ChemSearch Journal 15(2): 135 – 146, December, 2024
Publication of Chemical Society of Nigeria, Kano Chapter

Received: 28/10/2024 Accepted: 07/12/2024
http://www.ajol.info/index.php/csj

Synthesis, Characterization and Anti-Fungal activity of Cu(II), Ni(II) and Cd(II) complexes of 5-Bromosalicylidene -2-Nitroaniline

[1*]M. S. Iorungwa, [1]Q. M. Amua, [2]G. S. Ngantem, [1]P. T. Shimaibo, E. C. Oggah, [3]T. M. Apav, J. I. Ona and [4]S. T. Iningev

[1]Inorganic/ Physical Chemistry Research Group, Department of Chemistry, Joseph Sarwuan Tarka University, Makurdi – 970001, Benue State, Nigeria
[2]Department of Chemistry, Federal University, Wukari – Nigeria
[3]Department of Microbiology, Joseph Sarwuan Tarka University, Makurdi – 970001, Benue State, Nigeria
[4]Department of Chemistry, Benue State University, Makurdi P.M.B. 102119, Nigeria
***Correspondence Email:** iorungwa.moses@uam.edu.ng

ABSTRACT

The synthesis, characterization and the antifungal activities of some selected transition metal complexes (Cu^{2+}, Ni^{2+} and Cd^{2+}) were carried out. The salts of these metals were complexed with the Schiff base obtained from 5-Bromosalicylaldehyde and 2-Nitroaniline yielding the compound; 5 – Bromosalicylidene – 2- nitroaniline complexes of Cu(II), Ni(II) and Cd(II). The new compounds were characterized on the basis of physicochemical properties, spectral analysis (FTIR, UV-visible), molar conductance, magnetic susceptibility and PXRD analysis. The metal complexes exhibited various range of colours such as dark green, dark brown and milk white with the Schiff base being dark yellow; giving yields of 69.2, 56.7 and 62.5 % respectively; high melting points (126, 320 and 128 ^{0}C) and molar conductance values (591, 620 and 631 $\Omega^{-1}cm^2mol^{-1}$) for the Cu(II), Ni(II) and Cd(II) complexes respectively. The synthesized complexes were soluble in ethanol, methanol, DMSO, acetone, slightly soluble in DMF but insoluble in water and n-Hexane. The IR spectra of the synthesized complexes showed bands characteristic of azomethine (C=N) vibration mode as well as evidence of azomethine carbons, protons and formation of the M-N, M-O, O-H bonds. The spectral study also showed the complexes obtained as monomeric structures and the central metal moieties are four-coordinated, with tetrahedral geometry, except for the Cu(II) and Ni(II) complexes, which had square planar geometries. The complexes formed were of the general formula ML where L is the ligand and M is the respective metal ions. The PXRD studies revealed average crystallite size of 34.75, 69.75 and 39.11; the FWHM value of 0.23, 0.13 and 0.21; the hkl value of 101and 201. The antimicrobial activities of the ligand and its complexes were tested using Agar-well diffusion techniques for zone of inhibition while Agar dilution techniques were used for minimum inhibitory concentration and fungicidal concentration. The metal complexes of Schiff base showed broad spectrum antifungal activity against certain range of fungi; *A. flavus, A. fumigates, A. niger, R. stolonifer, R. bataicola and C. albicans*. The results showed that the complexes exhibited a higher fungicidal property than the ligand.

Keywords: Antifungal, Antimicrobial, Azomethine; Metal complex, Schiff base

INTRODUCTION

Coordination compound or metal complex can be seen as central metal atom attached with the sheath of ions or molecules (Lee, 1996; Iorungwa *et al*., 2020). The interesting aspects of transition metals are their ability to form coordination compounds. Such compounds are formed between a metal ion and a molecule with one or more unshared electron pairs called a ligand (Chakraborty *et al*., 2009; Iorungwa *et al*., 2020). Recently, the transition metal (II) Schiff base complexes have acquired special attention in medicinal and pharmaceutical field since they show excellent biological activities (Iorungwa *et al.*, 2020). Some of the transition metal complexes are used in biomedical analysis as Magnetic Resonance Imaging (MRI) contrast agents (Ashraf *et al.*, 2011).

Compounds containing the -C=N- (azomethine group) structure are known as Schiff bases, usually synthesized from the condensation of primary amines and active carbonyl groups (Asiri and Khan, 2010; Bhusnure *et al*., 2015).

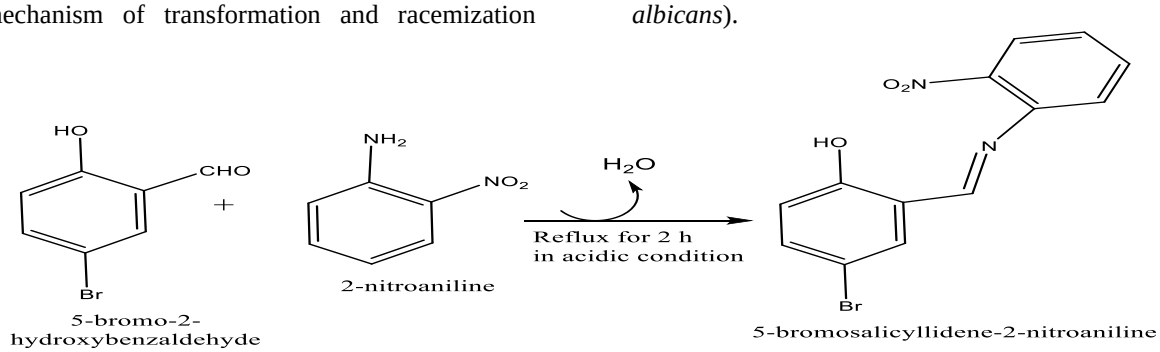
They are known to exhibit potent antibacterial, antiulcer and analgesic activities (Cleiton *et al*., 2011; Iorungwa *et al*., 2020). Schiff bases are well known for their biological applications as antibacterial, antifungal, anticancer and antiviral agents; furthermore, they have been used as intermediates in medical substrates and as ligands in complex formation with some metal ions (Fun *et al*., 2009). Polydentate ligands obtained

from Schiff bases, assisted by metal ions, provide highly organized supramolecular metal complexes. Such complexes possess binding sites and cavities for various cations, anions and organic molecules (Dixit *et al*., 2009).

Metal complexes with ligands containing N, O or S donor have been found to be useful as potential drugs (Chandra *et al.*, 2012). Similarly, phenolic Schiff bases have been found to have various applications in different spheres ranging from inorganic chemistry, physical chemistry and analytical chemistry to biochemistry and biology (Tarafder *et al*., 2002; Vicini *et al*., 2003). They have also been reported as effective corrosion inhibitors on mild steel such as copper and aluminium (Solmaz *et al*., 2011). They are known for their antibacterial (Kabeer *et al*., 2001; Cohan *et al*., 2004; Khan *et al*., 2009), antifungal (Cohan *et al*., 2006; Guo *et al*., 2007) and anticancer (Vicini *et al*., 2003) activities.

