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SYNTHESIS, GRAVIMETRIC ANALYSIS AND ANTIMICROBIAL STUDIES OF TRANSITION METALS (Cu(II), Zn(II)) COMPLEXES OF SCHIFF DERIVED FROM 2-HYDROXY-1-NAPHTHALDEHYDE AND 2-AMINO-3-METHYLPYRIDINE

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ABSTRACT

The interaction between 2-hydroxy-1-naphthaldehyde with 2-amino-3-methylpyridine give an orange- yellow Schiff base and its metals complexes of Cu (II) and Zn (II) were green and dark-green respectively, both Schiff base and metals complexes were characterized using different analytical techniques such as melting point, solubility test, conductivity, measurement, magnetic susceptibility measurement, IR spectroscopy and TGA. The Schiff base and its respective metal complexes showed a sharp melting point and are soluble in ethanol, dimethylsulfuroxide and methanol but insoluble in water and slightly soluble in other solvent. The conductivity value obtained revealed that the synthesized complexes are non-electrolytes while an octahedral geometry was suggested for all complexes based on the data obtained from magnetic susceptibility analysis. The IR results revealed bands at 1596 cm^{-1} indicating the formation of azomethine (C=N) confirming the formation of Schiff base. 747 cm^{-1}, 773 cm^{-1}, for (M-N) while 465 cm^{-1}, 469 cm^{-1} for (M-O) bands in the spectra of the complexes supporting coordination of Schiff base to respective metals. The thermo-gram (TGA) data of all complexes, exhibited three stages of decomposition which include loss of water, decomposition of the complexes and the formation of metal (II) oxide as the final product/residue. The in vitro antimicrobial screening of Schiff base and its metals complexes showed that they are potent antimicrobial agents against the tested microorganisms.

Keywords: synthesis, gravimetry, antimicrobial, activities, transition metals

INTRODUCTION

Metal ions play many critical functions in humans. Deficiency of some metal ions can lead to diseases like pernicious anemia resulting from iron deficiency, growth retardation arising from insufficient dietary zinc, and heart disease in infants owing to copper deficiency. The ability to understand at the molecular level and to treat diseases caused by inadequate metal-ion function constitutes an important aspect of medicinal bioinorganic chemistry. Metal ions are required in biology for their role as pharmaceuticals as well as diagnostic agents. Metals are endowed with unique characteristics that include redox activity, variable coordination modes, and reactivity towards organic substrates. Due to their reactivity, metals are tightly regulated under normal conditions and aberrant metal ion concentrations are associated with various pathological disorders, including cancer. For these reasons, coordination complexes, either as drugs or pro-drugs, become very attractive probes in medicinal chemistry. In nature, many biological systems make extensive use of metal ions, such as zinc and copper, which play critical roles in the normal functioning of organisms (Orvig and Abrama, 1999). Transition metals such as copper, iron, and manganese, among others, are involved in multiple biological processes, from electron transfer to catalysis to structural roles, and are frequently associated with active sites of proteins and enzymes (Orvig and Abrama, 1999).

Schiff bases are compounds formed by condensation of a primary amine with a carbonyl compound and it was first discovered by German chemist Hugo Schiff in 1864 (Ashraf *et al.,* 2011). Schiff bases with aryl substituents are substantially more stable and readily synthesized, while those with alkyl substituents are relatively unstable. Schiff bases of aliphatic aldehydes are relatively unstable and readily polymerisable (Hine and Yeh 1986), while those of aromatic aldehydes having effective conjugation are more stable (Kumar *et al.,* 2013). In general, aldehydes react faster than ketones in condensation reactions, leading to the formation of Schiff bases as the reaction Centre of aldehydes is sterically less hindered than that of the ketone. Furthermore, the extra carbon of ketone donates electron density to the azomethine carbon and thus makes the ketone less electrophilic compared to aldehydes (Fessenden 1998). Schiff bases are ligands capable of forming very stable complexes with transition metal and could be bidentate, tridentate or polydentate ligands depending on the number of donor sites they contain.(Arulmurugan *et al.*, 2010).

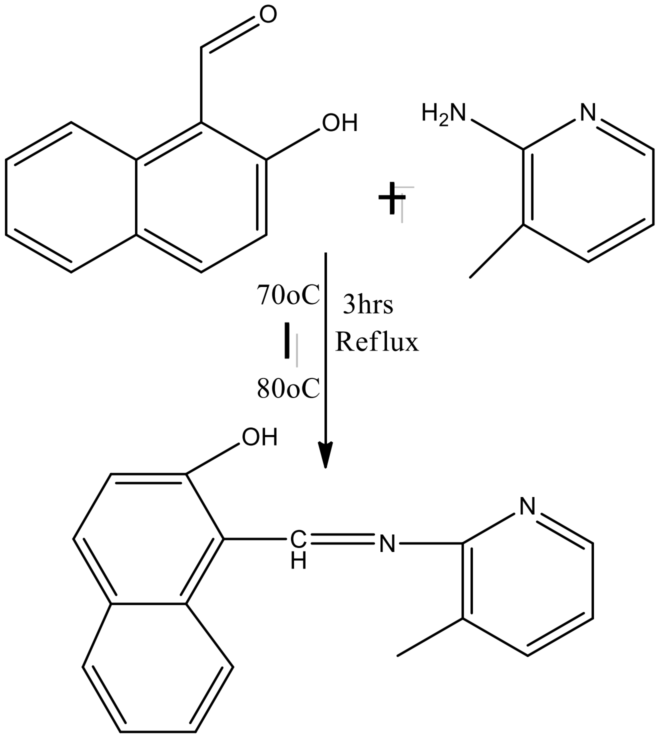
Schiff base complexes have broad applications in the biological field including enzyme inhibitors, antitumor, antioxidant, anticancer activity, antimalarial, antibacterial, anticonvulsant and ant proliferative (Patil *et al*. 2017). They are also used in the treatment of diabetes and AIDS. As biological models, they help in understanding the structure of biomolecules and biological processes occurring in living organisms. They participate, interact, in photosynthesis and oxygen transport in organisms. They are involved in the treatment of cancer drug resistance, and are often tested as antimalarial. It also could be used for the immobilization of enzymes (Boghaei *et al*., 2008). Schiff base complexes is one of the compounds reported to possess remarkable antibacterial, antifungal, anticancer and antimalarial activities (Annapoorani and Krishnan, 2013).

