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# Synthesis and Antimicrobial Activity of New imine Derivatives Containing Drug Molecule

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*P A P E R  I N F O*

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*A B S T R A C T*

The research involved the synthesis four of new Schiff base derivatives ($SC_1$, $SC_3$, $SC_4$, $SC_6$) through the condensation reaction of Three amines (drugs) with four aldehydes, all conducted under mild conditions. To validate their chemical structures, the produced compounds were analyzed utilizing spectroscopic methods such as FT-IR, 1H-NMR, and 13C-NMR. The antibacterial activity of Schiff base derivatives was tested against *(Pseudomonas aeruginosa, Escherichia coli, Klebsiella pneumoniae, Proteus spp., and Staphylococcus aureus)* using the agar well diffusion technique.

The findings revealed that SC1 was the most powerful and broad-spectrum antibacterial activity of all of the chemicals tested, with inhibition zone widths ranging from 18 to 30 mm, while SC3 showed moderate activity against most tested strains, with the highest activity against *E. coli* (21 mm) and *S. aureus* (25 mm). The structure-activity relationship (SAR) research revealed that electron-donating and electron-withdrawing substituents on the aromatic ring affected biological activity. These findings indicate that Schiff bases may be viable candidates for the creation of novel antibacterial medicines.

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## 1. INTRODUCTION

Schiff bases are a kind of imine chemical generated by the condensation of primary amines with carbonyl compounds like aldehydes or ketones. The imine (-C=N-) linkage determines the biological and chemical properties of these molecules (Raczuk E. et al., 2022) .Schiff bases have been widely researched for their antibacterial, antifungal, anticancer, and antioxidant effects, due to their ease of synthesis, structural diversity, and ability to interact with metal ions (Ceramella J. et al., 2022) (Hassan A. M. et al., 2022) (Soroceanu A. & Bargan A., 2022).

The proliferation of multidrug-resistant (MDR) bacterial species constitutes a substantial threat to public health, prompting the quest for novel antimicrobial drugs with new modes of action (Salam M. A. et al., 2023) . Schiff bases, generated from aromatic amines and aldehydes, have demonstrated potential antibacterial action, which is frequently attributed to their capacity to interfere with bacterial enzymes or membrane function (Khan R. et al., 2024).

Studies show that adding electron-donating or electron-withdrawing groups to the aromatic ring of Schiff base derivatives can considerably impact their biological activity (Rana M. S. et al., 2024) .Furthermore, the presence of heteroatoms such as nitrogen, sulfur, and oxygen in the molecular framework improves the ability of these compounds to interact with biological targets (Waziri I. et al., 2024) (Yasmeen Z. et al., 2025) (Yasmeen Z. et al., 2025) (Uddin E. et al., 2025). In this respect, the current study seeks to create a variety of new Schiff base derivatives by condensing different substituted aromatic amines with aldehydes under moderate circumstances. The produced compounds are characterized spectroscopically and tested for antibacterial activity against chosen Gram-positive and Gram-negative bacterial strains. This study also

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looks at the link between the chemical structure and antibacterial activity of the produced compounds.

## 2. MATERIALS AND METHODS

Analytical-grade chemical compounds from Sigma Aldrich, Fluka, CDH, and Thomas Backer are utilized. We bought sulfadiazine and mesalzine from the Leyan Company in China. A Bruker Multinuclear spectrometer was used to determine the 1H NMR (400 MHz) and 13C NMR (100 MHz) FTIR spectra, while the Gallenkamp MFB-600-Melting point Stuart equipment was used to perform the melting point.

### Synthesis of 2-hydroxy-5-((pyridin-2-ylmethylene)amino)benzoic acid[SC1]

In 40 ml of ethanol (1g, 9.33mmole) of pyridine2-carbaldehyde) and (1.45g, 9.33 mmole) of mesalazine prodrug was dissolved and transferred to (100 ml) round bottom flask. The mixture was refluxed for 3 hrs. until no spot of mesalazine shown on TLC plat. Then the formed precipitate was filtered and recrystallized from hot ethanol to afforded 1.9 g, 83% yield of [SC1] as light brown powder, m.p 179 C. FTIR vmax, cm-1: 2520-3000 (COOH and OH), 1651 (CO, acid), 1593 (C=N, imine), 1487 and 1446 (aromatic rings); 1H NMR (500 MHz, DMSO), ppm: 11.00 (s, 1H, COOH), 9.67 (s, 1H, Ar-OH), 7.88 (1 H, CH=N), 7.34 -6.36 (Ar-H). 13C NMR (125 MHz), ppm: 171.05 (1C, COOH), 133.02-101.45 (13C, Ar-C).