Schiff bases are studied widely due to their synthetic flexibility, selectivity and sensitivity towards the central metal atom (Zoubi, 2013), structural similarities with natural biological compounds and also due to presence of azomethine group (-N=CH-) which imports in elucidating the mechanism of transformation and racemization reaction biologically (Gao and Zheng, 2002). Schiff bases having chelation with oxygen and nitrogen donors and their complexes have been used as drugs and reported to possess a wide variety of biological activities against bacteria, fungi and certain type of tumors and also, they have many biochemical, clinical and pharmacological properties (Zoubi, 2013).

The Schiff base metal complexes are active against micro-organisms, because the Schiff base ligands containing azomethine or imine, with the presence of nitrogen atom take part in chemical and biological processes. Here, preparation, characterization and biological studies of a novel Schiff base obtained by condensation of 5-Bromosalicylaldehyde and 2-Nitroaniline and its complexes with transition metal ions has been reported as seen in Scheme 1 below. The aim of this research work is to synthesize and characterize metal complexes of Cu(II), Ni(II) and Cd(II) with the Schiff base ligand obtained from 5-Bromosalicyl-aldehyde and 2-Nitroaniline and carry out their anti-fungal activities against six (6) different species of fungi (*Aspergillus niger*, *Aspergillus flavus*, *Aspergillus fumigatus*, *Rhizopus stolonifer*, *Rhizoctonia bataicola* and *Candida albicans*).



Scheme 1: Reaction pathway for the synthesis of 5- Bromosalicylidene – 2- nitroaniline Schiff Base

MATERIALS AND METHODS

The reagents and solvents include: 2-Nitroaniline (BDH, 99 %) and 5-Bromosalicylaldehyde (Sigma Aldrich, 98 %) used to synthesize the Schiff base. Cadmium(II) chloride hemi-hydrate, $CdCl_2.5/2H_2O$ (BDH, 79.5-81 %), Copper(II) chloride dihydrate, $CuCl_2.2H_2O$ (BDH 99 %), and Nickel(II) chloride hexahydrate, $NiCl_2.6H_2O$ (BDH 98 %) used to synthesize the metal(II) complexes respectively. Sodium acetate (BDH 99 %) and sodium hydroxide (Loba Chemie 97 %) used as buffer for pH adjustment; glacial acetic acid (Sigma Aldrich 99 %) were used in buffer preparation and as indicator; ethanol (JHD 99.7 %) used as media for the synthesis; ether (Sigma Aldrich 98 %), dimethylsulfoxide, DMSO (Sigma Aldrich 99 %) and dimethylformamide, DMF (Loba Chemie 99.8 %) were used as solvents for solubility test; doubly distilled water for the washing and purification process; nutrient agar (TM Media) Potato Dextrose Agar, PDA (Tulip Diagnostic), Salmonella Shigella Agar, SSA (Sigma Aldrich) and Acetone (JHD 99 %) were used for culture media preparation. These reagents were purchased commercially and used as purchased.

Synthesis of the Schiff Base Ligand

An equimolar mixture of nitroaniline (0.001 mol), 10 mL and 5-Bromosalicylaldehyde (0.001 mol), 10 mL in ethanol (20 mL) was refluxed with a catalytic amount of glacial acetic acid (2 drops) for about 2 h at 75 ^oC. The reaction mixture was then cooled to room temperature so as to obtain a crystalline deep yellow compound and further filtered, dried and recrystallized in 20 mL of alcohol (Scheme 1). The newly synthesized compounds were then taken for characterization to confirmed evidence of the formation of Schiff base.

Synthesis of the Obtained Schiff base Metal Complexes

Exactly 2.0 g each of the hydrated metal salts was dissolved in 25 mL of hot absolute

ethanol and about 2.0 g of the synthesized Schiff base was dissolved in 20 mL of hot absolute ethanol. The metal salt solution was added with constant stirring to the solution of the synthesized Schiff base respectively and heated on SB160 heat-stirrer for about 2 h using magnetic stirrer. The resulting mixture was transferred into a beaker and left overnight to crystallize; after which the resulting crystals were recrystallized in 20 mL of hot ethanol. The final crystals obtained was oven dried (OV/100/F) at 50 ^{o}C, weighed and finally taken for the characterization process.

Characterization of Ligand and Complexes

Solubility test

The solubility test of the ligand and the metal complexes was carried out in different solvents such as water, ethanol, methanol, acetone, dimethylsulfoxide, (DMSO) dimethylformamide (DMF) and ether by shaking 0.5 g of each compound in a test tube containing 10 mL of the solvent and the results recorded (Iorungwa *et al.*, 2019).

Melting point determination

About 0.1 g of the synthesized compounds (the ligand and the metal complexes) were loaded in separate capillary tubes and inserted into the heating block of the Barnstead Electro-thermal (9100) melting point apparatus and heated separately and the temperature at which each of the samples melted were noted from the digital screen. The physicochemical properties of the Schiff base ligand and metal complexes are presented in Table 1.

Electrical conductivity measurement

The electrical conductivities of the complexes were obtained in DMSO using pH/Conductivity series 510 meters.

Magnetic susceptibility measurement

Since magnetic susceptibility measurement gives or provide information about the magnetic moment of the metal in the complexes, its paramagnetic properties and the number of unpaired electrons present was measured using Evans Balance (Dufera *et al.*, 2019).

Infrared spectra studies for the ligand and their complexes

The infrared spectra data of the synthesized Schiff base alongside the complexes were obtained by using carry 630 FT-IR spectrophotometer for the Schiff base ligand while proRamman-L-785-B1S FT-IR spectrophotometer for the complexes. five stages are involved; sample preparation, background measurement, spectral acquisition, data analysis and interpretation of results.

Electronic spectra studies for the ligand and its complexes

The electronic spectra of the ligand and the complexes were obtained using Shimadzu UV-1800 PC series Spectrophotometer in solution state in the range 190 to 800 nm wavelength.

X-ray diffraction (XRD) for the ligand and the metal complexes

Exactly 0.5 g of the synthesized compounds were used. XRD characterization of thin film samples was done in Umaru Musa Yar'adua University Katsina state, Nigeria in the Central Research laboratory with X-ray Diffractometer Thermoscientific model: ARL'XTRA X-ray and serial number 197492086. The powder x-ray diffraction (PXRD) pattern of the ligand and metal(II) complexes was recorded by employing Bruker d8 Advance X-ray diffractometer, using Cu Kα radiation (λ = 1.5406 Å), 40 kV- 40mA, 2θ/θ scanning mode. Data was taken for the 2θ range of 10 to 70 degrees with a step of 0.0202 degrees.

