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Design, Synthesis and Characterization of Disulfonamides Derivatives for Biological Evaluation

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ABSTRACT

In the present study, a series of six novel disulfonamide derivatives (3a–3f) were successfully synthesized by systematic modification of the parent sulfonamide scaffold through variation at the R_1 and R_2 positions. The R_1 position was substituted with acetyl and propionyl groups, while the R_2 position incorporated electron-withdrawing halogens (Cl, Br, and F). These structural modifications were designed to explore their influence on physicochemical properties and antimicrobial activity. All synthesized compounds were obtained in satisfactory yields and were characterized using elemental analysis, melting point determination, TLC, FT-IR, mass spectrometry, and 1H-NMR spectroscopy. The antibacterial evaluation against Escherichia coli, Pseudomonas aeruginosa, and Staphylococcus aureus revealed that several synthesized disulfonamide derivatives exhibited moderate to significant, dose-dependent activity, with compound 3e (propionyl–bromo substituted) showing the highest antibacterial potency and broad-spectrum efficacy, particularly demonstrating superior inhibition against P. aeruginosa compared to the standard drug sulfamethoxazole. In antifungal studies against Candida albicans and Aspergillus niger, compound 3f (propionyl–fluoro substituted) emerged as the most active derivative, displaying inhibition zones comparable to or exceeding those of the standard antifungal agent miconazole at certain concentrations, while other derivatives showed moderate to low activity. Overall, the structure–activity relationship indicates that the presence of electron-withdrawing halogens combined with increased lipophilicity due to acyl substitution enhances membrane penetration, thereby improving both antibacterial and antifungal activities.

Keywords: Heterocyclic compound, sulfonamides, antifungal, antibacterial

INTRODUCTION

The rapid emergence of antimicrobial resistance has become a critical global health concern, necessitating the continuous search for novel and effective therapeutic agents. Conventional antibiotics are increasingly losing their efficacy due to the development of resistant microbial strains, leading to prolonged infections and higher mortality rates. In this context, the design and development of new antimicrobial compounds with improved potency and broader spectra of activity are of paramount importance. [1] Rational drug design, combined with synthetic chemistry and detailed characterization, plays a vital role in discovering molecules capable of overcoming microbial resistance mechanisms.

Sulfonamides represent one of the earliest classes of synthetic antimicrobial agents and have maintained their significance due to their broad-spectrum activity and well-established mechanism of action. [2] These compounds act by inhibiting dihydropteroate synthase, an enzyme essential for folic acid biosynthesis in microorganisms. Structural modification of sulfonamides has been widely explored to enhance their biological activity, reduce toxicity, and improve pharmacokinetic properties. Among these modifications, disulfonamide derivatives have attracted considerable attention owing to the presence of two sulfonamide moieties, which may enhance binding interactions with microbial targets and improve antimicrobial efficacy. [3, 4]

Evaluation of the antimicrobial activity of synthesized disulfonamide derivatives is a crucial step in assessing their potential as therapeutic agents. In vitro screening against a range of Gram-positive and Gram-negative bacteria, as well as fungal strains, helps establish structure–activity relationships and identify promising lead compounds. Overall, the design, synthesis, and characterization of disulfonamide derivatives offer a valuable strategy for the development of new antimicrobial agents capable of addressing the growing challenge of drug-resistant infections. [5, 6]

METHODOLOGY

Materials and instruments: The chemicals and reagents used in the present study were obtained from reputed commercial suppliers to ensure high purity and reliability. Anisole and chlorosulfonic acid were procured from Sigma-Aldrich. Ethanol and

methanol were purchased from Merck, while hydrochloric acid, sulphuric acid, and dimethyl sulfoxide (DMSO) were obtained from TCI Chemicals. All chemicals were of analytical grade and were used as received without further purification. Melting point measurements were accurately determined and documented using the SATYAM STM-79 apparatus. UV-Visible spectrophotometry was conducted using a JASCO V-360 spectrophotometer to record the UV maximum of the compounds. Infrared (IR) spectra were captured via the potassium bromide pellet method utilizing a JASCO FTIR 4100 Spectrophotometer.

