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Design, Synthesis, Bioactivity Screening and Molecular Docking Analysis of Phenylthiazole Derivatives Containing Nitrobenzylidine Moiety

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ABSTRACT

Thiazole, a heterocyclic compound known for its versatile biological, pharmaceutical, industrial, and therapeutic significance, is a focal and increasingly studied area within organic chemistry. Aseries of thiazole derivatives (1b-4b) were synthesized and then characterized by spectroscopic methods followed by antimicrobial and antioxidant screening. Compound 3b showed potential antimicrobial activities. On the other hand, compounds (1b-3b) displayed excellent antifungal activities. In antioxidant screening, compound 3b showed the highest activity with IC_{50} value of 31.82µg/mL. To validate bioactivity screening, molecular docking studies and ADMET prediction were performed. All four compounds showed binding affinity-8.4to -9.5kcal/molwith targeted proteins.

Keywords: Synthesis, Thiazole, Bioactivity, Docking studies, ADMET prediction.

INTRODUCTION

In nations with emerging economies, the issue of antimicrobial resistance remains a concern because it makes it harder to treat infectious diseases, which are responsible for a substantial portion of disease and death[1,2]. For a long time, diseases from microorganisms have been the second most common cause of death[3-5]. Heterocyclic compounds, widely studied because of their diverse biological, medicinal, industrial, antimicrobial, and therapeutic applications, are a focal and increasingly studied area within organic chemistry[6,9]. Schiff base compounds are precious in medicine and play a vital role in combatting various organisms[10]. Hugo Schiff first reported imine synthesis in the 19th century (1864) and since then, multiple methods for producing imines have been recognized[11]. Schiff bases are chemical compounds but they contain an imine or azomethine group in place of the carbonyl group. Schiff bases exhibit a diverse range of biological characteristics, suggesting their

potential utility as agents with antioxidant, antifungal, anti-inflammatory, antitumor, antibacterial as well as anticancer activities[12–18]. Furthermore, heterocyclic thiazole compounds, which contain both sulfur and nitrogen atoms, have relevance to diverse research fields[19-21]. Several synthetic as well as naturally occurring substances that incorporate the thiazole unit have exhibited physiological potential as anti-microbial, free radical scavenging, anti-fungal, anti-cancer, anti-candida and cytotoxicity, anti-inflammatory agents[22–27]. Reactive oxygen species (ROS) are essential contributors to the development of several significant diseases including cancer[28], heart diseases[29], diabetes[30], arteriosclerosis[31] and cataracts[32] causing biological harm through oxidative stress induced by free radicals[33]. Oxidative strain occurs when there is a disparity, with the production of oxidants exceeding their degradation rate[34]. Antioxidants, neutralizing free radicals, offer protection against severe and potentially severe diseases[35]. An antioxidant is a compound with the ability to hinder the oxidation process of other molecules[36-38]. Due to ongoing microbial resilience against antibiotics, scholars are constantly exploring substitutes for traditional medications, recognizing essential role played by thiazoles in the biological diversity of various drugs.

To explore the combined effectiveness of a novel pharmacophore, we aim to generate a set of innovative compounds by synthesizing Schiff bases that include thiazole-nitro hybrids by changing substituents at various positions into the ring of thiazole. This will facilitate advancement in novel and more potent drugs. In current scientific studies, understanding the electronic structure of chemical compounds is essential for unraveling the mechanisms behind pharmacological activities[39]. Theoretical predictions play a crucial role in identifying potent biologically active compounds by generating results such as Molecular orbitals (LUMO, HOMO) and other electronic characteristics that closely align with experimental data[40], while the research involves evaluating computational toxicity, adherence to drug characteristics, and pharmacokinetic scoring for the synthesized compounds and includes studies on molecular docking to understand how proteins interact with the synthesized analogs.

MATERIALS AND METHODS

Chemicals

Reagents purchased from Sigma-Aldrich and Merck were used as received, without additional purifications.

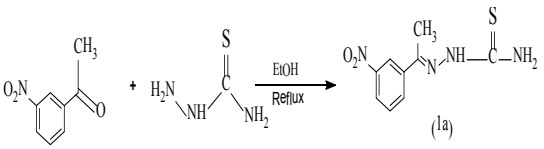
EXPERIMENTAL

Measurements

Infrared spectra were recorded by Shimadzu FTIR spectrophotometer (Model FTIR-IR Affinity-1) and melting points with a Fisher JOHNm.p. apparatus (Model 1A 9000). The Proton and Carbon-^{13}NMR spectra (DMSO-d_6, δ, ppm, J: Hz), including DEPT-135, COSY, HSQC, and HMBC were recorded by Bruker HD spectrometer (operated at 400 and 100 MHz). Structure of synthesized compounds was drawn in ChemDraw Ultra 12.0 software, *In silico* Molecular Docking was performed using Gaussian 09, PyMol (version 2.4), AutoDock Vina in PyRx 08 and Discovery Studio 4.1 soft wares.

