

Synthesis, Characterization and Evaluation of Pyridine Derivatives

Alka Tyagi*, Pravin Roman, Renuka Doiphode, Sanjivani Chaudhary

Abstract

Background: Schiff bases, a class of organic compounds, have garnered significant attention due to their diverse applications in various fields such as pharmaceuticals, materials science, and coordination chemistry. This study provides a comprehensive overview of the synthesis of Schiff bases amino pyridine derivatives and aromatic ketones along with their anti-microbial activity. **Method:** The synthesis of Schiff bases primarily involves the condensation reaction between a primary amine and a carbonyl compound (ketone) along with glacial acetic acid. Various methods have been developed for the synthesis of Schiff bases. Classical methods typically involve refluxing the amine and carbonyl compound in a suitable solvent with or without a catalyst. In this research, nine new compounds of Schiff bases have been synthesized along with characterization and antibacterial and anti-fungal activities. **Result:** It was discovered that all elemental analyses, IR, ^1H NMR, and mass spectrometry values were significant. According to antimicrobial and antifungal screening results, compounds PS-1 and compound PS-9 were found to be more active against all tested strains, while Schiff bases demonstrate substantial activity against *Staphylococcus aureus* and *Candida albicans*. PS-1 compound was found to have most activity in anti-bacterial test while PS-9 was found to possess best anti-fungal activity. **Conclusion:** The current study examines the pharmacological properties of pyridine derivatives. Pyridine derivative PS-1 was found to be most active antibacterial agent and PS-9 most active antifungal agent. The results of the study have important implications for future investigations into possible therapies for bacterial infections.

Keywords: Schiff base, synthesis, pharmacological evaluation, NMR spectroscopy, pyridine derivatives

INTRODUCTION

Schiff bases were discovered by German chemist noble prize winner Hugo Schiff in 1864 [1]. An important class of chemicals with the azomethine ($-\text{C}=\text{N}-$) group in their structure are called Schiff bases. Under particular circumstances, a primary amine and an aldehyde or ketone reacts to generate them. Schiff bases are members of the adaptable imine family [2]. Because of their steric and electrical properties, aldehydes and imines react in condensation processes more quickly than ketones [3].

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Nitrogen-containing heterocyclic compounds with a Schiff-base clubbed structure have demonstrated impressive biological properties, including antibacterial, antifungal, anti-inflammatory, antioxidant, and anticancer properties [4–10]. In the current research scenario, Schiff base complex formulation has been thoroughly explored due to its many uses, including common chemistry materials, magnetic crystal engineering synthase, and catalysis [11–15]. Molecular docking and antimicrobial testing have proven the efficacy of the Schiff base as a bioactive molecule [16]. Pyridine derivatives with either an

amino or a formyl group easily go through the Schiff base condensation process under the right circumstances and with the right substrate. Schiff bases are regarded as a subclass of imines and are the condensation products of primary amines and carbonyl compounds. Their existence of imine nitrogen, which is basic by nature and has acceptor characteristics, makes them an excellent organic ligand. Additionally, the Schiff bases operate as multidentate ligands with flexible structures if other heteroatoms such as nitrogen, oxygen, or sulfur of a particular functional group are present next to the azomethine group. Thus, in terms of strong binding, structural flexibility, and increased bioactivity, Schiff bases of pyridine might be thought of as far better ligands than pyridine itself. Biologically Schiff bases of pyridine also act as bioactive ligands and versatile pharmacophore. Protein-ligand interactions are necessary for every living thing's process. Proteins are the building blocks of all living cells and are essential to a variety of biological processes. This type of interaction is reversible and non-covalent. It involves molecular biological recognition, wherein molecules such as ligands and proteins recognize one another through stereo specificity. The formation of certain sites that are intended to bind ligand molecules is essential to the evolution of protein activities. The ability of ligands to bind is crucial for the control of biological processes that arise from the molecular mechanics of protein conformational changes. This alteration sets off a series of actions that result in various cellular processes. Thus, a thorough comprehension of protein-ligand interactions is essential to comprehending biology at the molecular level. Additionally, an in-depth understanding of the drug-receptor interaction and the discovery, design, and development of new therapeutic compounds are made possible by an understanding of the mechanisms underlying protein-ligand recognition and binding. Molecular docking is a contemporary computer method based on protein-ligand interactions that is currently widely utilized in drug research and design processes [17]. Vitrimers synthesized from Schiff bases gave excellent performance [18]. The human rhodopsin (visual purple found in rod cells of the retina) is an aldimine-type Schiff base, which is essential in the photoreception mechanism [19]. Due to their superior biological, spectroscopic, and catalytic activity, based phenylenediamine Schiff base metal complexes are currently receiving more attention [20]. Numerous studies have been conducted on the formation of Schiff bases between L-arginine and aldehydes, such as the Schiff bases salicylaldehyde-arginine, disalicylaldehyde-arginine, and metal-disalicylaldehyde-arginine. Under mild circumstances, the Schiff base exhibited exceptional selectivity and significant catalytic activity [21].

MATERIALS AND METHODS

Chemistry

The title Compounds (PS-1 to PS-9) were prepared by reaction sequence described in schemes 1, 2 and 3. In the first scheme, o-amino pyridine reacts with ketone compounds (isatin, p-benzoquinone and acetanilide) to give Schiff bases PS-1 to PS-3. In the second scheme, m-amino pyridine reacts with ketone compounds (isatin, p-benzoquinone and acetanilide) to give Schiff bases PS-4 to PS-6. In the third scheme, p-amino pyridine reacts with ketone compounds (isatin, p-benzoquinone and acetanilide) to give Schiff bases PS-7 to PS-9. The completion of reaction was confirmed by TLC.

Materials Used

Ketones: isatin, benzoquinone, acetanilide.

Amines: o-pyridine, m-pyridine, p-pyridine.

Solvent: Glacial acetic acid, acetone, distill water.

Methodology

The Schiff bases (PS-1 to PS-9) were synthesized using the below mentioned schemes (scheme 1, 2 and 3) (Figures 1–3), followed by their characterization using IR, ^1H NMR, Mass and Elemental analysis. The synthesized compounds were evaluated for their anti-bacterial and anti-fungal activity.

Procedure for Scheme

Equimolar pyridine derivative and ketone is taken in round bottom flask and 20 ml of glacial acetic acid is added to the above mixture and then the solution is refluxed for 1 h.