Antifungal Activity/Screening

The anti-fungal activity studies were carried out in the microbiology laboratory of Joseph Sarwuan Tarka University, Makurdi using the Agar-well diffusion technique. The *in vitro* antifungal property of the Schiff base ligand and its Cu(II), Ni(II) and Cd(II) complexes were assayed using six fungal isolates (*Aspergillus niger, Aspergillus flavus, Aspergillus fumigates, Rhizopus stolonifer, Rhizoctonia bataicola and Candida albicans*) by Disc Diffusion Technique.

Potato Dextrose Agar was used to prepare the culture media and incubated at room temperature for seven days. The results obtained is being compared with the activity of Ketoconozole (600 µg) as a standard antifungal drug (Sani and Dailami, 2015). Potato dextrose agar plates containing five concentrations of 100,75,50,25 and 12.5 5 μgmL^{-1} of each test compound and their respective metal chlorides would be inoculated with 100 μgmL^{-1} of 7 days old spore suspension of each fungal culture (108 spore/mL). These plates were kept for incubation at 32 ^{o}C for about 48 h. One control plate of potato dextrose agar without test compound would be kept for incubation with its test strains of fungi at the same condition. Soon after the completion of incubation period of 48 h, minimum inhibitory concentration (MIC)/ minimum fungicidal concentration (MFC) of each test compound was recorded as the lowest concentration of compound with no visible growth of fungi. The experiment was done in triplicate and the average values were calculated for antifungal activity.

RESULTS AND DISCUSSION

Colour, Yield and Melting Points of the Ligand and the M(II) Complexes

Reaction between the bromosalicylaldehyde and nitroaniline in ethanol medium gave a crystalline coloured Schiff base ligand. Also the synthesized Schiff base ligand, copper(II), cadmium(II) and nickel(II) chloride produced metal complexes that were crystalline and coloured in nature with percentage yield ranging from 56.7 – 70.8 % (Table 1). All the synthesized compounds were found to be in crystalline/powdery form, indicating their polymeric nature (Iniama *et al.*, 2018).

The high melting points displayed by the complexes suggested strong metal-ligand bonds. Also, high melting /decomposition temperature in the complexes is an indication of their high thermal stability (Table 1).

Table 1: Physicochemical Characteristics of the Ligand and Metal Complexes

Compd	Mol. Form.	Mol. Wt. ($gmol^{-1}$)	Colour	Yield (%)	M.pt (ºC)
L	$C_{12}H_9N_2BrO$	204.9	Dark yellow	70.8	81-83
[CuL_2]	$[Cu(C_{12}H_9N_2BrO)_2]\ Cl_2$	544.3	Dark green	69.2	126-128
[NiL_2]	$[Ni(C_{12}H_9N_2BrO)_2]\ Cl_2$	539.5	Dark brown	56.7	320-322
[CdL_2]	$[Cd(C_{12}H_9N_2BrO)_2]\ Cl_2$	593.2	Milk white	62.5	228-230

Keys: L = Schiff Base Ligand; Mol. Form. = Molecular formula; Mol. Wt. = Molecular weight

Solubility of the Synthesized Schiff base and the Metal Complexes

The synthesized Schiff base ligand and the metal complexes were dissolved in some organic solvents and water; the result of the solubility test is presented in (Table 2). From the result, the synthesized compounds were insoluble in water and hexane but soluble in ethanol, methanol, acetone and dimethylsulfoxide (DMSO) and sparingly soluble in dimethylformanide (DMF).

Table 2: Solubility of the Schiff base and the Metal Complexes

Compounds	Acetone	Ethanol	Methanol	Hexane	DMSO	DMF	Water
L	S	S	S	IS	S	SS	IS
[CuL_2] Cl_2	S	S	S	IS	S	SS	IS
[NiL_2] Cl_2	S	S	S	IS	S	SS	IS
[CdL_2] Cl_2	S	S	S	IS	S	SS	IS

Keys: S = Soluble; SS = Slightly Soluble; IS = Insoluble; L = Schiff base Ligand; DMSO = dimethylsulfoxide; DMF = dimethylformanide

Magnetic Susceptibility Studies of the Ligand and the Metal Complexes

The magnetic moments for the complexes are shown in Table 3 with the results suggesting a diamagnetic behavior for the Cd(II) complex. The complex of cadmium is diamagnetic, which means it has zero magnetic moments and no unpaired electrons in the degenerate 4*d* orbitals of the metal ion, as expected for a d^{10} electronic system. The absence of *d-d* bands in the visible spectra of the complexes further supports this and is due to the filled 4*d* orbital of the Cd(II) ion. This result aligns with findings from previous studies on Cd(II) complexes. The magnetic moment value (1.94 B.M) for the Cu(II) complexes suggests a square planar geometry with $dx^2–y^2$ ground state. The magnetic moment (2.83 B.M) value confirmed the presence of two unpaired electrons for the Ni(II) ion. This also shows the possibility of a square planar local symmetry around nickel in this complex as square planar complex of d^8 electronic systems are usually diamagnetic. Conversely, another square planar structure appears more reasonable for the Schiff base complex of Ni(II) under investigation (Lee, 2013).

Molar Conductivity Measurements

The molar conductivity values for the Schiff base ligand and the metal(II) complexes in 10^{-3} $moldm^{-3}$ DMSO are presented in Table 3. The values were observed to be in the range of *ca*. 308 – 631 Ω^{-1} mol^{-1} cm^2 suggesting that the complex compounds are electrolytic. This implies that there are ions outside the coordination sphere typical of electrolytic species. Hence, the presence of the degree of dissociation of the compounds with more ions in solution is noticed (Ogunniran *et al.*, 2008). Conductivity measurements have frequently been used in the structure elucidation of metal complexes (mode of coordination) within the limits of their solubility. They provide a method of probing the degree of ionization of the complexes, the molar ions a complex liberates in solution. It becomes clear from the conductivity data that the complexes under study are most likely to be electrolytes. This would only infer that the complexes all form in a 1:2 metal-ligand ratio (Iorhemba *et al*., 2018).

