

SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL ACTIVITY OF SOME SCHIFF BASE METAL COMPLEXES**Samar S. Mohammed**

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Abstract: This study presents the synthesis and characterization of five metal complexes (C1–C5) derived from the reaction of a newly synthesized ligand (HL) with various metal chlorides, specifically Zn, Co, Ni, Mn, and Fe. **General Background:** Transition metal complexes have garnered significant interest due to their diverse biological activities and potential therapeutic applications. **Specific Background:** The ligand (HL) was synthesized from equimolar amounts of p-anisidine and salicylaldehyde, yet the influence of different metal ions on the biological properties of such complexes remains underexplored. **Knowledge Gap:** While several metal complexes exhibit antimicrobial properties, there is limited research on the biological activities of complexes formed with this specific ligand. **Aims:** This work aims to synthesize and characterize the metal complexes and evaluate their antibacterial activity against various bacterial strains. **Results:** Characterization via FT-IR and ¹H NMR spectroscopy confirmed the successful formation of the complexes, indicating strong metal-ligand interactions. Preliminary biological testing revealed varying degrees of antibacterial activity among the complexes, with notable effectiveness against certain bacterial strains. **Novelty:** The study contributes to the understanding of how different metal ions influence the biological properties of metal-ligand complexes. **Implications:** These findings suggest that the synthesized metal complexes could serve as potential candidates for further development in antimicrobial therapies, prompting additional research into their mechanism of action and broader biological applications.

Keywords: : Schiff base, Metal complexes, Biological activity

This is an open-access article under the [CC-BY 4.0](https://creativecommons.org/licenses/by/4.0/) license**Introduction**

The amino compound undergoes a reaction with the carbonyl compound, resulting in the formation of Schiff bases. Schiff bases are a significant class of ligands due to their inclusion of C=N as the active group. These Schiff bases can then couple with metal ions through azomethine (1), a molecule that is now the subject of much investigation. The presence of a C=N bond is essential for the biological activity of azomethine derivative products. Several azomethine derivatives have demonstrated remarkable antibacterial, antifungal, anticancer, and antimalarial characteristics (2). Schiff base ligands have garnered significant attention in the field of coordination chemistry owing to their straightforward production, abundant accessibility, and favorable electrochemical characteristics. Schiff base coordination chemistry has garnered significant interest in recent times because to its crucial role in several fields such as chemical synthesis, analytical chemistry, metal refining, metallurgy, electroplating, and photography (3- 5). Schiff bases have several uses in the dye market, in catalytic reactions, fungicides, and as agricultural chemicals (6- 7). Several Schiff bases are known to have exceptional antibacterial, antifungal, and anticancer properties (8).

Metal compounds have been utilized in medical science for thousands of years due to their diverse properties. However, it was only in the past forty years that the scientific community became

interested in the modes of action of complexes composed of metal ions and organic ligands. This development established a significant connection between inorganic and organic chemistry. The field of inorganic medicinal chemistry mostly focuses on investigating the anticancer properties of metal complexes. However, there is also considerable interest in exploring the antimicrobial and anti-inflammatory effects of metal-based medications, such as Auranofin, which is a gold-based treatment for rheumatoid arthritis (9, 13).

Methods

2.1. General and instrumentals

All the reagents, starting chemicals, and solutions were obtained from a commercial source and used without additional purification. On a Gallen Kamp melting point apparatus with a heated stage, the melting points were recorded. FTIR Bucker Spectrophotometer was used to record the infrared (FTIR) spectrum. On a Bucker 500 MHz spectrometer, ^1H NMR spectra were acquired with deuterated d_6 -DMSO as the solvent.

2.2 Synthesis of the Schiff base ligand (HL) (14- 15)

The P-anisidine (0.01 mol, 1.23 g) reacted with salicylaldehyde (0.01 mmol, 1.22 g, 1.39 ml) in 15 ml of EtOH, refluxed more than 2 hours. Finally, produce yellowish solid compound separated via filtration, then washed with diethyl ether, and dried.

