Synthesis, Characterization and *In -Vitro* Antimicrobial Activities of a Schiff Base Derived From Benzaldehyde with Nitroaniline and Their Cobalt (II) and Nickel (II) Metal Complexes

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Abstract: **Schiff basederived from an equimolar amount of benzaldehyde with P-nitroaniline was synthesized by stirring. The Schiff base was subsequently reacted with cobalt(II) chloride hexahydrate and nickel (II) chloride hexahydrade to form the metal complexes.The compounds were characterized using FT-IR, UV-visible, melting point/decomposition and solubility test. The solubility test of the compounds showed that they are soluble in most organic solvents and the melting point of the schiff base ligand was found to be 147.8 ^oC and the decomposition temperature of the Cobalt (II) and Nickel(II) were found to be 158.8 ^oC and 157.9 ^oC for the cobalt(II) and Nickel(II) complexes respectively. The UV and the IR spectroscopy confirmed the formation of complex. The antimicrobial studies of the synthesized ligands and their Cobalt(II) and Nickel(II) metal complexes were carried out in against *Candida albican* fungal species, Gram positive bacteria *Staphylococcusaureus* and Gram negative bacteria *Eschaerichia coli*.The results indicated that the metal complexes were more active than the ligand but less active compared to standard drugs (ciprofloxacin and floconazole).**

I. INTRODUCTION

Schiff base is a nitrogen analog of an aldehyde or ketone in which the C=O group is replaced by a compound containing C=N-R group (Maher A.K., and Mohammed R. S.,2015). It is formed by condensation of an aldehyde or ketone with a primary amine (Alka P. and Anil K.,2015) according to the following scheme: Where R, may be an alkyl or an aryl group. Schiff bases that contain aryl substituents are substantially more stable and more readily synthesized, while those which contain alkyl substituents are relatively unstable. Schiff bases of aliphatic aldehydes are relatively unstable and readily polymerizable while those of aromatic aldehydes having effective conjugation are more stable (Nasira N. S., *et al* 2016). The formation of a Schiff base from an aldehydes or ketones is a reversible reaction and generally takes place under acid or base catalysis, or upon heating (Nasira N. S., *et al* 2016) .

Schiff bases are also known as anils, azomethines or imines In the polydentate Schiff base ligands(Mohammed A.A., *et al*, 2011), along with main functional group azomethine, the other donor sites contain various electronegative atoms such as oxygen, nitrogen and sulphur(Thierry Y. F., 2018). Schiff bases can be synthesized using various methods such as microwave irradiation method (Yang & Sun, 2006), green or environmental friendly method and normal conventional method (Zarei & Jarrahpour, 2011). The aim of this research is to synthesize, characterize and carry out antimicrobial activities for a Schiff base derived from P-nitroaniline and benzaldehyde and its Cobalt (II) and Nickel(II) metal complexes.

II. MATERIAL AND METHODOLOGY

2.1 *Materials*

2.2 *Reagents*

Benzaldehyde, p-nitroaniline, ethanol, acetic acid, ammonia, nickel (ii) chloride hexahydrate, andcobalt (ii) chloride hexahydrate,

Instruments/Apparatus

Magnetic plate and stirrer, watch glass, conical flask beaker and measuring cylinder, infra-red spectrophotometer, Ultraviolet- Visible spectrophotometer, analytical balance, and melting point apparatus

2.3 *Methodology*

2.3.1. *Synthesis of Benzaldehyde and P-nitroaniline Schiff base*

A solution of 1.02 ml of benzaldehyde [0.01m] in 10ml of ethanol, and 1.38gm 0f 4-nitroaniline[0.01m] in 10ml ethanol was added in a beaker. a few drops of glacial acetic acid was added to adjust the pH of the solution. the reaction mixture was stirred in 5 hours. after stirring add cool water, the obtained precipitate as collected by filteration. it was well dried and recrystallize from ethanol and dried at room temperature. the yellow product of schiff base ligand was obtained. for re-crystalization of Schiff base ligand, the product was dissolved in same solvent used for synthesis i.e ethanol and heat it on till product is dissolved completely, and clear solution is obtained and filter it through cotton at hot condition. Cool filterate in ice bath for overnight to get yellow crystalline solid particles of Schiff base ligand of benzaldehyde and 4-nitroaniline.