Table 3: Magnetic Susceptibility and Molar Conductivity Measurements of the Ligand and its metal Complexes

Complex	μ_{eff} (B.M)	Temperature (K)	$\Lambda(\Omega^{-1}mol^{-1}cm^2)$
L	-	-	308
[NiL$_2$] Cl_2	2.83	299.50	591
[CuL$_2$] Cl_2	1.91	299.50	620
[CdL$_2$] Cl_2	0.00	300.00	631

μ_{eff} = Effective magnetic moment, Λ= Molar conductivity, B.M=Bohr magnetons, K=Kelvin, molar conductivity in 1×10^{-3} moldm^{-3} DMSO solution

Infrared Spectral Data of the Synthesized Ligand and Metal Complexes

The formation of bonds on coordination was elucidated by critical observation and comparison with other related literature. The relevant IR spectra data and assignment of the Schiff base and the metal complexes are presented in Table 4. The IR spectrum of the ligand was compared with that of the metal complexes so as to identify the coordination sites of the ligand Thus, the broad band in the spectrum of ligand at *ca*. 3402 cm^{-1} is associated with the hydroxyl group, υ(O-H) which is present in the ligand molecule. Interestingly, a narrow band appeared in the spectrum of the metal complexes in a similar position. This has been ascribed to the presence of water of hydration in the synthesized metal complexes. The spectra of the Schiff base metal complexes of Cu(II), Ni(II), and Cd(II) showed a perturbation in the vibrational frequencies associated with the υ(C=N) when compared with that of the ligand. This indicates that the neighboring hydroxyl group in the ligand is coordinated with the transition metal ions. The shifts in bands at ca. 1250 cm^{-1} in the spectra of the ligand and the complexes for the C-O vibration supports this assertion further. The presence of peaks in the range of 1820 – 1890 cm^{-1} confirms the presence of the nitro group in the synthesized compounds. It is important to observe that the M–O vibration which is missing in the spectrum of the ligand becomes conspicuous in the spectra of the metal complexes. This is an indication that complexation has taken place with the coordination of the ligand to the metal occurring via M–O architectures. The findings herein are in agreement with those of other researchers (Hussain, 2014; Iorungwa *et al.*, 2020; Iorungwa *et al.*, 2020a). The shifting of this group to a lower frequency compared to the Schiff base ligand suggest a metal ion coordination through the nitrogen atom of the azomethine group (Abdelsalam *et al.*, 2019).

Table 4: **FTIR spectra data for the synthesized ligand and the metal complexes**

Complex/bands (cm^{-1})	O-H	N-O	C=N	C-N	C-O	M-O
L	3402	1891	1597	1318	1224	-
[NiL$_2$]	3438	1887	1682	1322	1262	695
[CuL$_2$]	3394	1887	1624	1320	1246	682
[CdL$_2$]	3438	1885	1693	1406	1264	722

