

Characterization of 4-(1′-(7-Chloroquinolin-4-yl)-5-(4-fluorophenyl)-3′-(thiophen-2-yl)-3,4-dihydro-1′*H*,2*H*-[3,4′-bipyrazol]-2-yl)benzenesulfonamide (9g). Yield 82%, mp 237−239 °C; IR (KBr) λ_{max}:3352 (N−H stretching), 3324 (N−H stretching), 3061 (Ar−CH stretching), 2950 (C−H aliphatic stretching), 1610 (C=C stretching), 1599 (C=N), 1170 (O=S=O); ^{1}H NMR (DMSO-d^6, 400 MHz):3.81 (dd, 1H, J = 20 Hz, −CH_2 group), 3.86 (dd, 1H, J = 20 Hz, −CH_2 group), 5.15 (dd, 1H, J = 12 Hz, −CH group), 6.20−8.20 (m, 19H, Ar−H & −SO_2NH_2); ^{13}C NMR (DMSO-d^6, 100 MHz): 42.4, 55.0, 115.2, 115.4, 115.8, 120.2, 120.8, 121.6, 121.7, 123.2, 124.2, 125.9, 127.0, 127.2, 128.2, 128.3, 128.5, 129.4, 130.8, 131.9, 133.3, 135.0, 148.8, 150.0, 152.2;ESI-MS: m/z = 629.1(M^+); anal. Calcd for $C_{31}H_{22}ClFN_6O_2S_2$:C, 59.18, H, 3.52; N, 13.36%; found: C, 59.22, H, 3.57; N, 13.38%.

Characterization of 4-(1′-(7-Chloroquinolin-4-yl)-5-(4-fluorophenyl)-3′-(furan-2-yl)-3,4-dihydro-1′*H*,2*H*-[3,4′-bipyrazol]-2-yl)benzenesulfonamide (9h). Yield 84%, mp 248−250 °C; IR (KBr) λ_{max}:3341 (N−H stretching), 3324 (N−H stretching), 3038 (Ar−CH stretching), 2925 (C−H aliphatic stretching), 1611 (C=C stretching), 1599 (C=N), 1170 (O=S=O); ^{1}H NMR (DMSO-d^6, 400 MHz):3.80 (dd, 1H, J = 20 Hz, −CH_2 group), 3.84 (dd, 1H, J = 20 Hz, −CH_2 group), 5.14 (dd, 1H, J = 16 Hz, −CH group), 6.20−8.20 (m, 19H, Ar−H & −SO_2NH_2); ^{13}C NMR (DMSO-d^6, 100 MHz): 44.5, 56.1, 115.2, 115.5, 115.8, 120.2, 120.8, 121.6, 121.7, 123.2, 124.2, 125.9, 127.0, 127.2, 128.2, 128.3, 128.5, 129.4, 130.8, 131.8, 133.3, 135.0, 148.8, 150.0, 152.3;ESI-MS: m/z = 613.12(M^+); anal. Calcd for $C_{31}H_{22}ClFN_6O_3S$: C, 60.73, H, 3.62; N, 13.71%; found: C, 60.76, H, 3.63; N, 13.73%.

Characterization of 4-(5-(4-Bromophenyl)-1′-(7-chloroquinolin-4-yl)-3′-(thiophen-2-yl)-3,4-dihydro-1′*H*,2*H*-[3,4′-bipyrazol]-2-yl)benzenesulfonamide (9i). Yield 82%, mp 242−244 °C; IR (KBr) λ_{max}:3348 (N−H stretching), 3322 (N−H stretching), 3061 (Ar−CH stretching), 2950 (C−H aliphatic stretching), 1610 (C=C stretching), 1599 (C=N), 1176 (O=S=O); ^{1}H NMR (DMSO-d^6, 400 MHz):3.81 (dd, 1H, J = 20 Hz, −CH_2 group), 3.86 (dd, 1H, J = 20 Hz, −CH_2 group), 5.15 (dd, 1H, J = 12 Hz, −CH group), 6.20−8.20 (m, 19H, Ar−H & −SO_2NH_2); ^{13}C NMR (DMSO-d^6, 100 MHz): 42.4, 55.0, 115.2, 115.4, 115.8, 120.2, 120.8, 121.6, 121.7, 123.2, 124.2, 125.9, 127.0, 127.2, 128.2, 128.3, 128.5, 129.4, 130.8, 131.9, 133.3, 135.0, 148.8, 150.0, 152.2;ESI-MS: m/z = 689.2(M^+); anal. Calcd for $C_{31}H_{22}ClBrN_6O_2S_2$: C, 53.96, H, 3.21; N, 12.18%; found: C, 53.95, H, 3.24; N, 12.20%.