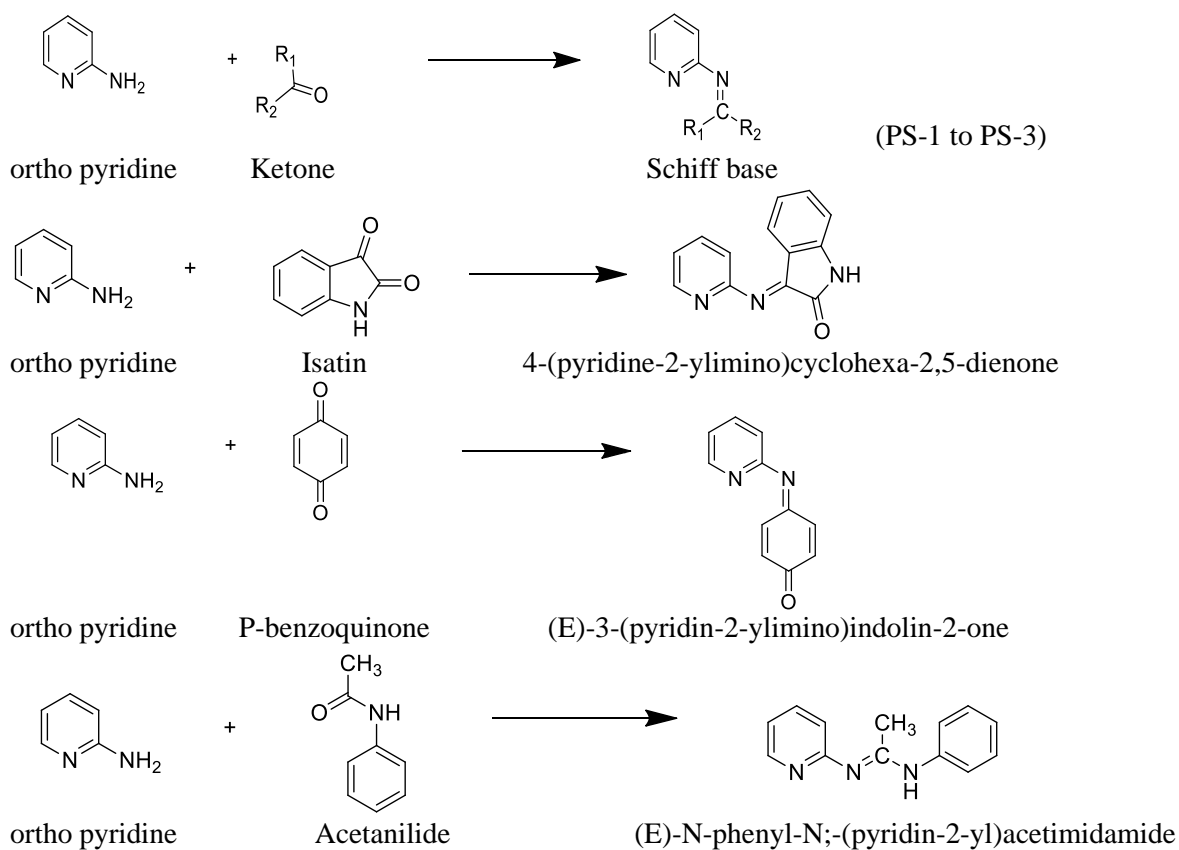


Figure 1. Scheme 1.

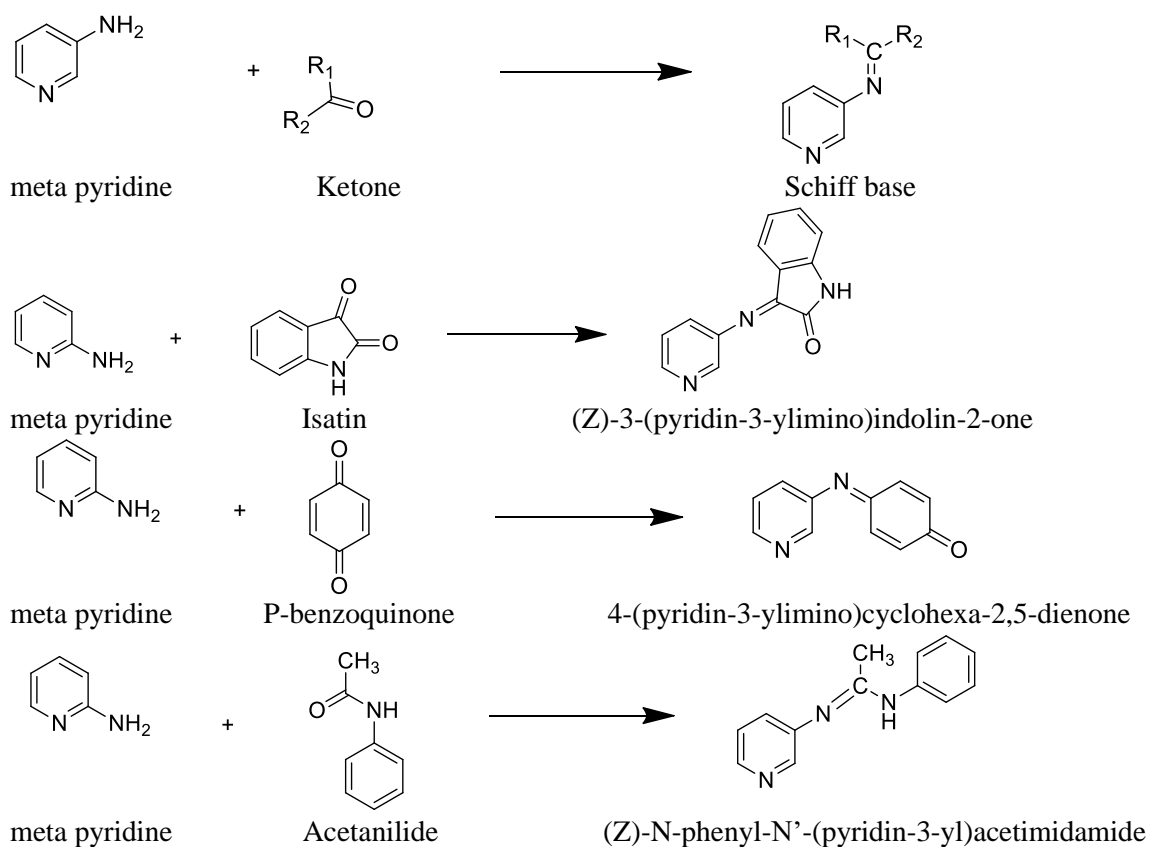


Figure 2. Scheme 2.

