



SOME METAL (II) COMPLEXES OF SCHIFF BASE LIGAND DERIVED FROM ACETONE AND 2-PHENYLGLYCINE: STRUCTURAL ASPECTS AND *IN VITRO* ANTIMICROBIAL INVESTIGATION



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Abstract: Five Schiff base complexes, namely [FeL₂(H₂O)₂] (1), [CoL₂(H₂O)₂] (2), [NiL₂] (3), [CuL₂] (4), and [ZnL₂] (5) were synthesized and characterized via solubility, melting points, molar conductivity, magnetic susceptibility, UV-Vis and IR spectroscopies. The complexes showed a metal-to-ligand ratio of 1:2 and were observed to be non-electrolytic, as per the results of molar conductivity tests. The IR spectra showed that the coordination between the carbonyl groups, the methanolic oxygen atom of the Schiff base, and the metal centers occurred in a bidentate manner. Electronic spectra and magnetic susceptibility tests revealed that complexes 1 and 2 had an octahedral geometry with a six-coordinate local symmetry around the metal ions. In contrast, complexes 3–5 were observed to be square planar. Studies on magnetic susceptibility further showed that complexes 3 through 5 are paramagnetic, whereas complex 5 is expectedly diamagnetic. As a result of forming high spin complexes with Fe(II) and Co(II) ions, the results further revealed that the Schiff base ligands are weak field ligands. The antimicrobial tests revealed that the metal complexes had more inhibition activity when compared to the free ligands. Thus, the Schiff base complexes have potential as powerful, all-purpose antimicrobial agents.

Keywords: Schiff base, Ligand, Metal (II) complex, Characterization, Spectra, Antibacterial, Antifungal.

Introduction

Antimicrobial resistance remains a global challenge. Infections and the emergence of resistance to the drugs used to prevent and treat them have readily spread across geographical borders, threatening global health security (WHO, 2016). For example, people with methicillin-resistant *Staphylococcus aureus* (MRSA) are 64 % more likely to die than people with a non-resistant form of the infection. Resistance also increases the cost of health care with lengthier stays in hospitals and more intensive care. In the search for new antimicrobials effective in the treatment of infections caused by multi-resistant bacteria, due consideration ought to be given to the synthesis of drugs with new activation targets, as well as modification of the activity of compounds with known antimicrobial activity (Saga and Yamaguchi, 2009). Most metal ions are essential components to maintaining human homeostasis and play crucial roles in many biological processes by involving as cofactors in the biological function of proteins, and operating many regulations, stabilization, and completion courses of cellular functions (Gkouvatso *et al.*, 2012; Zheng *et al.*, 2020).

Medicinal inorganic chemistry, the most attractive research area in the field of knowledge concerned with the implementation of metal-based complexes to the therapy or diagnosis of diseases (Mjos and Orvig, 2014) has played an important role in this perspective. Although the historically proven use of metal-based remedies and drugs traces back to very ancient times. Medicinal inorganic chemistry seems to be considered a young discipline among the medicinal chemistry fields of biological drugs or small organic molecules. Silver, for instance, was used to treat wounds and ulcers by the Greek physician Hippocrates, and gold was used to treat diseases thousands of years ago in China (Magner and Kim, 2017; Iorungwa *et al.*, 2020). The introduction of metal ions or metal ion binding components into a biological system for the treatment of diseases is one of

the main subdivisions in the field of bioinorganic chemistry (Magner and Kim, 2017; Iorungwa *et al.*, 2020).

Many of the current antifungal agents that are used in therapy are either becoming resistant or have severe adverse side effects. This has led to the continued search for new antifungal compounds, including coordination complexes of biologically important molecules (Farrell *et al.*, 2003). The medicinal uses and applications of Schiff base and Schiff base complexes are of increasing commercial importance. The use of chelating agents in the treatment of Wilson's disease is a good example of how chelating agents have arrested medicinal problems due to free metal ion toxicity (Sarkar, 1999). Continued research aimed at developing Schiff-base drugs which can perhaps work by a different mode of action and therefore arrest the challenge of resistance, is, therefore, a way forward (Agbaje *et al.*, 2014). Thus, the present study aims to synthesize, characterize, and evaluate the antifungal properties of Schiff base complexes of Fe²⁺, Co²⁺, Ni²⁺, Cu²⁺, Zn²⁺ ions derived from acetone and 2-phenylglycine.

