



Synthesis, Identification and Molecular Docking Evaluation of Novel Sulfonamide-Levofloxacin Targeting *Pseudomonas Aeruginosa*

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Abstract

Background: *Pseudomonas aeruginosa* is a Gram-negative rod-shaped bacterium that can be found in diverse environments and causes severe infections in immunocompromised patients and burn victims. Because of its extensive antibiotic resistance, effective eradication of *Pseudomonas aeruginosa* is still a significant therapeutic issue. **Objective:** This study was to improve the bactericidal activity of levofloxacin through structural modification. **Methodology:** Fifty clinical samples were collected. From May 2025 to August 2025, 50 samples were taken from Al-Yarmouk Hospital, including urine, mouth, and wound samples. Sixteen of these were identified as *P. aeruginosa*. Levofloxacin and its synthetic derivatives were assayed against these isolates at concentrations of 25, 50, and 100 µg/mL. A new series of sulfonamide derivatives A1, B1 were synthesized using the levofloxacin scaffold through the Hinsberg reaction and characterized using FT-IR and ¹H-NMR. **Results:** Molecular docking results showed strong binding affinities of the derivatives toward bacterial topoisomerase. **Conclusion:** Levofloxacin showed the highest binding energy (−12.522 kcal/mol), while the methyl and nitro analogs exhibited favorable hydrogen bonding with GLU474, GLU475, and ARG456, indicating promising antibacterial potential. [Bangladesh Journal of Infectious Diseases, June 2026;13(1):308-318]

Keywords: FT-IR; Hinsberg reaction; ¹H-NMR; levofloxacin; *Pseudomonas aeruginosa*

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Introduction

Antibiotic-resistant microorganisms are responsible for thousands of deaths each year. The prevalence of microorganisms resistant to commonly used antibiotics is increasing rapidly, posing a significant threat to public health¹. The phenomenon of antibiotic resistance is demonstrated by *Pseudomonas*, which is difficult to treat due to its inherent resistance, which includes altering the permeability of its outer wall and possessing multiple groups of β -lactamases (β -Las), also producing a variety of enzymes that break down a variety of antimicrobials, particularly Metallo β -Lactamases (M β LS)². *Pseudomonas*

aeruginosa is a gram-negative pathogen, rod shaped, aerobic bacteria, can be isolated from a variety of sources³, and multidrug-resistant (MDR) opportunistic bacterium that induces acute or chronic infections in impaired persons with chronic obstructive pulmonary disease (COPD) and other diseases⁴, among the leading bacteria responsible for hospital-acquired infections, commonly associated with medical device⁵. Many species have peculiar physiological traits that allow them to live and proliferate quickly in a variety of environments, including soil, freshwater, and oral. The release of extracellular enzymes, peptide signal molecules, peptide antibiotics, and stress-resistant endospores

are physiological characteristics crucial to their survival⁶. NSAIDs (non-steroidal anti-inflammatory drugs) also possess neuroprotective properties, and prolonged use of NSAIDs reduces the likelihood of developing Alzheimer's disease^{7,8}. Furthermore, studies have suggested that recognizing NSAID derivatives shows potential for anticancer effects⁹ while levofloxacin is a fluoroquinolone antibiotic utilized for various ailments, such as allergies, prostatitis, and urinary tract infections¹⁰. Levofloxacin functions as a DNA synthesis inhibitor in bacterial cells by blocking the bacterial type II topoisomerases, specifically DNA gyrase and topoisomerase IV¹¹. Research indicates that this rapidly eliminates bacteria while protecting human DNA. Levofloxacin acts as a bactericidal agent, and Topoisomerase IV is essential for separating DNA that is duplicated before bacterial cell division¹². Investigate the prevalence of antibiotic resistance in clinically important bacteria, *Pseudomonas aeruginosa*, as well as the possibility of NSAIDs and levofloxacin as treatments for resistant infections and related illnesses. Current studies have highlighted the critical role of oxidative stress and microbial infections in wound healing, particularly in cases involving multidrug-resistant bacteria.

Methodology

Study Settings and Population: This was a cross-sectional study. A total of 50 samples were collected from urine, oral, and wound samples from May 2025 to August 2025 from Al-Yarmouk Hospital, Iraq.

Bacterial Isolation and Identification: Bacterial samples were activated with Brain Heart Broth for 24 hours at 37°C. After that, they were cultured on Blood, MacConkey, and Cetrimide agar for the first characterization¹³. Then, transfer a single colony to the Nutrient agar medium for secondary diagnosis using VITEK 2.

Antimicrobial Susceptibility Test: Measure bacterial sensitivity and resistance to antibiotics by the well diffusion method. Choose a fresh bacterial colony that is between 18 and 24 hours old. To create a consistent bacterial solution, suspend the bacteria in 0.9% normal saline. The suspension's turbidity should be adjusted to meet the 0.5 McFarland criterion, or around 1.5×10^8 CFU/mL.

Using a sterile swab, evenly spread the calibrated bacterial suspension over the surface of Mueller-Hinton Agar. Punch wells (6 mm) into the agar using a sterile tool¹⁴. Then fill each well with the antibiotic [levofloxacin and derivatives compounds such as N'-(9-fluoro-3-methyl-10-(4-methylpiperazin-1-yl)-7-oxo-2,3-dihydro-7H-[1,4]oxazino[2,3,4-ij]quinoline-6-carbonyl)-4-nitrobenzenesulfonohydrazide (A1) and N'-(9-fluoro-3-methyl-10-(4-methylpiperazin-1-yl)-7-oxo-2,3-dihydro-7H-[1,4]oxazino[2,3,4-ij]quinoline-6-carbonyl)-4-methylbenzenesulfonohydrazide (B1).