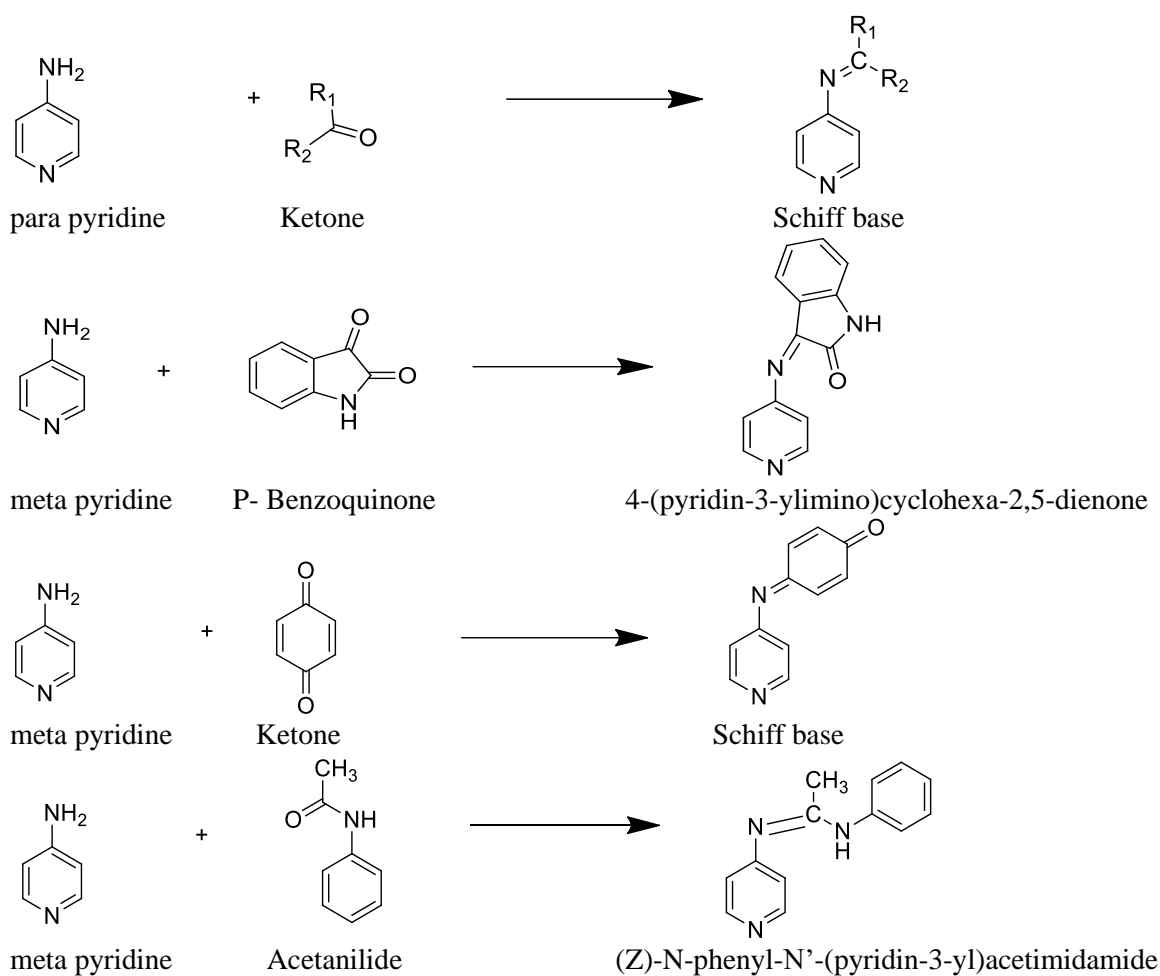


Figure 3. Scheme 3.

Pharmacological Evaluation

The synthesized compounds (PS-1 to PS-9) were evaluated for their anti-bacterial activity using the below mentioned procedure.

Anti-Microbial-Zone Inhibition Test: *S. aureus*

Requirements

- Mueller-Hilton Agar (MHA-SRL Chem- 24756) Plates.
- Bacterial Culture (*S. aureus*, MTCC96).
- Whatman No. 1 filter paper discs (5 mm).
- Solvent (vehicle control): Dimethyl Sulfoxide: DMSO (SRL Chem 28580).
- Ciprofloxacin (SRL Chem-78079).
- Amount Loaded: (0–1000 $\mu\text{g}/\text{disc}$).

Anti-microbial Activity Assay

The antibacterial activity was checked by following Zone Inhibition Method (Kirby-Bauer Method). The MHA plates were inoculated by spreading with 100 μl of Bacterial culture, *S. aureus* adjusted to 0.5 McFarland Unit, Approx cell density (1.5×10^8 CFU/ml), and followed by placing the discs containing 10 μl of different concentration (0 to 100 mg/ml). One disc in each plate was loaded with solvent alone which served as vehicle control and Ciprofloxacin disc (10 μg), were taken as positive control. The plates of *S. aureus* were incubated (Basil Scientific Corp. India) at 37°C for 24 h. The clear zones created around the disc were measured and recorded [22].

Anti-Fungal-Zone Inhibition Test *C. albicans*

The synthesized compounds (PS-1 to PS-9) were evaluated for their anti-fungal activity using the below mentioned procedure.

Requirements

- Sabouraud dextrose agar: SDA (SRL Chem, Cat no. 19427) plates.
- Fungal Culture (*C. albicans*, MTCC 854).
- Whatman No. 1 filter paper discs (5 mm).
- Solvent (vehicle control): Dimethyl Sulfoxide: DMSO (SRL Chem 28580).
- Amphotericin B: (Amphocare): 5 mg/ml.
- Amount Loaded: (0 to 1000 µg/disc).

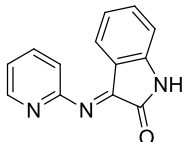
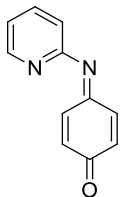
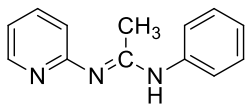
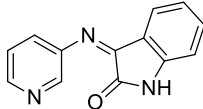
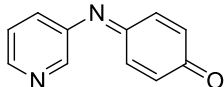
Anti-microbial Activity Assay

The antifungal activity was checked by following Zone Inhibition Method (Kirby-Bauer method). The SDA plates were inoculated by spreading with 100 100 µl of fungal culture, *C. albicans* (adjusted to 0.5 McFarland Unit- Approx cell densities (1.5×10^8 CFU/mLml) and followed by placing the discs containing 10 10 µl of different concentration (0 to 100 100 mg/ml). One disc in each plate was loaded with solvent alone which served as vehicle control and Amphotericin B disc (50 µg) was taken as positive control. The plates of *C. albicans* were incubated (Basil Scientific Corp. India- Incubator) at 37°C for 24 24 hrs. The clear zones created around the disc were measured and recorded [22].

RESULT AND DISCUSSION

The physical data (R_f value, melting point and solubility) of synthesized compounds was recorded (Table 1), followed by the characterization of the compounds by IR, ^1H NMR, mass spectrometry (M/z) and Elemental analysis (Table 2). The synthesized compounds were evaluated for their anti-bacterial and anti-fungal activity.

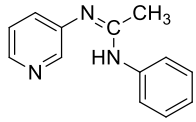
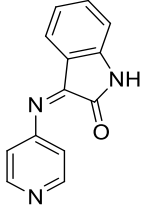
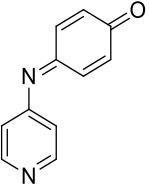
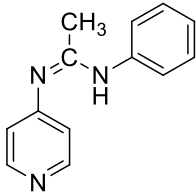
Table 1. Physical CHARACTERISTICS table of compounds (PS-1 to PS-9).