Synthesis of Thiosemicarbazone 1a

Synthesis of hydrazinecarbothioamide (1a): 3-nitroacetophenone (5mmol) and thiosemicarbazide (5mmol) weretaken in two-neck flask with 15.0 mL of ethanol followed by refluxed at 80°C with stirring. After completion (checked by TLC), it was cooled and separated by filtration. The product was recrystallized from ethyl acetate, affording the compound in an excellent yield (77%).

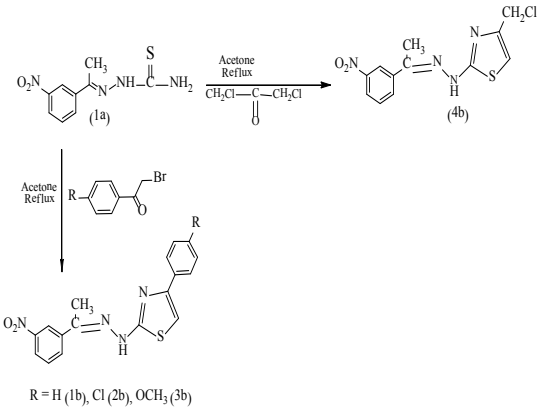


Scheme 1. Synthesisof hydrazinecarbothioamide

Synthesis of Thiazole (1b-4b)

Procedure for the synthesis of thiazolederivatives (1b-4b)

Thiosemicarbazone derivatives (g, mmol) and substituted phenacyl bromide (5 mmol) was refluxed in acetone (15.0mL) at approximately 60°C with stirring. After completion (checked by TLC), it was allowed to cool down and subsequently filtered to isolate the finaldesired products. Thesolid was further purified by recrystallization from acetone, affording the final compounds in excellent yields (72–78%).



Scheme 2. Synthesis of thiazolederivatives

Antibacterial and antifungal screening

In vitro antimicrobial studies of the compounds (1b-4b) were evaluated by using the agar disc diffusion[41] method. Potato dextrose agar (PDA) and mueller–hinton agar (MHA) were employed for the cultivation offungal and bacterial strains. Both PDA and MHA plates were incubated for 24 h to ensure sterility and confirm the absence of contamination. Following incubation, sterile cotton swabs were employed to uniformly inoculate the test microorganisms onto the respective media. Discs loaded with 25µL of a DMSO solution containing 300 µg of each synthesized compound were placed on the plates surfaces. Then,it was incubated aerobically for 24 h at 37°C for antibacterial studies and 48 h at 26°C for antifungal evaluation. For comparison, discs containing equivalent volumes of ceftriaxone (for antibacterial assays) and amphotericin B (for antifungal assays) dissolved in DMSO were used as standard drugs. Finally, the zones of inhibition were determined.

Antioxidant activity

The 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging method[42-44] was used to assess the antioxidant properties. DPPH (EtOH) solution (6µg/mL) was prepared and kept in stirring for 24 hours. Sample solutions were prepared in ethanol at concentrations 500µg/mL to 31.25µg/mL. For each test, 100µL of the sample solution was mixed to 4.0 mL of the DPPH followed by incubation in an ice bath under dark conditions. Ascorbic acid, dissolved in ethanol at corresponding concentrations, was used as the standard. After brief centrifugation (10 seconds), all samples were kept in the dark for an additional 15 minutes. The absorbance (Asample) of each sample was then recorded at 517 nm and compared with the control (Acontrol). Antioxidant activitywas determinedby the equation:

$$(\%)\ \text{Inhibition}\ \% = \frac{A_{control} - A_{sample}}{A_{sample}} \times 100$$

Molecular docking

In silico docking studies were undertaken to clarify how the proposed inhibitors interact with the binding site of the target protein. In this purpose, the crystal structure corresponding to PDB ID: 5JBO45 (taken from protein data bank), representing the co-crystal of *T. harzianum*. Protein was prepared using PyMol (version 2.4) by removing crystallographic H_2O molecules, ligands and attached heteroatoms. Energy minimization of the processed protein was subsequently conducted using Swiss-PdbViewer.