Synthesis of Acid Hydrazide: The target compound was prepared previously according to the reported method¹⁵.

Synthesis of Sulfonamide Derivatives A1, B1: To a solution of acid hydrazide (1 gm, 2 mmol) dissolved in (10 mL) dry pyridine, p-toluenesulfonyl chloride and p-nitrosulfonyl chloride (2 mmol) were added slowly while stirring at a temperature below 40 °C. The mixture was refluxed for 4 hours, then stirred thoroughly before being poured into cold water. The formed precipitate was subsequently filtered, rinsed with cold water, dried, and recrystallized with a suitable solvent¹⁶.

Statistical Analysis: Data were entered, organized, and analyzed utilizing IBM's Statistical Package for the Social Sciences (SPSS) Statistics for Windows, Version 26.0. Descriptive analysis was employed to summarize the elements of the sample's continuous variables, represented by the mean and standard deviation. The paired-samples t-test was utilized to examine the averages of two related variables from the same subjects. The criterion for significance was set at $p < 0.05$.

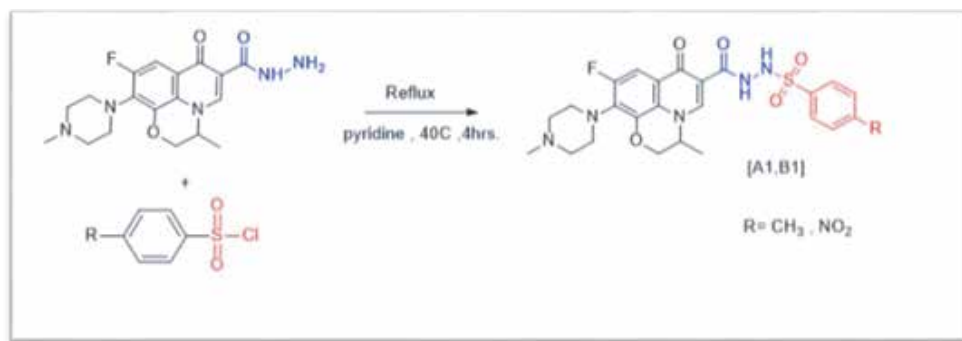
Ethical Consideration: The Medical Laboratory Techniques Department's local committee agreed to the experiments mentioned in this research SC1TUH-0007; 20 December 2024, and all volunteers gave oral consent with details and advantages. The study was supervised by specialists at the Al-Yarmouk Hospital.

Results

A total of 50 bacterial samples were collected from various sources; only 16 samples were selected. Table 1 presents the types of bacteria identified.

Table 1: Types of Bacteria

Types of Bacteria	Oral	Urine	Wound	Total
<i>Pseudomonas aeruginosa</i>	2 (4.0%)	6 (12.0%)	8 (16.0%)	16 (32.0%)



Scheme 1: Synthesis of Sulfonamide Derivatives

Characterization of Sulfonamide Derivatives (A1)^{17,18} Orange solid ; yield: (74.0%); m.p 253-255 °C; FT-IR ν_{max} (cm⁻¹): 3006 (C-H) arom. , 2914, 2883 (C-H) aliph. , 1683 (C=O amide) , 1598 (Olefinic C=C) , 1504 asym , 1342sym (NO₂) , (sulfone amide SO₂-NH)1375 asym , 1173 sym ; ¹H-NMR (400 MHz, DMSO-d₆ , ppm) 1.40-1.45 (d, 3H, CH₃-CH) ; 2.38-2.51 (m, 1H, CH₃-CH in ring Oxazine ; t, 2H, N-CH₂CH₂-N) ; 4.39-4.59 (d, 2H, CH-CH₂O) ; 4.94 (s, 3H, CH₃-N) ; 7.19-7.53 (m, 5H, Ar-H) ; 8.64 (s, 1H , (O=C-CH=C) ; 8.96 (s, 1H , (O=C-NH) ; 14.99 (s, 1H , -NH-S-(O)₂).

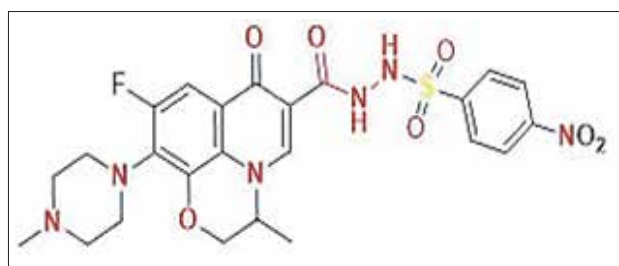
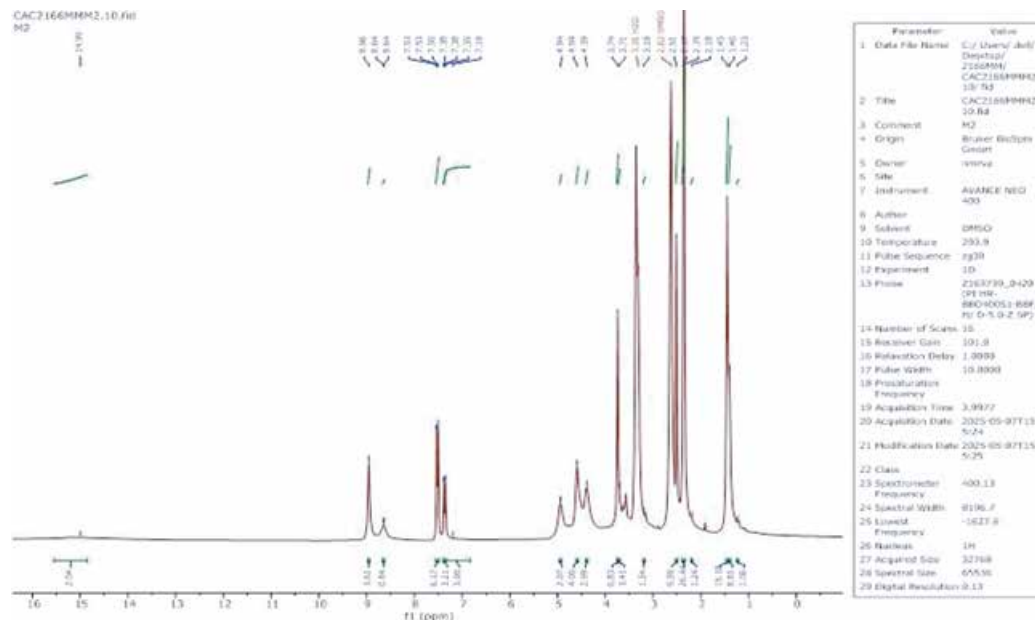