Characterization of 4-(5-(4-Bromophenyl)-1′-(7-chloroquinolin-4-yl)-3′-(furan-2-yl)-3,4-dihydro-1′*H*,2*H*-[3,4′-bipyrazol]-2-yl)benzenesulfonamide (9j). Yield 79%, mp 244−246 °C; IR (KBr) λ_{max}:3342 (N−H stretching), 3318 (N−H stretching), 3042 (Ar−CH stretching), 2925 (C−H aliphatic stretching), 1611 (C=C stretching), 1599 (C=N), 1175 (O=S=O); ^{1}H NMR (DMSO-d^6, 400 MHz):3.80 (dd, 1H, J = 24 Hz, −CH_2 group), 3.84 (dd, 1H, J = 24 Hz, −CH_2 group), 5.14 (dd, 1H, J = 16 Hz, −CH group), 6.20−8.24 (m, 19H, Ar−H & −SO_2NH_2); ^{13}C NMR (DMSO-d^6, 100 MHz): 44.5, 56.1, 115.2, 115.5, 115.8, 120.2, 120.8, 121.6, 121.7, 123.2, 124.2, 125.9, 127.0, 127.2, 128.2, 128.3, 128.5, 129.4, 130.8, 131.8, 133.3, 135.0, 148.8, 150.0, 152.3;ESI-MS: m/z = 673.04(M^+); anal. Calcd for $C_{31}H_{22}ClBrN_6O_3S$:C, 55.25, H, 3.29; N, 12.47%; found: C, 55.27, H, 3.30; N, 12.48%.

Characterization of 4-(5-(4-Chlorophenyl)-1′-(7-chloroquinolin-4-yl)-3′-(thiophen-2-yl)-3,4-dihydro-1′*H*,2*H*-[3,4′-bipyrazol]-2-yl)benzenesulfonamide (9k). Yield 82%, mp 242−243 °C; IR (KBr) λ_{max}:3348 (N−H stretching), 3322 (N−H stretching), 3061 (Ar−CH stretching), 2950 (C−H aliphatic stretching), 1610 (C=C stretching), 1599 (C=N),1172 (O=S=O);^{1}H NMR (DMSO-d^6, 400 MHz):3.81 (dd, 1H, J = 20 Hz, −CH_2 group), 3.86 (dd, 1H, J = 20 Hz, −CH_2 group), 5.17 (dd, 1H, J = 12 Hz, −CH group), 6.18−8.23 (m, 19H, Ar−H & −SO_2NH_2);^{13}C NMR (DMSO-d^6, 100 MHz): 42.4, 55.0, 115.2, 115.4, 115.8, 120.2, 120.8, 121.6, 121.7, 123.2, 124.2, 125.9, 127.0, 127.2, 128.2, 128.3, 128.5, 129.4, 130.8, 131.9, 133.3, 135.0, 148.8, 150.0, 152.2;ESI-MS: m/z = 645.06(M^+); anal. Calcd for $C_{31}H_{22}Cl_2N_6O_2S_2$: C, 57.68, H, 3.44; N, 13.02%; found: C, 57.69, H, 3.45; N, 13.03%.