Frontier Molecular OrbitalAnalysis

The energies of the HOMO and LUMO orbitals are key indicators for interpreting theelectronic behavior, charge-transfer capability, and overall chemical reactivity of a molecule, which together contribute to its biological activity[46]. Various biological activity descriptors of the compounds were computed based on the frontier molecular orbital values using the standard quantum chemical equations.

$$\eta = \frac{(E_{LUMO} - E_{HUMO})}{2}\ (1)\zeta = \frac{1}{2\eta} \qquad (2)$$

$$\mu = \frac{(E_{LUMO} + E_{HUMO})}{2}\ (3)\psi = \frac{\mu^2}{2\eta} \qquad (4)$$

In silico ADMET prediction

Assessment of absorption, distribution, metabolism, and excretion (ADME) characteristics for the synthesized analogs was carried out using the online versions of SwissADME andMolinspiration tools. The absorption (%ABS) for each compound was estimated by the equation:

$$(\%)\ ABS = 109 - (0.3459 \times TPSA)$$

Table 1: Synthesis of the compounds with yield (%) and time (hour)

Compounds	Colors and Textures	m.p.°C	Reaction Time (h)	Yield
1a	Yellow amorphous solid	210-212	9	77%
1b	Brown amorphous solid	228-230	6	74%
2b	Light yellow amorphous solid	178-180	8	78%
3b	Brown am orphous solid	182-184	6	72%
4b	White amorphous solid	195-197	6	75%

RESULTS AND DISCUSSION

Chemistry

Four novel thiazole derivatives (1b–4b) were successfully synthesized, and their molecular structures were confirmed through IR, Proton and Carbon-^{13}NMR, DEPT-135, COSY, HSQC, and HMBC spectroscopic analyses.

Characterization of compounds

2-(1-(3'-nitrobenzylidene)ethylidene) hydrazine carbo thioamide(1a): amorphous solid, m.p. 210~212°C. IR: υ_{max}. (KBr, cm^{-1}): 3402 and 3199 (N-H) and 1598(C=N). ^{1}H-NMR: 8.61 (1H, s, H2′), 8 .22 (1H, d, *J* = 8.0,H4′), 7.67 (1H, t, *J* = 8.0, H5′), 8.41 (1H, d, *J* = 8.0, H6′) 8.61 (1H, s, NH), 10.39 (2H, s, NH_2) and 2.37 (3H, s, CH_3); ^{13}C-NMR: δC1'(139.9), C2′(121.4), C3′(148.6), C4′(124.0), C5′(130.1), C6′(133.4), C=N(146.0), C=S(179.6) and CH3(14.5).

4''-Phenyl-2''-(2-(1-(3'-nitrobenzylidene) ethylidene) hydrazinyl)thiazole (1b): Brown amorphous solid, m.p. 228~230°C.IR: $\upsilon_{max.}$ (KBr, cm^{-1}):. 3130 and 3115(N-H) and 1610 (C=N). ^{1}H-NMR :δ 8.57 (1H, s, H2′), 7.73 (1H, t, *J* = 7.2, H4′), 7.42 (1H, t, *J* = 8.4, H5′), 8.22 (1H, t, *J* = 8.4, H6′) 7.37 (1H, s, H5′′), 7.87 (1H, d, *J* = 7.6, H2′′′), 7.33 (1H, t, *J* = 7.2, H3′′′),7.31 (1H, t, *J* = 7.2, H4′′′), 8.22 (1H, t, *J* = 8.4, H5′′′),7.87 (1H, d, *J* = 7.6, H6′′′), 8.57(1H, s, NH) and 2.39 (3H, s, CH_3); ^{13}C-NMR:δ C1′(140.0), C2′(120.3), C3′(148.5), C4′(123.4), C5′(130.5), C6′(132.3), C=N(144.7), C2''(169.9), C4''(134.9), C5''(104.9), C1′′′(134.9), C2′′′(129.1), C3′′′(126.0), C4′′′(128.0), C5′′′(126.0), C6′′′(129.1) and CH_3(14.3).

4′′-(4′′′-Chlorophenyl)-2′′-(2-(1-(3 nitrobenzylidene)ethylidene)hydrazinyl) thiazole (2b): Light yellow amorphous solid, m.p. 178~180°C, IR: υ_{max}. (KBr, cm^{-1}): 3066 and 3026 (N-H) and 1606 (C=N). ^{1}H-NMR:δ 8.56 (1H, s, H2′), 7.72 (1H, d, *J* = 7.2, H4′), 7.46 (1H, t, *J* = 8.4, H5′), 8.22 (1H, d, *J* = 8.4, H6′)7.44 (1H, s, H5′′), 7.91 (1H, d, *J* = 7.6, H2′′′), 7.49 (1H, d, *J* = 7.2, H3′′′),7.49 (1H, d, *J* = 7.2, H5′′′), 7.91 (1H, d, *J* = 7.6, H6′′′), 8.18 (1H, s, NH) and 2.37 (3H, s, CH_3);^{13}C-NMR:δ C1 (139.9), C2′(120.3), C3''(148.5), C4''(123.4), C5''(130.5), C6''(132.3), C=N (144.7), C2''(149.7), C4''(133.9), C5''(105.7), C1'''(132.4), C2'''(129.1), C3'''(127.7), C4'''(144.7), C5'''(127.7), C6'''(129.1) and CH_3(14.3).