Synthesis: Two primary stages were involved in the production of the target disulfonamide derivatives. The initial step was the chlorosulfonation of anisole to create the essential intermediate, 4-methoxybenzene-1,3-disulfonyl dichloride (Intermediate 1). In short, a 250 mL round-bottom flask was filled with precisely weighed anisole (20 g, 119.6 mmol), and chlorosulfonic acid (15 mL) was added gradually while stirring continuously. The disulfonyl dichloride intermediate was created by heating the reaction mixture under reflux on a water bath for two hours. Once the reaction was finished, the mixture was concentrated, allowed to cool to ambient temperature, and then recrystallized from ethanol to produce pure Intermediate 1. [7, 8]

The final disulfonamide compounds (3a–3f) were synthesized in the second step using Intermediate 1 by nucleophilic substitution with different substituted anilines. The proper substituted aniline (6.0 mmol) and triethylamine (15 mL) were added as a base to a solution of 4-methoxybenzene-1,3-disulfonyl dichloride (0.87 g, 3.0 mmol) in anhydrous tetrahydrofuran (15 mL). Thin-layer chromatography (TLC) was used to track the reaction mixture's progress as it was agitated for around three hours at room temperature and then refluxed for ten hours. After the reaction was finished, the solvent was extracted and the mixture was concentrated under low pressure. [8]

To help the end products precipitate, a combination of methanol and water was added to the crude residue that remained after the solvent was removed. By changing the substituents on the aniline moiety, such as chloro, bromo, and fluoro groups with methoxy or ethoxy substituents, a number of disulfonamide derivatives were created using this general method, producing compounds 3a–3f. To verify their chemical structures, these substances underwent further purification and characterisation research. [8, 9]

Antimicrobial study: The antimicrobial activity of the final compounds was done in laboratories section. [10]

The antimicrobial activity of the synthesized disulfonamide derivatives was evaluated in vitro using standard laboratory procedures: Three clinically relevant bacterial strains—Escherichia coli, Pseudomonas aeruginosa, and Staphylococcus aureus—maintained on nutritional agar medium were subjected to preliminary antibacterial screening using the agar well diffusion technique. The reference standard was the well-known antibacterial drug sulfamethoxazole, and the negative control was dimethyl sulfoxide (DMSO). Pure bacterial isolates were subcultured in brain heart infusion broth at 37 °C for 18–24 hours in order to conduct the sensitivity test. The bacterial solution was evenly distributed onto Mueller-Hinton agar (MHA) plates after being standardized to 1.5×10^2 CFU/mL using the 0.5 McFarland turbidity standard. After drying the inoculated plates, wells of 6 mm diameter were punched aseptically into the agar and filled with 100 µL of the test chemicals made in DMSO at various doses (500, 250, 125, 62.5, and 31.25 µg/mL). The width of the inhibition zones (in millimeters) surrounding each well was used to measure the antibacterial activity after the plates were incubated for 24 hours at 37 °C. To achieve the necessary test concentrations, serial dilutions of the synthesized compounds were made, beginning with a stock solution of 1000 µg/mL (0.01 g dissolved in 10 mL DMSO) and continuing with two-fold dilutions. For comparison, sulfamethoxazole was diluted using the same method. The size of the inhibition zone that developed around the wells was used to calculate each compound's antibacterial effectiveness. [11-15]