Characterization of 4-(5-(4-Chlorophenyl)-1′-(7-chloroquinolin-4-yl)-3′-(furan-2-yl)-3,4-dihydro-1′*H*,2*H*-[3,4′-bipyrazol]-2-yl)benzenesulfonamide (9l). Yield 83%, mp 244−245 °C; IR (KBr) λ_{max}:3342 (N−H stretching), 3318 (N−H stretching), 3042 (Ar−CH stretching), 2925 (C−H aliphatic stretching), 1611 (C=C stretching), 1599 (C=N), 1171 (O=S=O); ^{1}H NMR (DMSO-d^6, 400 MHz):3.80 (dd, 1H, J = 24 Hz, −CH_2 group), 3.84 (dd, 1H, 24 Hz, −CH_2 group), 5.16 (dd, 1H, 16 Hz, −CH group), 6.58−8.22 (m, 19H, Ar−H & −SO_2NH_2); ^{13}C NMR (DMSO-d^6, 100 MHz): 44.5, 56.1, 115.2, 115.5, 115.8, 120.2, 120.8, 121.6, 121.7, 123.2, 124.2, 125.9, 127.0, 127.2, 128.2, 128.3, 128.5, 129.4, 130.8, 131.8, 133.3, 135.0, 148.8, 150.0, 152.3;ESI-MS: m/z = 629.2(M^+); anal. Calcd for $C_{31}H_{22}Cl_2N_6O_3S$: C, 59.15, H, 3.52; N, 13.35%; found: C, 59.16, H, 3.54; N, 13.36%.

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Characterization of 4-(1′-(7-Chloroquinolin-4-yl)-5-(4-hydroxyphenyl)-3′-(thiophen-2-yl)-3,4-dihydro-1′*H*,2*H*-[3,4′-bipyrazol]-2-yl)benzenesulfonamide (9m). Yield 78%, mp 213-215 °C; IR (KBr) λ_{max}:3410 (−OH stretching), 3351 (N−H stretching), 3325 (N−H stretching), 3053 (Ar−CH stretching), 2940 (C−H aliphatic stretching), 1615 (C═C stretching), 1599 (C═N), 1210 (C−O stretching), 1178 (O═S═O); ^{1}H NMR (DMSO-d^6, 400 MHz):3.81 (dd, 1H, J = 20 Hz, −CH_2 group), 3.86 (dd, 1H, J = 20 Hz, −CH_2 group), 5.18 (dd, 1H, J = 12 Hz, −CH group), 6.17−8.21 (m, 19H, Ar−H & −SO_2NH_2), 9.83 (s, 1H, −OH); ^{13}C NMR (DMSO-d^6, 100 MHz): 43.4, 56.0, 115.2, 115.4, 115.8, 120.2, 120.8, 121.6, 121.7, 123.2, 124.2, 125.9, 127.0, 127.2, 128.2, 128.3, 128.5, 129.4, 130.8, 131.9, 133.3, 148.8, 150.0, 151.2;ESI-MS: m/z = 627.01(M^+); anal. Calcd for $C_{31}H_{23}ClN_6O_3S_2$:C, 59.37, H, 3.70; N, 13.40%; found: C, 59.39; H, 3.73; N, 13.42%.

Characterization of 4-(1′-(7-Chloroquinolin-4-yl)-3′-(furan-2-yl)-5-(4-hydroxyphenyl)-3,4-dihydro-1′*H*,2*H*-[3,4′-bipyrazol]-2-yl)benzenesulfonamide (9n). Yield 80%, mp 254−256 °C; IR (KBr) λ_{max}:3412 (−OH stretching), 3350 (N−H stretching), 3323 (N−H stretching), 3053 (Ar−CH stretching), 2940 (C−H aliphatic stretching), 1615 (C═C stretching), 1599 (C═N), 1210 (C−O stretching), 1178 (O═S═O); ^{1}H NMR (DMSO-d^6, 400 MHz):3.81 (dd, 1H, J = 20 Hz, −CH_2 group), 3.86 (dd, 1H, J = 20 Hz, −CH_2 group), 5.17 (dd, 1H, J = 12 Hz, −CH group), 6.15−8.22 (m, 19H, Ar−H & −SO_2NH_2), 9.85 (s, 1H, −OH); ^{13}C NMR (DMSO-d^6, 100 MHz): 43.4, 56.0, 115.2, 115.4, 115.8, 120.2, 120.8, 121.6, 121.7, 123.2, 124.2, 125.9, 127.0, 127.2, 128.2, 128.3, 128.5, 129.4, 130.8, 131.9, 133.3, 148.8, 150.0, 151.2;ESI-MS: m/z = 611.2(M^+); anal. Calcd for $C_{31}H_{23}ClN_6O_4S$: C, 60.93, H, 3.79; N, 13.75%; found: C, 60.90; H, 3.81; N, 13.76%.

