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Synthesis, Characterization and Antimicrobial Evaluation of Co(II), Ni(II) and Cu(II) Schiff base complexes of (Z)-4-(1-pyridin-4-ylimino) propyl)phenol

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ABSTRACT

The demand for discovery and development of new antimicrobial agents has continued to increase due to the emergence and increasing prevalence of drug resistant pathogens. The study evaluated the synthesis, characterization and antimicrobial activity of Co(II), Ni(II) and Cu(II) Schiff base complexes derived from condensation of (Z)-4-(1-pyridin-4-ylimino) propyl) phenol with their respective metal chlorides. The synthesized Co(II), Ni(II) and Cu(II) Schiff base complexes were characterized by UV-Visible analysis, FTIR, Molar conductivity measurement and Magnetic susceptibility test. The results of the FTIR suggest that the metal complexes possess coordinated water molecules and the absorption band with wavenumber 1651.12 and 1658.84 cm^{-1} shows that the nitrogen of the imine bond participated in the coordination to the metal center. The magnetic susceptibility measurements show magnetic moments of 4.68 BM, 3.10 BM and 1.95 BM corresponding to Co (II), Ni (II) and Cu (II) complexes, respectively, thus, indicating the metal complexes possess octahedral geometry. The molar conductivity tests show values of 82.90 $\Omega^{-1}mol^{-1}cm^2$, 62.60 $\Omega^{-1}mol^{-1}cm^2$ and 50.80 $\Omega^{-1}mol^{-1}cm^2$ which corresponds to Co(II), Ni(II) and Cu(II) complexes respectively. The molar conductivity values for the complexes show that they do not readily dissociate in solution and are non-electrolytic in nature. The metal to ligand ratio for each of the metal complexes is 1:2. The metal complexes were evaluated for their antimicrobial activity against two Gram positive bacteria, two Gram negative bacteria and two fungi organisms. The synthesized metal complexes show significant activities against most of the test organisms.

Keywords: Schiff base, FTIR, UV-Visible, metal complexes, antimicrobial.

Introduction

Pharmaceutical companies are continuously challenged when new form of antibiotics resistance emerged in previously susceptible pathogens. Despite efforts to provide new and improved antibiotics, resistant bacteria continue to evolve in response to the new antibacterial agents that they encounter.[1] The increasing identification of antibiotic-resistance pathogens cannot be ignored thus the need to restock the antibiotic pipeline.[2] The medicinal uses and applications of metals and metal complexes are of increasing clinical and commercial importance.[3] The biological activities of metal complexes maybe related to their redox properties and the pharmacological efficiencies of metal complexes depend on the nature of the metal ions and the ligands.[4] Schiff base which possess aryl or heterocyclic residue are known to be stable and possess excellent biological activities, hence have attracted attention of researchers in recent years.[5] Studies have shown that Schiff base metal complexes of the transition metals possess potential biological activities such as antibacterial, antifungal, antiviral and antitumor properties.[6] The increase in the mortality rate associated with infectious diseases is directly related to bacteria that exhibit multiple resistances to antibiotics. Thus, the development of new antibacterial agents with novel and more efficient mechanisms of action is of urgent medical need .[7]

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Phenols are antiseptic, disinfectants and are active against a wide range of micro-organisms but are slowly effective against spores. They are used to relieve pains and irritation caused by sore throat, sore mouth or canker sores.[8] This research is aimed at synthesizing and characterizing Co(II), Ni(II) and Cu(II) Schiff base complexes of (Z)-4-(1-pyridin-4-ylimino)propyl)phenol and their antimicrobial activity.

Materials and Methods

Chemicals and Instruments

All chemicals used are of analytical grade and were used without further purification. Melting points were determined on a Stuart automatic melting point apparatus model SMP40 using open capillary tubes with temperature of 40ºC at a temperature ramp of 15ºC, FTIR spectra were obtained using Shimadzu FTIR-8400S Spectrophotometer within the wavenumber 4000-650cm^{-1}. Electronic spectra for compounds in UV-Visible region 200-800nm were recorded using UV-Visible 2012PC Spectrophotometer. Molar conductivity measurements were performed using Jenway 4010 conductivity meter while magnetic moments were obtained using Sherwood Scientific AUTO magnetic susceptibility Guoy balance.