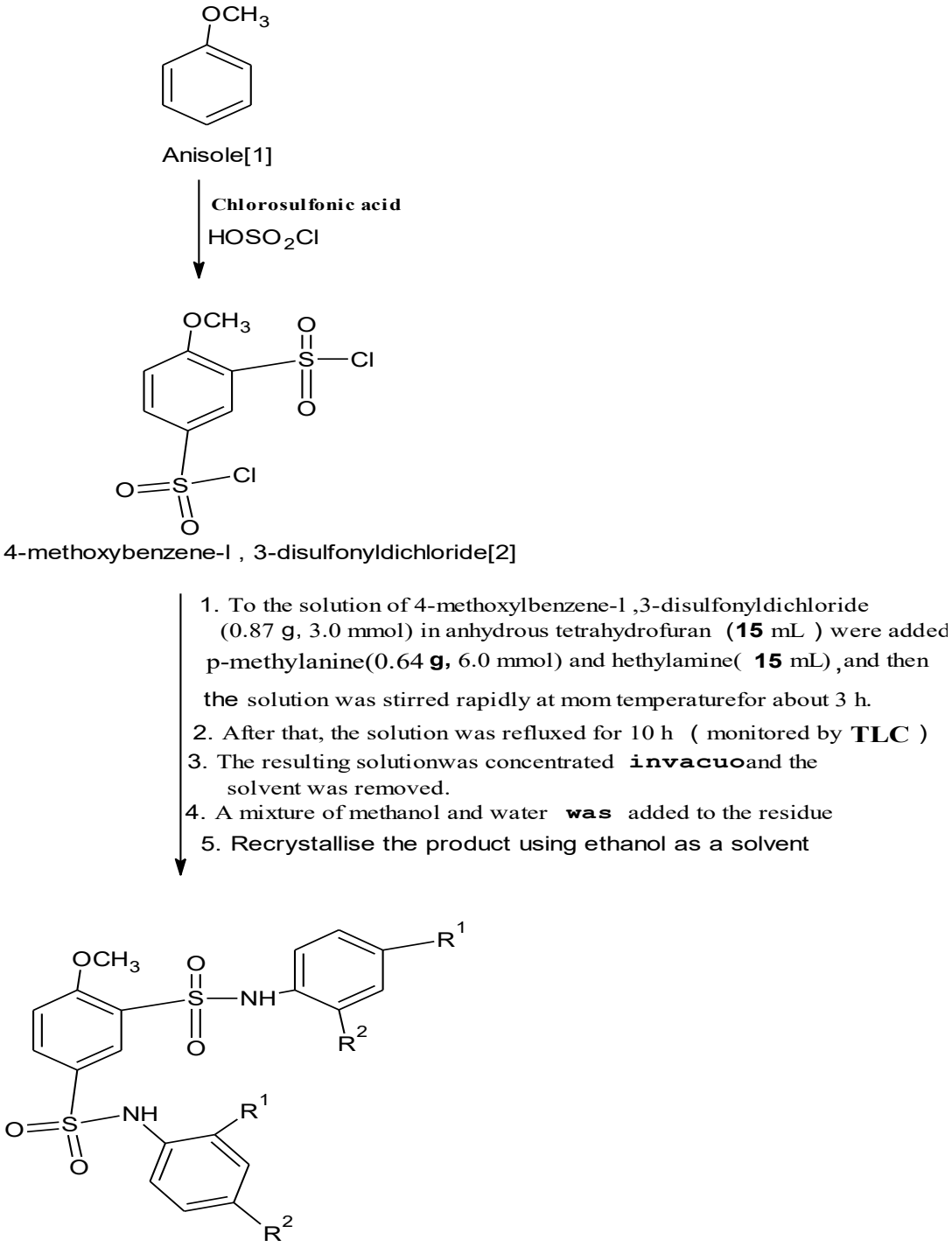
Antifungal activity: The serial broth dilution technique was used to assess the newly synthesized compounds' antifungal efficacy against Aspergillus niger and Candida albicans. Miconazole was utilized as the reference standard for comparison, and the solvent was dimethyl sulfoxide (DMSO). The minimum inhibitory concentration (MIC), which is the lowest concentration of the substance at which no discernible fungal growth was seen, was calculated to assess antifungal activity. The test chemicals and miconazole were first dissolved in 10% DMSO to achieve a stock concentration of 20,000 µg/mL in order to prepare the working inoculum. After incubating fungal cultures on Sabouraud dextrose agar slants for 48 hours, a loopful of the generated culture was added to new Sabouraud dextrose broth and cultured for an additional 48 hours to reach a concentration of 10–10 CFU/mL. This suspension served as the inoculum after being suitably diluted. To produce concentrations ranging from 100 to 1.56 µg/mL, sterile test tubes containing Sabouraud dextrose broth were serially diluted two times. There was a growth control with just the culture medium and a vehicle control with 10% DMSO. The tubes were incubated at 25–27 °C for 48 hours following inoculation with 0.1 mL of fungal solution, and MIC values were noted based on the lack of discernible growth. [16-19]

RESULTS AND DISCUSSION

In the present study, six novel disulfonamide derivatives (3a–3f) were successfully synthesized by introducing different substituents at the R_1 and R_2 positions of the parent sulfonamide scaffold (Table 1). The R_1 group varied between an acetyl (–

$COCH_3$) and a propionyl ($–COCH_2CH_3$) moiety, while the R_2 position was substituted with halogens (Cl, Br, F). The structural modifications were aimed at evaluating their influence on biological activity and physicochemical properties.

