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SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL ACTIVITY OF SCHIFF BASE AND ITS METAL COMPLEXES

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ABSTRACT: The biological effects of transition metal complexes that include a wide range of ligands are distinguishable from one another. In an effort to produce a novel metal (II) complexes the conventional reflux method has been used to the interaction of two ligands, N-(2H-benzo[d] [1,2,3] triazol-2-yl)-1-(4-nitrophenyl) ethanimine as L_1 and an amino acid Alanine as L_2 with freshly produced Zinc, Nickel, Manganese chloride's solution in a 1:1:1 molar ratio. In order to characterize the ligand and metal (II) complexes that have been synthesized, several approaches such as elemental analysis, molecular weight analysis, thermal analysis and spectroscopic analysis are used. A comparison was made between the antibacterial activity of all of the compounds that were created and that of Streptomycin, Ciprofloxacin and Nystatin. The compounds were tested against Gram-positive and Gram-negative bacteria as well as a variety of fungal strains. The insecticidal activity of each compound was evaluated against *Plodia interpunctella* and the findings revealed that the compounds exhibited promising results.

INTRODUCTION: There is a crucial class of substances known as Schiff bases [1]. Many of these ligands have been the subject of heavy research recently due to their desirable physical and chemical properties. Catalysts for the hydrogenation and oxidation of olefins in industrial processes may be effective when using the flexible Schiff base ligands. Aside from that, they may detect detrimental metal ions via their fluorescence. The progress of coordination chemistry was greatly aided by the creation of schiff base compounds [4].

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Furthermore, Schiff bases have been the subject of intense interest for the last 10 years because of the wide variety of biological, biochemical, analytical and commercial uses for these compounds [5]. It has been shown that some Schiff bases possess antibacterial, antiviral, antifungal, anticancer and antitumor properties [6]. The demand for antibacterial materials has risen rapidly due to the growing awareness of the negative impacts, foul odors and unsightly stains that bacteria and other microbes may create.

Many different industries rely on these materials for various tasks, including healthcare, personal care, water purification, clothing, food packaging and storage. They are also used in orthodontics and hospital surgical tools [7-9]. Additional research on the biological effects of Schiff bases is necessary [10]. Recent synthesis and description of spectroscopic and structural features of Zn, Ni and Mn(II) complexes containing Schiff base ligands [11]. Synthesis, structural characterisation and computational studies of two Schiff bases exhibiting fascinating antibacterial properties have been the primary focuses of this work [12] (Scheme 1). In addition to their role as ligands, the Schiff bases listed above have also been used in the azomethine functionality (-HC=N-) complexes [13].

MATERIALS AND METHODS: All chemicals and solvents used were of an analytical grade. The chemicals were prepared and preserved in a manner that prevented any contamination from air or moisture. The separations were carried out using silica gel-treated thin-layer chromatography plates. Anhydrous KBr pellets were utilized to collect the FTIR spectra of molecules and their complexes using a Perkin-Elmer Series 2000 equipment. In order to track electronic transitions in the UV-visible band as nujol mulls and in DMSO solutions with concentrations ranging from 105 to 103M, we used a Shimadzu 160 spectrophotometer. The Simultaneous Thermal Analyzer TG-DTA was used to record TGA studies in air with a heating range of 10-800°C. To prove the complexes thermal stability and find out whether the complexes structures include lattice or coordinated water molecules or both, TGA tests were carried out. Data from an LECO CHNS 932 model micro analytical instrument coincided with the predicted findings for elemental analyses by more than 0.3%. An internal standard of TMS was used to collect ^{1}H NMR spectra in DMSO solvent using a Varian-Mercury 300 MHz spectrometer. At room temperature, the Systronics Direct Reading Conductivity Meter-304 and Gouy's Balance Model no. HO-ED-EM-08 were used to measure molar conductance and magnetic moment, respectively, using glass cells with a cell constant of exactly 1.0 cm^{-1}.

Characterization of Ligand: Crystals, yeild: 72.4%, m.p: 257.30-259.32°c, IR (KBr) υ: 1365-1370, 1500–1550 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6, δppm)δ 2.47 (s, 3H, CH_3), 7.49 (m, 2H, Ar-H), 7.75 (m, 2H, Ar-H), 7.93 (m, 2H, Ar-H), 8.32 (m, 2H, Ar-H); ^{13}C NMR (100MHz, DMSO-d_6,δppm); 21.31, 113.06, 124.03, 124.61, 125.56, 142.69, 143.03, 148.98, 157.75; MS: (M+H); *m/z* 281.09, Found: 281.27; Anal. Cacld for $C_{14}H_{11}N_5O_2$; C, 59.78; H, 3.94; N, 24.90; Found: C, 59.80; H, 3.96; N, 24.93.