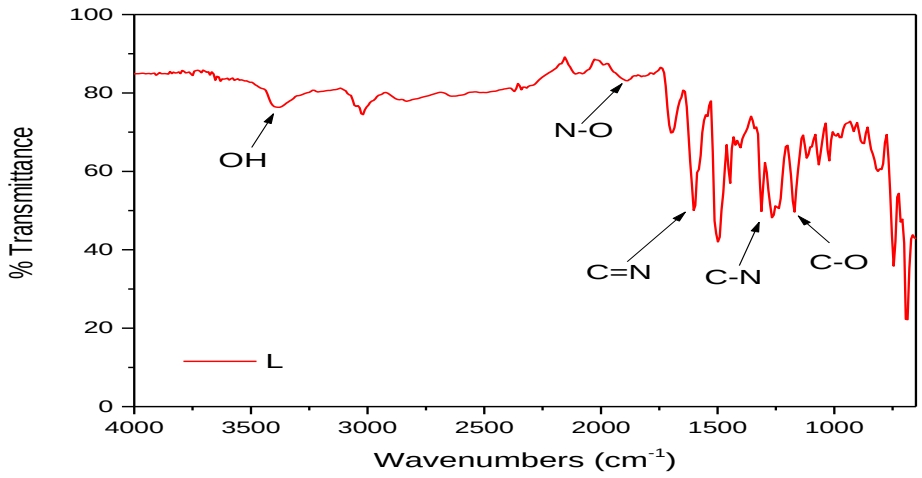


Figure 1: FTIR Spectrum of the ligand

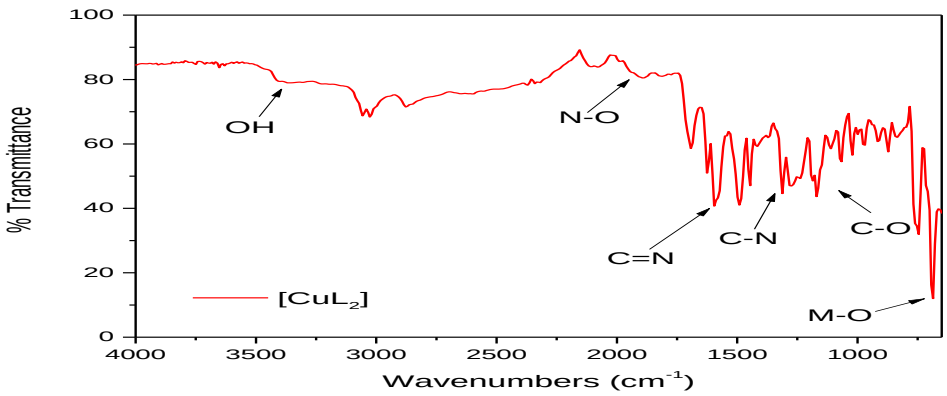


Figure 2: FTIR Spectrum of Cu Complex

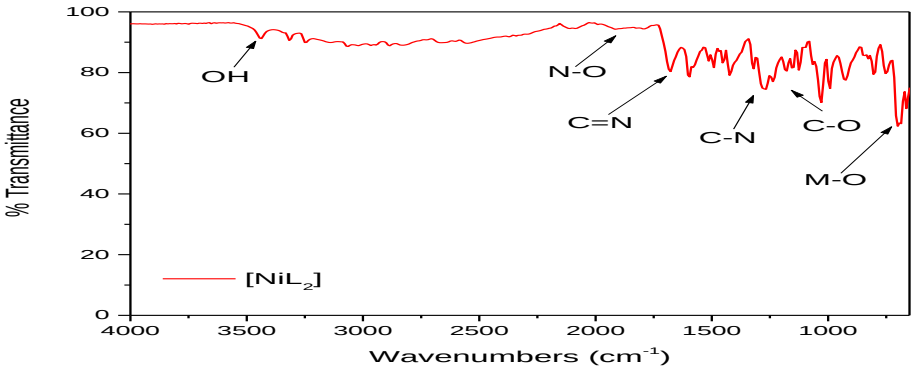


Figure 3: FTIR Spectrum of Ni complex

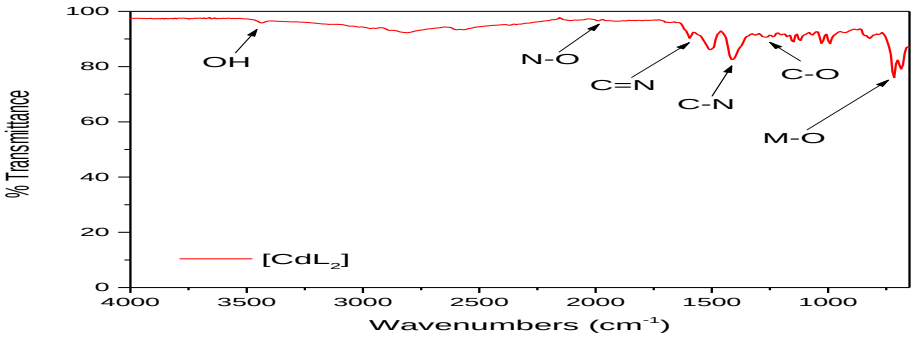


Figure 4: FTIR Spectrum of Cd complex

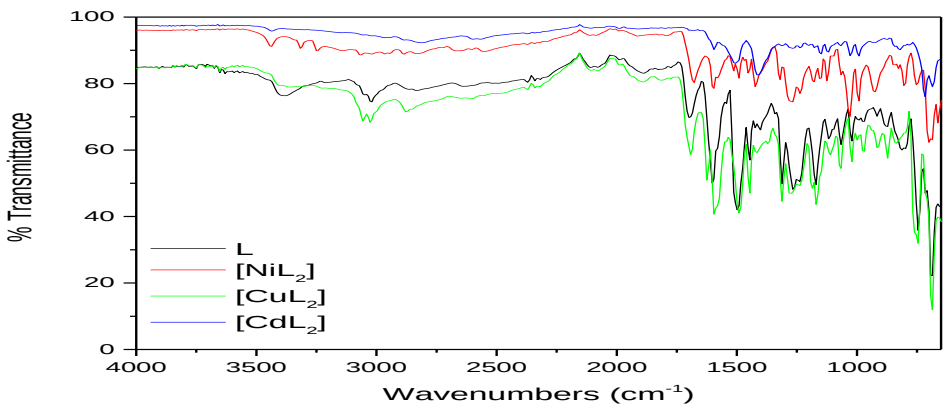


Figure 5: Stacked FTIR Spectra of the Synthesized Ligand and Metal(II) Complexes

Electronic Absorption Spectra of the Ligand and Metal Complexes

The UV-visible absorption spectra of the synthesized ligand and the metal complexes in DMSO were recorded within the range of 200 to 900 nm. The absorption wavelength and band assignments for the ligand and its metal complexes are shown in Table 5. The electronic spectrum of the free ligand shows a strong band at 198 nm assignable to π–π* transition of the aromatic ring. As a result of complexation, the absorption bands were shifted and observed to appear at 351 nm which may be assigned to n–π* transition associated with the azomethine (-C=N-) linkages for Cu(II) complex, 593 and 574 nm in the spectra of Ni(II) and Cd(II) complexes respectively may be assigned to *d-d* transitions. These spectral bands are consistent with that of a four-coordinate environment around the metal ions in the complexes. Thus, square planar geometry may be assigned for the Cu(II) complex while tetrahedral geometry has been assigned to the complexes of Ni(II) and Cd(II) ions (Sani *et al*., 2017).

Table 5: Electronic Spectra Data of the Ligand and the Metal Complexes

Compounds	λ(nm)	$\bar{\upsilon}$(cm^{-1})	Assignment	Geometry
L	198	50,505	$\pi - \pi^*$	-
[CuL_2]	351	28,490	n– π^*	Square planar
[NiL_2]	593	16,863	$d - d$	Square planar
[CdL_2]	574	17,422	$d - d$	Square planar

X-ray Diffraction (XRD) Measurement Studies of the Ligand and the Metal Complexes

The PXRD data and its analysis are given in Tables 6 and 7. The diffractogram of the ligand appeared to be distinct from those of the metal(II) complexes. This further rationalized the formation of complex compounds. This is supported by the fact that the diffractogram of the ligand showed a single peak which is associated with the 100 Miller index whereas those of the metal complexes showed multiple peaks with their Miller indices as assigned accordingly. This indicates that the ligand contains an amorphous phase while the complexes are made up of a mixture of both amorphous and crystalline phases.

Furthermore, the most prominent peaks in the thermograms of L, [NiL_2], [CuL_2], and [CdL_2] occurred at 2θ values of 46.94, 8.11, 38.00, and 33.25◦ with *d*-spacing of 1.93, 10.83, 2.37, and 2.76Å respectively. These peaks were used to estimate the average crystallite size of the synthesized complexes by employing the Debye-Scherrer formula, $D=\frac{0.9\lambda}{\beta Cos\ \theta}$ where λ is the wavelength of the X-rays used for diffraction and β is full width at half maximum (FWHM) of the peak (Sharma *et al*., 2014). Thus, the average crystallite sizes of L, [NiL_2], [CuL_2], and [CdL_2] were estimated to be 0.63, 34.75, 63.75, and 39.11 nm respectively. This observation provides evidence that the complexes were formed with relatively high crystallinity with the complex of Cu demonstrating the highest crystallinity evidenced by the appearance of five narrow and high-intensity peaks in its diffractogram. Consequently, a monoclinic Bravais lattice system is proposed for the complexes under investigation.

Some of the low-intensity peaks observed in the diffractogram have been identified to be due to ligands, which might not have reacted completely and hence remained in the sample in minute quantity. It is important to note that the average crystallite size of L is rather an outlier when compared with that of the metal (II) complexes. This further confirms the amorphous nature of the ligand.

Table 6: Some Lattice Data of the Synthesized Ligand and Metal (II) Complexes

S/N	2θ (◦)	*d*-spacing (Å)	Peak Int. (cps)	FWHM	*Hkl*
L					
1	46.94	1.93	637	13.80	100
[NiL_2]					
1	8.11	10.83	1160	0.23	101
2	15.91	5.51	199	1.87	110
3	20.09	4.43	703	0.42	111
[CuL_2]					
1	34.20	2.62	334	0.15	200
2	38.00	2.37	1876	0.13	201
[CdL_2]					
1	8.47	10.38	486	0.18	101
2	29.02	3.08	723	0.17	200
3	33.25	2.76	3682	0.21	201
4	45.73	1.98	862	0.19	211
5	56.78	1.62	2146	0.15	301

Table 7: **Some Important Lattice Parameters of the Synthesized Ligand and Metal (II) Complexes**

Sample	2θ (◦)	θ (◦)	Cos θ (◦)	FWHM (◦)	FWHM (rad)	δ (nm)	*hkl*
L	46.94	23.47	0.9173	13.8	0.2409	0.63	201
[NiL_2]	8.11	4.06	0.9974	0.23	0.0040	34.75	101
[CuL_2]	38.00	19.00	0.9455	0.13	0.0023	63.75	201
[CdL_2]	33.25	16.63	0.9582	0.21	0.0037	39.11	201

Key: FWHM = full width at half maximum, δ = Average crystallite size, *hkl* = Miller index of the most prominent peak, rad = radians

Antimicrobial Analysis

The fungi species used include *Aspergillus flavus; Aspergillus fumigatus; Aspergillus niger; Rhizopus stolonifer; Rhizoctonia bataicola* and *Candida albicans*. They were obtained and identified from the Department of Microbiology, Federal University of Agriculture, Makurdi – Nigeria.