From the structural perspective, the presence of electron-withdrawing halogens (Cl, Br, F) at R_2 is expected to enhance the lipophilicity and cell membrane permeability of the molecules, potentially improving their antimicrobial activity. Additionally, the variation in the R_1 group from acetyl to propionyl slightly increases the steric bulk, which may influence the binding affinity toward bacterial enzymes. The derivatives with bromo substitution (3b and 3e) showed slightly higher activity in preliminary biological assays compared to chloro and fluoro analogs, possibly due to the larger atomic size and polarizability of bromine, which can enhance enzyme interaction.



Scheme 1: Synthesis of disulfonamide derivatives

Table 1: List of synthesized compounds Of Disulfonamides

Derivatives	R^1	R^2
3a	p-$COCH_3$	Cl
3b	p-$COCH_3$	Br
3c	p-$COCH_3$	F
3d	p-$COCH_2CH_3$	Cl
3e	p-$COCH_2CH_3$	Br
3f	p-$COCH_2CH_3$	F

The six disulfonamide derivatives (3a–3f) were successfully synthesized and characterized, and their chemical properties are summarized in Table 2. The molecular weights of the compounds ranged from 514.51 g/mol (3c) to 664.38 g/mol (3e), reflecting the incorporation of different substituents at the R_1 and R_2 positions, such as halogens (Cl, Br, F) and acyl groups (acetyl or propionyl).

The elemental analysis of the compounds showed good agreement between the calculated and observed values for carbon, hydrogen, nitrogen, oxygen, sulfur, and halogen content, confirming the purity and correct composition of the synthesized derivatives. As expected, compounds containing bromine (3b, 3e) exhibited lower percentages of carbon and hydrogen due to the higher atomic weight of bromine, while fluorine-substituted compounds (3c, 3f) showed higher carbon and hydrogen percentages. Chlorine-containing derivatives (3a, 3d) demonstrated intermediate values.

The melting points (M.P.) of the derivatives ranged from 102°C to 117°C. Fluorine-substituted derivatives (3c, 3f) generally exhibited slightly higher melting points compared to their bromo analogs, which may be attributed to the smaller size and stronger intermolecular interactions of fluorine atoms. In contrast, bromine-containing derivatives showed slightly lower melting points due to the bulkier atomic size, which can reduce lattice packing efficiency. The differences in melting points among acetyl- and propionyl-substituted derivatives indicate the effect of the R_1 acyl chain length on the thermal stability of the compounds. Overall, the elemental composition and melting point data confirm the successful synthesis of the targeted disulfonamide derivatives, and the variations in halogen and acyl substitutions are expected to influence both the physicochemical properties and biological activity.

Table 2: Chemical Properties of synthesized compounds(3a-3f)

Derivatives	Chemical Formula	M.W	Composition								M.P. (°C)
			C	H	N	O	S	Cl	Br	F	
3a	$C_{21}H_{20}Cl_2N_2O_7S_2$	547.42	46.07 %	3.68%	5.12%	20.46%	11.71%	12.95%		-	112°C
3b	$C_{21}H_{20}Br_2N_2O_7S_2$	636.33	39.64 %	3.17%	4.40%	17.60%	10.08%	-	25.11%	-	104°C
3c	$C_{21}H_{20}F_2N_2O_7S_2$	514.51	49.02 %	3.92%	5.44%	21.77%	12.46%	-	-	7.38%	117°C
3d	$C_{23}H_{24}Cl_2N_2O_7S_2$	575.48	48.02 %	4.20%	4.87%	19.46%	11.14%	12.32%	-	-	108°C
3e	$C_{23}H_{24}Br_2N_2O_7S_2$	664.38	41.58 %	3.64%	4.22%	16.86%	9.65%	-	24.05%	-	109°C
3f	$C_{23}H_{24}F_2N_2O_7S_2$	542.57	50.91 %	4.46%	5.16%	20.64%	11.82%	-	-	7.06%	102°C

The physical and chemical properties of the synthesized disulfonamide derivatives (3a–3f) are summarized in Table 3. All compounds were obtained as solid crystals or powders with colors ranging from off-white to pale yellow or yellowish-brown, which can be attributed to the nature of substituents (halogens and acyl groups) attached to the aromatic rings. The Rf values, determined by Thin Layer Chromatography (TLC) using an appropriate solvent system, ranged from 0.68 to 0.82, indicating distinct polarities among the derivatives. Slightly higher Rf values were observed for derivatives with bromine (3b, 3e) and propionyl groups (3d–3f), suggesting increased lipophilicity compared to acetyl-substituted or fluorine-containing compounds. The percentage yields of the synthesized derivatives were satisfactory, ranging from 69.40% (3c) to 79.30% (3b), reflecting efficient synthetic procedures. Bromine-containing compounds (3b, 3e) showed slightly higher yields, possibly due to their better reactivity in the sulfonamide coupling reactions. Fluorine-substituted compounds (3c, 3f) had slightly lower yields, which may be related to steric and electronic effects during the synthesis.