2.3 Synthesis of metal complexes C1 – C5 (16-18)

0.02 mole of the Schiff base ligand (HL) reacted with 0.01 mole of metal chloride ($\text{ZnCl}_2 \cdot \text{H}_2\text{O}$ as C1, $\text{CoCl}_2 \cdot \text{H}_2\text{O}$ as C2, $\text{NiCl}_2 \cdot \text{H}_2\text{O}$ as C3, $\text{MnCl}_2 \cdot \text{H}_2\text{O}$ and $\text{FeCl}_2 \cdot \text{H}_2\text{O}$) in 2:1 molar ratio. In hot ethanol dissolved the mixture, reflux for 3 hours and led to form colored products.

Table 1: The physicochemical properties of synthesized compounds.

Compound No.	Melting point °C	Color	Yielded %
HL	129 - 131	Yellow	59
C1	125 - 127	Yellowish green	70
C2	119 - 121	Blue	69
C3	97 - 100	Green	72
C4	89 - 91	Yellowish green	68
C5	102 - 104	Black	69

Results and Discussion

The ligand HL, FT-IR (cm^{-1}) as shown in figure 1: FT-IR (cm^{-1}): The $\nu(\text{OH})$ appeared at 3333 ^(19, 20), $\nu(\text{C}=\text{N})$ 1621, $\nu(\text{C}-\text{N})$ 1333, $\nu(\text{C}-\text{O})$ phenolic 1253, $\nu(\text{C}-\text{H})$ Aromatic 3089 ⁽²¹⁾.