MATERIALS AND METHODS

All reagents and solvents used for this research were of analytical grade and were purchased from Sigma Aldrich and Merck and were used without further purification the melting point was recorded on the hot stage Gallen kamp melting point apparatus. the infrared spectra were recorded using Agilent carry 630 FTIR spectrometer in the frequency range of 400-4000 cm^{-1}. The magnetic susceptibility was obtained at room temperature using magnetic susceptibility balance MK1 Sherwood. Conductivity measurement was carried out using Jan way conductivity meter 401

Synthesis of Schiff Base

Exactly 0.03 mol (5.1654 g) of 2-hydroxy-1-naphthaldehyde was mixed with 0.03 mol (3.023 ml) of 2-amino-3-methylpyridine in 50 cm^3 of ethanol. The mixture was heated under reflux at 70°C-80°C for 3hours and the solid product formed was separated by filtration, purified by recrystallization from ethanol, washed with ethanol, and then dried in desiccators over calcium chloride $cacl_2$ for 18 hrs. (Sani and Iliyasu 2018).



Synthesis of Copper (II) Complexes

An aqueous solution of a hydrated copper (II) chloride (0.01 mol, 1.7048 g) in 10 cm^3 ethanol was added to an ethanolic solution of the prepared Schiff base ligand (0.02 mol, 5.241 g) the mixture was refluxed at 70°C-80°C for 2 hrs. The precipitated complex formed was separated by filtration recrystallized and washed with ethanol and dried in a desiccator over calcium chloride ($cacl_2$) for 18 hrs. The same procedure was repeated for the synthesis of Zn (II) chloride (Ashraf et al., 2011).

Antibacterial and Antifungal screening

The sterilized (Gillespie, 1994) (autoclaved at 121°C for 15 min) medium was inoculated with the suspension of ($5x10^{-5}$ cfu/ml) of the microorganism (matched to McFarland turbidity standard) and poured into a Petridish to give a depth of 3–4 mm. Three wells was made containing different concentrations of (100, 200 and 300 ppm in dimethylsulfuroxide) of both Schiff base and its metal (II) complexes.The plates was pre-incubated for 1 hr at room temperature and incubated at 37°C for 24 and 48 hrs for antibacterial and antifungal activities, respectively. ciproflaxacin (500 mg) and ketoconazole (200 mg) were used as standard. After the incubation period, the plates wasobserved for zones of inhibition in (mm) (Govindaraj *et al.*, 2015)

Determination of Minimum Inhibitory Concentration (MIC)

The concentration of Schiff base and its metal(II) complexes(1000 ppm) was diluted using double-fold serial dilution by transferring 1ml of the Schiff base and metal(II) complexes each (stock solution) into 1ml of sterile nutrient agar to obtain 500 ppm concentration the above process was repeated to obtain other dilution ; 100, 200, 300 ppm. Having obtained different concentrations, Suspension of the microorganism was prepared to contain approximately ($5x10^{-5}$cfu/ml and incubation was done at 37°C for 24 hrs. The positive control was Muller Hinton ager with standard reference antibiotic ciproflaxacin for bacteria and (ketoconazole) for fungal with inoculums and negative control was Muller Hinton broth with inoculum as described by (Kuete et al., 2008). After 24 hrs of incubation at 37°C for the bacterial and 72 hrs of incubation for the fungal, the tubes use observed for turbidity. The least concentration where no turbidity was observed and noted as MIC value or the least concentration that inhibits the growth of bacteria/fungal (Ogbonnia *et al.*, 2008)

RESULT AND DISCUSSION

Table 1: Physical Properties and Analytical Data of Schiff Base and its Metal (II) Complexes

Compound	Color	Melting point	Decomposition Temperature (^{O}C)	Percentage Yield
Ligand	Orange yellow	188		76
$[CuL_2Cl_2]$	Green		267	70
$[ZnL_2Cl_2]$	Dark green		269	71

L= Ligand, $C_{17}H_{14}N_2O$

Physical Data of Schiff Base and metals Complexes

The interaction between 2-hydroxy-1-naphthaldehyde and 2-amino-3-methylpyridine gives an orange-yellow Schiff base and its metal complexes of Cu (II) Zn (II) appeared to be green and dark green respectively. This is typical for transition metal complexes due to d-d electrons transition as reported by Oladipo *et al.,* (2005). The purity and stability of the Schiff base and metal complexes are established by the observance of sharp melting/decomposition temperature and for Schiff base and metal complexes were 188 ºC, 267 ºC, and 269 ºC respectively. The complexes showed a steady trend of higher melting points than the ligand which may be due to the intermolecular bonding as a result of metallic lattice and increase in molecular weight as reported by Ogunniran *et al.,*(2008). The consistent range difference of +2 ºC melting points observed indicates that the synthesized compounds are presumed pure (Putaya *et al.,* 2020). An appreciable percentage yield of all new compounds was obtained which range from 71% to 76%. The ligands and their metal (II) complexes were observed to be non-hygroscopic solids, air and photo stable under normal conditions. These findings agreed with that of Aliyu and Sani (2011).