Materials and Methods

The reagents used for the research work were acetone (Sigma Aldrich; 97 % assay), 2-phenylglycine (Sigma Aldrich; 95 % assay), zinc(II) chloride hexahydrate, nickel(II) chloride hexahydrate, copper(II) chloride dihydrate, iron(II) chloride tetrahydrate and cobalt(II) chloride hexahydrate (all BDH products with 99, 98, 99, 99 and 98 % assays respectively). Solvents used include ethanol (EtOH), methanol (MeOH), ammonia, dimethylsulphoxide (DMSO), and dimethylformamide (DMF) which were all Sigma Aldrich products. Others are ethylester and distilled water. The standard drugs used were ciprofloxacin and Econazole (May and Baker Pharmaceutical Company). All the reagents and solvents were of analytical grade and were obtained from commercial supplies. The reagents were used as received

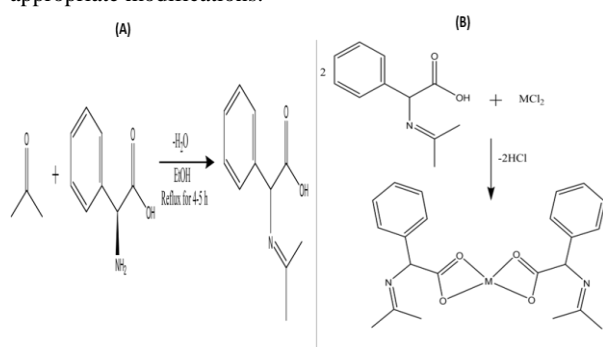
without further purification, except for ethanol and acetone which was redistilled using standard procedures. The following apparatus and equipment were used: water bath (improvised), oven (heating and drying oven DGH-9053), furnace (Nabertherm programmable furnace, Model GmbH), digital weighing balance (FINLAB Electronic Balance Model ESJ200-4), melting point apparatus (Stuart Automatic Model SMP40) and magnetic stirring hot plate (BIBBY STERILIN Model HC500). Others were scientific magnetic susceptibility balance (Sherwood AUTO scientific MSB), conductivity meter (HACH conductivity meter: Sension5), UV-visible spectrophotometer (Agilent Cary Series), and IR spectrophotometer (Agilent Cary 360).

Synthesis of the Schiff Base Ligand

The method described by Goreci *et al.*, (2016) was adopted. About 1 mmol of acetone was stirred for 30 min together with 2-phenylglycine and dissolved in 10 mL of dry ethanol in a 500 mL round bottom flask. A few anti-bumping granules were introduced into the flask. A refluxed condenser was attached, and the mixture was refluxed on a steam bath for 4 – 5 h and then allowed to cool overnight. The precipitated Schiff base was filtered, washed with cold ethanol several times, and dried in air at room temperature. The solid crystal were thereafter recrystallized with ethanol. The reaction proceeded according to Scheme 1A.

Synthesis of the Metal(II) Complexes

The method for the synthesis of the M(II) complexes (Scheme 1B) was carried out by adopting the procedure described by Shakir, (2014). For Fe(II), the iron(II) chloride salt was dissolved in 5 mL of absolute ethanol and 1 mmol of the Schiff base ligand at a metal-to-ligand molar ratio of 1:2. The metal salt was gradually added drop by drop to the solution of the ligand. The reaction mixture was allowed to magnetically stirred for 1 h at room temperature. The reaction mixture was filtered, washed with ethanol, and dried at 50 °C in an oven for 1 h. The same method was employed for the synthesis of Ni(II) L, Co(II) L, Zn(II) L, and Cu(II) L complexes with appropriate modifications.



Scheme 1. Synthesis of the Schiff base ligand (A), synthesis of the metal(II) complexes, M = Cu, Co, Fe, Ni, and Zn (B)

Characterization of the M(II) Complexes

The synthesized complexes were characterized by some classical and spectroscopic methods of analyses. These include solubility studies, melting point determination, molar conductivity measurement, magnetic susceptibility, infrared and electronic spectroscopies.

Antimicrobial Studies

Antimicrobial studies were carried out in the microbiology laboratory of Ahmadu Bello University, Zaria, with the agar-well diffusion technique employed

as described by Girish and Satish, (2008). The test organisms used for this analysis were clinical isolates of bacteria and fungi obtained from the Department of Microbiology, Ahmadu Bello University, Zaria. The isolates were: *Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli*, *Salmonella typhi*, *Proteus species*, *Pseudomonas aeruginosa*, *Candida albicans*, *Aspergillus niger*, and *Aspergillus flavus*. The culture media used were Mueller Hinton agar (MHA), Mueller Hinton broth (MHB), Potato dextrose agar (PDA), and Nutrient agar (NA), the media were used for sensitivity test, determination of minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC). All media were prepared according to the manufacturer's instructions and sterilized by autoclaving at 121 °C for 15 min.