S.N.	Compound code	Compound structure	IUPAC name	Chemical formula	Rf value	Melting point (°C)	Solubility
1.	PS 1		E-3-(pyridine-2-ylimino)indolin-2-one	$\text{C}_{13}\text{H}_9\text{N}_3\text{O}$	0.7	223.23	ethanol
2.	PS 2		4-(pyridine-2-ylimino)cyclohexa-2,5-dienone	$\text{C}_{11}\text{H}_8\text{N}_2\text{O}$	0.955	184.19	Acetone
3.	PS 3		E-N-phenyl-N'-(pyridine-2-yl)acetimidamide	$\text{C}_{13}\text{H}_{13}\text{N}_3$	0.588	211.26	ethanol
4.	PS 4		(Z)-3-(pyridine-3-ylimino)indolin-2-one	$\text{C}_{13}\text{H}_9\text{N}_3\text{O}$	0.89	223.23	ethanol
5.	PS 5		4-(pyridine-3-ylimino)cyclohexa-2,5-dienone	$\text{C}_{11}\text{H}_8\text{N}_2\text{O}$	0.95	184.19	acetone

6.	PS 6		(Z)-N-phenyl-N'-(pyridine-3-yl)acetimidaamide	C ₁₁ H ₁₃ N ₃	0.6	211.26	acetone
7.	PS 7		(Z)-3-(pyridine-4-ylimino)indolin-2-one	C ₁₃ H ₉ N ₃ O	0.96	223.23	ethanol
8.	PS 8		4-(pyridine-4-ylimino)cyclohexa-2,5-dienone	C ₁₁ H ₈ N ₂ O	0.86	184.19	ethanol
9.	PS 9		(Z)-N-phenyl-N'-(pyridine-4-yl)acetimidamide	C ₁₃ H ₁₃ N ₃	0.98	211.26	ethanol

Table 2. Characterization table of compounds (PS-1 to PS-9).

S.N.	Compound Code	Structure	IR	NMR	M/z	Elemental Analysis
1.	PS-1		C=O)=1650–1750; (N=C)=1603–1616	¹ H NMR (500 MHz, CDCl ₃ -d)δ (7.00–8.52 ⁴ H Pyridine), (7.00–7.86 ⁴ H Benzene), (8.0, H, NH)	m/z: 223.07 (100.0%), 224.08 (14.2%), 225.08 (1.1%), 224.07 (1.1%)	C, 69.95 H, 4.06 N, 18.82 O, 7.17
2.	PS-2		C=O)=1640–1750; (N=C)=1600–1610	¹ H NMR (500 MHz, CDCl ₃ -d)δ (7.00–8.52 ⁴ H Pyridine), (6.30–8.61 ⁴ H Benzene)	m/z: 184.06 (100.0%), 185.07 (12.0%)	C, 71.73 H, 4.38 N, 15.21 O, 8.69
3.	PS-3		C=O)=1650–1755; (N=C)=1603–1618	¹ H NMR (500 MHz, CDCl ₃ -d)δ (7.00–8.52 ⁴ H Pyridine), (6.43–7.20 ⁴ H Benzene), (4.0, H, NH)	m/z: 211.11 (100.0%), 212.11 (15.2%)	C, 73.91 H, 6.20 N, 18.89
4.	PS-4		C=O)=1640–1750; (N=C)=1605–1616	¹ H NMR (500 MHz, CDCl ₃ -d)δ (7.71–8.45 ⁴ H Pyridine), (7.26–7.86 ⁴ H Benzene), (8.0, H, NH)	m/z: 223.07 (100.0%), 224.08 (14.2%), 225.08 (1.1%), 224.07 (1.1%)	C, 69.95 H, 4.06 N, 18.82 O, 7.17
5.	PS-5		C=O)=1650–1751; (N=C)=1603–1620	¹ H NMR (500 MHz, CDCl ₃ -d)δ (7.37–8.61 ⁴ H Pyridine), (6.30–8.61 ⁴ H Benzene)	m/z: 184.06 (100.0%), 185.07 (12.0%)	C, 71.73 H, 4.38 N, 15.21 O, 8.69

6.	PS-6		C=O)=1650–1750; (N=C)=1603–1616	¹ H NMR (500 MHZ, CDCl ₃ -d) ₃ δ (7.34–8.44 ⁴ H Pyridine), (6.43–7.20 ⁴ H Benzene), (4.0, H, NH)	m/z: 2.11.11 (100.0%), 212.11 (15.2)	C, 73.91 H, 6.20 N, 19.89
7.	PS-7			¹ H NMR (500 MHZ, CDCl ₃ -d) ₃ δ (7.40–8.42 ⁴ H Pyridine), (7.26–7.86 ⁴ H Benzene), (8, H, NH)	m/z: 223.07 (100.0%), 224.08 (14.2%), 225.08 (1.1%), 224.07 (1.1%)	C, 69.95 H, 4.06 N, 18.82 O, 7.17
8.	PS-8			¹ H NMR (500 MHZ, CDCl ₃ -d) ₃ δ (7.40–8.61 ⁴ H Pyridine), (6.30–8.61 ⁴ H Benzene)	m/z: 184.06 (100.0%), 185.07 (12.0%)	C, 71.73 H, 4.38 N, 15.21 O, 8.69
9.	PS-9			¹ H NMR (500 MHZ, CDCl ₃ -d) ₃ δ (7.40–8.42 ⁴ H Pyridine), (6.43–7.20 ⁴ H Benzene), (4.00, H, NH)	m/z: 211.11 (100.0%), 212.11 (15.2%)	C, 73.91 H, 6.02 N, 19.89

Antibacterial Activity

All the synthesized derivatives (PS-1 to PS-9) were evaluated for anti-bacterial activity using Kirby-Bauer method. All the compounds showed moderate to good anti-bacterial activity (Tables 3–6 and Figures 4–6).

Table 3. Antibacterial activity of synthesized compounds.