Figure 1: Synthesis of sulfonamide derivatives A1

Figure II: ¹H-NMR spectrum of sulfonamide derivatives A1

Characterization of sulfonamide derivatives (B1) Brown solid ; yield: (81.0%); m.p 213 to 215 °C; FT-IR ν_{max} (cm⁻¹): 3013 (C-H) arom. , 2972, 2860 (C-H) aliph. , 1665 (C=O amide) , 1570 (Olefinic C=C) , 1514 asym , 1336sym (NO₂) , (sulfone amide SO₂-NH)1363 asym , 1181 sym ; ¹H-NMR (400 MHz, DMSO-d₆ , ppm) 1.43-1.47 (d, 3H, CH₃-CH) ; 2.28-2.75 (m, 1H, CH₃-CH in ring Oxazine ; t, 2H, N-CH₂CH₂-N) ; 3.16 (s, 3H, CH₃-Ar) ; 4.38-4.61 (d, 2H, CH-CH₂O) ; 4.91 (s, 3H, CH₃-N) ; 7.30-7.63 (m, 5H, Ar-H) ; 8.90 (s, 1H , (O=C-CH=C) ; 8.99 (s, 1H , (O=C-NH) ; 12.98 (s, 1H , -NH-S-(O)₂).

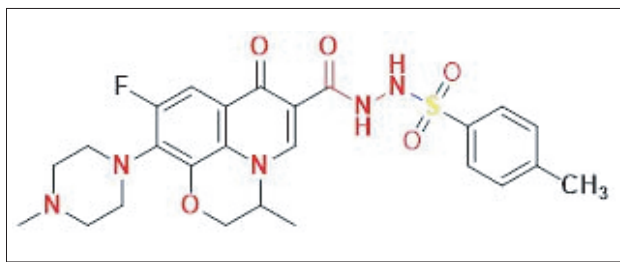


Figure III: Synthesis of sulfonamide derivatives B1

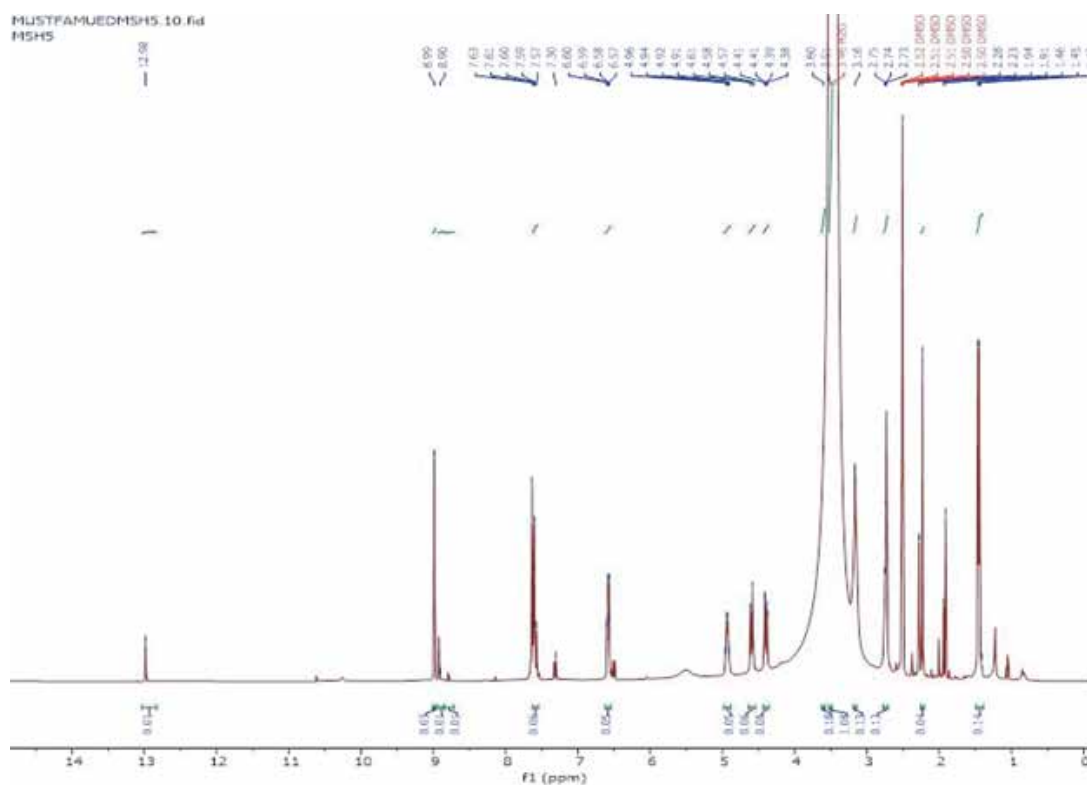


Figure IV: ¹H-NMR spectrum of sulfonamide derivatives B1

Among the diagnosed samples, 16 were classified as *Pseudomonas*. The remaining samples represented other bacterial species that were excluded from further consideration.