The standardized inocula of both the bacterial and fungal isolates were streaked on sterilized Mueller Hinton agar and Potato dextrose agar plates respectively with the aid of sterile swab sticks. Four wells were punched on each inoculated agar plate with a sterile cork borer. The well was properly labeled according to the different concentrations of the extract prepared which were 100, 50, 25, and 12.5 mg/mL respectively. Each well was filled up with approximately 0.2 mL of extract. The inoculated plates with the extract were allowed to stay on the bench for about one hour; this is to enable the extract to diffuse on the agar. The plates were then incubated at 37 °C for 24 h (plates of Mueller Hinton agar), while the plates of Potato dextrose agar were incubated at room temperature for about 3-5 days. At the end of the incubation period, the plates were observed for any evidence of inhibition which will appear as a clear zone that was completely devoid of growth around the wells (zone of inhibition). The diameter of the zone was measured using a transparent ruler calibrated in millimeters and the result was recorded.

The minimum inhibitory concentration (MIC) of the compounds was determined using the tube dilution method with the Mueller Hinton broth used as diluents. The lowest concentration of the compounds showing inhibition for each organism when the compounds were examined during the sensitivity test was serially diluted in the test tubes containing Mueller Hinton broth. The standardized organisms were inoculated into each tube containing the broth and extract. The inoculated tubes were then incubated at 37 °C for 24 h. At the end of the incubation period, the tubes were examined/ observed for the presence or absence of growth using turbidity as a criterion, the lowest concentration in the series without visible sign of growth (turbidity) was minimum inhibitory concentration. The result from the minimum inhibitory concentration was used to determine the minimum bactericidal concentration (MBC) of the compounds. A sterilized wire loop was dipped into the test tubes that did not show turbidity (clear) in the MIC test and a loopful was taken and streaked on sterile Nutrient agar plates. The plates were incubated at 37 °C for 18 – 24 h. At the end of the incubation period, the plates were examined/ observed for the presence or absence of growth. This is to determine whether the antimicrobial effect of the extract is bacteriostatic or bactericidal.

Strict adherence to the method was ensured and at least 30 days zone diameter was accurately measured with a ruler and the nearest millimeter recorded. The diameters were toward the middle of the acceptable range and

temporary performance limits were then calculated as the mean \pm standard deviation. Discs for diffusion were handled correctly within the laboratory and stocks of discs were stored at -20°C with working stock refrigerated with an indicating desiccant and protected from light. Discs were allowed to reach room temperature before opening for use.

Physical Properties of the Metal Complexes

The physicochemical properties of the synthesized metal complexes (**1–8**) are summarized and presented in Table 1. The complexes were all coloured with the ligand showing a white colour, while complexes **1**, **2**, **3**, and **4**

showed brown, pink, deep green, and dark blue respectively. Expectedly, the complex of Zn (**5**) showed a white colour. Relatively high yields were also obtained for the ligand (78.45 %) and metal complexes (77 – 91 %), with the highest yield recorded for complex **3** (90.50 %), while complex **5** gave the lowest percentage yield (76.89 %). The melting point or decomposition temperature of the ligand was observed to be in the range of 63.50 – 66.30 while those of the complexes were higher as expected. This is further evidence of the formation of metal complexes.

Table 1: Physical Properties of the Ligand and Metal Complexes

Compound	Formula weight (gmol ⁻¹)	Decomposition temperature (°C)	Colour	Yield (%)
L	191.24	63.50 – 66.30	Off white	78.45
[FeL ₂ (H ₂ O) ₂] (1)	472.33	185.30 – 188.10	Brown	86.47
[CoL ₂ (H ₂ O) ₂] (2)	475.41	109.20 – 112.20	Pink	88.76
[NiL ₂] (3)	439.17	244.60 – 247.10	Deep green	90.50
[CuL ₂] (4)	444.03	117.60 – 121.20	Dark blue	81.74
[ZnL ₂] (5)	445.87	146.40 – 147.10	White	76.89

Infrared spectral characterization

A comparative study of IR spectral data of the reported complexes with that of the free ligand has proven to offer sufficient evidence towards a better understanding of the coordinating behaviour of Schiff base ligand towards metal ions. Thus, the infrared spectra analyses of the Schiff base ligand, and its corresponding coordination complexes were carried out and the relevant peaks (cm⁻¹) are given in Table 2 and some selected spectra are shown in Figure 1. The absorption band due to $\nu(\text{C}=\text{N})$ was observed to overlap with that of $\nu(\text{C}=\text{O})$ occurring at ca. 1581 cm⁻¹ in the spectrum of the free ligand, L. This signal was observed to be shifted to higher wave

numbers appearing at 1591, 1605, 1609, 1638, and 1619 cm⁻¹ for complexes **1**, **2**, **3**, **4**, and **5** respectively, indicating the coordination of the M(II) ions to the carbonyl oxygen of $\nu(\text{C}=\text{O})$ group. This assertion is consistent with the presence of bands at ~691–898 cm⁻¹ in the spectra of all the complexes, attributed to $\nu(\text{M}-\text{O})$ vibrations. The lower value of $\nu(\text{C}=\text{O})$ stretching observed in the spectra of the complexes may be explained based on a drift of lone pair density of carbonyl oxygen towards the metal ion indicating that coordination takes place through the oxygen of (C=O) groups (Chandra and Sharma, 2002; Lodeiro *et al.*, 2003).