Characterization of 4-(1′-(7-Chloroquinolin-4-yl)-5-(4-nitrophenyl)-3′-(thiophen-2-yl)-3,4-dihydro-1′*H*,2*H*-[3,4′-bipyrazol]-2-yl)benzenesulfonamide (9o). Yield 85%, mp 248−250 °C; IR (KBr) λ_{max}:3348 (N−H stretching), 3321 (N−H stretching), 3054 (Ar−CH stretching), 2948 (C−H aliphatic stretching), 1610 (C═C stretching), 1599 (C═N), 1318 (N═O), 1168 (O═S═O); ^{1}H NMR (DMSO-d^6, 400 MHz):3.78 (dd, 1H, J = 20 Hz, −CH_2 group), 3.86 (dd, 1H, J = 20 Hz, −CH_2 group), 5.17 (dd, 1H, J = 12 Hz, −CH group), 6.20−8.23 (m, 19H, Ar−H & −SO_2NH_2);^{13}C NMR (DMSO-d^6, 100 MHz): 42.4, 55.0, 115.2, 115.4, 115.8, 120.2, 120.8, 121.6, 121.7, 123.2, 124.2, 125.9, 127.0, 127.2, 128.2, 128.3, 128.5, 129.4, 130.8, 131.9, 133.3, 140.0, 148.8, 150.0, 152.2;ESI-MS: m/z = 656.09(M^+); anal. Calcd for $C_{31}H_{22}ClN_7O_4S_2$: C, 56.75, H, 3.38; N, 14.94%; found: C, 56.75, H, 3.39; N, 14.95%.

Characterization of 4-(1′-(7-Chloroquinolin-4-yl)-3′-(furan-2-yl)-5-(4-nitrophenyl)-3,4-dihydro-1′*H*,2*H*-[3,4′-bipyrazol]-2-yl)benzenesulfonamide (9p). Yield 84%, mp 250−252 °C; IR (KBr) λ_{max}:3342 (N−H stretching), 3320 (N−H stretching), 3055 (Ar−CH stretching), 2948 (C−H aliphatic stretching), 1610 (C═C stretching), 1599 (C═N), 1318 (N═O), 1168 (O═S═O); ^{1}H NMR (DMSO-d^6, 400 MHz):3.78 (dd, 1H, J = 20 Hz, −CH_2 group), 3.86 (dd, 1H, J = 20 Hz, −CH_2 group), 5.15 (dd, 1H, J = 12 Hz, −CH group), 6.16−8.26 (m, 19H, Ar−H & −SO_2NH_2); ^{13}C NMR (DMSO-d^6, 100 MHz): 42.4, 55.0, 115.2, 115.4, 115.8, 120.1, 120.8, 121.7, 121.7, 123.2, 124.2, 125.9, 127.0, 127.2, 128.2, 128.3, 128.5, 129.4, 130.8, 131.9, 133.3, 140.0, 148.6, 150.2, 152.4;ESI-MS: m/z = 640.3(M^+); anal. Calcd for $C_{24}H_{20}N_{10}O_2$: C, 58.17, H, 3.46; N, 15.32%; found: C, 58.19, H, 3.47; N, 15.33%.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.4c10198.

Supplementary figures demonstrating the characterization of synthesized compounds by ^{1}H NMR, ^{13}C NMR, Mass, and IR spectra. Additionally, the molecular docking study and methodology for the biological assay are also provided (PDF)

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Notes

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