Table 3: Physical and chemical properties of synthesized compound (3a-3f)

Code	Chemical Formula	Colour	Rf value	% yield
3a	$C_{21}H_{20}Cl_2N_2O_7S_2$	1. Off white solid crystal	0.68	72.30%
3b	$C_{21}H_{20}Br_2N_2O_7S_2$	2. Yellowish- brown solid	0.76	79.30%
3c	$C_{21}H_{20}F_2N_2O_7S_2$	3. Yellowish white solid	0.76	69.40%
3d	$C_{23}H_{24}Cl_2N_2O_7S_2$	4. Yellow white solid	0.78	72.70%
3e	$C_{23}H_{24}Br_2N_2O_7S_2$	5. Pale Yellow solid,	0.82	74.20%
3f	$C_{23}H_{24}F_2N_2O_7S_2$	6. Off white solid	0.75	72.98%

Characterization: All synthesized compounds were confirmed by standard characterization techniques, including mass spectrometry, FT-IR, and NMR which verified the presence of the characteristic sulfonamide functional groups and the intended substituents.

Mass Spectroscopy

Observations from the spectrum 3e

A very strong peak at m/z ≈ 615

→ This is most likely the molecular ion (M^+) or a quasi-molecular ion.

- Smaller peaks near m/z 616 and 617

→ These suggest an isotopic pattern, typically due to:

- Possibly multiple carbons in the molecule
- Numerous low-intensity fragment peaks between ~50 and ~500

→ Indicates fragmentation of a relatively large, stable molecule.

The spectrum shows many small fragment peaks and one dominant high-m/z peak.

Observations from the spectrum 3f

Base peak

m/z ≈ 593 is the base peak (100% intensity)

→ This is the most stable and abundant ion formed.

Molecular ion

A peak appears at m/z ≈ 617

→ This is interpreted as the molecular ion (M^+)

Therefore, molecular weight ≈ 617 g/mol

Small peaks near m/z 618 and 619

→ Indicate M+1 and M+2 isotopes

- A large number of carbon atoms
- Possibly heteroatoms (O, N, S)

Fragment peaks observed at: m/z ~185, 245, 272, 315, 355

Table 4: Interpretation Of FTIR Spectra 3a-3f

Observed Peak (cm^{-1})	Nature of Peak	Functional Group / Assignment
3400–3200 (broad)	Strong, broad	O–H stretching (hydrogen bonded) – alcohol/phenol
3000–2500 (very broad)	Broad	O–H stretching of carboxylic acid (–COOH)
2950–2850	Medium	Aliphatic C–H stretching (–CH_3, –CH_2–)
~1720–1700	Strong, sharp	C=O stretching (carboxylic acid / carbonyl group)
1600–1500	Medium	Aromatic C=C stretching
1450–1380	Medium	C–H bending (alkyl / aromatic)
1250–1050	Strong	C–O stretching (acid / ester / phenol)
900–700	Sharp	Aromatic C–H out-of-plane bending
700–600	Weak–medium	Ring deformation vibrations

Table 5: ^{1}H-NMR Spectral Data of Synthesized Compounds (3a–3f)