Characterization of Metal Complexes:

FT-IR Spectroscopy: In the FTIR spectrum, an absorption band shifts to lower frequencies when C=N is coordinated to a metal ion. Also, the usual carboxylate (C=O) absorption band is located at 1730 cm^{-1}, while the alanine complex occurs at 1620cm^{-1}. A new absorption band appears in the spectrum at 609 cm^{-1}, with the M-O band occupying 650 cm^{-1} and the M-N band occupying 450 cm^{-1} and 430 cm^{-1}, respectively.

^{1}H and ^{13}C NMR Spectroscopy: The spectrum of the synthesized compound was obtained using ^{1}H NMR spectroscopy after being dissolved in DMSO. In ^{1}H NMR the metal complexes of $Zn(L_1L_2)$, $Ni(L_1L_2)$ shows aromatic peaks at 7.22–7.92 (m), 7.27–7.55 (m)ppm which is slightly higher than the ligand. The molecular ion peaks shows at *m/z* 433.77, 427.07 and Shows ^{13}C NMR at the range 142.92–158.42 and 116.42–136.52 ppm, $Mn(L_1L_2)$ shows ^{1}H at 7.26–8.45 (m)ppm and ^{13}C NMR at the range 124.30–132.72 ppm and the molecular ion peaks shows at *m/z* 424.89.The thermogram of Ni(II) 250°C and the last decomposition at 1020°C and Mn(II) at 1450°C and Zn(II) at 210°C.

Mass Spectroscopy: All of the investigated metal chelates may be seen in the mass spectrum of the resulting complex. The formula of the complex's molecular substance [$ZnC_{17}H_{17}N_6O_4$] was found to be well supported by the mass spectrum of the substance (MW 433.06). In the ESI-MS spectra of the synthetic mixed ligand complex [$ZnC_{17}H_{17}N_6O_4$], the molecular ion peak can be detected at *m/z* 433.06. The synthetic mixed ligand complex [Ni $C_{17}H_{17}N_6O_4$] shows MW-427.07 and [Mn $C_{17}H_{17}O_4N_6$] shows 424.89.

UV-Spectra and Conductivity Measurements: The conductivity of complexes was measured in 1:1 mixture of methanol and water at room temperature. The visible bands at 425 and 598 nm in the UV spectra of the Mn(II) complex were ascribed to the electronic transitions $^6A_1\rightarrow{}^4T_2$ and $^6A_1\rightarrow{}^4T_1$ respectively. The paramagnetic nature and high spin tetrahedral geometry of the Mn(II) complex are confirmed by the magnetic moment value of 4.65 B.M. The three bands seen in the visible spectrum at 450, 765 and 920 nm in the Ni(II) complex are attributed to the reactions $^3A_2g \rightarrow ^3T_2g$ and $^3A_2g \rightarrow ^3T_1g$ respectively of nickel(II) was 2.45 B.M. for its magnetic moment. The band at 315 nm corresponding to $^3A_2g \rightarrow ^3T_1g$ are seen in the visible area of the Zn (II) complex. There was a 3.20 B.M. value for the magnetic moment of Zn(II).

TABLE 1: PHYSICAL AND ANALYTICAL PROPERTIES OF LIGANDS AND COMPLEXES

Compound/ Empirical Formula	Colour	Formula Weight	Yield(%)	Melting Point/ Decomposition temp.(0C)	Elemental analysis (%) found (calc.)
Ligand $C_{14}H_{11}N_5O_2$	Pale Yellow	281.01	72 %	257.30-259.32^{0}C	C-59.78 (59.82), H-3.94 (3.96), N-24.90 (24.92)
[Zn $C_{17}H_{17}O_4N_6$]	Grey	433.06	78 %	Above 300^{0}C	C-46.97 (46.99), H-3.94 (3.98), N-19.33 (19.36)
[Ni $C_{17}H_{17}O_4N_6$]	Silver white	427.07	73 %	Above 300^{0}C	C-47.07 (47.10), H-4.00 (4.04), N-19.63 (19.66)
[Mn $C_{17}H_{17}O_4N_6$]	Grey white	424.07	76 %	Above 300^{0}C	C-48.12 (48.15), H-4.04 (4.08), N-19.81(19.84)

RESULTS AND DISCUSSIONS:

Synthesis of N-(2H-benzo[d] [1,2,3]triazol-2-yl)-1-(4-nitrophenyl)ethanimine (L_1): The ligand was prepared by mixing 1.34g of 1-(4-nitrophenyl) ethanone (0.1M) with 0.1g of 2-aminobenzotriazole. Over the course of five or six hours, we monitored the reaction mixture's development using a Silica Gel-G TLC plate as it was heated on a heating plate with condensing reagent and glacial acetic acid. Following completion of the reaction, the product was recrystallized in alcohol, cooled and then vacuum dried.