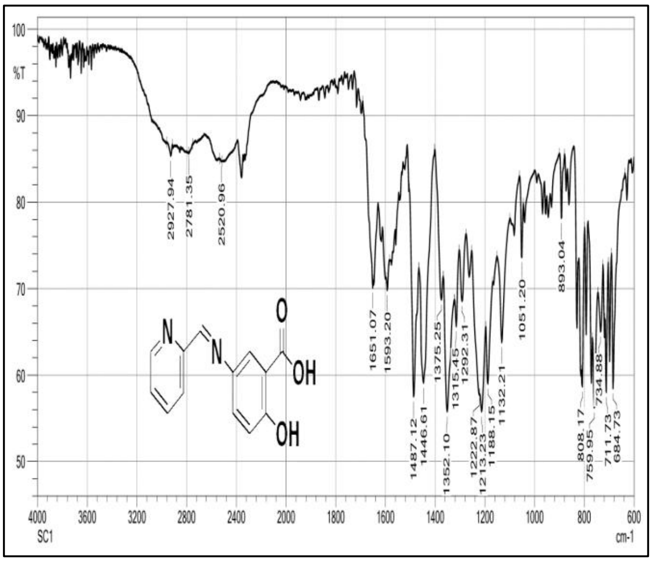


**Figure 1.** IR spectrum of compound SC1

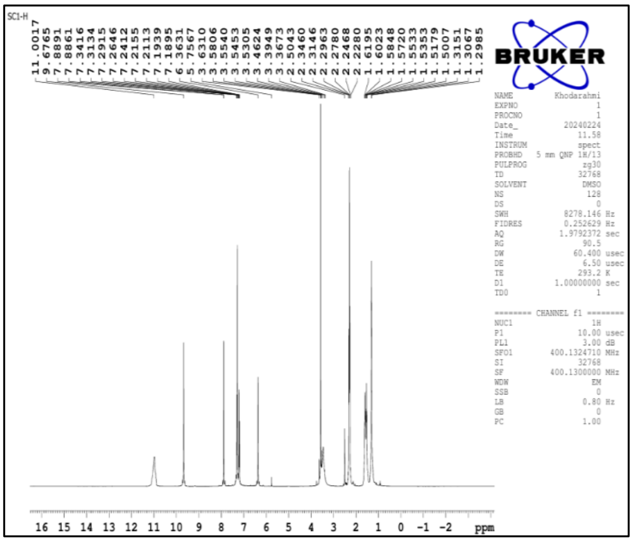


**Figure 2.** 1H-MNR spectrum of compound SC1

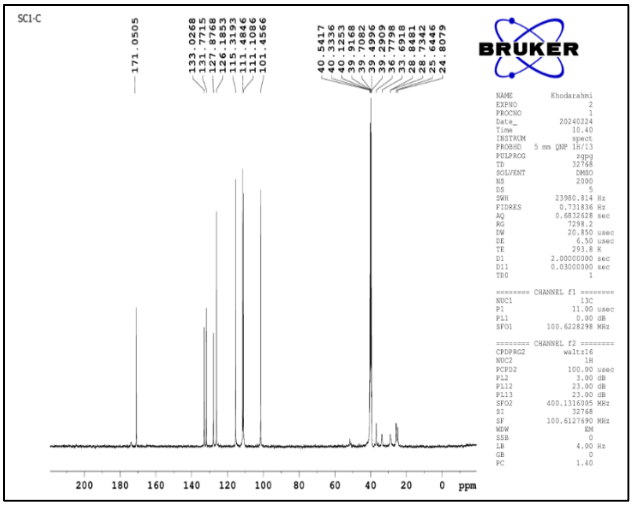


**Figure 3.** 13C-MNR spectrum of compound SC1

### Synthesis of 5-((2,5-dimethoxybenzylidene)amino)-2-hydroxybenzoic acid [Sc3]

In 40 ml of ethanol (1g, 6 mmole) of 2,5-dimethoxybenzaldehyde and (0.92g, 6 mmole) of mesalazine prodrug was dissolved and transferred to (100 ml) round bottom flask. The mixture was refluxed for 3 hrs. until no spot of mesalazine shown on TLC plat. Then, the formed precipitate was filtered and recrystallized from hot ethanol to afforded 1.4 g, 77% yield of [SC3] as beige color powder, m.p 158 C. FTIR vmax, cm-1: 2520-3000 (COOH and OH), 2977 (O-$CH_3$), 1645 (CO, acid), 1612 (C=N, imine), 1557-1446 (aromatic rings);