Table 2: FTIR Spectra of the Ligand and the Synthesized Complexes

Compound/bands (cm ⁻¹)	Ar-H	O-H	C-H	C=N/ C=O	C-N	M-O
L	3339	3164	2900	1581	1120	-
[FeL ₂ (H ₂ O) ₂] (1)	3358	3131	2895	1597	1086	502
[CoL ₂ (H ₂ O) ₂] (2)	3395	3009	2895	1605	1101	507
[NiL ₂] (3)	3513	3405	3169	1609	1110	517
[CuL ₂] (4)	3315	3146	3037	1638	1110	493
[ZnL ₂] (5)	3395	3193	2985	1619	1101	507

Furthermore, in the spectrum of the free ligand, the $\nu(\text{O}-\text{H})$ stretching vibrations appeared at 3164 cm⁻¹ which is an indication of the presence of a phenolic OH group in the Schiff base ligand. Similar signals appeared in the spectra of the complexes with increased intensities at ca. 3131, 3009, 3405, 3146, and 3193 cm⁻¹ for complexes **1**, **2**, **3**, **4**, and **5** respectively which may rather be ascribed to the OH from water of hydration, and/or water of coordination as in the cases of complexes **1** and **2**. Interestingly, the band assigned to $\nu(\text{C}-\text{N})$ vibrations in the spectrum of the ligand was observed at 1120 cm⁻¹. In the spectra of the complexes, however, this band is shifted towards lower wavenumbers at 1086, 1101, 1110, 1110, and 1101 cm⁻¹ for the complexes **1**, **2**, **3**, **4**, and **5** respectively (Warad *et al.*, 2014). The fact that these

peaks appear to have shifted bathochromically in the spectra of the respective complexes can be additional evidence for the involvement of the carbonyl oxygen in M-O bonding. Furthermore, the low-intensity bands that appear in the spectra of the complexes around 493 – 517 cm⁻¹ could be attributed to the $\nu(\text{M}-\text{O})$ vibrations. This provides strong evidence that the intended complex compounds were successfully formed, which is consistent with the findings of other researchers who studied similar compounds. (Warad *et al.*, 2014; Sani *et al.*, 2017).

Electronic Spectra Studies

The electronic spectra of the Schiff base ligand, L, and its complexes **1**, **2**, **3**, **4**, and **5** were measured in DMSO

(Figure 2), and the spectra data is presented in Table 3. The electronic spectrum of the free ligand showed two strong bands at 299 and 408 nm which may be assigned respectively to $\pi-\pi^*$ of the aromatic ring and $n-\pi^*$ transition associated with the carbonyl ($-C=O-$) linkages. Following complexation, the position of the bands associated with $\pi-\pi^*$ transitions were observed to have

shifted to 310, 300, 290, 355, and 302 nm for complexes **1**, **2**, **3**, **4**, and **5** respectively, while those ascribed to $n-\pi^*$ transitions shifted to 364, 386, 404, 397, and 415 nm for complexes **1**, **2**, **3**, **4**, and **5** respectively suggesting the coordination of the carbonyl oxygen to the metal centers.