Table 2: Solubility of Schiff Base and Its Metal (II) Complexes

Compound	**Water H_2O**	**Ethanol CH_3CH_2OH**	**Methanol CH_3OH**	**DMSO $(CH_3)_2SO$**	**Chloroform $CHCl_3$**	**Acetone $CH3COCH3$**
Ligand	IS	S	S	S	SS	SS
$[CuL_2Cl_2]$	IS	S	S	S	SS	SS
$[ZnL_2Cl_2]$	IS	S	S	S	SS	SS

Key S = soluble SS = sparingly soluble IS = Insoluble

Solubility of a compound in various solvents depends on the nature of the compound, type of bonding and solvent (Satya *et al.,* 2006) The solubility test was carried out in methanol, ethanol dimethylsulphoxide, water, chloroform and acetone both the Schiff base and metals complexes were found to be soluble in some solvent such as dimethylsulfuroxide, methanol and ethanol. This is because polar solvents dissolve polar compounds due to similar attractive force between them. This finding is similar to that of Sani and Siraj (2020). However, they are slightly soluble in acetone and chloroform because many non-polar solvents can dissolve compounds containing oxygen atoms which is used in forming a bond with polar hydrogen of the carbon-hydrogen in the solvent as reported by Satya *et al.,* (2006).Both Schiff base and complexes are insoluble in water which is similar to the report of Aliyu and Ado (2011).

Table 3. Magnetic Susceptibility of Metal (II) Complexes

Compound	Magnetic susceptibility (cm^3 g^{-1})	molar magnetic susceptibility (cm^3 mol^{-1})	B.M(μ_{eff})	Magnetism
$[CuL_2Cl_2]$	21.63×10^{-7}	15.702×10^{-6m}	1.93	Paramagnetic
$[ZnL_2Cl_2]$	-2.81×10^{-7}	-	-	Diamagnetic

L= Ligand, $C_{17}H_{14}N_2O$

Magnetic Susceptibility Result

Magnetic susceptibility measurement carried out at room temperature showed that the effective magnetic moment of the complexes as determined from the magnetic susceptibility balance were found to be 1.93BM for Cu (II) Which suggests a high spin complex and is paramagnetic (Imran *et al.,* 2010). But Zn showed diamagnetism which may attribute to the d^{10} configuration of the metal. All the magnetic moment values of the metal (II) complexes prepared were found within the range of octahedral complexes as reported by Figgis *et al.,* (1960).

Table 4: The Infrared Spectral Data of Schiff Base and Its Metal (II) Complexes

Compound	**v(OH) cm^{-1}**	**v(C-O) cm^{-1}**	**v(C=N)cm^{-1}**	**v(M-N)cm^{-1}**	**v(M-O)cm^{-1}**
Ligand	3365	1149	1596		
$[CuL_2Cl_2]$	3048	1134	1622	747	
$[ZnL_2Cl_2]$	3257	1186	1618	773	

L= Ligand, $C_{17}H_{14}N_2O$

IR Analysis

The IR analysis carried out for Schiff base showed an absorption band at 3365 cm^{-1} which could be attributed to *V*(O-H) vibration frequency. This is a consequence of strong intramolecular hydrogen bonding between the hydroxyl proton and the imine nitrogen (OH…NH).The presence of the hydroxyl group was further substantiated with the appearance of the phenolic C–O stretch band at 1196 cm^{-1}which is similar to that of Sabola *et al., (*2020). The band shifted to a different frequencies of 3048 cm^{-1}, and 3257 cm^{-1} for Cu (II) and Zn (II) Complexes respectively. However, the weak OH band of the Schiff base ligands was still evident in the spectra of most of the complexes, undergoing a blue or red shift upon chelation with the metal (II) ions. This indicates that the phenolic OH was not deprotonated in the metal complexes but rather coordinates as neutral species(Sabola *et al.,* 2020).The band at 1596 cm^{-1} could be due to v(C=N) (Jamuna *et al.,* 2011) On complexation with metal (II) ions the v(C=N) band shifted to a higher frequencies (Putaya *et al.,* 2020) at the following regions; 1622 cm^{-1} and 1618 cm^{-1}respectively, indicating coordination of the Schiff base ligands *via* the imine nitrogen (Sabry *et al.*, 2016). The coordination of the Schiff base ligands to the metal (II) ions was further substantiated by the appearance of new bands in the far-infrared spectra of the complexes at (747 cm^{-1} and 773 cm^{-1}) which were absent in the spectra of Schiff base ligand and could be assigned to *v*(M-N) similarly the bands at (465 cm^{-1} and 449 cm^{-1}) could be due to v(M-O) stretching frequencies (Bharat *et al.*, 2015).

Table 5: **Conductivity Measurement of Complexes In DMSO Solution (1x10 ^{3}moldm^{-3})**

Compound	Concentration (mol^{-1} dm^{-3})	Specific conductance Ohm^{-1}cm^{-1}	Molar conductance Ohm^{-1}cm^{2} mol^{-1}
[CuL_2Cl_2]	**1 x 10^{-3}**	**8.23x10^{-6}**	**8.23**
[ZnL_2Cl_2]	**1 x 10^{-3}**	**5.52x10^{-6}**	**5.52**

L= Ligand, $C_{17}H_{14}N_2O$

Conductivity Data

Electrolytic conductivity is the measure of the mobility of ions present in the solution. The ionic mobility in turn depends on the charge and size of metal ions and interaction with a solvent molecules. When a metal ion forms a complex with solvent molecules or some ligands, the conductivity is reduced (David *et al.*, 1999). In this study the electrical conductivity of divalent metal ions (M^{+2}) in 10^{-3}M DMSO solution was studied. It is observed that the molar conductance value of Cu (II) and Zn (II) complexes determined in 10^{-3}M DMSO solution at room temperature are (8.23 and 5.52 Ohm^{-1}cm^{2} mol^{-1}) their molar conductance values are low which suggest a non-electrolytic nature (Sabola *et al.*, 2020), It could also because the metal (II) ions form stable complex with DMSO solution, and therefore mobility and conductance of these metal (II) complexes is lowered(David *et al.*, 1999). Thus it has been established that ionization is an important factor in the activity of synthetic drugs (Lewis, 1954).