1H NMR (500 MHz, DMSO), ppm: 11.15 (s, 1H, COOH), 8.68 (s, 1H, Ar-OH), 8.30 (1 H, CH=N), 7.99 -6.34 (Ar-H). 13C NMR (125 MHz), ppm: 171.41 (1C, COOH), 155.78 (1C, C=N), 140.52-111.88 (12C, Ar-C), 53.48 (2C, O-$CH_3$).

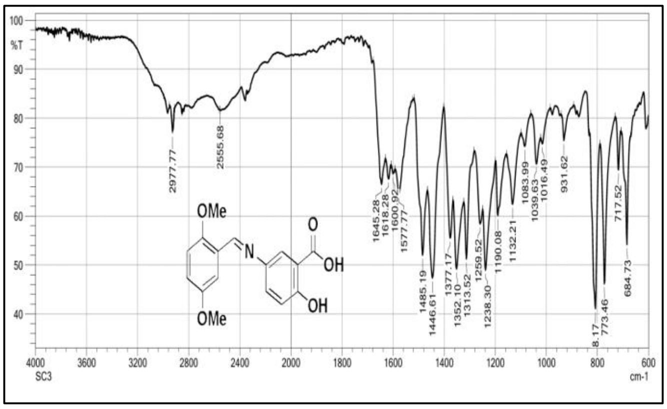
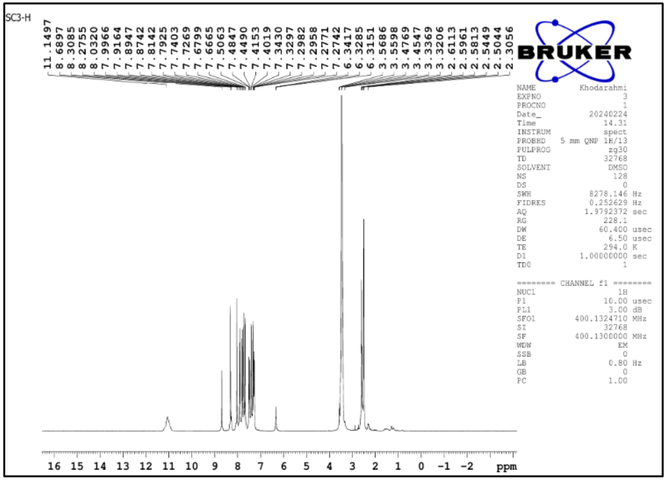


**Figure 4.** IR spectrum of compound SC3



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AQ              1.9792372 sec
RG                  228.1
DW                 60.400 usec
DE                   6.50 usec
TE                  294.0 K
D1             1.00000000 sec
TD0                     1

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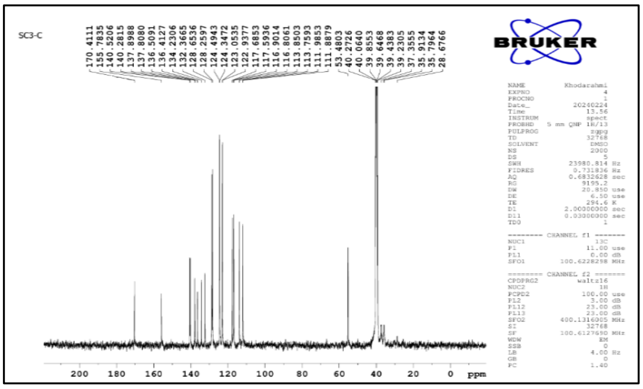
**Figure 5.** 1H-NMR spectrum of compound SC3