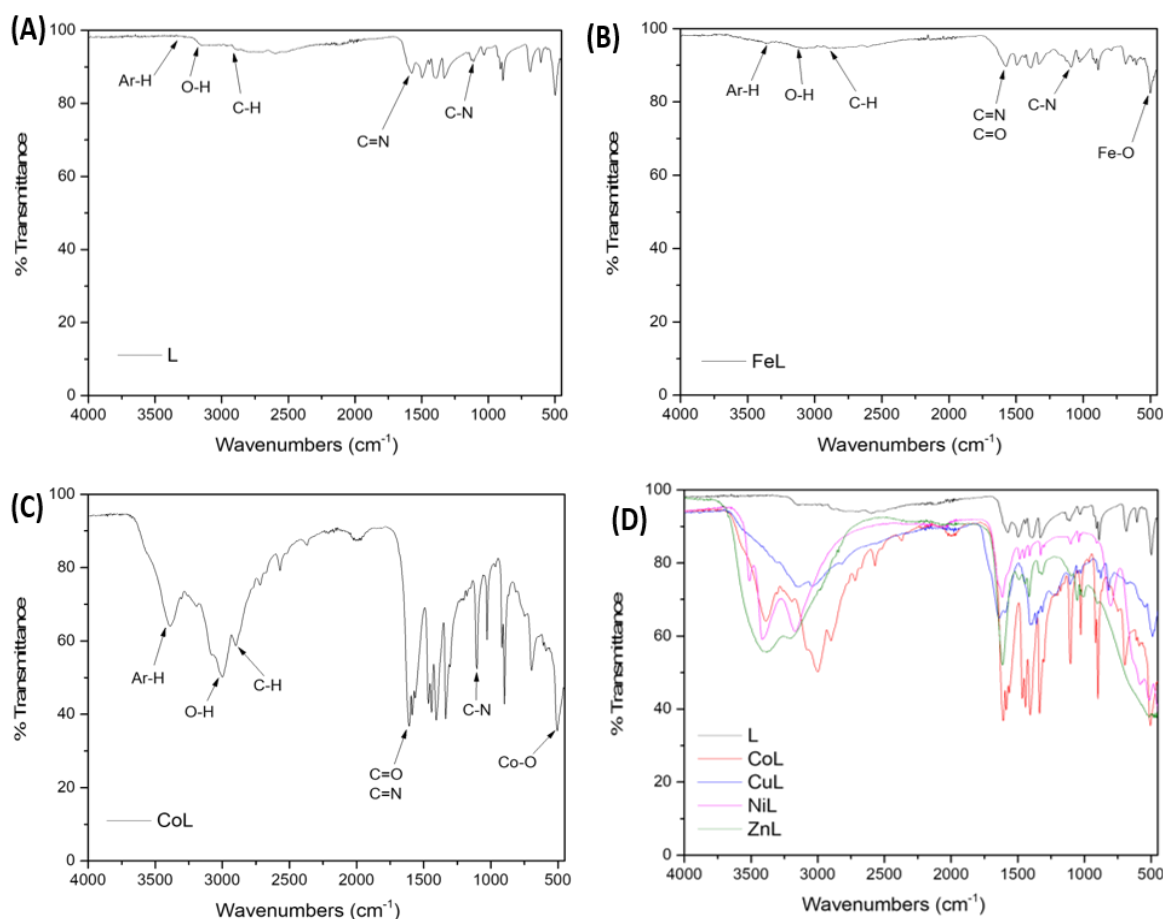


Figure 1. FT-IR spectra of the synthesized compounds; Schiff base ligand (A), $[\text{CoL}_2(\text{H}_2\text{O})_2]$ (B), $[\text{FeL}_2(\text{H}_2\text{O})_2]$ (C), and stacked spectra of the ligand and the complexes (D)

The bands observed at 509, 528, 670, and 740 nm in the spectra of complexes **1**, **2**, **3**, and **4** may be assigned respectively to $d-d$ transitions. Consequently, the $d-d$ spectral bands of complexes **1** and **2** are consistent with that of six-coordinate geometry around Fe(II) and Co(II), on the basis of which an octahedral geometry may be assigned for these complexes while those of **3** and **4** are consistent with a square planar geometry around Cu(II) and Zn(II) (Patil *et al.*, 2011). Complex **5** showed no $d-d$ bands as expected since Zn(II) ion has a d^{10} electronic configuration.

Table 3: UV-vis Spectra Data for the Ligand and the Synthesized Complexes

Compound/peaks (nm)	$(\pi-\pi^*)$ transition	$(n-\pi^*)$ transition	$d-d$ transition
L	299.91	408.07	-
$[\text{FeL}_2(\text{H}_2\text{O})_2]$ (1)	310.94	364.98	509.98
$[\text{CoL}_2(\text{H}_2\text{O})_2]$ (2)	300.55	386.59	528.32
$[\text{NiL}_2]$ (3)	290.15	404.10	670.86; 746.52
$[\text{CuL}_2]$ (4)	355.57	397.67	740.90
$[\text{ZnL}_2]$ (5)	302.87	415.18	-