Zones of inhibition of the synthesized complexes

The zone of inhibition of the antimicrobial agents (L, Cu^{2+}, Ni^{2+} and Cd^{2+} complexes) against the fungal species used, at 100 mg/mL, measured in millimetre is given in Table 8. This was evaluated by Agar-well diffusion technique described by Iorungwa *et al.,* (2020a). The results of the zones of inhibition recorded showed that the complexes inhibited the growth of all the fungi species (*Aspergillus flavus; Aspergillus fumigatus; Aspergillus niger; Rhizopus stolonifer; Rhizoctonia bataicola and Candida albicans*), except for the Ni complex which showed no activity against *Rhizoctonia bataicola* and the ligand complex which had no activity against *Aspergillus flavus; Aspergillus fumigates* and *Aspergillus niger* used for the study. On the other hand, the data showed that the Cu^{2+} complex gave the highest inhibition (21 mm) on the *C. albicans* strains when compared to the other synthesized complexes. The Ni^{2+} and Cd^{2+} complexes also gave good inhibition against *C. albicans* with inhibition zones of 11 and 12 mm respectively. On the *R. Stolonifer.* strain, the Cu^{2+} complex presented inhibition zone of 16 mm against 13 and 15.5 mm recorded for Ni^{2+} and Cd^{2+} complexes respectively. This result showed that the Cu^{2+} complex gave better inhibition compared to Ni^{2+} and Cd^{2+} complexes against *R. Stolonifer.* The Ni^{2+} complex had the highest inhibition zone of 16 mm against *A. niger* when compared to 13 and 13.5 mm values for the Cu^{2+} and Cd^{2+} complexes respectively. Meanwhile for the *R. Bataicola*., Cu^{2+} complex inhibited the highest with 13 mm than Cd^{2+} complex with inhibition value of 10.5 mm leaving Ni^{2+} complex with no inhibition value against the fungi strain. But for the *A. fumigates*, the Ni^{2+} complex exhibited the highest inhibition zone with 14 mm when compared to Cu^{2+} and Cd^{2+} complexes with 12.5 and 12 mm zones of inhibition respectively. While Cu^{2+} complex gave the highest zone of inhibition of 16 mm against *A. flavus* compared to Ni^{2+} and Cd^{2+} complexes with 12 and 14.5 mm respectively. In general, the standard drug (Fluconazole complex) showed the highest zone of inhibition against all the fungi strain with 23, 25, 22, 28, 20, 32.5 mm for *A. flavus, A. fumigates, A. niger, R. stolonifer, R. bataicola* and *C. albicans* respectively.

According to the data obtained, all the metal complexes showed significant activity against the fungi strain but lower when compared to the standard drug used (Fluconazole). This finding however agreed with Yiase *et al*. (2018) who reported that Mn(II) and Co(II) complexes were effective but had lower activity compared to Ciprofloxacin and Fluconazole. Meanwhile the Ni(II) complex exhibited significant activity on five out of the six fungi species while Cu(II) and Cd(II) complexes displayed wide biological activity on all the fungi; a similar work was reported by Terhemba and Aondoaver (2021).

Table 8: Zone of Inhibition (in mm) of Ligand, Standard and the Complexes (0.5 µg/mL)

Test Organisms	L	[CuL_2]	[NiL_2]	[CdL_2]	Fluconazole
A. flavus	NA	15, 17	12, 12	14, 15	23, 23
A. fumigatus	NA	13, 12	15, 13	12, 12	26, 24
A. niger	NA	12, 14	16, 16	14, 13	22, 22
R. stolonifer	8, 9	16, 16	13, 13	16, 15	27, 29
R. bataicola	11, 11	13, 13	N.A	10, 11	19, 21
C. albicans	13, 12	21, 20	10, 11	12, 12	32, 33

Keys: *A. flavus = Aspergillus flavus; Aspergillus fumigates; Aspergillus niger*; NA= No activity; L = Schiff base ligand; *R. stolonifer; R. bataicola = Rhizoctonia bataicola; C. albicans = Candida albicans*

Minimum inhibitory concentrations (MIC) of the synthesized complexes

Minimum inhibitory concentration is defined as the lowest concentration of an antimicrobial agent that can inhibit the growth of microorganisms but may or may not eliminate them. If it inhibits the growth and activities of bacteria without eliminating them, it is said to be a bacteriostatic agent. But if it inhibits the growth of fungi without eliminating them, it is said to be

fungistatic. The results of the Minimum Inhibitory Concentration (MIC) recorded for the complexes are shown on Table 9. On the *Candida albicans* and *Rhizopus stolonifer* strains, the Cu(II) complex had the lowest MIC values of 3.125 and 6.25 mg/mL while the Ni(II) and Cd(II) complexes had higher MIC values of 25.00 and 12.50 mg/mL each respectively. There is no activity recorded for the Ni(II) complex against *Rhizoctonia bataicola* strain but higher values of 25.00 and 12.50 mg/mL were seen for Cd(II) and Cu(II) complexes against the same fungi. In the case of *Aspergillus niger*, Ni(II) complex recorded the lowest MIC value of 6.25 mg/mL, while Cu(II) and Cd(II) complexes recorded higher MIC values of 12.50 mg/mL respectively. For the *Aspergillus fumigatus* strain, Cd(II) complex gave the highest MIC value of 25.00 mg/mL against it while Cu(II) and Ni(II) complexes gave lower MIC of 12.50 mg/mL respectively. Hence, on the *Aspergillus flavus strain,* Ni(II) complex recorded the highest MIC value of 25.00 mg/mL against it compared to that of Cu(II) and Cd(II) complexes with lower MIC values of 12.50 mg/mL respectively.

The MIC values indicated that all the complexes exhibited promising results compared to the ligand against mentioned microorganisms, and this activity is found to be enhanced on coordination with the metal ions. This enhancement in the activity may be rationalized on the basis that ligands mainly possess C=N bond. The enhanced activity of the complexes over the ligand can be explained on the basis of chelation theory.

Table 9: Minimum Inhibitory Concentrations (MIC) of Ligand and the Complexes (mg/mL)

Test Organisms	L	$[CuL_2]$	$[NiL_2]$	$[CdL_2]$	Fluconazole
A. flavus	NA	12.50	25.00	12.50	21.00
A. fumigatus	NA	12.50	12.50	25.00	26.00
A. niger	NA	12.50	6.25	12.50	21.00
R. stolonifer	25.00	6.25	12.50	12.50	25.00
R. bataicola	25.00	12.50	NA	25.00	33.00
C. albicans	12.50	3.125	25.00	25.00	33.50

Keys: *A. flavus = Aspergillus flavus; Aspergillus fumigates; Aspergillus niger*; NA= No activity; L = Schiff base ligand; *R. stolonifer= R. bataicola = Rhizoctonia bataicola; C. albicans= Candida albicans*