In this study, levofloxacin was used at concentrations of 25, 50, and 100 $\mu\text{g/mL}$, and its relative efficacy was compared with that of its modified derivative compounds (A1, B1) against *Pseudomonas aeruginosa* (Scheme 1).

Ligand Preparation Two-dimensional structures of synthesized compounds (A1, B1) were drawn using ChemDraw Ultra 12 software, subsequently converted to three-dimensional structures, and saved as mol files. The energy minimization synthesized compounds (A1, B1) were calculated using Avogadro 3.0 with the MMFF94s force field.

Protein Preparation The three-dimensional structure of DNA gyrase protein (PBP) (PDB ID: 3RAE) was obtained from the Protein Data Bank (<https://www.rcsb.org/>) and prepared by Protein Preparation wizard of Maestro 12.5 software suite using default settings. These settings include bond order assignment, hydrogen addition, creation of zero-order bond for metals, creation of disulfide bonds, removal of water molecules beyond 5 Å from het groups, energy optimization, and restrained minimization using the OPLS3e force field¹⁹.

Molecular Docking The protein grid for molecular docking studies was prepared using the Glide-Grid wizard of Maestro 12.5 software suite. The binding site was identified by selecting one atom of the

co-crystallized ligand (Ciprofloxacin). Other settings were applied as default. Molecular docking studies were conducted using the Glide Docking wizard of Maestro 12.5 software suite with standard precision (SP) mode. The remaining settings were applied as default. Results were visualized and analyzed using BIOVIA Discovery Studio 2021.

Molecular Docking Study Molecular docking was performed to assess the binding affinity and interaction pattern of levofloxacin and its synthetic derivatives with bacterial topoisomerase, an important enzyme in DNA replication as well as an established antibacterial target. Levofloxacin, a clinically approved fluoroquinolone and the co-crystallized ligand of the topoisomerase complex, was selected to be the reference standard. Table 1 summarizes the docking scores (Glide GScore) and interaction analyses. For the co-crystallized ligand, levofloxacin,²¹ the binding affinity was the highest, as indicated by the lowest docking score of -12.522 kcal/mol and Glide RMSD value of 1.05 Å.²¹, which verified the good affinity of the docking method and will be a reference for the synthesized derivatives. Of the existing analogs investigated, there was a high docking score for the starting compound (-10.313 kcal/mol, similar to that of the reference ligand). Methyl (-9.610 kcal/mol) and nitro (-9.198 kcal/mol) derivatives also exhibited optimal binding behavior. This means that small electron donating groups (methyl and nitro) are more effective in binding the compound. Detailed analysis revealed that hydrogen bonding was most consistent with critical residues, as GLU474, GLU475, ARG456 and SER79²², known to stabilize ligand orientation

within the topoisomerase binding pocket. As an example, levofloxacin had multiple hydrogen bonds with GLU474 and GLU475 as well as strong electrostatic contacts with ARG456, demonstrating the optimum binding mode. Methyl and nitro derivatives remained characterized by similar hydrogen bonding configurations and this probably indicates that modification conserved major pharmacophoric interactions.

Hydrophobic interactions including π - π stacking and π -alkyl contacts, were abundant across all compounds, particularly with DNA nucleotides DA1, DA5, DT4, and DT15. These interactions were essential for stabilizing the ligands within the enzyme-DNA complex. The nitro and methyl derivatives exhibited enhanced hydrophobic contacts, compensating for modest reductions in hydrogen bonding.

Metal coordination with the Mg^{2+} ion (MG101) was consistently observed for levofloxacin and all derivatives, underscoring its importance for topoisomerase inhibition. Additionally, electrostatic interactions with GLU474, GLU475, and ARG117 were conserved across most ligands, further confirming their role as anchoring residues in ligand stabilization. Overall, the comparative docking analysis highlights the critical role of GLU474, GLU475, ARG456, and Mg^{2+} coordination in ligand binding to topoisomerase. The co-crystallized levofloxacin ligand remains the most optimized pharmacophore, while the methyl and nitro derivatives exhibit promising activity profiles. These findings warrant further investigation of the methyl and nitro derivatives in in vitro and in vivo

Table 2: Molecular Docking Results and Interpretations of the Studied Acid Hydrazide Compounds