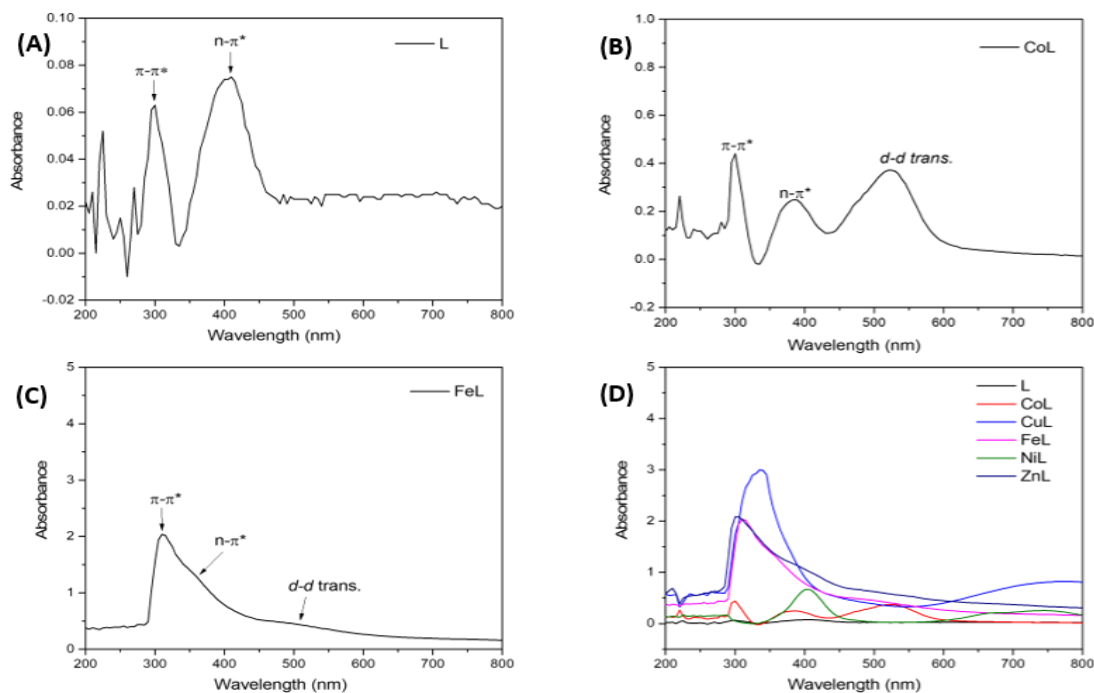


Figure 2. UV-vis spectra of the synthesized compounds; Schiff base ligand (A), $[\text{CoL}_2(\text{H}_2\text{O})_2]$ (B), $[\text{FeL}_2(\text{H}_2\text{O})_2]$ (C), and stacked spectra of the ligand and the complexes (D)

Molar Conductivity Measurements

Conductivity measurements are commonly used to determine metal complex structure within solubility limits. The molar ions a complex liberates in solution can be used to determine the degree of ionization of the complexes (Refat, 2007; Refat *et al.*, 2013). The molar conductivity values for the Schiff base ligand and its complexes in $1.0 \times 10^{-3} \text{ mol dm}^{-3}$ DMSO are presented in Table 4. The observed molar conductivity values of both the ligand ($68.34 \Omega^{-1} \text{ mol}^{-1} \text{ cm}^2$) and the complexes ($47.41 - 70.56 \Omega^{-1} \text{ mol}^{-1} \text{ cm}^2$) suggest that the compounds are non-electrolytic. This indicates the absence of an outer coordination sphere in the structure of complexes since charge neutrality is maintained when an M^{2+} ion combines with 2L^- to give the most likely primary structure $[\text{ML}_2]$. This observation implies that a metal-ligand ratio of 1:2 could be at play. Higher conductivity readings are usually observed in the electrolytic range

Table 4: Room Temperature Magnetic Susceptibility and Molar Conductivity of the M(II)Complexes

Compound	μ_{eff} (B.M)	Temperature (K)	Λ ($\Omega^{-1} \text{ mol}^{-1} \text{ cm}^2$)
L	-	300.00	62.30
$[\text{FeL}_2(\text{H}_2\text{O})_2]$ (1)	4.97	300.00	66.60
$[\text{CoL}_2(\text{H}_2\text{O})_2]$ (2)	5.31	300.50	70.56
$[\text{NiL}_2]$ (3)	3.16	300.50	47.41
$[\text{CuL}_2]$ (4)	1.86	300.00	51.63
$[\text{ZnL}_2]$ (5)	0.00	300.50	55.38

B.M = Bohr magnetons

Magnetic Susceptibility Studies

The spin-only magnetic moments of the complexes are shown in Table 4 with the results suggesting paramagnetic behaviour for complexes 1 – 4, while diamagnetic character was observed for complex 5. Complexes 1 and 2 showed spin-only magnetic moments of 4.97 and 5.31 BM respectively which are close to the

($106-311 \Omega^{-1} \text{ mol}^{-1} \text{ cm}^2$) when ions beyond the coordination sphere (electrolytes) are present (Refat *et al.*, 2013).

Based on the conductivity data, it is evident that the complexes being studied are probably non-electrolytes. This indicates that the complexes are formed in a metal-ligand ratio of 1:2, as charge neutrality can only be maintained when 1 mole of M^{2+} combines with 2 moles of L. This fact is important in establishing that there is the absence of such ions as Cl^- in the outer coordination sphere of these complexes which eliminates the possibility of a 1:1 or 1:3 metal-ligand ratio. (Mohamed *et al.*, 2009; Abou-Hussein and Linert, 2015). This fact was strongly supported by simple qualitative analysis where Cl^- ions were not precipitated following the addition of aqueous solutions of silver nitrate to a solution of the complexes (Refat, 2007).

theoretical spin-only moments predicted for four and three unpaired electrons in Fe^{2+} and Co^{2+} ions respectively suggesting an octahedral geometry around these ions (Lots, 2008). Furthermore, the magnetic moments of complexes 3 and 4 were observed at 3.16 and 1.86 BM respectively suggesting the existence of these complexes in a high spin state which is

characteristic of Ni²⁺ and Cu²⁺ ions in square planar environments. This could infer that the Schiff base ligand under study is a weak field ligand as it gave high spin complexes with the M(II) ions. These claims are backed by *d-d* transitions that are indicative of an octahedral local symmetry around Fe(II) and Co(II) ions, and a square planar symmetry around Ni(II) and Cu(II) ions as seen in the visible spectrum of these complexes.