Synthesis of Schiff base ligand

The Schiff base was synthesized according to the method described by Nagesh *et al*., (2015).[9] Equimolar quantities of 4-aminopyridine (0.02mol) and 4-hydroxypropiophenone (0.02 mol) were each dissolved in hot ethanol (20 mL) then the mixtures were added together. Glacial acetic acid (2 drops) was also added to the mixture and refluxed for 8 h on a water bath (Figure 1). The crystals formed were filtered and washed with distilled water and then recrystallized from methanol, air dried and kept in a desiccator for further analysis.

Synthesis of Schiff base metal complexes

The synthesis of the Schiff base metal complex was carried out according to the method reported by Nagesh *et al*., 2015.[9] To 0.010 mole of (Z)-4-(1-pyridin-4-ylimino)propyl)phenol(Schiff base ligand which was previously synthesized) in ethanol (20 mL) was added a hot ethanolic solution (15 mL) of the respective metal chlorides (0.005 mole) i.e. 1:2 metal to ligands ratio. The reaction mixture was heated under reflux for 3 h until complete precipitation and the precipitate was separated by filtration, purified by washing several times with distilled water, recrystallized with methanol as solvent and dried in a desiccator.

Antimicrobial Screening

The antimicrobial test was carried out in accordance with the Laboratory Standard using the agar well diffusion method as reported by Offiong and Martelli, (1994).[10] The test microorganisms were of clinical strains, which were identified and characterized in the Department of Microbiology, Ahmadu Bello University Zaria; they include two gram positive bacteria (*Staphylococcus aureus* and *Bacillus subtilis*), two gram negative bacteria (*Escherichia coli* and *Proteus vulgaris*) and two fungal strains (*Aspergillus flavus* and *Aspergillus niger*).

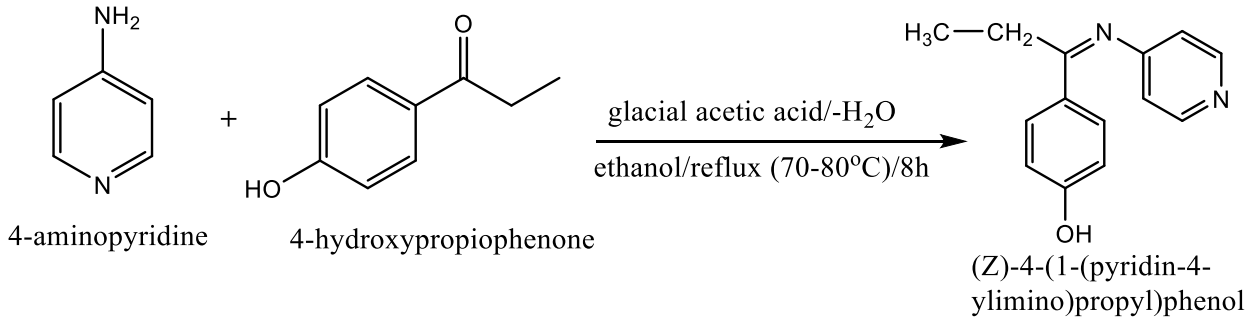

Figure 1: Reaction Scheme for synthesis of the Schiff base ligand.

Results and Discussion

The newly synthesized metal complexes were coloured solids with fairly sharp melting points and are stable at room temperature.

Molar conductivity measurement

The molar conductivity values for the complexes are shown in Table 1. The metal (II) complexes were dissolved in DMSO and the molar conductivities of 10^{-3} M of their solutions were measured at room temperature. The low molar conductivity values for all the complexes show that the complexes are non-electrolytic in nature. Complexes with molar conductivity values in the range of 106-311 are considered to be electrolytic in nature, such complexes have ions present outside the coordination sphere.[11] The molar conductivity value is a good pointer to the proposed $[ML_2.2H_2O]$ as the structure of the complex as in Figure 2, since the data obtained for the complexes are lower than those for electrolytic complexes and for the complex to achieve charge neutrality, the M^{2+} must combine with the ligand in ration 1:2, thus the conductance values of the metal complexes support their non-electrolytic nature. The values also show that there is no counter ion outside the coordination sphere of the complexes.