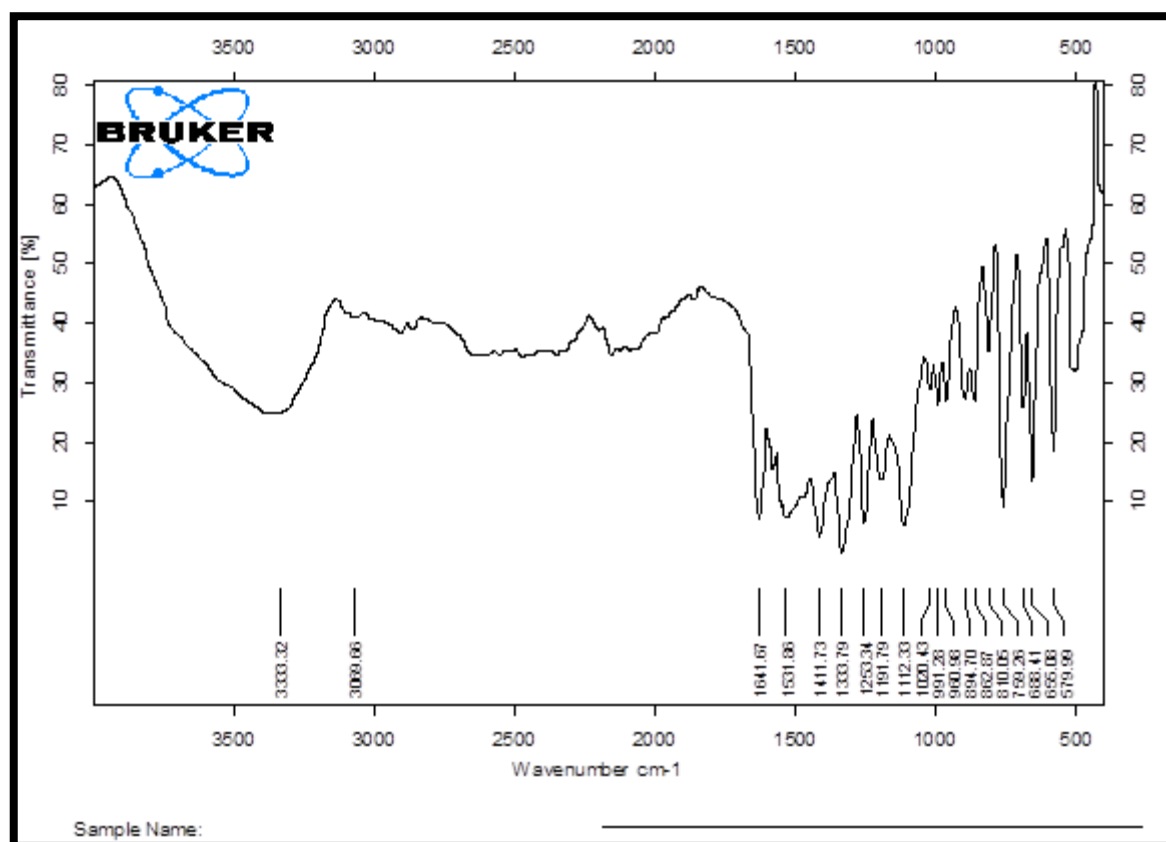


Figure 1: FTIR spectrum of compound HL.

The ligand HL, ^1H NMR (500 MHz, DMSO- d_6 , δ , ppm) as shown in figure 2: δ 9.66 (s, O-H), 8.44 (s, proton of azomethine), 7.90- 6.63 (C-H aromatic) ^(22, 23), 3.50 (H₂O), 2.45 (DMSO as solvent).