S.N.	Sample code	Max.Zi (mm) AVG	Conc. (μg)
1.	Ciprofloxacin (pc)	26.66	10
2.	Ps-1	20.00	50
3.	Ps-2	13.88	50
4.	Ps-3	10.80	50
5.	Ps-4	12.00	50
6.	Ps-5	18.33	50
7.	Ps-6	13.07	50
8.	Ps-7	12.00	50
9.	Ps-8	10.81	50
10.	Ps-9	15.90	50

Bioassay: Antibacterial Activity

Test Organism: *S. aureus*

X Axis : Amount (μg/disc)

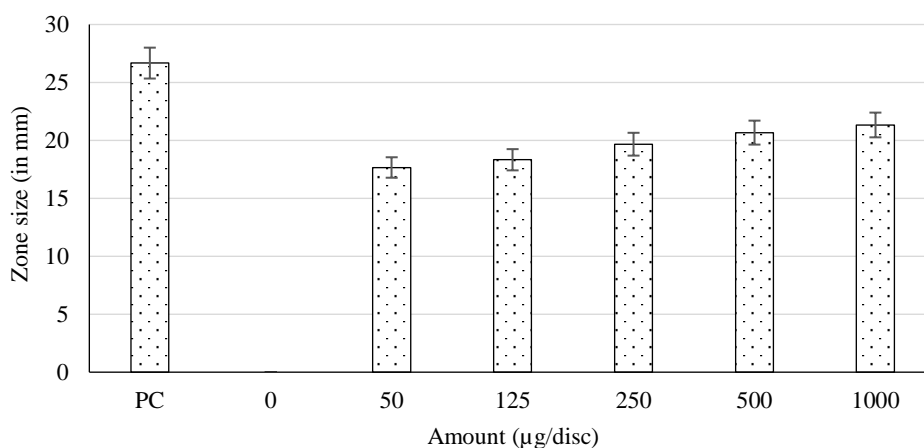
Y Axis: Zone Size (in mm)

Title: Antibacterial Activity: *S. aureus*

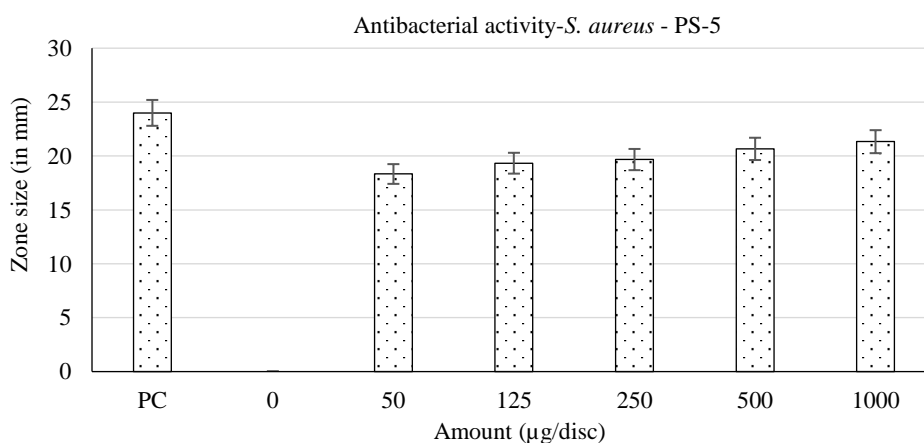
Max. Zi =maximum zone of inhibition

PS-1**Table 4.** Bioassay: antibacterial activity of compound PS-1.

Amount ($\mu\text{g}/\text{disc}$)	Plate A	Plate B	Plate C	Average	SD	SEM
PC	24	28	28	26.67	2.30	1.33
0	0	0	0	0	0	0
50	15.20	16.33	17.44	17.66	1.73	0.55
125	16.32	17.42	18.23	18.33	2.15	0.66
250	17.20	18.50	19.85	19.67	2.17	0.67
500	18.12	19.95	20.80	20.67	2.15	1.00
1000	20.98	21.45	22.00	21.33	2.28	1.66

**Figure 4.** Graphical representation of antibacterial activity of compound PS-1.**PS-5****Table 5.** Bioassay: antibacterial activity of compound PS-5.

Amount ($\mu\text{g}/\text{disc}$)	Plate A	Plate B	Plate C	Average	SD	SEM
PC	28	28	24	26.67	2.94	1.33
0	0	0	0	0	0	0
50	8.11	7.88	6.23	8.33	1.75	0.57
125	8.33	8.45	6.25	9.33	2.12	0.67
250	9.20	8.25	7.48	9.67	2.18	0.67
500	10.00	10.45	7.74	10.66	2.15	1.00
1000	12.88	12.66	7.67	12.33	2.28	1.66

**Figure 5.** Graphical representation of antibacterial activity of compound PS-5.

PS-9

Table 6. Bioassay: antibacterial activity of compound PS-9.

Amount (µg/disc)	Plate A	Plate B	Plate C	Average	SD	SEM
PC	24	24	24	24	2.30	1.33
0	0	0	0	0	0	0
50	17.05	18.02	19.05	18.33	1.73	0.52
125	18.12	19.07	20.44	19.33	2.15	0.67
250	18.81	19.02	20.77	19.67	2.17	0.77
500	19.08	20.00	21.33	20.66	2.15	1.67
1000	20.22	21.06	22.33	21.33	2.28	1.63

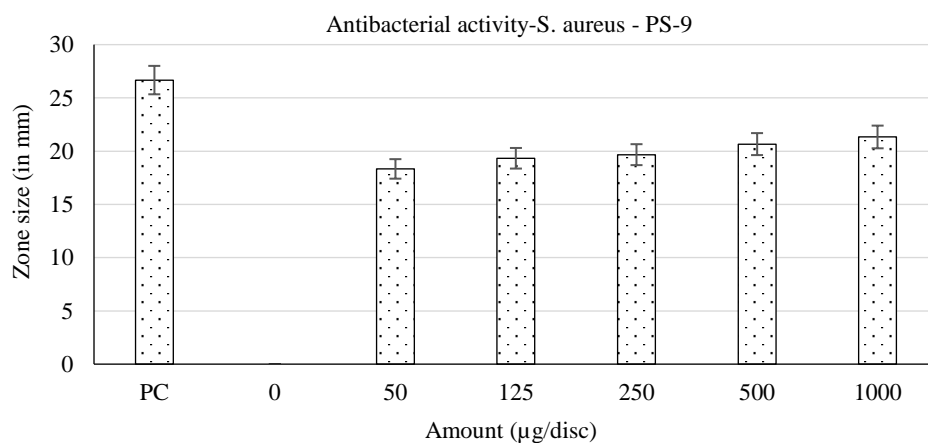


Figure 6. Graphical representation of Antibacterial Activity of compound PS-9.