Minimum Fungicidal Concentrations (MFC) of the Synthesized Complexes

The minimum fungicidal concentration (MFC) is the lowest concentration needed to inhibit fungi strains. The minimum fungicidal concentrations (MFC) were carried out to determine the smallest concentrations of the complexes that were required to inhibit the microbes completely. The smaller the value of the MFC, the more effective the sample is against the tested strains. Table 10 shows the results of the minimum fungicidal concentrations (MFC) of the synthesized complexes. The lowest MFC was presented by the Cu complex (6.25 mg/mL) while the Cd had the highest (50.00 mg/mL). The result showed that Cu complex was far more effective against *C. albicans* than the Cd complex since the minimum concentration of the Cu complex needed to inhibit *C. albicans* was 6.25 mg/mL, which is far lower than the 50 mg/mL required by the Cd complex. The result means that the Cd and Ni complexes require higher dosage to inhibit the *C. albicans* than the Cu complex. High dose of the Cu and Cd complexes (25 and 50 mg/mL each) were needed to inhibit the *R. bataicola* while Ni complex had no effect on it. This entails the Cu complex has more fungicidal properties than the Cd and Ni complexes. All the metal complexes showed fungicidal activity when tested against *A. flavus, A. fumigatus and A. niger* while the synthesized Schiff base ligand did not show any even when tested with 50 mg/mL. The *A. flavus* were inhibited by just 25 mg/mL of Cu and Cd complexes but required high concentration of 50 mg/mL to be inhibited when Ni complex was used. *A. fumigatus were* inhibited by just 12.5 mg/mL of Cu complex but 25 and 50 mg/mL of Ni and Cd complexes were used. And for *A. niger*, only 12.5 mg/mL of Ni and Cd complexes were used but 25 mg/mL of the Cu complex was required. Of all the fungi strains, Cu complex exhibited a better fungicidal activity except for *A. flavus* and *A. fumigatus.*

In general, all the MFCs recorded showed that the Cu complex was a better antifungal agent. This result agrees with the results of the MIC values obtained. On comparing the MIC and MFC values it was observed that the MFC values were higher for almost all the microbial strains. The implication is that at the MIC values, the microbes were just fungistatic but still alive. Their growths were only inhibited but they were not eliminated. Hence, the metal complexes displayed better antifungal activity than the synthesized ligand. This also is as a result of lipophilic character of the metal compounds (Iorungwa *et al*., 2020b).

Table 10: Minimum Fungicidal Concentrations (MFC) of the Ligand and the Complexes (mg/mL)

Test Organisms	L	[CuL_2]	[NiL_2]	[CdL_2]	Fluconazole
A. flavus	NA	25.00	50.00	25.00	21.00
A. fumigatus	NA	12.50	25.00	50.00	26.00
A. niger	NA	25.00	12.50	12.50	21.00
R. stolonifer	50.00	12.50	25.00	25.00	25.00
R. bataicola	50.00	25.00	NA	50.00	33.00
C. albicans	50.00	6.25	25.00	50.00	33.50

Keys: *A. flavus = Aspergillus flavus; Aspergillus fumigates; Aspergillus niger*; NA= No activity; L = Schiff base ligand; *R. stolonifera = Rhizopus stolonifer; R. bataicola = Rhizoctonia bataicola; C. albicans = Candida albicans*

CONCLUSION

The synthesis of azomethine linkages have been studied and it is an area of research that has great potentials in new drug design. The present work describes the synthesis of a Schiff base obtained from 5-Bromosalicyaldehyde and 2-Nitroaniline and its complexes of Cu(II), Ni(II) and Cd(II). From the results of the antimicrobial analysis obtained, they showed activity against various fungi such as *A. flavus, A. fumigates, A. niger, R. stolonifer, R. bataicola* and *C. albicans*. Both the transition metal complexes of the Schiff base prepared and the Schiff base are effective inhibitors of fungal growth but the metal complexes have a broader spectrum of inhibition on activities of the fungi than the Schiff base ligands and as such it can be concluded that the newly synthesized Cu(II), Ni(II) and Cd(II) complexes showed good antifungal activity when compared to the free ligand hence, the compounds are potential antimicrobial agents. With Cu(II) complex having the highest activity followed by Cd(II) complex and then Ni(II) complex. The Cu(II) complex exhibited better activity against *Candida albicans* while Ni(II) had no activity against *Rhizoctonia bataicola*. The antibacterial strength displayed by the compounds showed they can be used as raw materials for synthesis of broad spectrum antibiotics.

REFERENCES

Abdelsalam M.M., Ali M.H., Bassem H. H., Bedair M.A., Gamal E.N and Zaghlou I.E. (2019). Green Synthesis, Spectral, Thermal Characterization and Biological Activity of Schiff base Ligand Derived from 3-amino-1,2,4-triazol and its Metal Complexes. *Organic and Medicinal Chemistry International Journal* 8(3):1-10.

Ashraf M.A, Wajid A., Mahmood K., Maah M.J. and Yusoff I. (2011) Spectral Investigation of the Activities of Amino Substituted Bases. *Journal of Chemical science*.**27**(2): 363–372.

Asiri A.M. and Khan S.A. (2010). Synthesis and anti-bacterial activities of some novel Schiff bases derived from aminophenazone. *Molecules*, **15**(10): 6850–6858.

Bhusnure G.O., Vibhute B.Y., Giram S.P.and Vibhute Y.A. (2015). Innovative Green synthesis of Schiff bases and their Antimicrobial Activity. *Journal of Pharmacy Research,* **9**(12): 670-677

Chakraborty, J., Ray, A., Pilet, G., Chastanet, G., Luneau, D., Ziessel, R. F and Charbonnière, L. (2009): Syntheses, characterisation, magnetism and photoluminescence of a homodinuclear Ln(III)-Schiff base family. *Journal of inorganic chemistry* 46:10263–10272.

Chandra S., Raizada S. and Verma R. (2012). Synthesis, Characterization and Biological Activities of Copper (II) Complexes with Semicarbazones and thiosemicarbazones, *Journal of Chemical and Pharmaceutical Research*, **4**(3): 1612 – 1618

Cleiton M. da Silva. Daniel L. da Silva , Luzia V. Modolo , Rosemeire B. Alves , Maria A. de Resende and Cleide V.B. Martins (2011): A short review of their antimicrobial activities, *Journal of Advanced Research* 2: 1–8.

Cohan Z. H., Pervez H., Rauf A., Khan K.M., Maharvi G.M. and Supuran C.T. (2004); Antibacreial and Antifungal Mono and Di substituted Symmetrical and Unsymmetrical Triazine derived from Schiff bases and their Transition Metal complexes. *Journal Enzyme inhibition Medicinal Chemistry*, **19**: 161 – 168.

Cohan Z. H., Perez H., Rauf A., Khan K. M. and Supuran C. T. (2006): Antibacterial Study of Copper(II), Cobalt(II), Nickel(II) and Zinc(II) Complexes of Mercaptothiszole derived from furanyl, thienyl, pyyrolyl, salicyl and pyridinyl Schiff bases. *Journal Enzyme Inhibition Medicinal Chemistry*, **21**: 193 – 201.