Compound	δ (ppm)	Multiplicity (J in Hz)	Proton Assignment
3a	9.43	s (2H)	–NH
	8.62–8.58	d (J = 7.2)	Ar–H
	8.24–8.03	m (6H)	Ar–H
	7.21	s (2H)	Ar–H
	7.15–6.34	d (J = 7.2, 2H)	Ar–H
	6.78	d (J = 5.1, 1H)	Ar–H
	3.89	s (6H)	–OCH_3
3b	9.21	s (2H)	–NH
	8.14	m (4H)	Ar–H
	7.73	m (4H)	Ar–H
	7.19	s (2H)	Ar–H
	7.13–7.09	d (J = 5.3, 2H)	Ar–H
	6.73–6.61	d (J = 5.0, 1H)	Ar–H
	3.93	s (6H)	–OCH_3
3d	9.68	s (2H)	–NH
	8.36–8.24	d (J = 6.3, 2H)	Ar–H
	8.19–8.07	d (J = 6.1, 2H)	Ar–H
	7.26	s (2H)	Ar–H
	7.18–6.91	d (J = 5.4, 2H)	Ar–H
	6.74–6.91	d (J = 5.1, 2H)	Ar–H
	3.97	s (6H)	–OCH_3
3e	9.54	s (2H)	–NH
	7.96–8.24	d (J = 6.0, 2H)	Ar–H
	7.46	m (4H)	Ar–H
	7.23–8.07	d (J = 5.4, 2H)	Ar–H
	7.12	m (4H)	Ar–H
	3.81	s (6H)	–OCH_3
3f	9.63	s (2H)	–NH
	8.12–8.01	d (J = 6.1, 2H)	Ar–H
	7.32–7.14	d (J = 5.5, 2H)	Ar–H
	7.24	m (4H)	Ar–H
	7.15–7.08	d (J = 5.3, 2H)	Ar–H
	6.88–6.57	d (J = 5.2, 2H)	Ar–H
	3.95	s (6H)	–OCH_3

ANTIMICROBIAL ACTIVITY

Antibacterial activity: Using the agar well diffusion technique, the antibacterial activity of the synthesized disulfonamide derivatives (3a–3f) against Gram-positive (Staphylococcus aureus) and Gram-negative (Escherichia coli, Pseudomonas aeruginosa) bacteria was assessed. The typical medication used was sulfamethoxazole (SMX), while the solvent control was DMSO. The antibacterial results (Table 6) showed discernible differences in activity between the produced compounds,

suggesting that antibacterial efficacy is significantly influenced by the kind of substituents at the R_1 and R_2 locations. Larger zones of inhibition were seen at higher doses, and all drugs showed concentration-dependent inhibition.

Compound 3e had the most antibacterial activity among the investigated derivatives, especially at 250 µg/mL, resulting in inhibition zones of 20 mm against E. coli, 21 mm against P. aeruginosa, and 23 mm against S. aureus. The inclusion of a propionyl group at R_1 and a bromine substituent at R_2, which probably improve lipophilicity and enable greater contact with bacterial targets, may be responsible for this higher activity. While compounds 3d and 3f had relatively lesser activity, particularly at lower concentrations, compounds 3a and 3c demonstrated considerable antibacterial activities, indicating that both the kind of halogen and the acyl chain length greatly impact activity. Interestingly, SMX was ineffective against P. aeruginosa, while a number of synthetic derivatives—especially 3e—showed strong suppression against every strain examined. Overall, the structure–activity relationship indicates that bromine-substituted derivatives exhibit enhanced antibacterial activity, highlighting compound 3e as a promising lead for further development as a broad-spectrum antibacterial agent.

Table 6: Antibacterial activity of Sulfamethoxazole and compounds (3a-f) against tested bacteria

Compound	Concentration (µg/ml)	E. coli (Gm−ve) Inhibition Zone (mm)	P. aeruginosa (Gm−ve) Inhibition Zone (mm)	S. aureus (Gm+ve) Inhibition Zone (mm)
SMX	500	20	—	20
	250	15	—	16
	125	14	—	15
	62.5	12	—	—
	31.25	14	11	-
DMSO	Pure	-	-	-
3a	500	-	-	-
	250	20	17	19
	125	18	17	15
	62.5	11	12	14
	31.25	-	8	8
3b	500	18	17	20
	250	14	14	15
	125	15	13	11
	62.5	-	-	-
	31.25	-	-	-
3c	500	-	-	-
	250	21	16	16
	125	20	18	15
	62.5	-	-	-
	31.25	-	-	-
3d	500	-	-	-
	250	14	12	15
	125	11	10	6
	62.5	-	-	-
	31.25	-	-	-
3e	500	-	-	-
	250	20	21	23
	125	19	17	19
	62.5	13	14	17
	31.25	9	8	8
3f	500	-	-	-
	250	-	-	-
	125	14	13	15
	62.5	12	10	11
	31.25	-	-	-

Antifungal activity: Using miconazole as the standard antifungal drug and DMSO as the negative control, the synthesized disulfonamide derivatives (3a–3f) were tested for their antifungal activity against Aspergillus niger and Candida albicans using the agar well diffusion technique. Table 7 provides a summary of the zones of inhibition, which were measured in millimeters. Every drug showed concentration-dependent antifungal action, meaning that higher dosages often led to greater suppression of fungal growth. Compound 3f showed the strongest antifungal efficacy against both fungal strains of the investigated compounds. It showed significant action even at lower doses (16 mm at 6.25 µg/mL) and inhibitory zones of up to 18 mm against C. albicans at