4''-(4'''-Methoxyphenyl)-2''-(2-(1-(3 nitrobenzylidene)ethylidene)hydrazinyl) thiazole (3b): Brown amorphous solid, m.p. 182~184°C.IR: $\upsilon_{max.}$ (KBr, cm^{-1}): 3118 and 3080 (N-H) and 1608 (C=N). ^{1}H-NMR: δ 8.57 (1H, s, H2′), 8.22 (1H, t, *J* = 7.2, H-4'), 7.73 (1H, t, *J*= 8.4, H5′), 8.22 (1H, t, *J* = 8.4, H6′) 7.19 (1H, s, H5′′), 6.99 (1H, d, *J* = 7.6, H2′′′), 7.82 (1H, d, *J* = 7.2, H3′′′),7.80 (1H, d, *J* = 7.2, H5′′′) and 6.97 (1H, d, *J* = 7.6, H6′′′), 8.18 (1H, s, NH), 3.79 (3H, s, OCH_3) and 2.39 (3H, s, CH_3);^{13}C-NMR: C1''(140.0), C2''(120.3), C3''(148.5), C4''(123.4), C5''(130.5), C6''(132.3), C=N(144.7), C2''(169.8), C4''(140.0), C5''(102.7), C1'''(132.3), C2'''(114.4), C3'''(127.7), C4'''(159.3), 5'''(127.3), C6'''(114.4), CH_3(14.3) and OCH_3(55.5).

4''-(Chloromethyl)-2''-(2-(1-(3nitro-benzylidene)ethylidene)hydrazinyl)thiazole (4b): White amorphous solid, m.p. 195~197°C.IR: $\upsilon_{max.}$ (KBr, cm^{-1}): 3417 and 3126 (N-H) and 1598 (C=N). ^{1}H-NMR:δ8.57 (1H, s, H2′), 7.73 (1H, t, *J* = 7.2, H-4′), 7.42 (1H, t, *J* = 8.4, H5′), 8.22 (1H, t, *J* = 8.4, H6′), 7.37 (1H, s, H5′′), 8.54 (1H, s, NH), 2.37 (3H, s, CH_3) and 4.66 (2H, s, CH_2Cl); ^{13}C-NMR: δ C1 (139.8), C2′(120.3), C3′(148.5), C4′(123.5), C5′(130.5), C6′(132.4), C=N(147.3), C2′′(170.1), C4''(145.4), C5''(109.5), CH_3(14.3) and CH_2Cl(41.8).