Table 6; Thermo gravimetric data of the thermal decomposition of Schiff base complexes

Compound	Steps	T_1-T_2(°C)	Mass %	Assignment
[CuL2Cl2]	**1st**	**47-130**	**3.05 (2.8)**	**Water**
	2nd	**268-400**	**96.9 (94.2)**	**Ligand**
	3nd	**Residue**	**13.5 (12.4)**	**CuO**
[ZnL2Cl2]	**1st**	**50-120**	**3.05 (2.6)**	**Water**
	2nd	**270-450**	**96.9 (91.3)**	**Ligand**
	3nd	**Residue**	**13.78 (15.3)**	**ZnO**

L= Ligand, $C_{17}H_{14}N_2O$

TGA Result

The thermo-gram (TGA) data of the complexes, exhibited three stages of decomposition. The TGA curve for Cu-complex showed a total weight loss of (2.8% found, 3.05% cal) at the temperature range of (50-130°C) which is assigned to water loss and for the second step the complex decomposed at the temperature range of (265-380°C) with a weight loss of (94.2% found, 96.9 cal.). While the third step involves the formation of CuO as the final product with weight loss of (12.4% found, 13.5% cal.).The TGA curve of the Zn (II) complex showed three- stage of decomposition with weight loss of (2.6% found 3.05% cal.) assign to the loss of water and (91.3% found 96.9% cal) for complex decomposition and the formation of ZnO with the weight loss of (15.3% found 13.78%cal.) as the final product or residue. All the values obtained are in good agreement with the theoretical values and are similar to that of Abdelsalam *et al., (2019).*

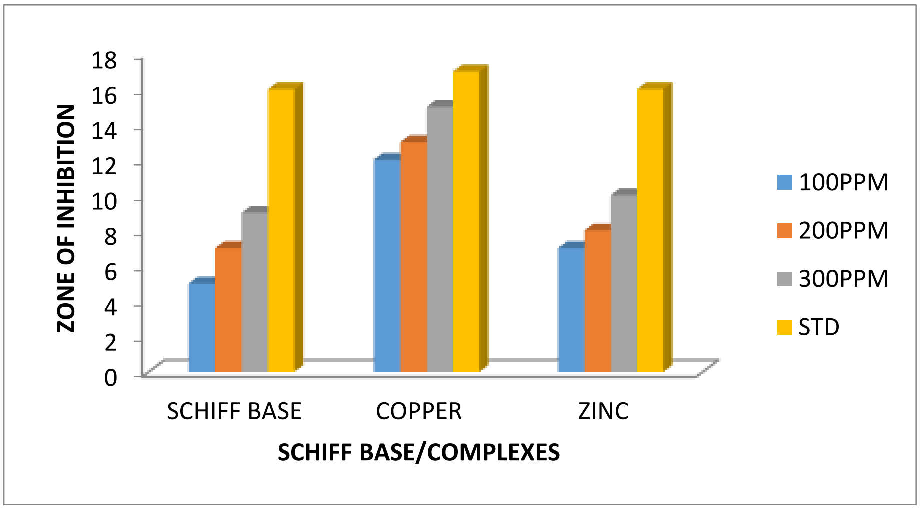


Figure 1: Sensitivity test for antibacterial activity of Schiff base and its Metal (II) Complexes against clinical isolate (*Staphylococcus.aureus*) using Well diffusion method

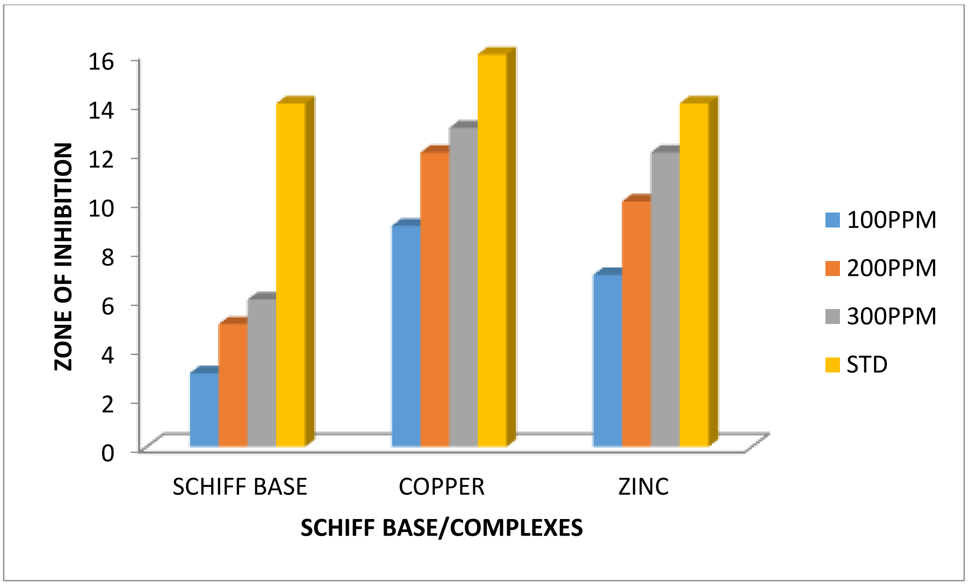


Figure 2: Sensitivity test for antibacterial activity of Schiff base and its Metal (II) Complexes against clinical isolate (*Escherichia Coli)* using Well diffusion method