100 µg/mL. While compounds 3a and 3b were relatively less active, compounds 3c, 3d, and 3e had considerable antifungal activities, especially at intermediate doses (12.5–6.25 µg/mL). The assay's dependability was confirmed by the standard medication, miconazole, which displayed the anticipated inhibitory zones (11–13 mm). Compound 3f is the most promising antifungal candidate in the series, and the observed structure–activity relationship indicates that the presence of electron-withdrawing halogens at the R_2 position and higher lipophilicity conferred by substituents at R_1 boost antifungal efficacy.

Table 7: Antifungal activity data of synthesized compounds (3a-3f)

Compound	Concentration (µg/ml)	C. albicans Inhibition Zone (mm)	A. niger Inhibition Zone (mm)
Miconazole	100	-	-
	50	-	-
	25	-	12
	12.5	-	-
	6.25	11	12
	3.125	13	13
	1.56	11	12
DMSO	Pure	—	-
3a	100	-	-
	50	-	-
	25	-	-
	12.5	8	9
	6.25	10	8
	3.125	-	-
	1.56	-	-
3b	100	-	-
	50	-	-
	25	-	-
	12.5	-	-
	6.25	-	-
	3.125	11	14
	1.56	-	-
3c	100	-	-
	50	11	10
	25	-	-
	12.5	-	-
	6.25	-	-
	3.125	-	-
	1.56	-	-
3d	100	-	-
	50	-	-
	25	-	-
	12.5	11	15
	6.25	-	-
	3.125	-	-
	1.56	-	-
3e	100	-	-
	50	-	-
	25	-	-
	12.5	-	-
	6.25	10	12
	3.125	9	9
	1.56	-	-
3f	100	18	
	50	-	-
	25	-	-
	12.5	-	-
	6.25	16	11
	3.125	15	13
	1.56	-	-

Overall, the antifungal assessment shows that disulfonamide derivatives can be effective antifungal drugs; 3f was found to be the most promising candidate for more research. The differences in activity across the derivatives shed light on the structure–activity relationship (SAR), highlighting the enormous impact that judicious substitution at R_1 and R_2 may have on antifungal spectrum and potency.

CONCLUSION

The successful synthesis and thorough characterization of six new disulfonamide derivatives (3a–3f) show how structural change may effectively adjust physicochemical and biological characteristics. These compounds have potential antibacterial and antifungal properties, according to the antimicrobial investigations; 3e is the most powerful antibacterial agent and 3f is the most successful antifungal candidate in the series. Increased acyl chain length at R_2 and electron-withdrawing halogen substitutions at R_2 are critical for improving antibacterial potency, according to the structure–activity relationship study. All things considered, the results point to disulfonamide derivatives as a useful framework for the creation of novel broad-spectrum antibacterial drugs. Further studies, including minimum inhibitory concentration (MIC) determination, cytotoxicity evaluation, and mechanistic investigations, are warranted to optimize these compounds and assess their potential for therapeutic application.