No.	Docking Score	Glide rmsd	Hydrogen Bond Amino Acids (Bond Length)	Hydrophobic Amino Acids (Bond Length)	Others (Type & Bond Length)
Acid Hydrazide	-10.313	90.554	GLU475 (3.20), GLU474 (4.24), SER79 (2.31), SER79 (2.13), GLU474 (2.84, Carbon H), GLU475 (3.19, Carbon H), DA5:O4' (3.46, Carbon H), ARG456 (3.75, Carbon H), DA5:N3 (3.28, Carbon H)	DA1 (3.75, Pi-Pi Stacked), DA1 (3.89, Pi-Pi Stacked), DA1 (3.79, Pi-Pi Stacked), DA1 (5.04, Pi-Pi Stacked), DT15 (4.74, Pi-Pi Stacked), DT4 (4.99, Pi-Pi Stacked), DA5 (5.02, Pi-Pi Stacked), DA5 (3.77, Pi-Pi Stacked), DA5 (4.47, Pi-Pi Stacked), ARG456 (5.30, Alkyl), DA1 (4.17, Pi-Alkyl), DA1 (4.55, Pi-Alkyl), DA1 (4.81, Pi-Alkyl), DA5 (4.93, Pi-Alkyl)	GLU475 (Salt Bridge, 3.20), GLU474 (Electrostatic, 4.24), MG101 (Metal-Acceptor, 2.02, 2.33), DT4 (Halogen, 3.18), DA5 (Halogen, 3.13, 3.54)

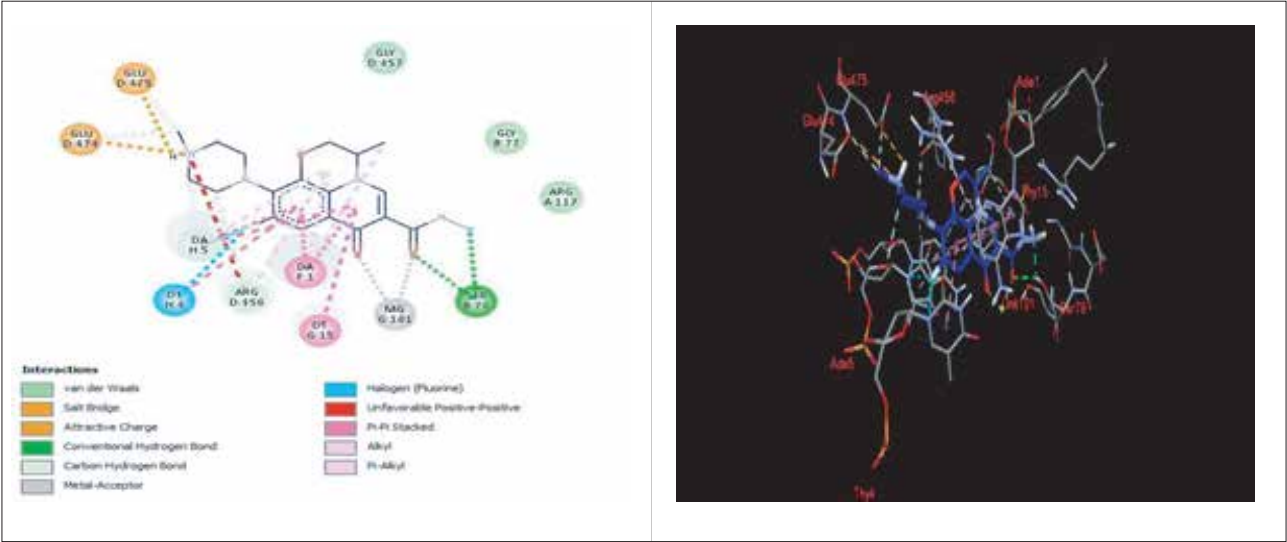


Figure V: Computational Analysis of Ligand-Protein Interactions of Acid Hydrazone Compounds

Table 3: Molecular Docking Results and Interpretations of the Studied A1 Compounds.

No.	Docking Score	Glide rmsd	Hydrogen Bond Amino Acids (Bond Length)	Hydrophobic Amino Acids (Bond Length)	Others (Type & Bond Length)
A1	-9.198	88.673	SER79 (2.36), DA1:N7 (2.45), DA1:O4' (2.53, Carbon H), GLU475 (2.47, 2.78, Carbon H), GLU474 (2.20, Carbon H), ARG456 (2.41, Carbon H), DA5:N3 (2.57, Carbon H)	DA1 (3.72, 3.88, 3.84, 5.02, Pi-Pi Stacked), DT15 (4.84, Pi-Pi Stacked), DT4 (5.16, Pi-Pi Stacked), DA5 (4.96, 3.83, 4.57, Pi-Pi Stacked), ARG456 (4.36, Alkyl), DA1 (3.94, 4.16, Pi-Alkyl), DA1:C (4.92, 3.77, Pi-Alkyl), DA5 (5.26, 5.38, Pi-Alkyl)	MG101 (Metal-Acceptor, 2.78, 2.01), DT4 (Halogen, 3.49), DA5 (Halogen, 3.60, 3.51)