Magnetic susceptibility measurement

The measurement was carried out at temperature of 35ºC. The observed magnetic moment for Co (II) complex was 4.68 BM, which is expected for an octahedral geometry.[1] The ground state of the Co (II) complex is $^4T_{1g}$ and a large orbital contribution to the singlet state lowers the magnetic moment values for the Co (II) complex which is usually in the range of 4.70-5.20 BM. In the Ni (II) complex, the magnetic moment of the complex was 3.1 BM which is within the expected range for Ni (II) complex having octahedral stereochemistry (2.83-4.00 BM). The value for Cu (II) complex is 1.95 BM, this implies that the complex is devoid of any spin interaction with distorted octahedral geometry.[12]

Electronic spectra

The electronic spectra of the metal (II) complexes in DMSO in the range of 200 – 800 nm is recorded in Table 1. The electronic spectra provide useful information on arrangement of the ligand around the metal ions.[13] The spectrum of the Co (II) complex shows absorption bands at 369 nm corresponding to n-π* transition. The band at 513 nm corresponds to $^4T_1g \rightarrow {}^4T_1g(P)$ which is v_3 transition, while the absorption band at 651 nm corresponds to $^4T_1g \rightarrow {}^4A_2g(F)$ which is the v_2 transition. Due to the low intensity of the d-d transition, v_1 was not observed in the spectrum.[11] For Ni (II) complex in an octahedral environment having ^3A_2g ground state, three spin allowed transitions are expected. In the spectrum for the Ni (II) complex, the band at 357 nm was assigned to $^3A_2g \rightarrow {}^3T_1g(P)$ while the 446 nm corresponds to $^3A_2g \rightarrow {}^3T_1g(F)$. The third transition was not observed in the spectrum probably due to low intensity of the d-d transition.[14] In the Cu (II) complex with d^9 configuration, a broad band ranging from 500 nm-700 nm with maximum at 596 nm was observed in the spectrum. The maximum absorption corresponds to $^2Eg \rightarrow {}^2T_2g$ transition which can be found in a tetragonally distorted octahedral complex.[15]

Infrared spectra

The vibrational modes of the synthesized metal(II) complexes carried out in the range of 4000 cm^{-1} to 650 cm^{-1} are presented in Table 2. The complexes display bands 3772.89, 3757.46 and 3873.19 cm^{-1} corresponding to Co(II), Ni(II) and Cu(II) complexes, respectively. This can be attributed to the presence of coordinated water molecules in the structure of the complexes which is confirmed by the presence of bands at 941.29 and 949.01 cm^{-1}, this corresponds to the position for vibrational bend mode for H_2O.[15] The band at 1651.12 and 1658.84 cm^{-1} can be assigned to azomethine ligand while the bands at 717.53 and 671.25 cm^{-1} show metal-oxygen bond.[15]

Based on the results of the physicochemical analysis, the proposed structure for the metal complexes indicates that the metal-ligand ratio is 1:2.

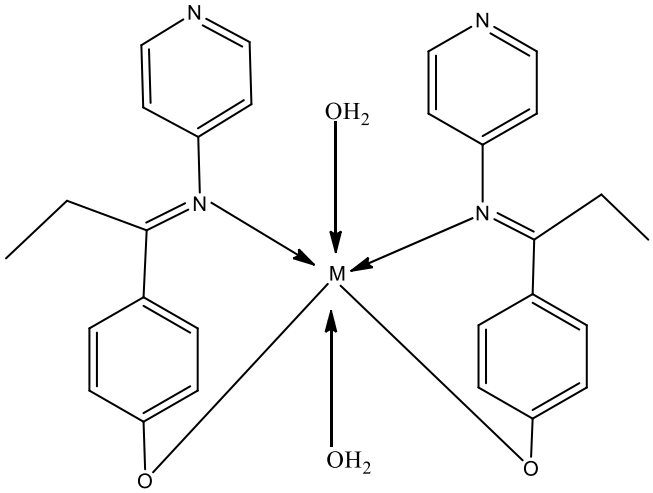

Figure 2: Proposed structure for the metal complexes.

Where M = Co(II), Ni(II) and Cu(II) ions.