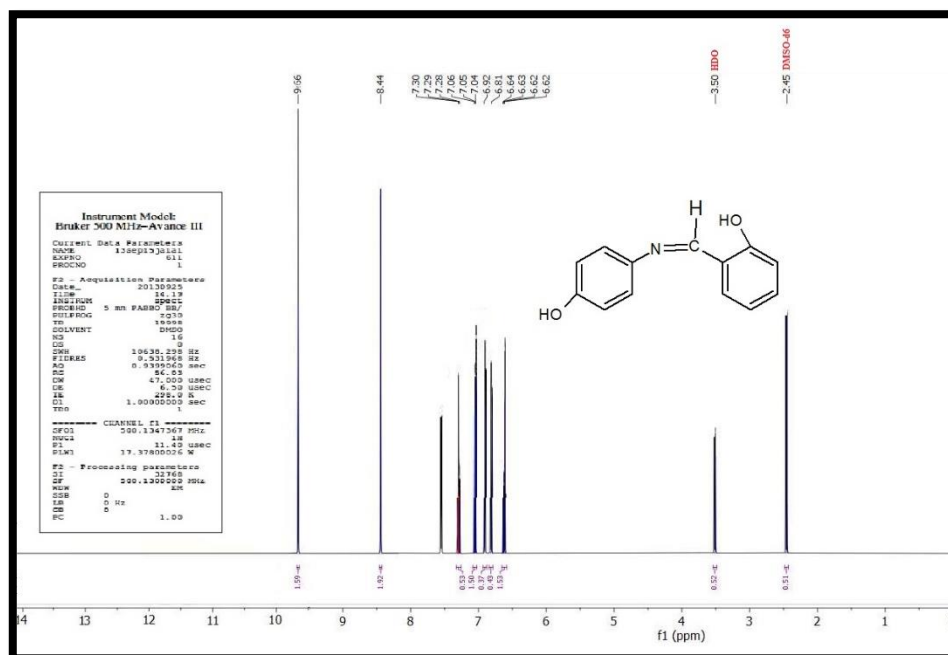


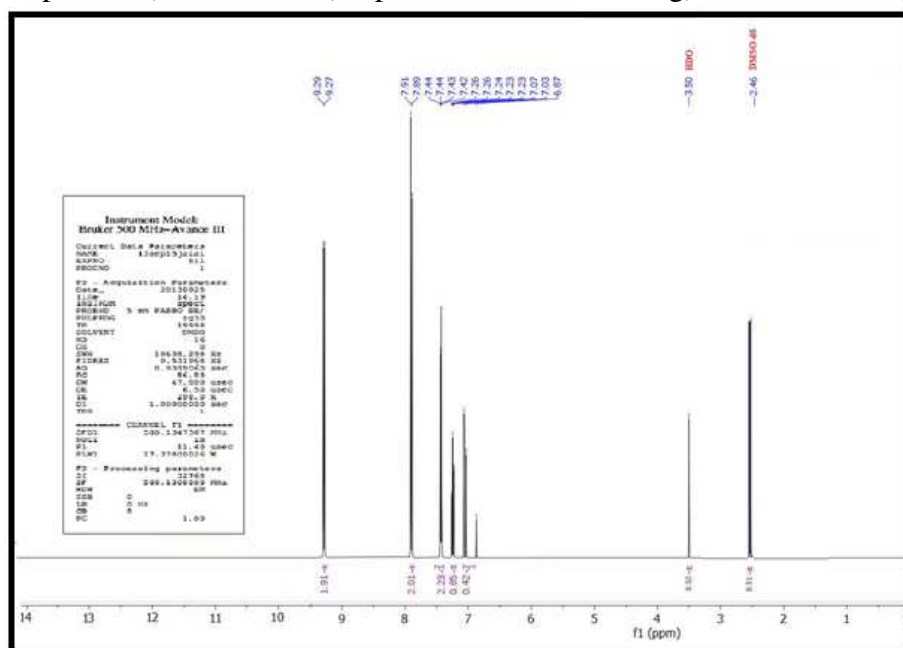
Figure 2: ^1H NMR spectrum of compound HL.

The complexes C1, FT-IR (cm^{-1}) as shown in figure 3: The ν (OH) hydroxyl group appeared

IR Spectrum Plot showing Transmittance [%] versus Wavenumber cm^{-1} . The plot includes a Bruker logo in the top left corner. The x-axis ranges from 3500 to 500 cm^{-1} , and the y-axis ranges from 20 to 100 % Transmittance. Key peaks are labeled with their wavenumbers:

Wavenumber (cm^{-1})
3421.15
3031.06
1627.04
1603.55
1600.40
1431.61
1374.94
1271.80
1228.28
1193.08
1161.09
1130.21
1003.66
981.34
847.64
765.00
692.02
664.27
641.25
612.57
501.00
410.00

The complexes C1, ¹HNMR (500 MHz, DMSO-d₆, δ, ppm) as shown in figure 4: 9.25 and 9.27 (s, proton of OH phenolic), 6.87– 7.44 (m, protons of aromatic ring), 7.89 and 7.91 (s, CH=N) ⁽²⁵⁾.



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The complexes C1, FT-IR (cm^{-1}) as shown in figure 5: the broad band of $\nu(\text{OH})$ appeared at 3383, the group $\nu(\text{C}=\text{N})$ appeared at band 1653, $\nu(\text{C}-\text{N})$ 1367, $\nu(\text{C}-\text{O})$ 1248. The stretching bands of $\nu(\text{H}_2\text{O})$ coordinated water showed two band 832 and 779, $\nu(\text{M}-\text{O})$ stretching bands of coordinated water 557, metal-oxygen band as $\nu(\text{M}-\text{O})$ that showed at 651. Finally, the band $\nu(\text{M}-\text{N})$ at 466^(26–28).