As expected for a *d*¹⁰ electronic system, the Zn complex (5) was found to be diamagnetic and have magnetic moments of zero. This shows that there are no unpaired electrons in the degenerate 4*d* orbitals of the Zn(II) ion ruling out the possibility of *d-d* transition. The result is in concomitance with the findings of other researchers for some complexes of Cd(II) (Iorhamba *et al.*, 2018). Thus, based on the structural data obtained from the present study, the geometries of the synthesized metal complexes are proposed in Figure 3.

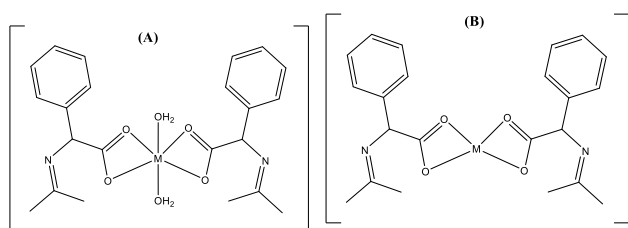


Figure 3. Proposed Structures of the Metal(II) Complexes (A), M = Fe, or Co; (B), M = Ni, Cu, or Zn.

Table 5: Zone of Antimicrobial Inhibition (nm) of the Ligand and M(II) Complexes

Test organism	L	(1)	(2)	(3)	(4)	(5)	C
Bacteria							
<i>B. subtilis</i>	0	12	26	28	21	18	25
<i>S. aureus</i>	0	8	27	32	34	21	40
<i>E. coli</i>	0	0	24	26	24	20	35
<i>S. typhi</i>	0	17	28	24	21	17	23
<i>P. specie</i>	0	0	27	22	18	19	20
<i>P. aeruginosa</i>	0	0	24	25	19	22	39
Fungi							
<i>C. albicans</i>	0	0	0	0	0	0	32
<i>A. niger</i>	0	0	21	40	25	18	40
<i>A. flavus</i>	0	0	19	32	27	20	35

C = ciprofloxacin, E = Econazole, L = Schiff base ligand. Furthermore, the Schiff base ligand demonstrated no activity on the studied fungi strains. However, after complexation, the complex compounds 2 – 5 showed induced potency against *A. niger* and *A. flavus* but no activity against *C. albicans*. Similarly, complex 1 was found to be inactive against all the studied fungal strains suggesting that the fungi strains under investigation are resistant to the Fe-based complex. It is important to note that the antifungal activity of complex 3 compared favorably to that of the standard drug, *C. albicans* and *A. flavus* respectively. It can be inferred that the new complexes demonstrated interesting inhibitory performance indicating their potential as alternative antifungal agents. Earlier reports have suggested that metal centers could enhance or induce the antimicrobial activity of ligands. This aligns with the findings of the investigation into these metallodrug candidates, as the inactive Schiff base ligands are induced rather than enhanced against the fungi strains being studied following complexation. These findings are in agreement

Antimicrobial Screening

A comparison was made between the antimicrobial potency of the Schiff base ligand L and the synthesized complexes 1 – 5 against two Gram-positive bacteria, four Gram-negative bacteria, and three fungi. The results are presented in Table 5. Ciprofloxacin and Econazole were used as standard reference drugs for bacteria and fungi respectively. The standard drug, ciprofloxacin demonstrated better activity against the bacteria species when compared to all the synthesized complexes except in a few cases. For example, complexes 2 and 3 showed better activity against *B. subtilis*, *S. typhi*, and *P. specie* than the standard drug suggesting the pharmaceutical potential of the complexes. Interestingly, the Schiff base ligand proved inactive against all the bacteria strains. However, the complexes demonstrated significantly induced biological potency which infers an induced lipophilicity of the complexes following coordination (Chang *et al.*, 2010). It is important to note that complexes 2 – 5 showed better activity against the bacteria strains than complex 1 which induced minimal activity on *B. subtilis*, *S. aureus*, and *S. typhi* while no activity was observed against all the other bacterial strains suggesting that the microbes are resistant to the Fe(II) complex. Thus, it may be indicative that activity is linked with chemical structural dynamics which in turn affect the lipophilicity of metallodrug candidates. Complexes 2 – 5 seem promising drug candidates as their activity aligns with the standard drug.

with previous reports for similar kinds of compounds (Iorungwa *et al.*, 2019; Iorungwa *et al.*, 2020).