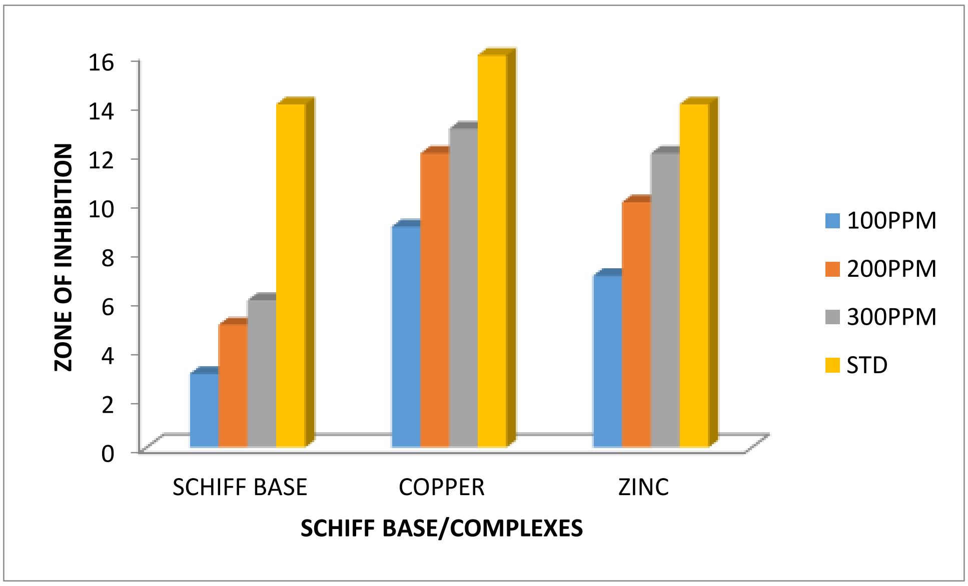


Figure 3: Sensitivity test for antibacterial activity of Schiff base and its Metal (II) Complexes against clinical isolate (*Streptococcus pneumoniae)* using Well diffusion method.

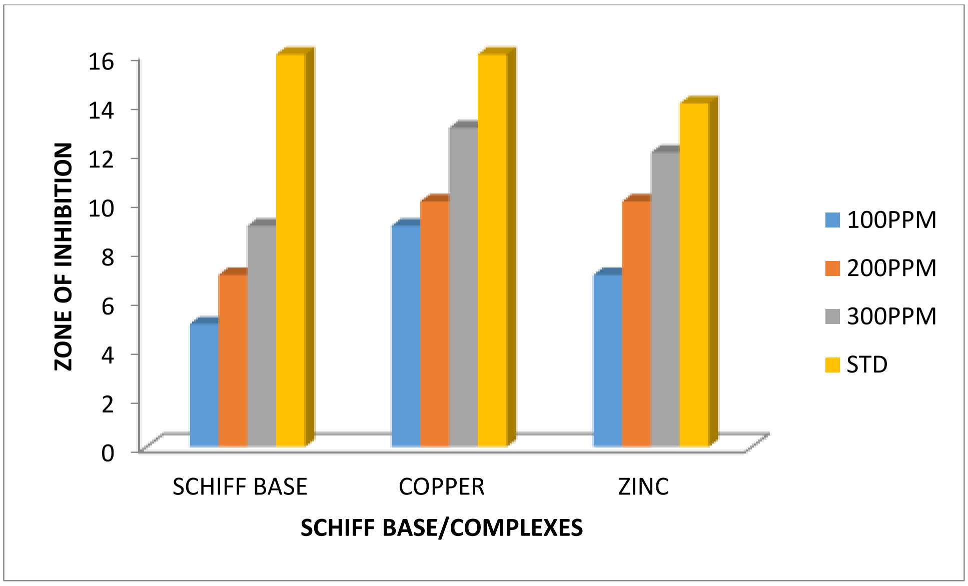


Figure 4: Sensitivity test for antibacterial activity of Schiff base and its Metal (II) Complexes against clinical isolate (*Klebsillapneumoniae)* using Well diffusion method.

Table 7. Minimum Inhibitory Concentration (MIC) of Schiff base ligand and its metal complexes

compound	Clinical isolate	concentration			
	S, aureus	50ppm	100ppm	150ppm	200ppm
Ligand		-	-	-	+
[CuL_2Cl_2]		-	+	+	+
[ZnL_2Cl_2]		-	+	+	+

L= Ligand, $C_{17}H_{14}N_2O$

Table 8. Minimum Inhibitory Concentration (MIC) of Schiff base ligand and its metal complexes

Compound	Clinical isolate	concentration			
	E, Coli	50ppm	100ppm	150ppm	200ppm
Ligand		-	-	-	+
[CuL_2Cl_2]		-	+	+	+
[ZnL_2Cl_2]		-	+	+	+

L= Ligand, $C_{17}H_{14}N_2O$

Table 9. Minimum Inhibitory Concentration (MIC) of Schiff base ligand and its metal complexes

compound	Clinical isolate	concentration			
	S,pneumoniae	50ppm	100ppm	150ppm	200ppm
Ligand		-	-	-	+
[CuL_2Cl_2]		-	+	+	+
[ZnL_2Cl_2]		-	+	+	+

L= Ligand, $C_{17}H_{14}N_2O$

Table 10. Minimum Inhibitory Concentration (MIC) of Schiff base ligand and its metal complexes

compound	Clinical isolate	concentration			
	K,pneumoniae	50ppm	100ppm	150ppm	200ppm
Ligand		-	-	-	+
[CuL_2Cl_2]		-	+	+	+
[ZnL_2Cl_2]		-	+	+	+