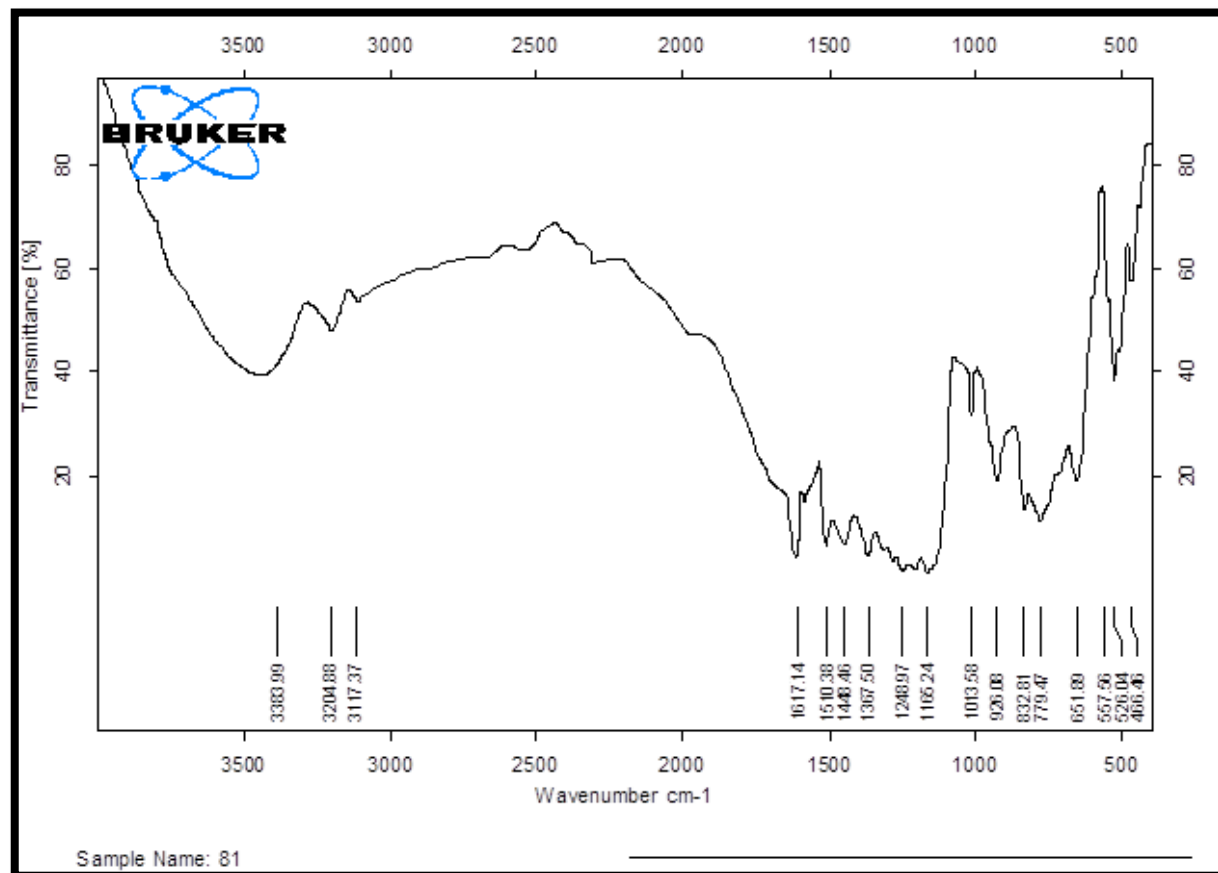


Figure 5: FTIR spectrum of complex C2.

The complexes C2, ^1H NMR (500 MHz, $\text{DMSO}-d_6$, δ , ppm) as shown in figure 6: 9.49 (s, proton of OH phenolic), 6.63 – 8.61 (m, proton of aromatic ring), 7.61 and 7.41 (s, H, $\text{CH}=\text{N}$)^(29, 30).