Antimicrobial analysis

The biological activities of the metal(II) complexes were carried out against two Gram positive bacterial strains; *Staphylococcus aureus* and *Bacillus subtilis*, two Gram negative bacterial strains; *Escherichia coli* and *Proteus vulgaris***,** two fungal strains; *Aspergillus flavus* and *Aspergillus niger* utilizing the agar well diffusion method and results obtained were compared to ciprofloxacin(antibacterial agent) and fluconazole(antifungal agent). The synthesized metal complexes were evaluated for their *in vitro* antimicrobial activities. All the metal complexes displays significant activity against *S.aureus* (Table 3). The Co(II) complex exhibited the highest activity against *S.aureus, E.coli* and *P.vulgaris*, the Ni(II) complex exhibited the highest activity against the fungi *A.niger* while the Cu(II) complex exhibited the highest activity against *B.substilis* when compared to the other complexes. None of the metal complex shows activity against *A.flavus*. The result shows that the type of metal ion and type of microorganism are the main controlling factors on biological action. The Minimum Inhibitory Concentration (MIC) was determined using the broth dilution method, the result is shown at Table 4. The result shows that Co(II) Schiff base complex inhibited the growth of *S.aureus* at concentration of 1.56 mg/mL. The Ni(II) and Cu(II) complexes inhibited the growth of *S.aureus* at 3.125mg/mL. For *A.niger*, all the complexes inhibited the growth at 25mg/mL. Generally, all the metal complexes were found to inhibit the test bacteria at 12.5 mg/mL.

Table 1: Physical and analytical data of Schiff base metal complexes.

Compounds	Molecular weight	Melting Point (°C)	Colour	% Yield	Molar Conductivity $\Omega^{-1}cm^{-1}mol^{-1}$	Magnetic Moment (BM)	Absorption Wavelength (nm)
$[Co(C_{14}H_{14}N_2O)_2.2H_2O]$	645.22	124-126	Blue	34.20	82.90	4.68	369 513 651
$[Ni(C_{14}H_{14}N_2O)_2.2H_2O]$	645.22	138-140	Light green	50.70	62.60	3.10	357 441 446
$[Cu(C_{14}H_{14}N_2O)_2.2H_2O]$	649.72	128-130	Green	28.80	50.80	1.95	350 500-700 (596)

Table 2: FTIR of M(II) complex (cm^{-1}).

Compounds	***v*(H$_2$O) str.**	***v*(O-H) Str.**	***v*(C=N) azomethine**	***v*(C=N) heterocyclic**	***v*(C-O) str**	***v*(H$_2$O) bend**	***v*(M-O)**
$[Co(C_{14}H_{14}N_2O)_2.2H_2O]$	3772.89	3410.26	1651.12	1535.39	1226.77	941.29	717.53
$[Ni(C_{14}H_{14}N_2O)_2.2H_2O]$	3757.46	3433.41	1651.12	1527.67	1234.48	949.01	671.25
$[Cu(C_{14}H_{14}N_2O)_2.2H_2O]$	3873.19	3433.41	1658.84	1527.67	1222.95	949.01	671.25

Table 3: Results of sensitivity test of the complexes (Zones of Inhibition, mm).

Samples	**Conc. mg/mL**	***S. aureus***	***B. substilis***	***E. coli***	***P. vulgaris***	***A. niger***	***A. flavus***
Co(II) complex	50	33	18	20	20	18	NS
	25	25	16	18	17	16	NS
Ni(II) complex	50	25	16	14	15	21	NS
	25	19	14	12	13	18	NS
Cu(II) complex	50	18	20	14	15	16	NS
	25	16	18	12	13	14	NS
Ciprofloxacin	50	35	32	37	39	ND	ND
Fluconazole	50	ND	ND	ND	ND	35	35

NS = Not sensitive, ND = Not determine.

Table 4: Minimum Inhibitory Concentration (MIC) of the Complexes in mg/mL.

Complexes	***S. aureus***	***B. subtilis***	***E. coli***	***P. vulgaris***	***A. niger***
Co(II) complex	1.56	12.5	3.125	3.125	25
Ni(II) complex	3.125	25	12.5	12.5	25
Cu(II) complex	3.125	25	6.25	6.25	25

Conclusion

The M(II) complexes derived from condensation of (Z)-4-(1-pyridin-4-ylimino)propyl)phenol with the hydrates of the metal chlorides were successfully synthesized and characterized by FTIR, molar conductivity, magnetic susceptibility and electronic spectroscopy. The result of the physicochemical properties reveal that the coordination of the ligand to the metal is bidentate with M:L mole ratio of 1:2. All the complexes displayed octahedral geometry. The metal complexes showed significant antimicrobial activity against the test organisms especially *S. aureus*. The Co(II) complex also showed MIC at a very low concentration of 1.56 mg/mL. None of the synthesized complex showed activity against *A. flavus.*

Conflict of interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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