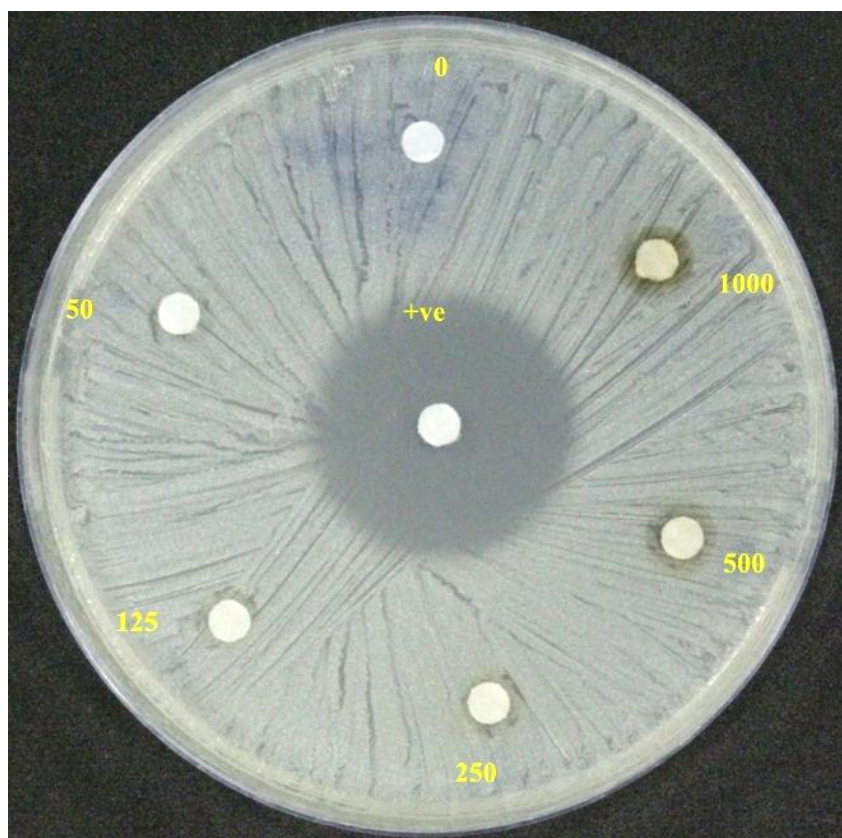


Figure 7. PS-1 antimicrobial zone inhibition test.

Anti-fungal Activity

All the synthesized derivatives (PS-1 to PS-9) were evaluated for anti-fungal activity using Kirby-Bauer method. All the compounds showed moderate to good anti-fungal activity (Tables 7–10 and Figures 7–11).

Table 7. Antifungal activity of synthesized compounds.

S.N.	Sample code	Max.zi (mm) avg	Conc. (μg)
1.	Amphotericin B (pc)	20.33	50.(μg)
2.	Ps-1	8	50
3.	Ps-2	8	50
4.	Ps-3	6	50
5.	Ps-4	6.22	50
6.	Ps-5	7.33	50
7.	Ps-6	6.87	50
8.	Ps-7	7.56	50
9.	Ps-8	7.66	50
10.	Ps-9	8.66	50

Bioassay: Antifungal Activity

Test Organism: *C. albicans*

X Axis: Amount: ($\mu\text{g}/\text{disc}$)

Y Axis: Zone Size (in mm)

Title: Antifungal Activity: *C. albicans*

PS-1

Table 8. Antifungal activity of compound PS-1.

Amount ($\mu\text{g}/\text{disk}$)	Plate A ($\mu\text{g}/\text{disk}$)	Plate B ($\mu\text{g}/\text{disk}$)	Plate C ($\mu\text{g}/\text{disk}$)	Average	SD	SEM
PC	20.00	20.00	21.00	20.33	0.57	0.40
0	0	0	0	0	0	0
50	8.23	8.66	8.77	8.66	0	0
125	8.22	8.66	8.67	8.55	0	0
250	8.66	8.67	8.77	8.67	0	0
500	8.67	8.66	8.67	8.77	0	0

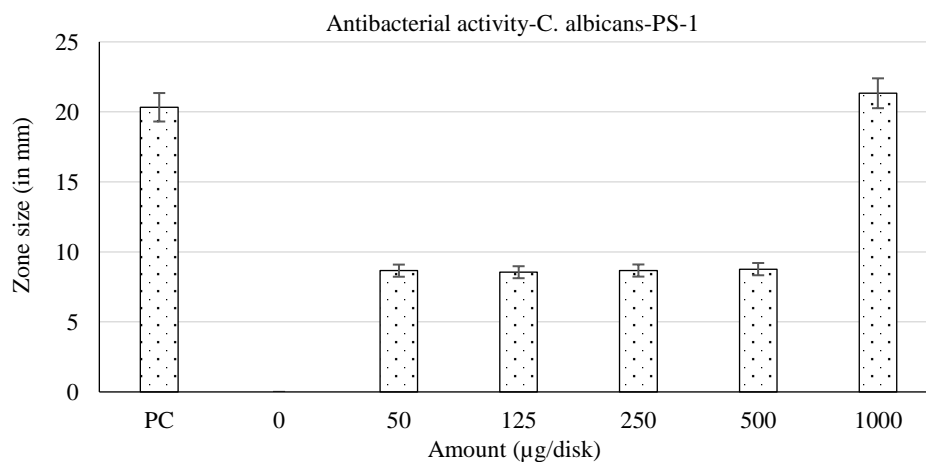


Figure 8. Graphical representation of Antifungal activity of compound PS-1.

PS-5

Table 9. Antifungal activity of compound PS-5.

Amount (µg/disk)	Plate A	Plate B	Plate C	Average	SD	SEM
PC	20.00	20.00	20.00	20.00	0	0
0	0	0	0	0	0	0
50	7.66	7.77	8.80	7.33	0.55	0.40
125	7.23	7.67	8.66	7.33	0.57	0.45
250	7.67	7.67	7.52	7.68	0	0
500	7.89	7.67	7.44	7.67	0	0
1000	6.88	6.67	6.67	6.67	0	0

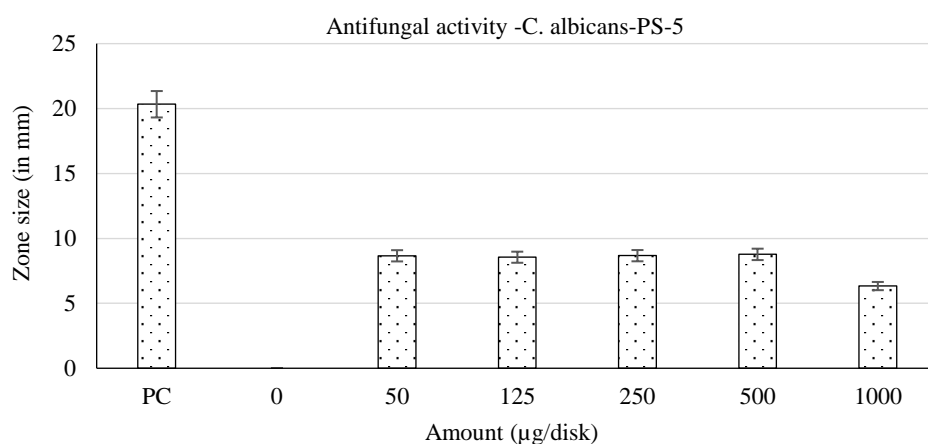


Figure 9. Graphical representation of Antifungal activity of compound PS-5.

PS-9

Table 10. Antifungal activity of compound PS-9.