Synthesis of Metal Complex: The metal complex was formed by adding pure HCl to a modest quantity of distilled water producing a 0.98 gram (0.01 M) metal solution. The compound was made by mixing 10 ml of an ethanolic N-(2H-benzo[d] [1,2,3] triazol-2-yl)-1-(4-nitrophenyl) ethanimine (2.49 gm, 0.01 ml) with 10 ml of water soluble L-alanine (0.89 gm, 0.01 ml) subsequently 10 ml of a metal solution that was acidic in nature was added to the mixture. A ratio of 2:1 was observed between the metal and ligands. No precipitation was observed even after the reaction mixture was turned vigorously. The reaction's development was monitored using TLC during the 6-hour refluxing duration. After the reaction was complete, the product was washed, recrystallized, dried and finally collected under vacuum. The subsequent fundamental methodologies are illustrated. The biological activity of these three complexes is much higher than that of other Schiff base metal complexes. When compared to other metal complexes, the azomethane in the Ni(II) complex exhibited stronger antifungal activity.

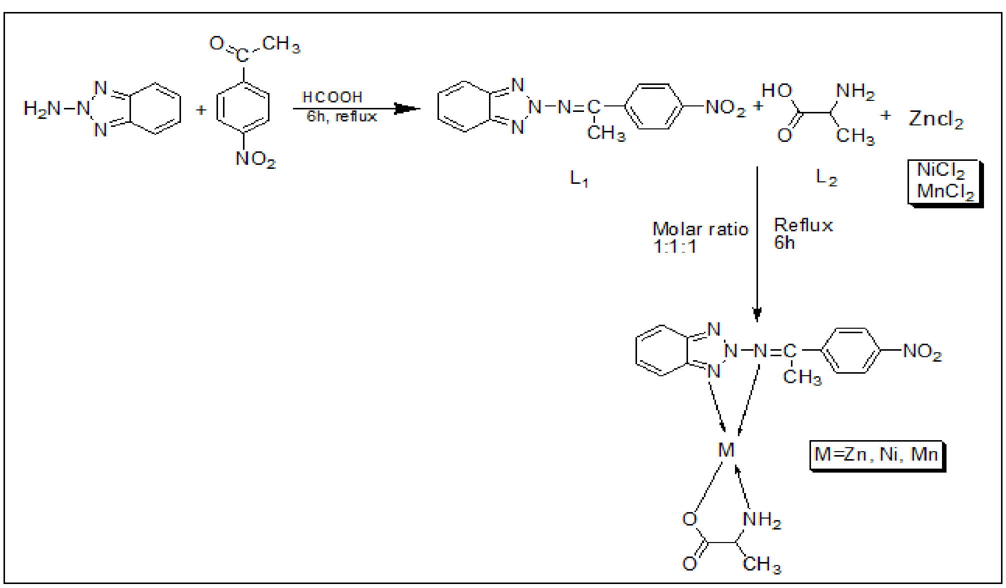

FIG. 1: SYNTHETIC STRATEGY PROPOSED FOR MIXED LIGAND COMPLEX

Antimicrobial Studies of Metal Complexes: Agar cup testing was used to determine the antibacterial activity of each drug against a variety of bacteria (*Bacillus megaterium*, *Micrococcus luteus*, *Salmonella typhi* and *Escherichia coli) and two different fungal strains (Aspergillus niger*, *Aspergillus flavus*). The growth-inhibiting zone's size was measured in centimeters. The substance was dissolved using dimethyl sulfoxide (DMSO). Ligand-1, Zn(II) metal complex were shown to have high levels of activity against *Escherichia coli, S. typhi*, *Micrococcus*, and *B. megaterium*, whereas Ni(II), Mn(II) were found to have moderate levels of activity. When tested against many strains of fungi, Ligand-1, Ni(II), Mn(II) Showed highest activity. The antibacterial activity of all of the compounds was promising when tested against two of the most successful antibiotics, streptomycin and ciprofloxacin. However, they showed low to moderate antifungal efficacy when tested against Nystatin. The results of this study might be used to other bio evaluations.