L= Ligand, $C_{17}H_{14}N_2O$

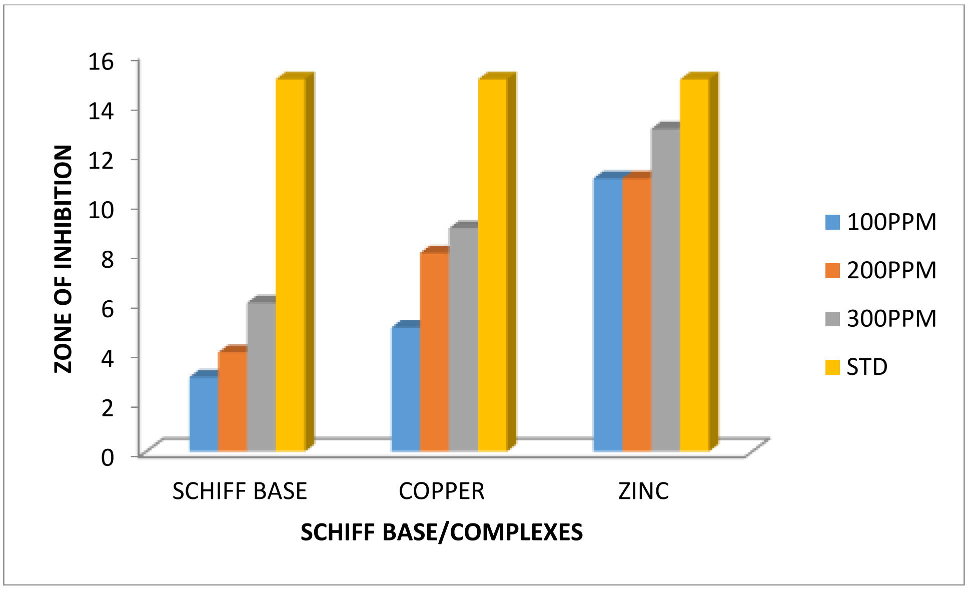


Figure 5: Sensitivity test for antifungal activity of Schiff base and its Metal (II) Complexes against clinical isolate (*Aspergillusniger*) using Well diffusion method.

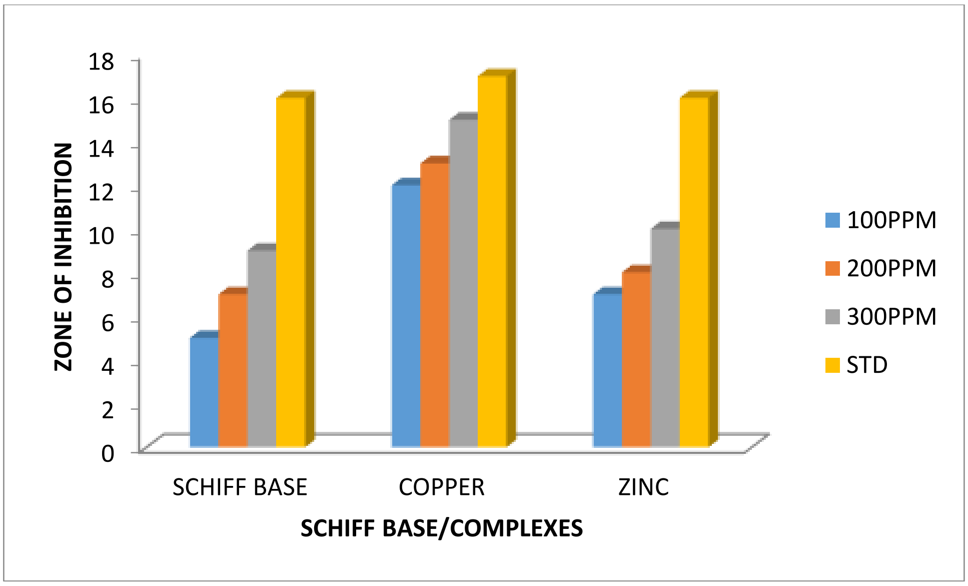


Figure 6: Sensitivity test for antifungal activity of Schiff base and its Metal (II) Complexes against clinical isolate (*Candida albican)* using Well diffusion method.

Antimicrobial Result

The Schiff base ligand and the metals (II) complexes were screened for their *in vitro* antimicrobial activity at different concentrations of 100 ppm, 200 ppm and 300 ppm against bacterial isolates (*Staphylococcus aureus*, *Escherichia coli*, *Streptococcus pneumonia, and Klebsiella pneumoniae*) using Ciprofloxacin (500 mg) as control. The Schiff base shows significant activity against tested organisms at all concentrations with inhibitory zone ranging 3 mm to 8mm but the activity is higher in *Staphylococcus aureus* with the inhibitory zone of 5mm-8mm as compared to that of *Escherichia coli*, *Streptococcus pneumonia, and Klebsiella pneumoniae with inhibitory zone ranging from 3mm-6mm.* The metal complexes on the other hand showed higher activities compared to the Schiff base ligand because of chelation and π-electron delocalization, which increase the lipophilic character, favoring its permeation into the bacterial membrane, causing the death of the organisms (Agwara *et al*., 2010). The activities of both Schiff base and its metal (II) complexes increase as the concentration increases (Sani *and Illiyasu, 2018*) As shown in figures 1- 4. It was also revealed that the copper complex showed higher activity as compared to Zinc complex. This finding collaborates with that of Kowol *et al.,(2009*) which reported that the effect of metal ions on the biological activity of a given bio-active compound is metal-specific. Both the complexes are less active than control (Sani *and Illiyasu, 2018*). The study also revealed that the minimum inhibitory concentration for (*Staphylococcus aureus, Escherichia coli, Streptococcus pneumonia, and*

Klebsiella pneumoniae) of Schiff base and metal complexes was found to be 200 ppm, 100 ppm, 150 ppm and 200 ppm respectively as shown in Table 7-10. The minimum inhibitory concentration of metal (II) complexes is higher than that of the Schiff base ligand. The increasing activity of the metal complexes against the Schiff base ligand could be explained based on oxidation state, overtone concept and chelation theory (Osowole *et al*., 2008) which reduces polarity of the metal ion by partial sharing of the positive charge with donor atoms of the ligand (imine & oxygen). This atomic shake-up increases the lipophilic character, favouring the permeation through lipid layers of the bacterial membrane and consequently restricting further growth of the organism (Obalaye et al., 2011).