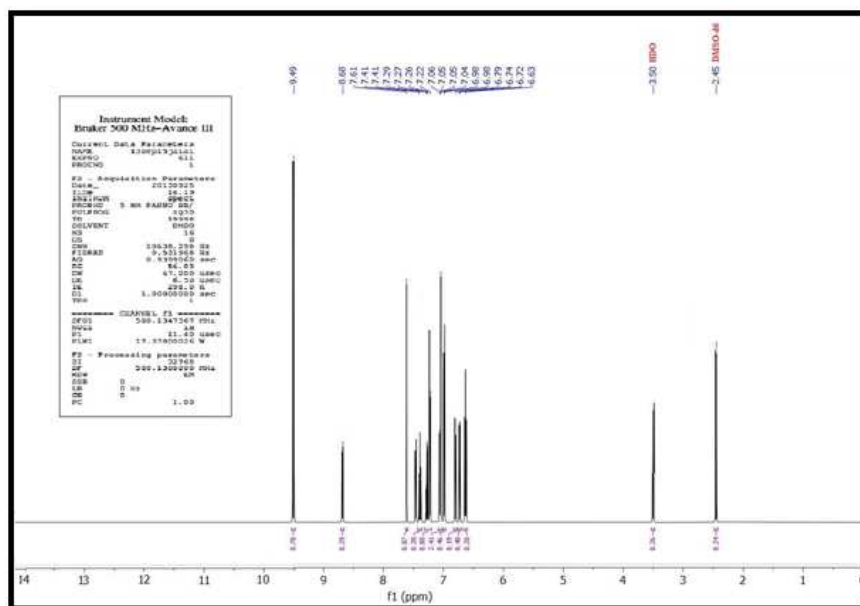


Figure 6: HNMR spectrum of complex C2.

Table (2): FTIR spectrum for compounds C1 – C5.

Compound NO.	O-H	C-H Aromatic	C=N	C-O	M-O	M-N
HL	3333	3089	1641	1239	---	---
C1	3461	3031	1627	1228	612	419
C2	3383	3117	1617	1248	651	466
C3	3401	3067	1632	1236	643	438
C4	3379	3146	1628	1231	647	426
C5	3301	3089	1616	1235	639	425

The molar conductivity (10^{-3} M, DMSO / Ω^{-1} cm² mol⁻¹): 19.40 for complex C1, 41.20 for complex C2, 43 for complex C3, 38.20 for complex C4 and 67 for complex C5.

Biological Activity of synthesized compounds C1-C3

The synthetic complexes C1 and C3 have undergone testing against both gram-positive and gram-negative bacteria, such as Staphylococcus, bacillus subtilis, pseudomonas aerugi, and escherichia coli. The microorganisms were provided as pre-cultured bacterial cultures at concentrations of 25 and 50 mg/ml using the Agar well Diffusion technique (31). The inhibitory diameter of each pore was measured using a ruler. The zone of inhibition refers to the translucent area that encloses the disc, including the unaffected diameter of the disk. All of these results are displayed in Table 2.

The cell wall of bacterial cells is composed of peptidoglycan, a complex network of elongated sugar polymers. The process of cross-linking the glycan strands in the peptidoglycan is facilitated by transglycosidases. This entails the extension of peptide chains from the sugars present in the polymers, resulting in the formation of cross linkages between peptides (32). In the presence of penicillin binding proteins (PBPs), the D-alanyl alanine segment of the peptide chain undergoes

crosslinking through glycine residues (33).

Table 2. Antibacterial activities of the compounds (C1 and C3).

Bacteria name	Zone of inhibition (mm)			
	Compound C1		Compound C3	
	[con. 25 mg/ml]	[con. 50 mg/ml]	[con. 25 mg/ml]	[con. 50 mg/ml]
<i>Staphylococcus</i>	37	40	36	39
<i>Bacillus subtilis</i>	40	43	43	45
<i>Pseudomonas aerug</i>	45	47	42	48
<i>Escherichia coli</i>	37	42	40	47

Conclusion

This study successfully synthesized and characterized five Schiff base metal complexes (C1–C5) from a novel ligand (HL), demonstrating strong metal-ligand interactions as confirmed by FT-IR and ^1H NMR spectroscopy. The antibacterial assays revealed varying degrees of activity among the complexes, highlighting their potential as effective antimicrobial agents against specific bacterial strains. These findings not only expand the knowledge base regarding the biological activities of metal-ligand complexes but also suggest that these synthesized compounds could serve as promising candidates for the development of new antimicrobial therapies. Future research should focus on elucidating the mechanisms underlying their antibacterial properties and exploring their efficacy against a broader spectrum of microbial pathogens. Additionally, investigating the structure-activity relationship will be crucial for optimizing these complexes for therapeutic applications.