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PL2                  3.00 dB
PL12                23.00 dB
PL13                23.00 dB
SFO2          400.1316005 MHz
SI                  32768
SF            100.6127690 MHz
WDW                    EM
SSB                     0
LB                   4.00 Hz
GB                      0
PC                   1.40
```

**Figure 6.** 13C-NMR spectrum of compound SC3

Synthesis of 4-((3-hydroxybenzylidene)amino)-1,5-dimethyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one [Sc4] In 40 ml of ethanol (1g, 8.2 mmole) 3-hydroxybenzaldehyde and (1.66 g, 8.2 mmole) of 4-Aminoantipyrine was dissolved and transferred to (100 ml) round bottom flask. The mixture was refluxed for 3 hrs. until no spot for reactants was shown on TLC plat. Then, the formed precipitate was filtered and recrystallized from hot ethanol to afforded 2 g, 80% yield of [SC4] as brown powder, m.p 181 $^{O}$C. FTIR νmax, cm-1: 3138 (OH), 2926 ($CH_3$), 1614 (CO, pryrazole), 1591 (C=N, imine), 1555-1448 (aromatic rings); 1H NMR (500 MHz, DMSO), ppm: 9.99 (s, 1H, OH), 8.70 (1 H, CH=N), 7.92 -6.34 (Ar-H). 13C NMR (125 MHz), ppm: 155.82 (1C, C=O), 140.58 (1C. C=N), 137.97-111.97 (14C, Ar-C), 37.44 and 35.94 (2C, -$CH_3$).

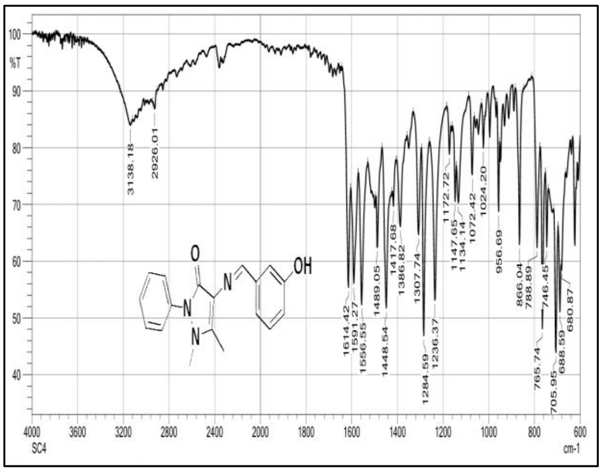
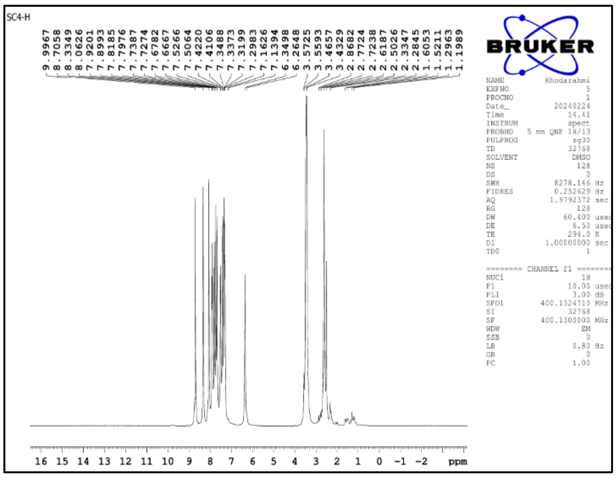


**Figure 7.** 1IR spectrum of compound SC4



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FIDRES           0.252629 Hz
AQ              1.9792372 sec
RG                    128
DW                 60.400 usec
DE                   6.50 usec
TE                  294.0 K
D1             1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
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**Figure 8.** 1H-MNR spectrum of compound SC4

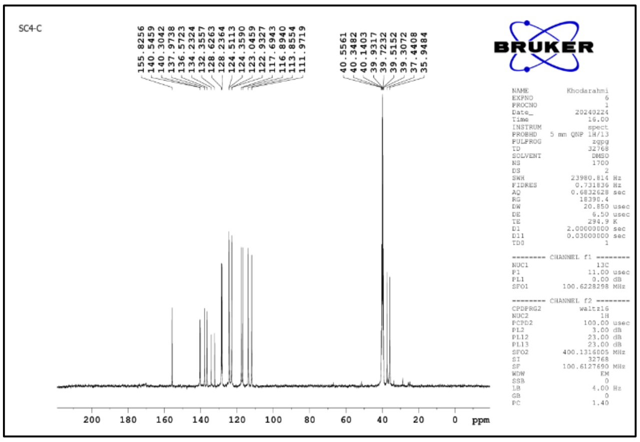