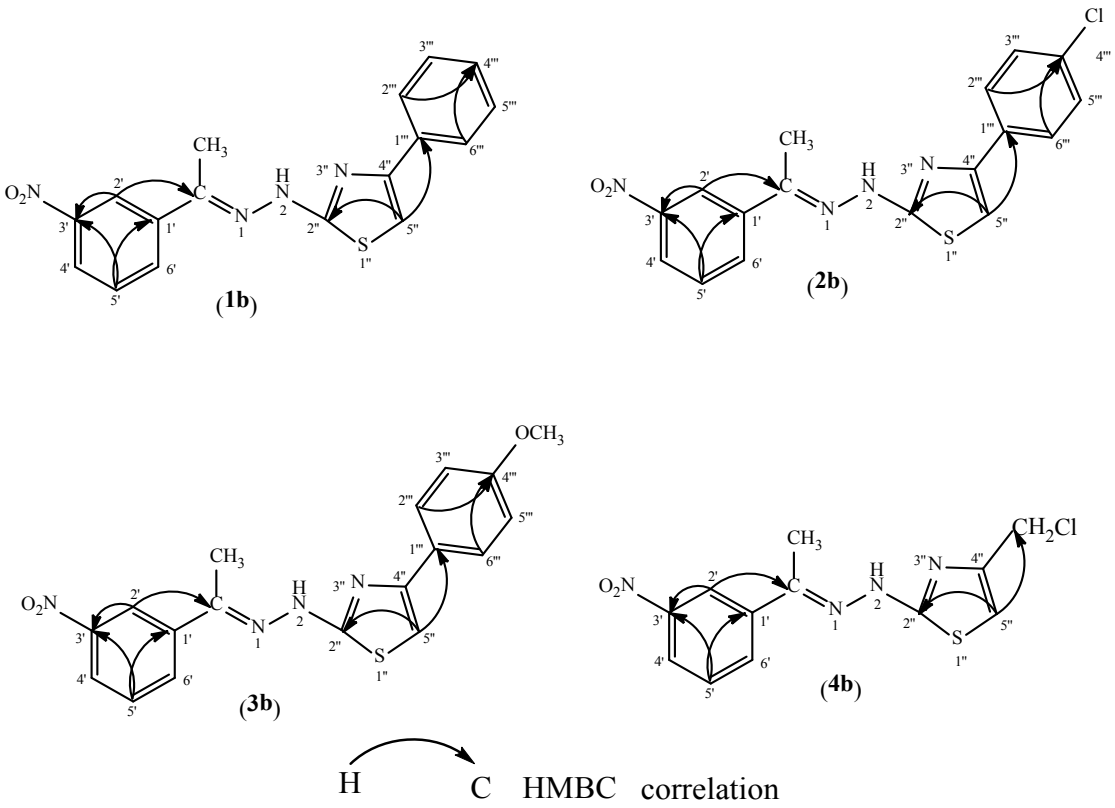


Fig. 1. Important ^{1}H-^{13}C HMBC correlations of compounds (1b-4b)

Antimicrobial studies

In vitro antimicrobial investigation of the synthesized derivatives (1b-3b) was assessed by bacterial and fungal species. The zones of inhibition (mm±SD) are summarized in Table 2. Amphotericin B (Amp B) and Ceftriaxone (Cef) were used asreference standards. Among the tested compounds, 3b exhibited the highest antibacterial activity, showing 13.7±0.6 mm against *Salmonella typhimurium*. All compounds demonstrated significant antifungal activity, particularly against *Aspergillus niger*.

Table 2: Antibacterial activities of compounds (1b-3b)

Compounds	*Gram (+)ve* bacteria		*Gram (-)ve* bacteria		Fungal strains	
	S. aureus	*B. subtilis*	*S. typhimurium*	*E. coli*	*T. harzianum*	*A. niger*
1b	11.3±0.6	–	6.3±0.6	7.0±1.0	21.0±1.0	26.3±1.5
2b	5.3±0.6	6.3±0.6	4.3±0.6	6.0±1.0	10.3±0.6	26.0±1.0
3b	10.3±1.5	12.0±2.0	13.7±0.6	12.0±1.0	10.7±1.2	36.3±1.5
DMSO	–	–	–	–	–	–
Cef	40.3±0.6	50.0±1.0	42.7±1.5	37.3±1.2	–	–
Amp B	–	–	–	–	17.7±0.6	15.3±0.6

Diameter±SD (standard deviation), –Represents no activity.

Antioxidant Activity Assay

The DPPH test was employed to examine the antioxidant capacity of the samples at varying concentrations. The compounds exhibited IC_{50} values ranging from 31.82 to 60.42 µg/mL. Among them, compound 3b demonstrated the highest activity (IC_{50} of 31.82 µg/mL) comparable to that of ascorbic acid (27.34 µg/mL). In particular, the para-positioned methoxy group in 3b enhances its radical scavenging ability through electron-donating effects, whereas compound 2b displayed the lowest activity in presence of halogen (chlorine). Due to limitations in laboratory facilities, compound 4b was not subjected to antimicrobial evaluation.

Table 3: Antioxidant activities of(1b-3b)

Compounds	IC_{50}(µg/mL)
1b	44.07±2.920
2b	60.42±3.90
3b	31.82±3.80
Ascorbic acid (AA)	27.34±1.86

Docking Analysis

Compounds (1b–4b) were subjected to docking studies against the co-crystal structure of5JBO (PDB ID) to evaluate their antifungal potential. All compounds exhibited favorable binding affinities (–8.4 to –9.5 kcal/mol). Among them, 1b demonstrated the highestaffinity, whereas compound 4b showed comparatively moderate binding (–8.4 kcal/mol) relative to the other synthesized analogs.