2.3.2. Synthesis of Metal Complex of Cobalt with Schiff base

A solution of 1.19gm of cobalt chloride [0.01m] in 10ml of ethanol, a hot solution of 2.26gm of Schiff base ligand in 10ml ethanol was added in beaker. Few drops of ammonia was added to adjust pH of solution. The reaction mixture was stirred in 2 hours. After stirring add cool water, the obtain precipitate was collected by filteration. Dry well and recrystallized from ethanol and dried at room temperature.

2.3.3. Synthesis of metal complex of Nickel with Schiff base ligand

A solution of 1.19gm of nickel chloride [0.01m] in 10ml of ethanol, a hot solution of 2.26gm of Schiff base ligand in 10ml ethanol was added in a beaker. a few drops of ammonia was added to adjust pH of solution. the reaction mixture was stirred in 2 hours. After stirring add cool water, the obtain precipitate was collected by filteration. Dry it well and recrystallized from ethanol and dried at room temperature.

2.3.4.. *FT-IR Analysis:*

Fourier transforms infrared spectrophotometer (FT-IR) analysis of each Schiff base and its metal complexes were done to confirm the formation of metal complex

2.3.5 Melting point Determination

Melting point or decomposition temperatures of the compounds were determined with a melting point apparatus and capillary tube.

2.3.6. UV spectra measurement

The UV spectra of title compound and its complex were recorded in the conventional region (400-800nm) using ethanol as solvent. The UV spectral study helps to decide the absorption (λmax) ofSchiff base ligand and its complex

2.3.7 Solubility Test

Solubility test was done using different solvents which includes ethanol, methanol, DMSO, ethylacetate, chloroform, acetone, and water in order to determine which solvent are suitable for subsequent analysis.

2.3.8. Antimicrobial Activity

2.3.9 Test Microorganisms:

The test microorganisms used for this analysis were pure cultures of bacteria and fungi obtained from Department of Microbiology, Nigerian institute of leather and science technology, Samaru. Zaria. The isolates were:*Staphylococcus aureus, Escherichia coli, andCandida albicans* .

2.3.10 Culture Media

The culture media used for the analysis includes Mueller hinton agar (MHA), Mueller hinton broth (MHB), Potato dextrose agar (PDA) and Nutrient agar (NA). These media were used for sensitivity test, determination of minimum inhibitory concentration (MIC), and minimum bactericidal/fungicidal concentration (MBC/MFC). All media were prepared according to manufacturer's instructions and sterilized by autoclaving at 121°C for 15minutes.

2.3.11 Determination of Inhibitory Activity (Sensitivity Test) of the Synthesized Samples Using Agar Well Diffusion Method

The standardized inocula of both the bacterial and fungal isolates were streaked on sterilized Mueller hinton and potato dextrose agar plates respectively with the aid of a sterile swab sticks. Four wells were punched on each inoculated agar plate with a sterile cork borer. The wells were properly labeled according to different concentrations of the synthesized samples which were 200, 100, 50, 25 and 12.5mg/ml respectively. Each well was filled up with 0.2ml of the sample. The inoculated plates with the sample were allowed to stay on the bench for about 1hour, this is to enable the extract to diffuse on the agar. The plates were then incubated at 37°C for 24hour (plates of Mueller hinton agar) while the plates of potato dextrose agar were incubated at room temperature for about 3-5 days. At the end of the incubation period, the plates were observed for any evidence of inhibition which will appear as a clear zone that was completely devoid of growth around the wells (Zone of inhibition). The diameter of the zones was measured using a transparent ruler calibrated in millimeter and the results were recorded.