Amount (µg/disk)	Plate A	Plate B	Plate C	Average	SD	SEM
PC	21.00	20.00	20.00	20.33	0.57	0.40
0	0	0	0	0	0	0
50	7.23	7.66	7.56	7	0	0
125	7.33	7.66	8.66	7.33	0.57	0.40
250	8.23	7.67	8.67	7.66	0.57	0.40
500	8.66	7.67	8.67	7.66	0.57	0.40
1000	7.67	8.67	7.67	7.33	0.57	0.40

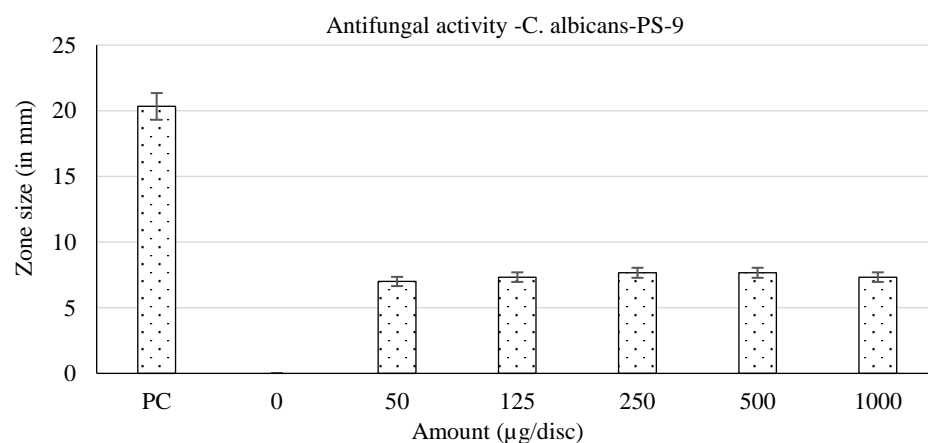


Figure 10. Graphical representation of antifungal activity of compound PS-9.

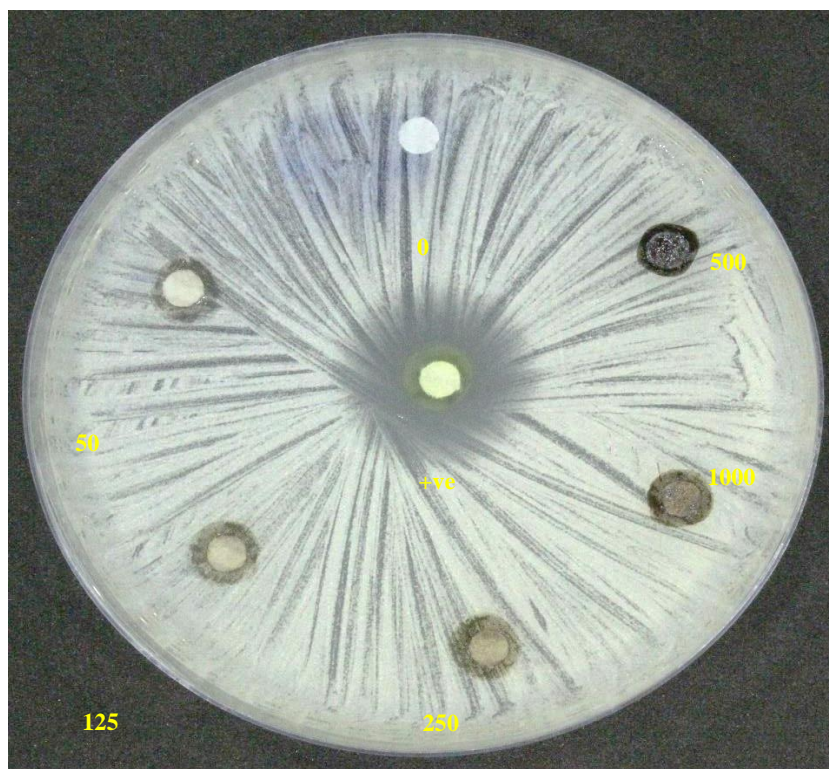


Figure 11. PS-5 Antifungal zone inhibition test.

CONCLUSION

Synthesizing Schiff bases involves condensation reactions between primary amines and carbonyl compounds. Once formed, Schiff bases have various applications in pharmaceuticals, dyes, and coordination chemistry due to their versatile properties. Here is a general result and conclusion for a typical Schiff base synthesis experiment:

In this research, the synthesis of Schiff bases involves the reaction between a primary amine and different ketones in a suitable solvent, typically under reflux conditions. The reaction proceeds via a condensation reaction, forming an imine intermediate which then undergoes tautomerization to yield the Schiff base product. The progress of the reaction can be monitored using technique IR (infrared spectroscopy).

Upon completion of the reaction, the Schiff base product is typically isolated by simple workup procedures. The product's identity and purity can be confirmed using analytical techniques such as NMR (nuclear magnetic resonance) spectroscopy, mass spectrometry, and elemental analysis.

Based on the results obtained from the study of antibacterial activity, when test organism *S. aureus* was treated with different amounts of sample on agar plate, maximum zone of inhibition (ZI) were estimated and compared to the positive control. In this research for antibacterial activity, ciprofloxacin was taken as control group and out of 9 samples been tested, Sample PS-1, PS-5, and PS-9 showed best results. The zone of inhibition is an area around a disc on an agar plate where no bacterial growth is observed due to the presence of an antimicrobial agent. It is used to determine whether a particular test organism is susceptible to the action of a particular antimicrobial agent or not.

Based on the results obtained from the study of antifungal activity, when test organism *C. albicans* was treated with different amounts of sample of PS (1–9) on agar plate, maximum zone of inhibition (ZI) were estimated by PS-1, PS-5, and PS-9. The zone of inhibition is an area around a disc on an agar plate where no fungal growth is observed due to the presence of an antimicrobial agent. It is used to determine whether a particular test organism is susceptible to the action of a particular antimicrobial agent or not.

The synthesis of Schiff bases provides an efficient route to access a wide range of compounds with diverse applications. The reaction conditions can be adjusted to modulate the selectivity and yield of the desired product. Additionally, the Schiff base formation can be catalyzed by various catalysts, including acids, bases, and transition metal complexes, to enhance the reaction rate and selectivity. PS-1 was found to be most active antibacterial agent and PS-9 most active antifungal agent.

Overall, the synthesis of Schiff bases offers a versatile and valuable tool in organic synthesis, allowing for the facile preparation of structurally diverse compounds with potential applications in various fields including medicinal chemistry, materials science, and catalysis. Further studies can focus on exploring new substrates, reaction conditions, and catalytic systems to expand the scope and utility of Schiff base synthesis.