**Figure 9.** 13C-MNR spectrum of compound SC4

### Synthesis of 4-((4-hydroxybenzylidene)amino)-N-(pyrimidin-2-yl)benzenesulfonamide [Sc6]

In 40 ml of ethanol (1g, 8.2 mmole) 3-hydroxybenzaldehyde and (2.05 g, 8.2 mmole) of sulfadiazine was dissolved and transferred to (100 ml) round bottom flask. The mixture was refluxed for 3 hrs. until no spot for reactants was shown on TLC plat. Then the formed precipitate was filtered and recrystallized from hot ethanol to afforded 2 g, 69% yield of [SC6] as off-white powder, m.p 213 C. FTIR vmax, cm-1: 3352 (N-H), 3257 (OH), 1614 (CO, pryrazole), 1557 (C=N, imine), 1489-1406 (aromatic rings); 1H NMR (500 MHz, DMSO), ppm: ~10.99 (s, 1H, N-H), ~9.50(1 H, O-H), ~8.50 (s, 1H, HC=N), 7.45 -7.04 (Ar-H). 13C NMR (125 MHz), ppm: 169.62 (1C, pyrimidine ring), ~158.82 (1C. C=N), 138.44-111.02 (9 C, Ar-C), 37.44 and 35.94 (2C, -CH$_3$).

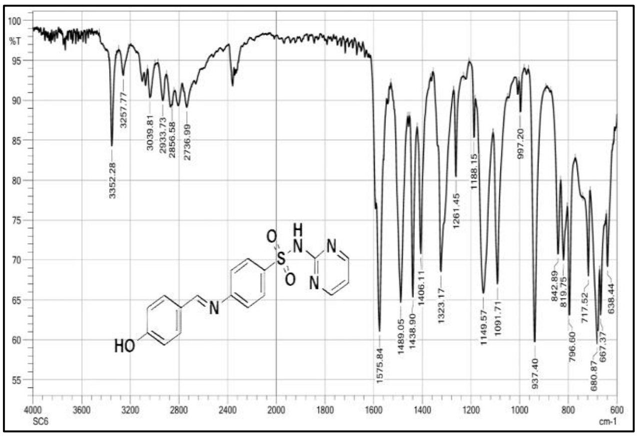


**Figure.10.** IR spectrum of compound SC6

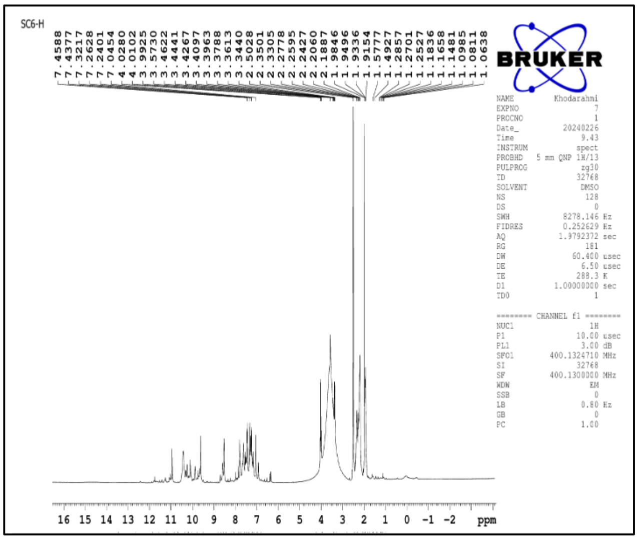


**Figure 11.** 1H-NMR spectrum of compound SC6

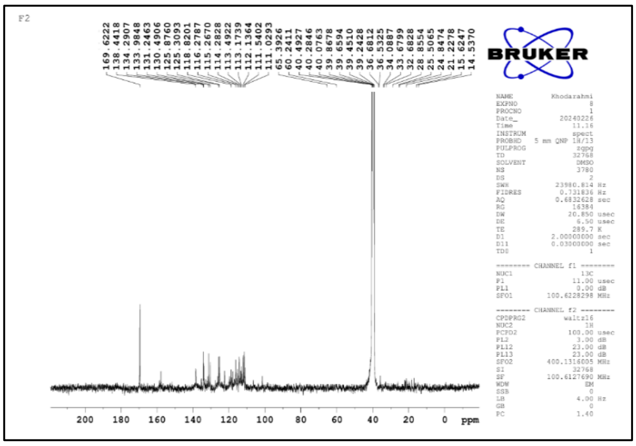
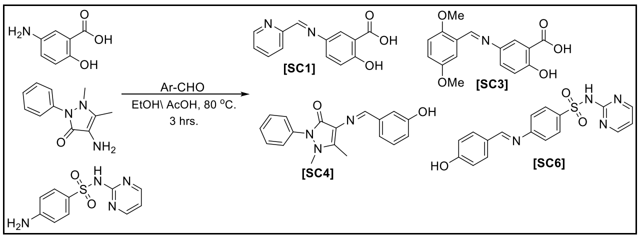


**Figure 12.** 13C-NMR spectrum of compound SC6

## 1- 3. RESULTS AND DISCUSSION

### 3.1. Chemistry

The new compounds (SC$_1$, SC$_3$, SC$_4$, SC$_6$) were synthesized through a direct condensation reaction between various aromatic amino drugs and an aromatic aldehyde, as illustrated in Scheme 1.



**Scheme 1**. Synthesis of compounds (SC$_1$, SC$_3$, SC$_4$, SC$_6$).

Several spectroscopic methods were used to confirm the structures of the prepared compounds. Successful synthesis was demonstrated by the FT-IR spectra's broad bands representing aldehydes carbonyls and amino groups disappearing, as well as the emergence of new bands for the imine (C=N) stretching vibrations at 1595, 1618, 1614, and 1575 cm⁻¹. The formation of the imine bonds and the elimination of the aldehyde proton signal were confirmed by the $^1$H NMR spectra, which displayed distinctive singlets for the imine protons at 7.88, 8.66, 8.70, and 8.50 ppm.