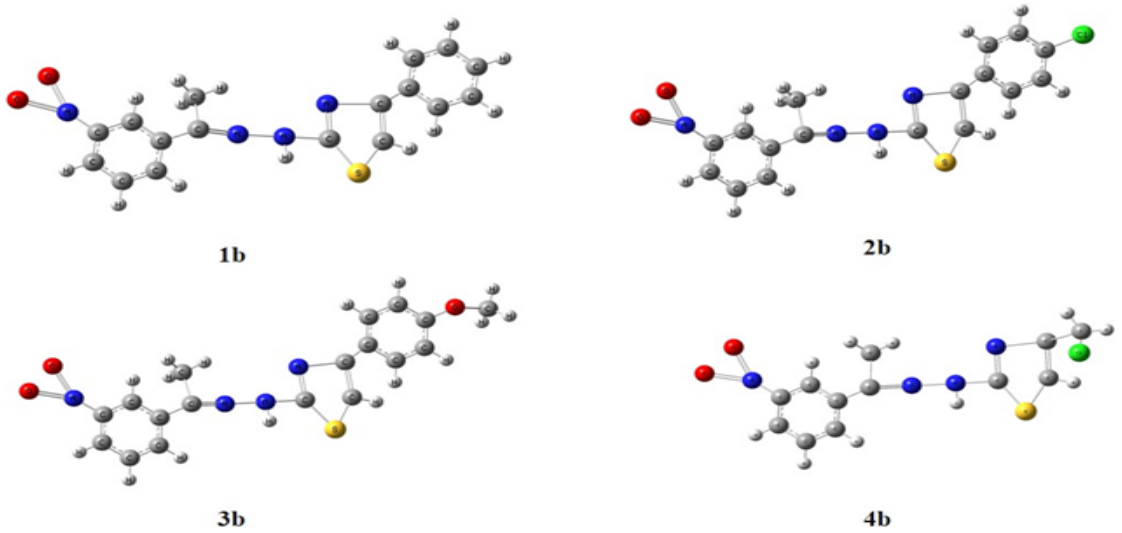


Fig. 2. Optimized molecular structures of the synthesized compounds (1b-4b)

Table 4: Docking Results of compounds(1b-4b)

Compounds	Protein (PDB ID)	Binding Affinity (Kcal/mol)	Residue in Contact	Types of Interactions	Bond Distance (Å)
1b	5JBO	-9.5	GLU172	AC	4.85981
			ASP243	AC	5.56333
			TYR245	CHB	2.91468
			GLU172	CHB	2.9389
			ARG262	CHB	2.89845
			ARG262	CHB	3.1789
			HIS266	CHB	2.87799
			ASP243	PA	3.59632
			ASP444	PA	3.89965
			HIS266	PDH	3.40432
			TRP126	PS	5.32234
			TRP126	PPT	5.4008
			ILE175	Pi-Al	4.91473
2b	5JBO	-9.4	GLU172	AC	4.75713
			ASP243	AC	5.33181
			GLU172	CHB	2.83221
			ARG262	CHB	2.89863
			ARG262	CHB	3.1345
			HIS266	CHB	2.82444
			ASP243	PA	3.36468
			ASP444	PA	3.86893
			HIS266	PDH	3.36524
			TRP126	PS	5.54955
			TRP126	PPT	5.47412
			ILE175	Pi-Al	4.89729
3b	5JBO	-9.3	ASP243	AC	4.48688
			TYR316	CHB	2.85983
			ASP243	CHB	2.89236

3b	5JBO	-9.3	ASP243	AC	4.48688
			TYR316	CHB	2.85983
			ASP243	CHB	2.89236
			TRP357	Pi-C	4.03109
			GLU172	PA	3.68864
			ASP243	PA	3.49978
			TRP434	PDH	4.19158
			GLN319	PDH	4.09525
			HIS266	PS	5.95345
			ILE175	Pi-Al	5.3695
			PHE356	Pi-Al	5.1782
4b	5JBO	-8.4	GLU172	AC	3.90228
			GLU172	CHB	2.55379
			GLU172	CHB	2.3281
			TYR179	CHB	2.42071
			TRP357	Pi-C	4.7087
			GLU384	PA	3.86456
			TRP357	PS	4.82807
			TYR316	PPS	4.52261
			TRP357	PPS	3.78312
			TRP357	PPS	4.34145
			TRP434	PPS	5.3004
			TRP434	Pi-Al	4.1378
			TRP434	Pi-Al	3.92438
			TRP442	Pi-Al	5.27478

CHB = Conventional Hydrogen Bond, PPS = Pi-Pi Stacked, AC = Attractive Charge, PA = Pi-Anion, PDH = Pi-Donor Hydrogen Bond, Pi-Al = Pi-Alkyl, PS = Pi-Sulfur, PPT = Pi-Pi T-shaped, Pi-C = Pi-Cation