Statements And Declaration

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REFERENCES

1. Khedr AM, Jadon S, Kumar V. Synthesis, Spectral analysis, and molecular modeling of bioactive Sn (II)-complexes with oxadiazole Schiff bases. *J Coord Chem*. 2011 Apr 20; 64(8): 1351–9.
2. Tsacheva I, Todorova Z, Momekova D, Momekov G, Koseva N. Pharmacological activities of Schiff bases and their derivatives with low and high molecular phosphonates. *Pharmaceuticals*. 2023 Jun 28; 16(7): 938. <https://doi.org/10.3390/ph16070938>
3. Gul R, Munir W, Saleh EA, Shujah S, Sirajuddin M, Tabassum S, ur Rehman K, Khan D, Al-Saeedi SI, Abdelrahman EA. Ferrocene based Schiff bases and their complexes: Synthesis, characterization and biological evaluation. *J Organomet Chem*. 2024 Jan 1; (1003): 122944. <https://doi.org/10.1016/j.jorganchem.2023.122944>
4. Gurav SS, Waghmode KT, Dandekar SN, Jadhav SD, Lotlikar OA, Jadhav SR, Mali SN, Naphade JG. New 2-Chloroimidazo [1, 2-a] pyridine induced Schiff bases: Synthesis, characterization, antimicrobial and A-498 and A-549 anticancer activity, molecular modeling, in-silico pharmacokinetics, and DFT studies. *Chem Phys Impact*. 2024 Jun 1; 8: 100494.
5. Ceramella J, Iacopetta D, Catalano A, Cirillo F, Lappano R, Sinicropi MS. A review on the antimicrobial activity of Schiff bases: Data collection and recent studies. *Antibiotics*. 2022 Feb 1; 11(2): 191.
6. Mishra N, Kumar K, Pandey H, Anand SR, Yadav R, Srivastava SP, Pandey R. Synthesis, characterization, optical and anti-bacterial properties of benzothiazole Schiff bases and their lanthanide (III) complexes. *J Saudi Chem Soc*. 2020 Dec 1; 24(12): 925–33.
7. Alok P, Dhansay D, Shekhar V, Achal M, Ravindra DD. Synthesis of Schiff bases of 2-amino-5-aryl-1,3,4-thiadiazole and its analgesic, anti-inflammatory and antibacterial activity. *Int J ChemTech Res*. 2011;3:178–184.
8. Shahraki S, Majd MH, Heydari A. Novel tetradentate Schiff base zinc (II) complex as a potential antioxidant and cancer chemotherapeutic agent: Insights from the photophysical and computational approach. *J Mol Struct*. 2019 Feb 5; 1177: 536–44. <https://doi.org/10.1016/j.molstruc.2018.10.005>
9. Saedi Z, Hoveizi E, Roushani M, Massahi S, Hadian M, Salehi K. Synthesis, characterization, anticancer properties and theoretical study of asymmetrical Cd (II) N2-Schiff base complexes. *J Mol Struct*. 2019 Jan 15; 1176: 207–16. <https://doi.org/10.1016/j.molstruc.2018.08.072>

10. Shabbir M, Akhter Z, Ahmad I, Ahmed S, Ismail H, Mirza B, McKee V, Bolte M. Synthesis, characterization, biological and electrochemical evaluation of novel ether based ON donor bidentate Schiff bases. *J Mol Struct.* 2016; 1116: 84–92. <https://doi.org/10.1016/j.molstruc.2016.03.008>
11. Deepika P, Vinusha HM, Begum M, Ramu R, Shirahatti PS, Prasad MN. 2-methoxy-4-(((5-nitropyridin-2-yl) imino) methyl) phenol Schiff base ligand and its Cu (II) and Zn (II) complexes: synthesis, characterization and biological investigations. *Heliyon.* 2022 Jun 1; 8(6): e09648. <https://doi.org/10.1016/j.heliyon.2022.e09648>
12. Pouralimardan O, Chamayou A-C, Janiak C, Hosseini-Monfared H. Hydrazone Schiff base-manganese(II) complexes: Synthesis, crystal structure and catalytic reactivity. *Inorganica Chim Acta.* 2007; 360(5): 1599–1608. <https://doi.org/10.1016/j.ica.2006.08.056>
13. Karvembu R, Hemalatha S, Prabhakaran R, Natarajan K. Synthesis, characterization and catalytic activities of ruthenium complexes containing triphenylphosphine/triphenylarsine and tetradentate Schiff bases. *Inorg Chem Commun.* 2003; 6(5): 486–490. [https://doi.org/10.1016/s1387-7003\(03\)00021-2](https://doi.org/10.1016/s1387-7003(03)00021-2)
14. İspir E. The synthesis, characterization, electrochemical character, catalytic and antimicrobial activity of novel, azo-containing Schiff bases and their metal complexes. *Dyes Pigm: An International Journal.* 2009; 82(1): 13–19. <https://doi.org/10.1016/j.dyepig.2008.09.019>
15. Mabad B, Cassoux P, Tuchagues JP, Hendrickson DN. Manganese(II) complexes of polydentate Schiff bases. 1. Synthesis, characterization, magnetic properties, and molecular structure. *Inorg Chem.* 1986; 25(9): 1420–1431. <https://doi.org/10.1021/ic00229a025>
16. Kaushik S, Paliwal SK, Iyer MR, Patil VM. Promising Schiff bases in antiviral drug design and discovery. *Med Chem Res.* 2023 Jun; 32(6): 1063–76. <https://doi.org/10.1007/s00044-023-03068-0>
17. Joshi KK. Chemistry with Schiff bases of pyridine derivatives: Their potential as bioactive ligands and chemosensors. In: *Exploring Chemistry with Pyridine Derivatives.* London (United Kingdom): IntechOpen; 2022 Oct 7. doi: 10.5772/intechopen.106749.
18. Jiang L, Tian Y, Cheng J, Zhang J. A biomass-based Schiff base vitrimer with both excellent performance and multiple degradability. *Polym Chem.* 2021; 12(45): 6527–37. <https://doi.org/10.1039/d1py01003d>
19. Sztanke M, Wilk A, Sztanke K. An Insight into Fluorinated Imines and Hydrazones as Antibacterial Agents. *Int J Mol Sci.* 2024 Mar 15; 25(6): 3341.
20. Zhao J, Xie Y, Fang J, Ling Y, Gao Y, Liu X, Zhang Q, Xu Q, Xiong H. P-phenylenediamine-benzoquinone Schiff base Ag (I) complexes chemically bonded to few-layered graphene as flexible materials for electromagnetic studies. *J Mater Sci.* 2016 Dec; 51(23): 10574–84.
21. Cui J, Sun Y, Wang L, Miao Q, Tan W, Guo Z. Preparation of l-arginine Schiff bases modified chitosan derivatives and their antimicrobial and antioxidant properties. *Mar Drugs.* 2022 Oct 31; 20(11): 688. <https://doi.org/10.3390/md20110688>
22. Christenson JC, Korgenski KK, Relich RF. Laboratory diagnosis of infection due to bacteria, fungi, parasites, and Rickettsiae. In: Long SS, Prober CG, Fischer M, editors. *Principles and Practice of Pediatric Infectious Diseases.* 5th ed. Washington (UK): Elsevier; 2018. p. 1422–1434.e3. Available from: <https://asm.org/getattachment/2594ce26-bd44-47f6-8287-0657aa9185ad/Kirby-Bauer-Disc-Diffusion-Susceptibility-Test-Protocol-pdf.pdf>.