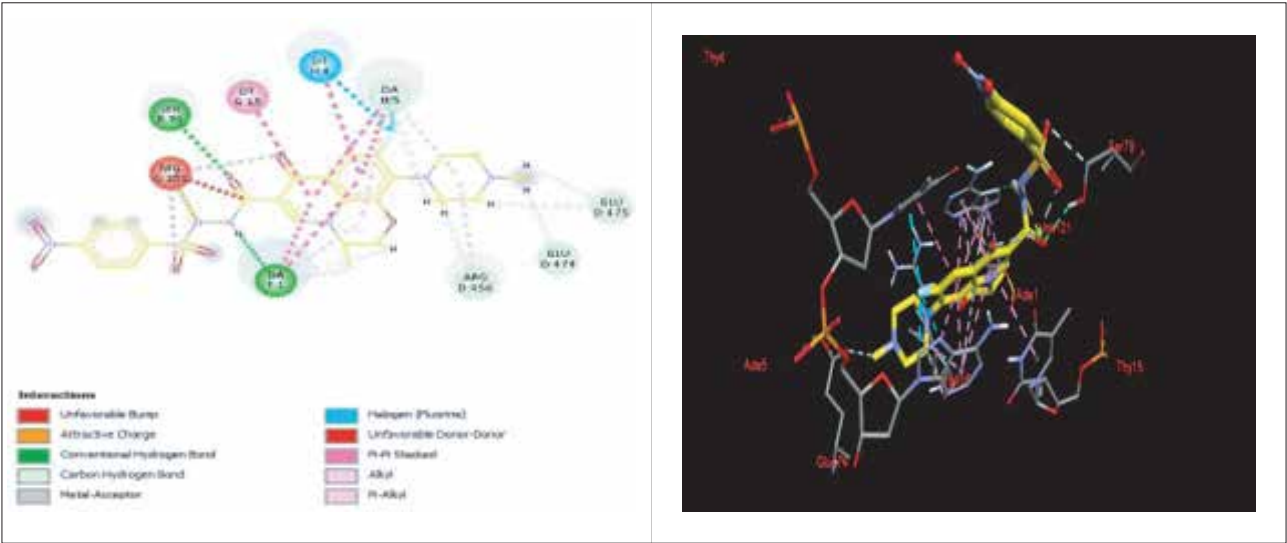
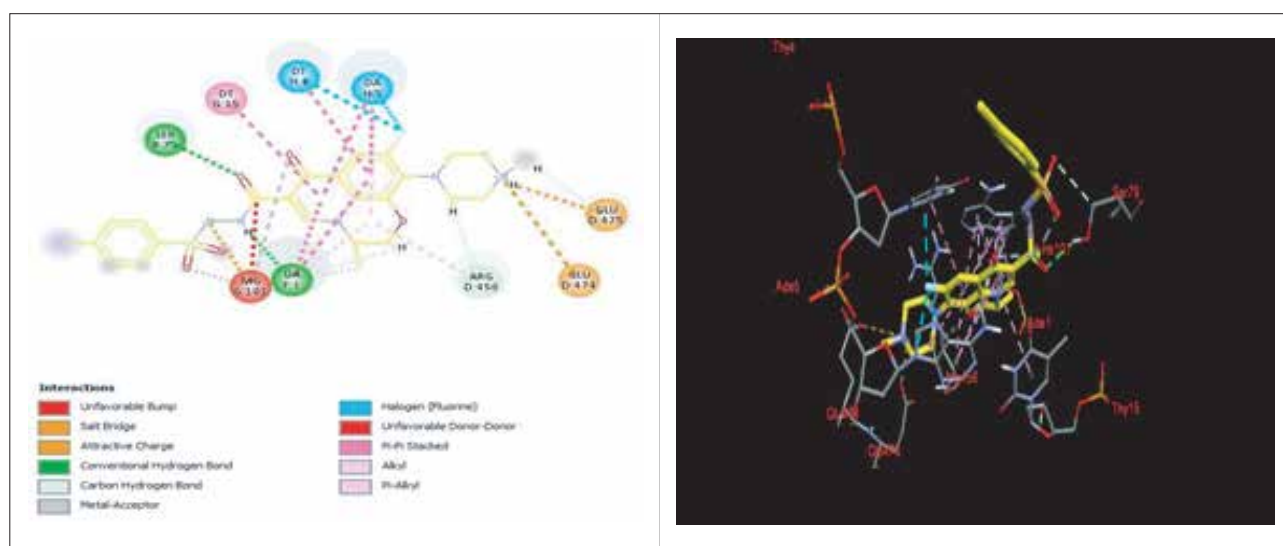


Figure VI: Computational analysis of ligand-protein interactions A1 compounds

Table 4: molecular docking results and interpretations of the studied B1 compounds

No.	Docking Score	Glide rmsd	Hydrogen Bond Amino Acids (Bond Length)	Hydrophobic Amino Acids (Bond Length)	Others (Type & Bond Length)
B1	-9.61	89.157	GLU475 (2.57, Salt Bridge), SER79 (2.37), DA1:N7 (2.45), DA1:O4' (2.55, Carbon H), GLU475 (2.62, Carbon H), ARG456 (2.21, Carbon H),	DA1 (3.72, 3.94, 3.86, 5.06, Pi-Pi Stacked), DT15 (4.83, Pi-Pi Stacked), DT4 (5.23, Pi-Pi Stacked), DA5 (4.93, 3.79, 4.56, Pi-Pi Stacked), ARG456 (5.49, Alkyl), DA1 (4.01, 4.22, Pi-Alkyl), DA1:C (4.94, 3.79, Pi-Alkyl), DA5 (5.25, Pi-Alkyl)	GLU475 (Salt Bridge, 2.57), GLU474 (Electrostatic Attractive Charge, 4.27), MG101 (Metal-Acceptor, 2.86, 2.01), DT4 (Halogen, 3.63), DA5 (Halogen, 3.62, 3.44)

**Figure VII: Computational analysis of ligand-protein interactions B1 compounds.****Table 5: Molecular Docking Results and Interpretations Of the Studied Levofloxacin Compounds**