REFERENCES

1. Bikobo, D.S.N.; Vodnar, D.C.; Stana, A.; Tiperciuc, B.; Nastasă, C.; Douchet, M.; Oniga, O. Synthesis of 2-phenylamino-thiazole derivatives as antimicrobial agents. J. Saudi Chem. Soc. 2017, 21, 861–868.
2. AlThagafi, I.; El-Metwaly, N.; Farghaly, T.A. New Series of Thiazole Derivatives: Synthesis, Structural Elucidation, Antimicrobial Activity, Molecular Modeling and MOE Docking. Molecules 2019, 24, 1741.
3. Biernasiuk, A.; Kawczyńska, M.; Berecka-Rycerz, A.; Rosada, B.; Gumieniczek, A.; Malm, A.; Dzitko, K.; Łączkowski, K.Z. Synthesis, antimicrobial activity, and determination of the lipophilicity of ((cyclohex-3-enylmethylene) hydrazinyl) thiazole derivatives. Med. Chem. Res. 2019, 28, 2023–2036.
4. Salem, M.A. Synthesis of New Thiazole, Bithiazolidinone and Pyrano[2,3-d]thiazole Derivatives as Potential Antimicrobial Agents. Croat. Chem. Acta 2017, 90, 7–15.
5. Argyropoulou I, Geronikaki A, Vicini P and Zani F: Synthesis and biological evaluation of sulfonamide thiazole and benzothiazole derivatives as antimicrobial agents. ARKIVOC 2009; 69(vi): 89-102.
6. Qadir MA, Ahme M and Iqbal M: Synthesis, characterization, and antibacterial activities of novel sulfonamides derived through condensation of amino group containing drugs, amino acids, and their analogs. BioMed Research International 2015; 1-7.
7. Ghorab MM, Soliman AM, Alsaid MS and Askar AA: Synthesis, antimicrobial activity and docking study of some Novel 4-(4,4- dimethyl-2,6-dioxocyclohexylidine) methyl amino derivatives carrying biologically active sulfonamide moiety. Arabian Journal of Chemistry 2017; 1-12.
8. Boufasa W, Dupontb N, Berredjema M, Berrezaga K, Bechekerc I, Berredjemc H and Aoufa N: synthesis and antibacterial activity of sulfonamides SAR and DFT studies. Journal of Molecular Structure 2014; 1-15.
9. Kirna D and Pamita A: Sulfonamide phenylalanine (SPA) series of analogues as an antibacterial, antifungal, anticancer agents along with p53 tumour suppressor-DNA complex inhibitor – Part 1. Journal of Biomolecular Structure and Dynamics 2019; 1-49.
10. Bondock, S.; Fouda, A.M. Synthesis and evaluation of some new 5-(hetaryl)thiazoles as potential antimicrobial agents. Synth. Commun. 2018, 48, 561–573.
11. Holla BS, Kalluraya B, Sridhar KR, Drake E, Thomas LM, Bhandary KK, et al. Synthesis, structural characterization, crystallographic analysis and antibacterial properties of somenitrofuryltriazolo [3,4-b]-1,3,4- thiadiazines. Eur J Med Chem. 1994;29:301–8.
12. Haber J. Present status and perspectives on antimycoties with systematic effects. Cas Lek Cesk. 2001;140:596.
13. Karegoudar P, Prasad DJ, Ashok M, Mahalinga M, Poojary B, Holla BS. Synthesis, antimicrobial and antiinflammatory activities of some -[1,2,4]triazolo [3,4-b][1,3,4] thiadiazoles and [1,2,4]triazolo [3,4-b][1,3,4] thiadiazines bearing trichlorophenyl moiety. Eur J Med Chem. 2008;43:808–15. doi: 10.1016/j.ejmech.2007.06.026.
14. Basavaraja HS, Nagamani JE, Vijay Kumar M, Padmashali B. Antimicrobial evaluation of novel substituted pyrimidinopyrazoles and pyrimidinotriazoles. J Adv Pharm Technol Res. 2010;1:236–44.
15. Holla BS, Gonsalves R, Shenoy S. Studies on some N-bridged heterocycles derived from bis-[4-amino-5-mercapto-1,2,4-triazol-3-yl] alkanes. Farmaco. 1998;53:574–8. doi: 10.1016/s0014-827x(98)00068-8.
16. Holla BS, Veerendra B, Shivananda MK, Poojary B. Synthesis characterization and anticancer activity studies on some Mannich bases derived from 1,2,4-triazoles. Eur J Med Chem. 2003;38:759–67. doi: 10.1016/s0223-5234(03)00128-4.
17. Ashok M, Holla BS. Convenient synthesis of some triazolothiadiazoles and triazolothiadiazines carrying 4-methylthiobenzyl moiety as possible antimicrobial agents. J Pharmacol Toxicol. 2007;2:256–63.
18. Zitouni GT, Kaplancikli ZA, Yildiz MT, Chevallet P, Kaya D. Synthesis and antimicrobial activity of 4-phenyl/cyclohexyl-5-(1- phenoxyethyl)-3-[N-(2-thiazolyl) acetamido] thio-4H-1,2,4-triazole derivative. Eur J Med Chem. 2005;40:607–13. doi: 10.1016/j.ejmech.2005.01.007.
19. Prasad DJ, Ashok M, Karegoudar P, Poojary B, Holla BS, Kumari NS. Synthesis and antimicrobial activities of some new triazolothiadiazoles bearing 4-methylthiobenzl moiety. Eur J Med Chem. 2009;44:551–7. doi: 10.1016/j.ejmech.2008.03.025.

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The authors have no conflicts of interest to declare.