### 3.2. Anti-Bacterial Activity

Five clinically relevant bacterial strains (*Pseudomonas aeruginosa, Escherichia coli, Klebsiella pneumoniae, Proteus spp., and Staphylococcus aureus*) were used to test the antimicrobial properties of the synthesized compounds SC1, SC3, SC4, and SC6. The antibacterial efficacy was measured using amoxicillin as the reference standard.

**TABLE 1.** The diameter of inhibition zone of compounds ($SC_1$, $SC_3$, $SC_4$, $SC_6$) against *P. aeruginosa, E. Coli, K. pneumonia, Proteus* and *S. aureus*

| **Sample code** | ***P. aeruginosa*** | ***E. Coli*** | ***K. pneumoniae*** | ***Proteus*** | ***S. aureus*** |
|---|---|---|---|---|---|
| SC1 | 30 | 18 | 26 | 18 | 30 |
| SC3 | 25 | 21 | 18 | 11 | 25 |
| SC4 | 11 | 19 | 12 | 18 | 11 |
| SC6 | 12 | 8 | 4 | 0 | 15 |
| Amoxicillin | 30 | 24 | 19 | 18 | 32 |

SC1 was the most powerful and broad-spectrum antibacterial activity of all of the chemicals tested, with inhibition zone widths ranging from 18 to 30 mm. It had notably robust action against *P. aeruginosa and S. aureus* (30 mm each), equivalent to that of amoxicillin (30 mm and 32 mm, respectively), as well as considerable suppression against *K. pneumoniae* (26 mm). This shows that SC1 may have a structural or functional characteristic that helps it engage with both Gram-positive and Gram-negative bacterial cell targets. SC3 showed moderate activity against most tested strains, with the highest activity against *E. coli* (21 mm) and *S. aureus* (25 mm). SC3 was significantly less effective than SC1, although it still demonstrated a wide spectrum of action, indicating that certain structural variations may impact its potency or bacterial target selectivity.

In contrast, SC4 and SC6 had relatively low antibacterial activity, notably SC6, which was ineffective against *Proteus* (0 mm) and had negligible inhibitory zones against other strains. SC4 has considerable effectiveness against *E. coli* (19 mm) and *Proteus* (18 mm), but low efficacy against *P. aeruginosa* and *S. aureus* (11 mm). These data suggest that SC4 and SC6 may lack crucial