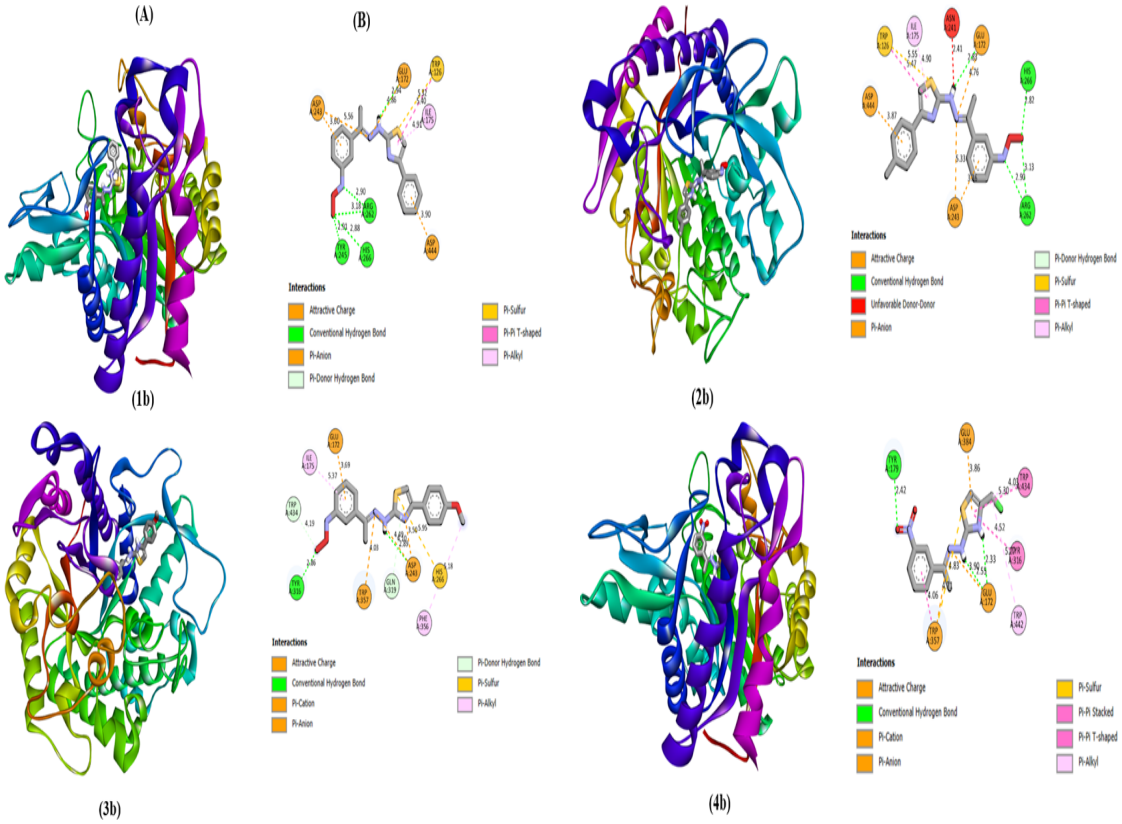


Fig. 3. (A) 3D conformer, (B) 2D docking predictions

In silico ADMET Prediction

Pharmacokinetic properties are commonly evaluated using Veber's and Lipinski's Rule of Five,provide insight into oral bioavailability. Key descriptors considered include molecular weight (MW)a, no. of H-bond acceptors (HBA)b,

no. of H-bond donors (HBD)c, lipophilicity (clogP) d, no. of rotatable bonds (NROTB)e, topological polar surface area (TPSA)f, solubility (logS)g, and percentage absorption (%ABS)h. TPSA is particularly important in drug design, as values above 140 often suggest limited oral bioavailability. The pharmacokinetic profiles of compounds 1b–4b, along with reference standards ascorbic acid (AA), ciprofloxacin (Cip), and miconazole (Mic), are summarized in Table 5.

Table 5: ADME Prediction's properties of Compounds(1b-4b)

Compound	Lipinski's violations	Lipinski's rule			Veber's rule			logSg	%ABSh
		MW[a](≤500)	HBA[b](≤10)	HBD[c](≤5)	clogP[d](≤5)	NROTB[e](≤10)	TPSA[f](140 Å^2)		
1b	0	338.39	6	1	5.05	5	111.3	-5.48	70.5
2b	0	372.84	6	1	5.67	5	111.3	-6.22	70.5
3b	0	368.42	7	1	4.99	6	120.5	-5.50	67.32
4b	0	310.76	4	1	3.90	5	111.3	-4.84	70.48
Cip	1	331	5	2	-1.53	3	72.88	-3.32	83.85
AA	0	176	6	4	-2.46	2	107.2	-0.35	71.91
Mic	1	416	3	0	4.85	6	27.5	-5.08	99.67

Frontier Molecular Orbital Analysis

The energy difference (EHOMO–ELUMO) is a significant descriptor that reflects a molecule's chemical hardness or softness, optical polarizability, kinetic stability, and electron transport capability. A smaller HOMO–LUMO gap indicates a softer and more chemically reactive molecule, whereas a larger gap is associated with greater hardness and lower reactivity. The most antioxidant-active compound is 3b (IC_{50} = 31.82±3.80 µg/mL) and the least active compound, is 2b (IC_{50} = 60.42±3.90 µg/mL). Compound 3b exhibited a narrower energy gap (′E = 3.97 eV) compared to 2b (′E = 4.22 eV), indicating higher reactivity. The corresponding HOMO–LUMO values are summarized in Table 6. Furthermore, compound 2b showed a greater hardness value (η = 2.1106 eV) relative to 3b (η = 1.935 eV), suggesting lower reactivity and enhanced stability, along with greater resistance to electron density distortion. Electrophilicity (ψ) analysis also indicated that compound 2b possesses the highest predicted toxicity among the studied compounds.