No.	Docking Score	Glide rmsd	Hydrogen Bond Amino Acids (Bond Length)	Hydrophobic Amino Acids (Bond Length)	Others (Type & Bond Length)
Levofloxacin (Crystallized Ligand)	-9.61	89.157	GLU475 (3.14, Salt Bridge), ARG456 (2.70, 3.05, Carbon H), DA1:O4' (2.84, 2.47, Carbon H), GLU474 (2.26, Carbon H), GLU475 (2.27, Carbon H)	DA1 (3.76, 3.76, 3.66, 4.80, Pi-Pi Stacked), DT15 (4.72, Pi-Pi Stacked), DT4 (5.21, Pi-Pi Stacked), DA5 (5.27, 3.91, 4.72, Pi-Pi Stacked), DA1 (3.92, 4.10, Pi-Alkyl), DT15:C (4.08, Pi-Alkyl), DA5 (5.36, Pi-Alkyl)	GLU475 (Salt Bridge, 3.14), ARG117 (Electrostatic Attractive Charge, 4.36), MG101 (Electrostatic Attractive Charge, 4.11, Metal-Acceptor 1.90, 2.21), GLU474 (Electrostatic Attractive Charge, 4.38), DT4 (Halogen, 3.36), DA5 (Halogen, 3.28, 3.58)

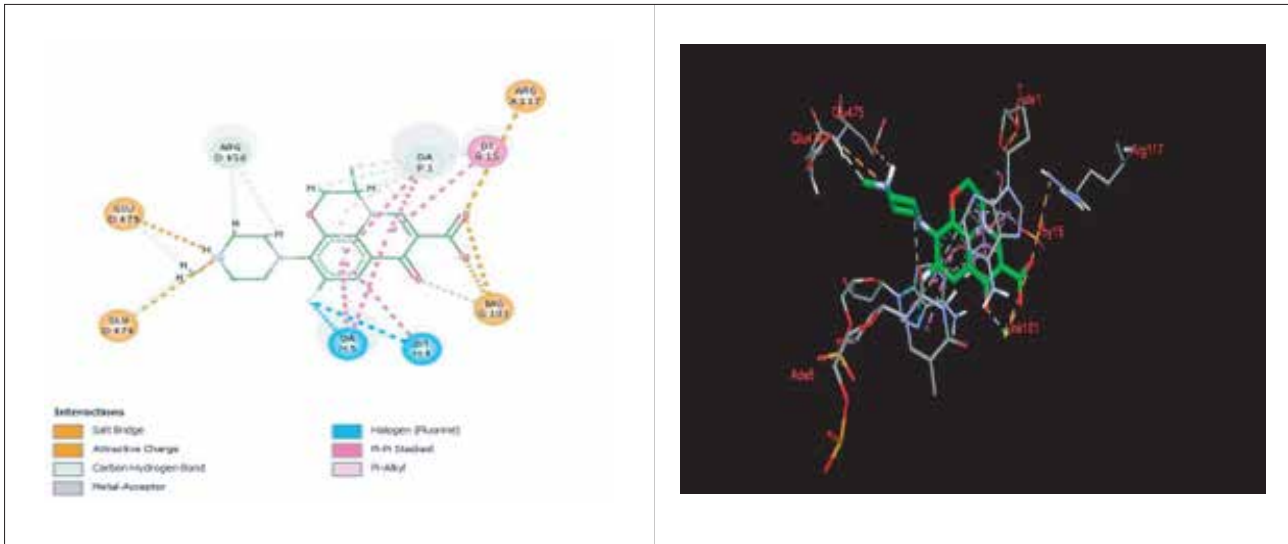


Figure VIII: Computational analysis of ligand-protein interactions of Levofloxacin compounds

Table 6: Inhibition Zone of *Pseudomonas aeruginosa* by the Well Diffusion Method

<i>P. aeruginosa</i> sample	Inhibition zone diameter (mm)								
	Levofloxacin			A1			B1		
	25.0%	50.0%	100.0%	25.0%	50.0%	100.0%	25.0%	50.0%	100.0%
P1	18	20	22	28	27	30	20	24	29
P2	19	21	23	40	13	21	21	23	28
P3	16	20	21	16	21	23	18	20	21
P4	18	22	23	40	40	25	19	20	21
P5	17	21	22	18	24	28	15	19	23
P6	18	20	21	40	40	41	40	35	38
P7	16	22	23	40	40	41	41	30	36
P8	19	23	23	15	20	22	18	30	25
P9	15	20	21	15	23	28	18	30	28
P10	16	21	20	25	30	20	19	25	30
P11	18	20	22	29	33	30	22	25	33
P12	19	22	23	20	24	28	27	23	30
P13	15	21	22	18	25	29	25	30	20
P14	19	20	23	25	30	38	23	35	40
P15	18	20	22	23	22	23	27	26	29
P16	17	20	21	21	21	22	24	22	24

assays to assess their potential as novel topoisomerase inhibitors²¹.

Table 6 shows the inhibition zones of bacterial samples when using different levofloxacin concentrations (25.0%, 50.0%, and 100.0%) and is compared to their derivatives (Figure IX).

The 12 most hazardous categories of super-drug-resistant bacteria that are the greatest threat to human health worldwide were listed by the World Health Organization (WHO). Since *Pseudomonas aeruginosa* is at the top of the ranking, the creation of novel antibiotics should be prioritized²⁴.

The natural resistance of *Pseudomonas aeruginosa* to numerous drug classes, its capacity to develop resistance (through mutations) against all pertinent treatments, its high resistance rates globally, and its frequent association with serious infections make it a particularly troublesome nosocomial pathogen. The prevalence of multidrug resistance (MDR) is rising. Several strains are currently known to be resistant to practically all effective antipseudomonal medications²⁵.