The MIC and MBC results for the bacteria (Tables 6 and 7) also revealed that the metal complexes are effective against microbial strains while the free ligand is not. Thus, among all the metal complexes synthesized, 2 proved to be the best drug candidate against *S. typhi* and complex 4 against *B. subtilis* with minimum inhibitory concentrations and minimum bactericidal concentrations of 3.13 and 6.25 µg/mL⁻¹ respectively in each case. This is again closely followed by complex 2 with MIC and MBC values of 6.25 and 12.50 µg/mL⁻¹ respectively against *B. subtilis*, *S. aureus*, and *E. coli*. It is important to state that complex 1 demonstrated no bactericidal or bacteriostatic potential against *S. aureus* as the complex compound showed a very high MIC value against the microbe. Similarly, the most promising metallodrug candidate against the studied fungi strains was found to be complexes 3 with MIC and MFC values of 6.25 and 12.50 µg/mL⁻¹ against *A. niger*. Fungicidal activities were absent for complex 2 against *A. niger* and *A. flavus* which

suggests that the complexes are not fungicidal but fungistatic against the respective organisms. The Schiff

base complexes investigated thus exhibit potential as antibacterial and antifungal agents.

Table 6: Minimum Inhibition Concentration ($\mu\text{g mL}^{-1}$) of the Ligand and M(II) Complexes

Test organism	L	(1)	(2)	(3)	(4)	(5)
Bacteria						
<i>B. subtilis</i>	-	-	6.25	6.25	3.125	6.25
<i>S. aureus</i>	-	100	6.25	25.00	25.00	12.50
<i>E. coli</i>	-	-	6.25	25.00	12.50	12.50
<i>S. typhi</i>	-	50	3.125	25.00	25.00	25.00
<i>P. specie</i>	-	-	12.50	12.50	25.00	6.25
<i>P. aeruginosa</i>	-	-	12.50	12.50	25.00	6.25
Fungi						
<i>C. albicans</i>	-	-	-	-	-	-
<i>A. niger</i>	-	-	50	6.25	12.50	25.00
<i>A. flavus</i>	-	-	50	12.50	12.50	25.00

L = Schiff base ligand, - = Not determined for MIC

Table 7: Minimum Bactericidal Concentration and Minimum Fungicidal Concentration ($\mu\text{g mL}^{-1}$) of the Ligand and the M(II) Complexes

Test organism	L	(1)	(2)	(3)	(4)	(5)
Bacteria						
<i>B. subtilis</i>	-	-	12.50	12.50	6.25	12.50
<i>S. aureus</i>	-	**	12.50	50.00	50.00	25.00
<i>E. coli</i>	-	-	12.50	50.00	25.00	25.00
<i>S. typhi</i>	-	100	6.25	50.00	50.00	50.00
<i>P. sp.</i>	-	-	6.25	25.00	50.00	12.50
<i>P. aeruginosa</i>	-	-	25.00	25.00	50.00	12.50
Fungi						
<i>C. albicans</i>	-	-	-	-	-	-
<i>A. niger</i>	-	-	**	12.50	25.00	50.00
<i>A. flavus</i>	-	-	**	25.00	25.00	50.00

L = Schiff base ligand, - = Not determined for MBC. ** = No MFC (compound is bacteristatic not bactericidal)

Conclusion

Five Schiff base complexes $[\text{FeL}_2(\text{H}_2\text{O})_2]$ (1), $[\text{CoL}_2(\text{H}_2\text{O})_2]$ (2), $[\text{NiL}_2]$ (3), $[\text{CuL}_2]$ (4), and $[\text{ZnL}_2]$ (5) where L = Schiff base derived from 2-phenylglycine and acetone were synthesized and characterized by melting point determination, solubility, molar conductivity, magnetic susceptibility, UV-Vis and IR spectroscopies. Molar conductivity measurements showed that complexes are non-electrolytic with their composition corresponding to a metal-ligand ratio of 1:2. The IR spectra showed that the Schiff base ligand acted in a bidentate fashion to the metal centers with coordination involving the carbonyl groups and the methanolic oxygen atom of the Schiff base. Electronic spectra and magnetic susceptibility measurements suggested a six-coordinate local symmetry around the metal ions in an octahedral geometry in the case of complexes 1 and 2 while 3 – 5 were observed to be square planar. Magnetic susceptibility studies also revealed that complexes 3 – 5 are paramagnetic while 5 was diamagnetic as expected. The result also suggested the Schiff base ligands to be weak field ligands as they formed high spin complexes with Fe(II) and Co(II) ions. The structural formula for the metal complexes is shown in Figures 6 and 7, based on obtained structural data. The antimicrobial studies suggested that the Schiff base

ligands are inactive against the studied bacteria and fungi, and their metal complexes showed significantly induced antimicrobial sensitivity against the studied microbial strains in comparison to the free ligands. The Schiff base complexes are thus promising potent broad-spectrum antimicrobial agents.

Competing Interests

The authors declare that there are no competing interests regarding the publication of this paper.

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