The antifungal activity of the Schiff base and its metal (II) complexes as carried out against fungal isolates (*Aspergillusniger and Candida albicans)* using Ketoconazole (200 mg) as control, The results of the findings revealed that metals (II) Complexes have higher activity compared to Schiff base with the inhibitory zone of 6 mm-14 mm and 5 mm-8 mm metal complex to Schiff base respectively. The better activities of the metal complexes are attributed to the metal ions, since the metal-free ligand has low antifungal activity (Lawal *et al.,* 2014).The activity of metal complexes differs from metal to metal with the zinc having the higher activity of 10 mm-13 mm as compared with copper with the inhibition zone 5 mm-8 mm for *Aspergillus niger* while for *Candida albicans* copper showed higher of 11 mm-14 mm as compared with the Zinc with inhibitory zone of 6mm-9mm as shown in figures 5-6. This could because the chelation of free ligands with metals ions selectively enhanced the biological activity of the compound (Osowole *et al.,* 2008). The activity increases with an increase in the concentration of both Schiff base ligand and metal (II) complexes (Sani *and Illiyasu, 2018*). The activity of both Schiff base and metal (II) complexes at all concentrations is less than that of control with the inhibitory zone of 17 mm.

CONCLUSION

The Schiff base and it is metal (II) complexes were synthesized, characterized and tested for their antimicrobial activity. The Schiff base was found to be a bidentate ligand with a sharp melting point and octahedral geometry was suggested for both two complexes. Thermo-gram data showed a three-stage of decomposition , loss of water, decomposition of the complexes and formation of metal oxide as the final product. Both the Schiff base and complexes were found to be active against the tested microorganism and could be used as potential antimicrobial agents.

REFERENCES

Agwara, M. O., Ndifon, P. I., Ndosiri, N. B., Paboudam, A. G., Yufanyi, D. M. and Mohamadou, A., (2010) Synthesis, characterization and antimicrobial activities of Co(II), Cu(II) and Zn(II) mixed – Ligand complexes containing 1,10-phe nanthroline and 2, 2’- bipyridine,”Bulletin of the Chemical Society of Ethiopia. 24 (3) 383-389.

Abdelsalam, M.M, Ali M.H., Bassem, H. H., Bader, M.A., Gamal, A., and Zaghloul I.E (2019):Green Synthesis, Spectral, thermal characterization and biological activities of Schiff base ligand derived from 3-amino-1,2,4-triazol and its metals complexes:Organic and Medicinal Chem IJ 8(3)

Aliyu H.N, Ado. I (2011): Synthesis, of Mn(II) and Ni(II) complexe with schiff base derived from 2-aminobenzoic acid and salicyldehyde: Biokemistri vol. 23 no. 1

Aliyu, H.N. and Sani, U., (2011). Synthesis, Physicochemical Characterization and Microbial Activity of N, N’ Bis (2 – hydroxyl – 1-Naphthalyl) propylenediiminato Metal (II) Complexes. *Journal of Asian scientific research*. **1**(8) Pp.399-406

Ashraf M. A., Mahmood K., Wajid A. (2011); Synthesis, Characterization and Biological Activity of Schiff Bases IPCBEE, 10 PP 1-7

Arulmurugan a., Halen P., Venkatraman B. R.(2010) Biological application of schiff and
Its complexes: A review Rasayan journal of chemistry 3(3) Pp385-410

Annapoorani, S., and Krishnan, C.,(2013). Synthesis and spectroscopic studies of trinuclear N_4 Schiff base complexes international. *Journal of Chemical and Technology Research*.**5** (1), 180–185.

Bharat, A M, Pratik, N. D and Pratik, B. T (2015). Synthesis of Schiff base and their transition metal complexes, characterization and application. *International Journal of Science,Technology and Management,* 04(1): 642-652.

Boghaei D. M., Askarizadeh E. and Bezaatpou, A., (2008). *Molecular and BiomolecularSpectroscopy*. Spectrochim. *Acta Part A*, **69**, 624–628.

David T. S., Balakumar S. and suganthi, S., (1999). Effect of Complexation on the ions mobility of some 3-d metal ions. *International journal of apply chemistry* 12:38-49

Fessenden R.J. and Fessenden, J.S.(1998**)**. Organic Chemistry, Brooks/Cole Publishing Company, USA,

Figgis, B. N.; Lewis, J. In Lewis, J., Wilkins, R. G Eds. (1960). Modern coordi nationchemsitry, *Interscience Publishers Inc.: New york*. pp400 - 454

Govindaraj,S., Veerachamy, A.,andChinnasamy R.P.,(2015).Synthesis, characterization and in vitro antimicrobial activity of some 1-(substitutedbenzylidene)-4-(4-(2-(methyl/phenyl)-4-oxoquinazolin-3(4H)-yl)phenyl)semicarbazide Derivatives. *Journal of Saudi Chemical Society*19, 3–11

Hine 1.J. and Yeh, C.Y. Journal of American Chemical Society 89 (1967) 2669

Imran, M, Liviu M, Shoomaila, L, Zaid, M, Imtiaz, N, Sana, S. Z and Surrya, F (2010). Antibacterial Co(II), Ni(II), Cu(II) and Zn(II) Complexes with Biacetyl-Derived Schiff Bases. *Journal ofSerbian Chemical Society*, 75(8):1075–1084.