Dixit N., Mishra L., Mustafi S. M., Chary K. V. R. and Houjou H. (2009) Synthesis of a ruthenium(II) bipyridyl complex coordinated by a functionalised Schiff base ligand: Characterisation, spectroscopic and isothermal titration calorimetry measurements of M^{2+} binding and sensing (M^{2+} = Ca^{2+}, Mg^{2+}). *Journal of Chemical science* 31, (3): 374–385.

Dufera, T.E., Tafesse S. and Duraisamy R. (2019). "Synthesis and Characterization of Tin (II) and Lead (II) Complexes with Benzylidene Aniline Ligand". *International Research Journal of Science and Technology*, **1**(1): 56-65.

Fun, H.K., Kia, R., Vijesh, A.M. and Isloor A.M. (2009). 5-Diethylamino-2-[(E)-(4- methyl-3-nitrophenyl) iminomethyl]phenol: a redetermination. Acta Crystallo- graphica E: Structure Reports Online, 65:0349–0350.

Gao W. T. and Zheng, Z. (2002). "Synthetic Studies on Optically Active Schiff-base Ligands Derived from Condensation of 2-Hydroxyacetophenone and Chiral Diamines," *Molecules*, **7**(7): 511-516.

Guo Z, Xing R, Liu S, Zhong Z, Ji X, Wang L, Li P (2007). Antifungal properties of Schiff base of chitosan, Nsubstituted chitosan and quatenised chitosan. *Carbohydrate Reserch.* **342**(10):1329-1332.

Hussain Z., Yousif E., Ahmed A. and Altaie A. (2014). "Synthesis and Characterization of Schiff's Bases of Sulfamethoxazole". *Organic and Medicinal Chemistry Letters*, **4**(1): 2191-2858.

Iniama G.E., Iorkpiligh, T.I. and Essien P.B. (2018). Synthesis, Characterization, Antibacterial and Antifungal activities of Co(II), Ni(II) and Cu(II) Schiff base Complexes derived from Methionine and Salicylaldehyde. *Chemistry Research Journal*, **3**(3): 34-39.

Iorhemba, M. A., Shallangwa, G. A., Idris S.O (2018). Spectroscopic, Structural, Molar Conductivity, Magnetic and Antibacterial Activity Studies of Co(II) and Ni(II) Complexes of L-methionine and L-leucine. *Federal University Wukari Trends in Science and Technology Journal,* 3(1):109 – 116

Iorungwa M. S., Ogara J. I., Wuana R. A. and Iorungwa P. D. (2019). Synthesis, spectral characterization of selected Schiff base transition metal complexes, and their biocidal activities: a review of green methods. *Ewemen Journal of Synthetic Organic Chemistry.* **3**: 17–25.

Iorungwa, M. S., Abuh, H., Wuana, R. A., Iorungwa P .D. and Surma N. (2020a). Synthesis, Characterization, Kinetics, Thermodynamics and Antimicrobial Studies of Carbonatotetraamine Complexes of Nd(III), Sm(III) and Gd(III) Nitrates. *FUW Trends in Science and Technology Journal,* **5**(1): 141–148.

Iorungwa, M. S., Wuana, A. R., Tyagher, L., Agbendeh, Z.M., Iorungwa, P.D., Surma, N. And Amua, Q.M. (2020b). Synthesis, Characterization, Kinetics, Thermodynamics and Nematicidal Studies of Sm(III), Gd(III) and Nd(III) Schiff Base Complexes. *ChemSearch Journal, Chemical Society of Nigeria Kano Chapter*, **11**(2): 24 – 34.

Kabeer A. S., Baseer M. and Mote N. (2001). Synthesis and Antimicrobial Activity of some Schiff bases from Benzothiazole, *Asian Journal of Chemistry*, **13**:496 – 500

Khan K. M., Ahmed A., Ambeeen N., Amyn A., Perveen S., Khan S. A., Choudhary M. I. (2009): Schiff bases of 3-formylchromones as Antibacterial, Antifungal and Phytotoxic agents, *Letter Drug Design and Discipline*, **6**:363 – 373.

Lee, J. D. (1996): Concise Inorganic Chemistry. Blackwell Science Ltd, France(5th ed) Pp. 194- 236.

Ogunniran K. O., Ajanaku K. O., James O. O., Ajani O. O., Nwinyi C. O., Allensela M. A. (2008). Fe (III) and Co (II) Complexes of Mixed Antibiotics: Synthesis, Characterization Antimicrobial Potential and their effect on Alkaline Phosphatase Activities of Selected Rat Tissues. *International Journal of Physical Science*, **3**(8): 177-182.

Sani U. and Dailami S. A. (2015). Synthesis, Characterization, Antimicrobial Activity and Antioxidant Studies of Metal (II) Complexes of Schiff Base Derived from 2–Hydroxy–1-Naphthaldehyde and Hydrazine Monohydrate. *ChemSearch Journal Chemical Society of Nigeria, Kano Chapter*, **6**(2): 35 – 41.

Sani, U., Na'ibi, H. U. and Dailami, S. A. (2017). In vitro antimicrobial and antioxidant studies on N-(2-hydroxylbenzylidene) pyridine-2-amine and its M (II) complexes. *Nigerian Journal of Basic and Applied Sciences*, *25*(1), 81-88.

Sharma K. K. and Sharma L. K., (1999). A Textbook of Physical chemistry, 4th Reviewed Edition, Vikas Publishing House, PVT Limited India, **160**: 165-167.

Solmaz R., Altunbas E. and Kardas G. (2011). Adsorption and Corrosion Inhibition Effects of 2-((5mercapto-1,3,4-thiadiazol-2-ylimino)methyl) phenol Schiff base on mild steel, *Meter. Chem. Phys.* **125**: 796–801.

Tarafder M., Kasbollah A., Saravanan N., Crouse K. A. and Ali A. M. (2002): Smethyldithiocarbazate and its Schiff bases: Evaluation of bondings and thiszole Schiff bases, *Bioorganic Medicinal Chemistry*, **6:** 85 – 91.

Terhemba, S. I. and Aondoaver, J. G. (2021). Chelation Effect of 2, 4-pentadione with Ni (II) and Cu (II) Ions. *Chemistry Research Journal*, 6(2): 48-57.

Vicini P., Geronikaki A., Incerti M., Busonera B., Poni G.m Cabras C. A. and La Colla P. (2003). Synthesis and biological Evaluation of Benzo[d]isothiazole, benzothiazole and thiazole Schiff bases, *Bioorganic Medicinal Chemistry*, **11**: 4785 – 4789.

Yiase, S. G., Adejo, S. O. and Iningev, S. T. (2018).Manganese (II) and cobalt (II) acetylacetonates as antimicrobial agents. *Nigerian Annals of Pure and Applied Sciences*,1: 176-185.

Zoubi W. A. (2013). Biological Activities of Schiff Bases and Their Complexes: Review of Recent Works. *International Journal of Organic Chemistry*, **2013**(3): 73-95.