The mean inhibition zones of Compound A1 (25.81 mm) and Compound B1 (23.56 mm) were substantially higher than those of Levofloxacin (17.38 mm) at a concentration of 0.25. At the

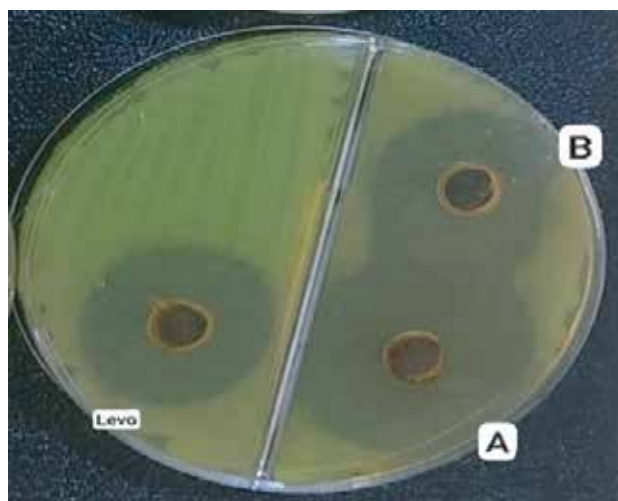


Figure VIII: Computational analysis of ligand-protein interactions of Levofloxacin compounds

concentration of 0.5, the mean inhibition zones of Compound A1 (27.0625 mm) and Compound B1 (26.0625 mm) were significantly higher than Levofloxacin (20.8125 mm). At a concentration of 1, they even show a mean inhibition zone higher in Compound A1(28.0625 mm) and Compound B1 (28.4375 mm) than Levofloxacin's (22.0000 mm) (Table 7).

According to the Centers for Disease Control and Prevention's 2019 report, there has been a rise in antibiotic resistance. *P. aeruginosa* causes 2.8

million illnesses and 35,000 deaths annually in the United States and 33,000 in Europe. An estimated 10 million cases of death and morbidity are predicted by 2050²⁶ found that, in vitro, levofloxacin has better bactericidal activity than ciprofloxacin, whereas the time-kill curve shows that ciprofloxacin has almost the same bactericidal activity as levofloxacin.

Discussion

All results for compounds A and B at different concentrations (25, 50, and 100) were higher than Levofloxacin, with a highly significant p-value recorded. Additionally, the table shows that compound A at a concentration of 50.0% was the highest in killing bacteria compared to the other concentrations, as the p-value was 0.006.

Kanafani et al²⁷ notes that levofloxacin therapy affects the growth rate and approaches the resistance breakpoint more quickly than ciprofloxacin treatment. Chamoun et al²⁸ detected an alarming non-susceptibility of 24.0% to ciprofloxacin among the *P. aeruginosa* clinical isolates, which is similar to the rate reported from nosocomial infections in Lebanon (22.7%).

Ciprofloxacin has greater capacity to eradicate *P. aeruginosa*, but some mutations and efflux pump overexpression may make the bacterium more vulnerable to resistance. These results show that whereas levofloxacin and ciprofloxacin are both FQs,

Table 7: Antibacterial Activity of Levo and Derivatives Against *Pseudomonas aeruginosa*

	Minimum	Maximum	Mean	Std. Deviation
Levo-0.25	15	19	17.38	1.408
Levo-0.5	20.00	23.00	20.8125	.98107
Levo-1	20.00	23.00	22.0000	.96609
A-0.25	15	40	25.81	9.446
A-0.5	13.00	40.00	27.0625	7.92017
A1	20.00	41.00	28.0625	6.78694
B-0.25	15	41	23.56	7.438
B-0.5	19.00	35.00	26.0625	5.07896
B1	20.00	40.00	28.4375	6.06596

Table 8: Paired T-Test for A and B compared to Levo at Various Concentrations.

	Mean	Std. Deviation	Std. Error Mean	Lower	Upper	P-value
A0.25 - Levo0.25	8.438	9.136	2.284	3.569	13.306	0.002**
B0.25 - Levo0.25	6.188	7.565	1.891	2.156	10.219	0.005**
A0.5 - Levo0.5	6.25000	7.91202	1.97800	2.03398	10.46602	0.006**
B0.5 - Levo0.5	5.25000	5.24722	1.31181	2.45395	8.04605	0.001**
A1 - Levo1	6.06250	6.64799	1.66200	2.52003	9.60497	0.002**
B1 - Levo1	6.43750	6.04394	1.51098	3.21691	9.65809	0.001**

** = mean highly significant

their bactericidal activity and resistance-inducing capabilities differ²⁹. Itoi and Willcox³⁰ study concludes that the combination of levofloxacin and cefmenoxime may enhance antibacterial activity against *P. aeruginosa* isolated from corneal keratitis, presenting a viable solution for combating antibiotic-resistant bacteria.

Conclusion

The structural modification of levofloxacin successfully produced new sulfonamide derivatives with enhanced antibacterial potential against *Pseudomonas aeruginosa*. Docking results confirmed strong interactions of the derivatives with key topoisomerase residues, supporting their potential as effective antibacterial agents. The findings highlight that small electron-donating substituents can improve binding affinity and may guide future drug design to overcome antibiotic resistance.

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Conflict of interest:

The authors declare that they have no conflict of interest.

Financial Disclosure

None.

Authors' contributions

Mustafa was responsible for the analysis and description. Esraa was responsible for collecting analyzing samples, while Safa was responsible for gathering sources. All authors reviewed the manuscript for significant intellectual content, approved the final version, and agreed to share responsibility for all aspects of the work.

Data Availability

Any questions regarding the availability of the study's supporting data should be addressed to the corresponding author, who can provide it upon justifiable request.

Ethics Approval and Consent to Participate

Ethical approval was granted by the Research Ethics Committee of Medical Laboratory Techniques Department's, Iraq (reference no. SC1TUH-0007; 20 December 2024). The study was conducted in accordance with the Declaration of Helsinki, and written informed consent was obtained from all participants.

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