pharmacophoric characteristics required for efficient bacterial suppression or they have low cell wall penetration. When all compounds are compared to normal amoxicillin, SC1 emerges as the most promising contender, with equivalent or slightly lower activity in most circumstances. The decreased activity of SC4 and SC6 suggests either suboptimal chemical properties or a low affinity for the bacterial targets tested.

Overall, the findings suggest that structural alterations to Schiff base derivatives have a major impact on their antibacterial properties. Further structure-activity relationship (SAR) studies, as well as mechanistic research, are needed to maximize the potency and selectivity of these compounds, particularly SC1 and SC3, as potential antimicrobial agents against resistant bacteria, including ESBL-producing strains.

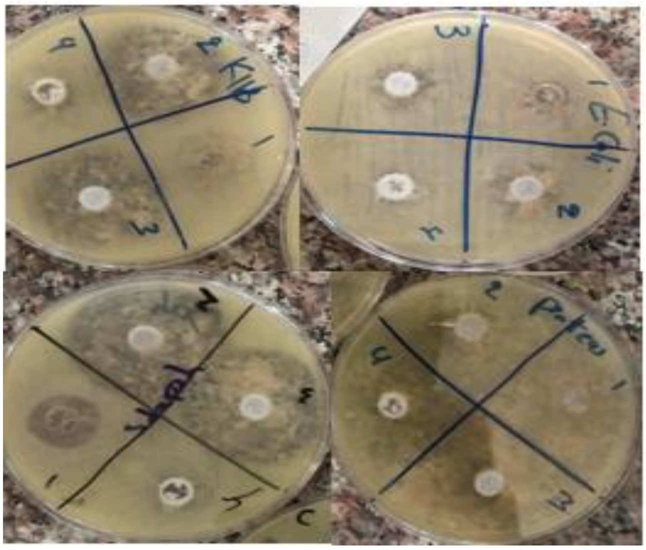


**Figure 13.** Antibacterial activity of ($SC_1$, $SC_3$, $SC_4$, $SC_6$): (1= SC1), (2= SC3), (3= SC4), (4= SC6).

## 4. CONCLUSION

In this study, a series of drug-derived Schiff base compounds (SC1, SC3, SC4, and SC6) were successfully synthesized and tested for antimicrobial activity against a panel of clinically significant bacterial strains such as *Pseudomonas aeruginosa, Escherichia coli, Klebsiella pneumoniae, Proteus spp., and Staphylococcus aureus*. SC1 had the most effective and broad-spectrum antibacterial action of the investigated compounds, with inhibitory zones equivalent to the conventional antibiotic amoxicillin, notably against P. aeruginosa and S. aureus.

The findings identify Schiff base derivatives, particularly SC1 and SC3, as attractive candidates for future development as antibacterial drugs. These findings further confirm the significance of structural change in increasing biological activity, implying that additional optimization and structure-activity relationship (SAR) research might provide even more effective analogues.

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