Table 6: Energies of HOMO–LUMO and other parameters of compounds(1b-4b)

Chemical reactivity indices (eV)	1b	2b	3b	4b
E_{HOMO}	-7.7384	-7.9620	-7.5059	-7.07
E_{LUMO}	-3.7067	-3.7408	-3.6354	-3.28
Energy Difference, ΔE	4.0317	4.2212	3.9705	3.79
Hardness, η′	2.01585	2.1106	1.93525	1.895
Softness, ζ	0.248	0.2369	0.2584	0.2638
Ionization potential, $I = -E_{HOMO}$	7.7384	7.9620	7.5059	7.07
Electron affinity, $A = -E_{LUMO}$	3.7067	3.7408	3.6354	3.28
Chemical potential, µ	-5.72255	-5.8514	-5.570	-5.175
Electrophilicity, ψ	8.12252	8.111	8.0174	7.066
Electronegativity, χ= – µ	5.72255	5.8514	5.570	5.175

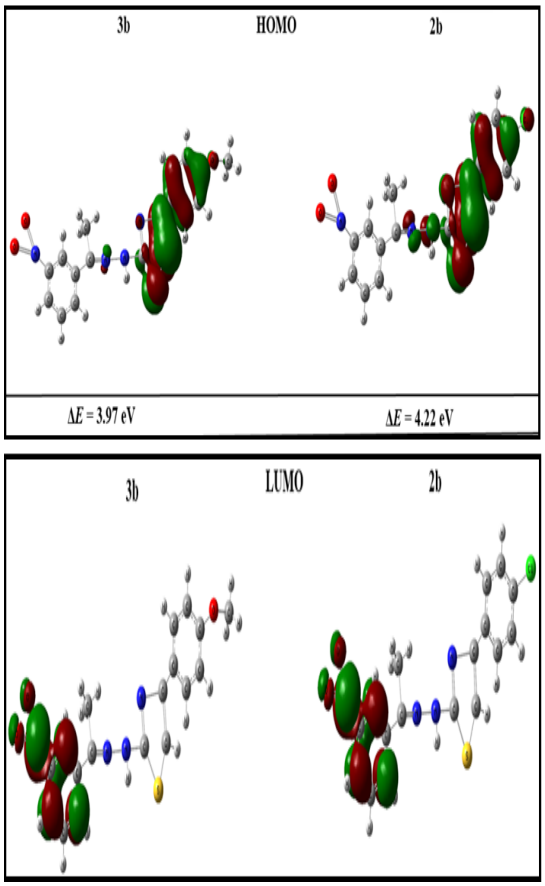


Fig. 4. Frontier molecular orbital of compound 2b and 3b

Toxicity And Drug-Score Properties

In silico evaluation of toxicity risks as well as Drug-Likeness Properties for Compounds (1b-4b), Ascorbic Acid, Ciprofloxacin and Miconazole. Reproductive (R), Irritating (I), Tumorigenic (T) and Mutagenic (M) are the four categories used to represent toxicity effects.

Table 7: *In silico* toxicity properties of Compounds (1b-4b)

Compound	Toxicity Effects				Drug-Likeness	Drug-Score
	R	I	T	M		
1b	L	L	H	L	-2.04	0.16
2b	L	L	H	L	-1.29	0.14
3b	L	L	H	H	-1.90	0.10
4b	H	L	H	H	-2.39	0.08
AA	H	L	H	H	0.02	0.16
Cip.	L	L	L	L	2.07	0.63
Mico.	L	L	L	L	7.64	0.18

L = Low, H = High, AA = Ascorbic Acid

CONCLUSION

A new series of thiazole derivatives (1b–4b) were synthesized and characterized to evaluate their antimicrobial and antioxidant activities against selected bacterial and fungal strains associated with severe or fatal infections. Compound 3b showed potential antimicrobial and antioxidant activities. On the other hand, compounds (1b-3b) showed excellent antifungal activities. In addition, docking studies, ADMET predictions were performed to analyze the potentiality of the compounds as drug candidates. Docking studies showed that all four compounds exhibited favorable binding affinities with the 5JBO proteinalong with multiple strong interactions at the binding sites of the receptor. *In silico* studies were consistent with the observed antimicrobial activity. Overall, the synthesized thiazole derivatives (1b–4b) demonstrated promising drug-like properties, suggesting their potential for further development as potent therapeutic agents.

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Authors' contributions

Ranajit Kumar Sutradhar: Paper writing, Supervision, Md. Abu Bakkar Siddiki: Methodology, Investigation,Md. Mohiuddin Emon: Formal analysis, Md. Din Islam: Formal analysis, Md. Aminul Haque: Biological Test and Analysis, Mohammad Mostafizur Rahman:Biological Test and Analysis.

Conflict of interest

No conflicts of interest among the authors on the publication of this article.

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