Jamuna, K, Harikishore, D, Reddy K, Naresh, B K, Venakata, D K R and Seshaiah, K (2011). Synthesis, Characterization and Biological Activity of Cu(II) and Ni(II) Complexes of 3-Hydroxy-4-(Pyridine-2-yl-Methylene Amino)benzoic Acid. *Oriental Journal of Chemistry*, 27(3):1141-1147.

Kowol, C. R. R. Trondl, P. Heffeter, V. B. Arion, M. A. Jakupec, A. Roller, M. Galanski,
W. Berger, B. K. Keppler, *J. Med. Chem.* 52 (2009) 5032.

Kuete, V, Mbaveng, A. T., Tsaffack. M., Beng, V. P., Etoa, F. X., Nkengfack, A, E., Meyer, J.J and Lall, N., (2008). Antitumour, Antioxidant and Antimicrobial Activities of BersamaEngeleriana (Melianthaceae).Journal of Ethnophamacology 15:494-501

Kumar, N, Pratima, S, Aastha, P and Prasad, AVGS (2013). Synthesis and characterization of some new shiff bases. *International Journal ofChemical and Pharmaceutical Sciences* 23(2):231-236.

Lawal, A., Obaleye, J.A., Adediji, J.F., Amolegbe S.A., Bamigboye, M.O., Yunus- Issa, Mt., (2014). Synthesis, Characterization and Antimicrobial Activities of Some Nicotinamide – metal Complexes, *Journal of Applied Science and Enviromental Managemen*t 18 (2): 205-208

Lewis G.P., (1954). The Importance of Ionization In The Activity of Sympathomimetic Amines. British Journal of Pharmacology 9, 488.

Obaleye, J. A., Adediji, J.F., Olayinka, E.T. and Adebayo, M. A.,(2009). 'Synthesis, antimicrobial potential and toxicological activities of Ni (II) complex of mefloquine hydrochloride. *Research in Pharmaceutical Biotechnology.* 1 (1), 009-015.

Ogbannia, S. O., Enwuru,; N. V., Oyemenem, G. A., Oyedele; G. A., and Enwuru; C. A.,(2008). Photochemical Evaluation and antibacterial profile of Treculia Africana Deene Bark Extract on Gastrointestinal Bacteria pathogens. *African Journal of Biotechnology* 7(10): 1383-389

Ogunniran KO, Ajanaku KO, James OO, Ajani OO, Nwinyi CO, Allensela MA.. Fe (III) and Co (II) Complexes of Mixed Antibiotics: Synthesis, Characterization Antimicrobial Potential and their effect on Alkaline Phosphatase Activities of (2008)

Oladipo, M.A, Woods J.A.O, Odunola O.A. 2005. Synthesis, Vibrational Spectra and Magnetic Properties of Cobalt (II), Nickel (II) and Copper (II) Complexes of Barbituric Acid. *Sci. Foc.*, 10(1): 49-52. https://scholar.google.com/scholar?hl

Osowole AA, Kolawole GA, Fagade OJ. 2008. Synthesis, Characterization and Biological Studies on Unsymmetrical Schiff base Complexes of Nickel(II), Copper(II) and Zinc(II) and Adducts with 2,2'-dipyridine and 1, 10 phenanthroline. *J. Coord. Chem.*, 61: 1046-1049.

Orvig C, Abrams MJ (1999) Medicinal inorganic chemistry: introduction. Chem Rev 99(9): 2201–2204.

Patil , C. J. Manisha C. P, and Mrunmayee C. Patil:(2017) Studies on Synthesis of Aromatic Schiff Bases: Part-II. Synthesis,Characterization and Biological Evaluation of Ketimines from Benzophenone with Substituted-anilines ACTA

Putaya A.N. Habila, Naomi P. Ndahi, Hauwa S. Bello, Grema Mala Adekunle A. Osunlaja And HussainiGarba (2020): Synthesis, characterization and antimicrobial analysis of Schiff bases of o-phenylenediamine and 2-aminopyridine-3-carboxylic acid with ofloxacin and their metal (II) complexes, Int. J. Biol. Chem. Sci. 14(1): 263-278

Sani U and Iliyasu S M (2018) Synthesis, Characterization And Antimicrobial Studies On Schiff Base Derived From 2- Aminopyridine and 2-Methoxybenzaldehyde and Its Cobalt (Ii) and Nickel (Ii) Complexes *Bayero Journal of Pure and Applied Sciences 11(1):pp 214 – 219* ISSN 2006 – 6996

Sabry, A. A, Saad, R F, El-Dine, A and Abdel- Hady M (2016). Synthesis Characterization and Antimicrobial Activity of Schiff Base (*E*)-*N*-(4-(2-Hydroxybenzylideneamino)phenylsulfonyl)acetamideMetal Complexes.*American Journal of Analytical Chemistry*, 7:233-245.

Sani S, Siraj, I,T. (2020): Mechanochemical Synthesis, Characterization, Thermal Analysis and Antimicrobial Studies Of Co (Ii) Complexes Nigerian Research Journal of Chemical Science Vol. 8 (1)

Satya, P., Tuli, G. D.,Basu, S.K. and Madan, R. D., (2006). *Advanced Inorganic chemistry*Chand S. and Company. Pp 33, 40-50.

Sobola, Abdullahi O., Gareth M. Watkins And Bernadus Van Brecht (2018): Synthesis, characterization and biological study of Cu(II) complexes of aminopyridine and (aminomethyl)pyridine Schiff bases, *J. Serb. Chem. Soc. 83* (7–8) 809–819