References

- [1] A. Z. El-Sonbati, W. H. Mahmoud, G. G. Mohamed, M. A. Diab, S. M. Morgan, and S. Y. Abbas, "Synthesis, Characterization of Schiff Base Metal Complexes and Their Biological Investigation," *Applied Organometallic Chemistry*, vol. 33, no. 9, p. e5048, 2019.
- [2] E. Yousif, A. Majeed, K. Al-Sammarrae, N. Salih, J. Salimon, and B. Abdullah, "Metal Complexes of Schiff Base: Preparation, Characterization and Antibacterial Activity," *Arabian Journal of Chemistry*, vol. 10, p. S1639-S1644, 2017.
- [3] P. Pfeiffer, E. Buchholz, and O. Bauer, "Innere Komplexsalze von Oxyaldimininen und Oxyketimininen," *Journal für Praktische Chemie*, vol. 129, no. 1, pp. 163-177, 1931.
- [4] P. Pfeiffer, E. Breith, E. Lübke, and T. Tsumaki, "Tricyclische Orthokondensierte Nebenvaleenzringe," *Justus Liebigs Annalen der Chemie*, vol. 503, no. 1, pp. 84-130, 1933.
- [5] S. Kumar, D. N. Dhar, and P. N. Saxena, "Applications of Metal Complexes of Schiff Bases—A Review," *Journal of Chemical Education*, 2009.
- [6] M. S. Gaur, "Physico-Chemical and Biological Properties of Mn(II), Co(II), Ni(II) and Cu(II) Chelates of Schiff Bases," *Asian Journal of Chemistry*, vol. 15, no. 1, pp. 250, 2003.
- [7] M. J. Genin et al., "Novel 1,5-Diphenylpyrazole Nonnucleoside HIV-1 Reverse Transcriptase Inhibitors with Enhanced Activity Versus the Delavirdine-Resistant P236L Mutant: Lead Identification and SAR of 3-and 4-Substituted Derivatives," *Journal of Medicinal Chemistry*, vol. 43, no. 5, pp. 1034-1040, 2000.

- [8] L. H. Abdel-Rahman et al., "Synthesis, Theoretical Investigations, Biocidal Screening, DNA Binding, In Vitro Cytotoxicity and Molecular Docking of Novel Cu(II), Pd(II) and Ag(I) Complexes of Chlorobenzylidene Schiff Base: Promising Antibiotic and Anticancer Agents," *Applied Organometallic Chemistry*, vol. 32, no. 12, p. e4527, 2018.
- [9] C. H. Leung, S. Lin, H. J. Zhong, and D. L. Ma, "Metal Complexes as Potential Modulators of Inflammatory and Autoimmune Responses," *Chemical Science*, vol. 6, no. 2, pp. 871-884, 2015.
- [10] B. Kupcewicz et al., "Copper(II) Complexes with Derivatives of Pyrazole as Potential Antioxidant Enzyme Mimics," *Medicinal Chemistry Research*, vol. 22, no. 5, pp. 2395-2402, 2013.
- [11] G. Gasser and N. Metzler-Nolte, "The Potential of Organometallic Complexes in Medicinal Chemistry," *Current Opinion in Chemical Biology*, vol. 16, no. 1-2, pp. 84-91, 2012.
- [12] B. Desoize, "Metals and Metal Compounds in Cancer Treatment," *Anticancer Research*, vol. 24, no. 3A, pp. 1529-1544, 2004.
- [13] G. G. Graham and A. J. Kettle, "The Activation of Gold Complexes by Cyanide Produced by Polymorphonuclear Leukocytes. III. The Formation of Aurocyanide by Myeloperoxidase," *Biochemical Pharmacology*, vol. 56, no. 3, pp. 307-312, 1998.
- [14] A. Z. El-Sonbati et al., "Synthesis, Characterization of Schiff Base Metal Complexes and Their Biological Investigation," *Applied Organometallic Chemistry*, vol. 33, no. 9, p. e5048, 2019.
- [15] M. A. Ashraf, K. Mahmood, A. Wajid, M. J. Maah, and I. Yusoff, "Synthesis, Characterization and Biological Activity of Schiff Bases," *IPCBE*, vol. 10, no. 1, pp. 185, 2011.
- [16] M. Azam et al., "Pyridine Solvated Dioxouranium Complex with Salen Ligand: Synthesis, Characterization and Luminescence Properties," *Journal of Saudi Chemical Society*, vol. 23, no. 5, pp. 636-641, 2019.
- [17] M. Mishra et al., "Synthesis, Characterization and Corrosion Inhibition Property of Nickel(II) and Copper(II) Complexes with Some Acylhydrazine Schiff Bases," *Polyhedron*, vol. 89, pp. 29-38, 2015.
- [18] M. Salehi et al., "Synthesis, Characterization, Structural Study and Antibacterial Activity of the Schiff Bases Derived from Sulfanilamides and Related Copper(II) Complexes," *Inorganic Chimica Acta*, vol. 453, pp. 238-246, 2016.
- [19] M. Consumi, G. Leone, G. Tamasi, and A. Magnani, "Water Content Quantification by FTIR in Carboxymethyl Cellulose Food Additive," *Food Additives & Contaminants: Part A*, vol. 38, no. 10, pp. 1629-1635, 2021.
- [20] T. Petit and L. Puskar, "FTIR Spectroscopy of Nanodiamonds: Methods and Interpretation," *Diamond and Related Materials*, vol. 89, pp. 52-66, 2018.
- [21] Â. Novais, A. R. Freitas, C. Rodrigues, and L. Peixe, "Fourier Transform Infrared Spectroscopy: Unlocking Fundamentals and Prospects for Bacterial Strain Typing," *European Journal of Clinical Microbiology & Infectious Diseases*, vol. 38, no. 3, pp. 427-448, 2019.
- [22] R. A. De Graaf, *In Vivo NMR Spectroscopy: Principles and Techniques*, John Wiley & Sons, 2019.
- [23] J. B. Lambert, E. P. Mazzola, and C. D. Ridge, *Nuclear Magnetic Resonance Spectroscopy: An Introduction to Principles, Applications, and Experimental Methods*, John Wiley & Sons, 2019.
- [24] A. C. Leri and A. P. Pavia, "Analysis of Plastic Waste for Sorting in Recycling Plants: An