Insecticidal Activity: Insects of the species *P. interpunctella* were collected and put in a 1000 ml glass jar. Dosage was determined for each drug by assuming a nominal concentration of 100% in the exposure jar. The compounds were transfered to filter paper that was put inside the jar. The stock was then diluted to provide solutions of varying concentrations (3, 6, 9, 12, and 15 µL/L). Toosendanin was produced at a concentration of 15 µL/L and used as the reference standard. A constant 27± 1°C temperature, 14L:10D light:dark cycle, and 65%±5 relative humidity were maintained throughout all trials. Values were averaged standard error of the mean. All reagents and chemicals used were purchased from Sigma and were of an analytical quality [14] **Table 3.**

TABLE 2: ANTIMICROBIAL ACTIVITIES OF COMPOUNDS. CONC. (MG/ML)

	Antibacterial activity				Antifungal activity	
	Gram +*ve* bacteria		Gram–*ve* bacteria			
Code	***B. megaterim***	***Micrococcs lut.***	***S. typhi***	***E. coli***	***A. niger***	***A. flavus***
Ligand (L_1)	2.6	2.8	2.5	2.5	3.5	3.4
Zn L_1L_2	2.8	2.9	2.6	2.5	3.5	3.4
Ni L_1L_2	2.2	2.1	2.0	1.9	3.6	3.9
Mn L_1L_2	2.4	2.5	2.5	2.4	3.7	3.8
Streptomycin	2.0	2.0	2.0	2.2	-	-
Ciprofloxacin	2.5	2.2	2.3	2.0	-	-
Nystatin	-	-	-	-	3.5	3.8

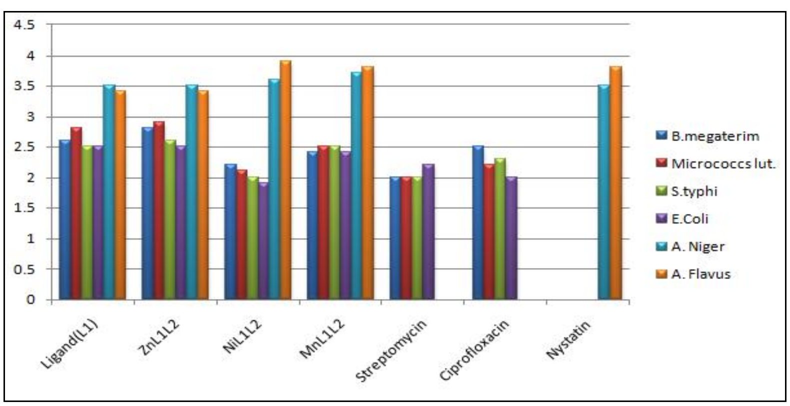

FIG. 2: CHART OF ANTIMICROBIAL ACTIVITIES OF LIGAND AND METAL COMPLEXES

TABLE 3: INSECTICIDAL ACTIVITY OF COMPOUNDS

Compounds	Insecticidal assay ±SE				
	Concentration in µL/L				
	3h	**6h**	**9h**	**12h**	**15h**
Ligand (L_1)	56.0±1.1	64.0±1.6	67.0±1.2	73.0±1.0	74.0±1.6
Zn L_1L_2	60.0±1.5	70.0±1.4	70.0±1.9	74.0±1.4	76.0±1.2
Ni L_1L_2	65.0±1.2	72.0±1.2	74.0±1.1	76.0±1.6	75.0±1.5
Mn L_1L_2	80.0±2.6	80.0±2.1	89.0±2.1	85.0±2.1	90.0±2.1
Toosendanin	100.0 ± 00	100.0 ± 00	100.0 ± 00	100.0 ± 00	100.0 ± 00

CONCLUSION: The physicochemical and spectroscopic data point to a four-coordinated geometry for the mixed ligand complex, which was calculated using the synthetic ligand as a bidentate chelating agent and the amino acid as a mono-ionic bidentate component. The tetrahedral structure and low conductance of the produced Zn(II), Ni(II) complex suggest that it is non-electrolytic and diamagnetic, whereas Mn(II) is paramagnetic, according to the hypothesis. Furthermore, when Zn(II), Ni(II) or Mn(II) are involved, the antibacterial activity of the Metal(II) complex against certain bacteria and fungi is often greater than that of the free ligand. The azomethine (C=N) link and the donor atoms (oxygen and nitrogen) allow the metal(II) complex to enter bacteria further. In this article, we highlight our efforts to find more substituted analogues that have outstanding biological activity. To improve the insecticidal performance of the compounds offered, further research into structure-activity correlations and assessment efficacy is definitely needed.

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CONFLICT OF INTEREST: The author's confirmed that there is no conflicts of interest.

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