- Inquiry-Based FTIR Spectroscopy Experiment for the Organic Chemistry Laboratory," *Journal of Chemical Education*, vol. 99, no. 2, pp. 1008-1013, 2022.
- [25] R. Youngman, "NMR Spectroscopy in Glass Science: A Review of the Elements," *Materials*, vol. 11, no. 4, p. 476, 2018.
- [26] M. J. Jeng et al., "Raman Spectroscopy Analysis for Optical Diagnosis of Oral Cancer Detection," *Journal of Clinical Medicine*, vol. 8, no. 9, p. 1313, 2019.
- [27] R. Selvaraj et al., "Advances in Mid-Infrared Spectroscopy-Based Sensing Techniques for Exhaled Breath Diagnostics," *Molecules*, vol. 25, no. 9, p. 2227, 2020.
- [28] J. A. Prananto, B. Minasny, and T. Weaver, "Near Infrared (NIR) Spectroscopy as a Rapid and Cost-Effective Method for Nutrient Analysis of Plant Leaf Tissues," *Advances in Agronomy*, vol. 164, pp. 1-49, 2020.
- [29] B. I. Ionin, B. A. Ershov, and A. I. Kol'tsov, *NMR Spectroscopy in Organic Chemistry*, Khimiya, Leningrad, 1983.
- [30] B. I. Ionin, *NMR Spectroscopy in Organic Chemistry*, Springer Science & Business Media, 2012.
- [31] G. Kapoor, S. Saigal, and A. Elongavan, "Review Article," 2020.
- [32] A. R. Hauser, *Cell Envelope*, in *Antibiotic Basics for Clinicians*, 2nd ed., New Delhi: Wolters Kluwer (India) Pvt. Ltd., 2015, pp. 3-5.
- [33] Kahne D, Leimkuhler C, Lu W, Walsh C. Glycopeptide and lipoglycopeptide antibiotics. *Chem Rev* 2005;105:425-48.