2.3.12 Determination of Minimum Inhibitory Concentration (MIC)

The minimum inhibitory concentration of the synthesized samples was determined using tube dilution method with the Mueller hinton broth used as diluents (Adeniyi *et al*., 2000). The lowest concentration of the synthesized samples showing inhibition for each organism when the sample was tested during sensitivity test which was serially diluted in the test tubes containing Mueller hinton broth. The organisms were inoculated into each tube containing the broth and the synthesized samples. The inoculated tubes were then incubated at 37°C for 24hours. At the end of the incubation period, the tubes were examined/observed for the presence or absence of growth using turbidity as a criterion, the lowest concentration in the series without visible sign of growth (turbidity) was considered to be the minimum inhibitory concentration (MIC).

2.3.13 Determination of Minimum Bactericidal/Fungicidal Concentration (MBC/MFC):

The result from the minimum inhibitory concentration (MIC) was used to determine the minimum bacteriocidal/fungicidal concentration (MBC/MFC) of the synthesized sample. A sterilized wire loop was dipped into the test tubes that did not show turbidity (Clear) in the MIC test and a loopful was taken and streaked on a sterile nutrient agar plates. The plates were incubated at 37°C for 18-24hours. At the end of incubation period , the plates were examined for the presence or absence of growth. This is to determine whether the antimicrobial effects of the synthesized samples are bacteriostatic or bactericidal. (Adeniyi *et al., 2000*).

2.4. Scheme of Reaction

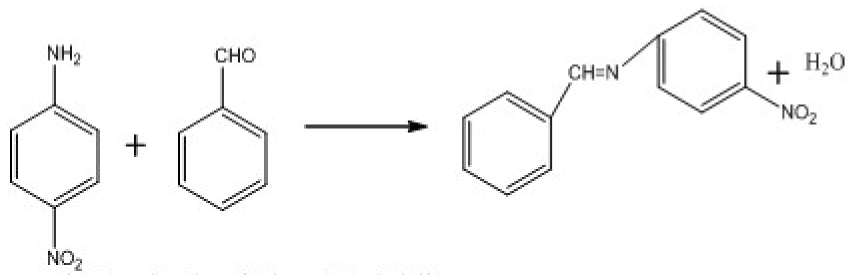

Fig. 5: Reaction scheme for the synthesized schiff base

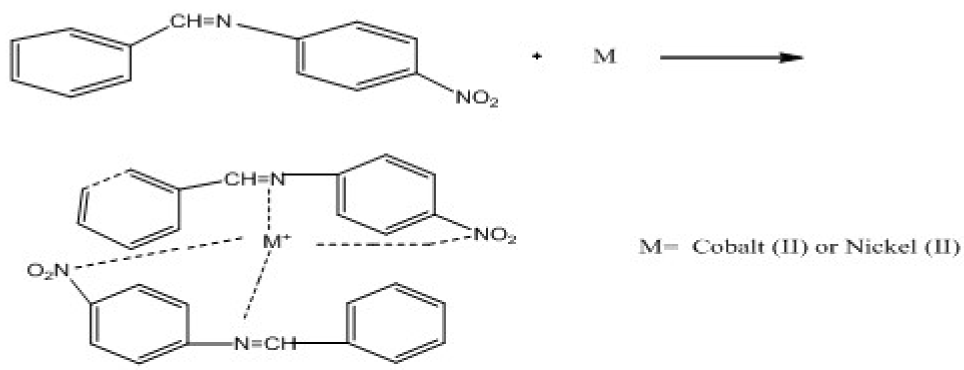

Fig. 6: Reaction scheme of Schiff base complex

III. RESULTS AND DISCUSSIONS

3.1 Physical Properties of Schiff Base and Their Metal Complex

Some of the physical properties of the Schiff base and its Co (II) and Ni (II) metal complexes were characterized and recorded as mentioned below.

Table 1: Physical properties of the Schiff base and their metal complex

Compound	Colour	Percentage yield
L	Yellow	66.37%
L-Ni	Greenish yellow	57.65%
L-Co	Yellow	60.78%

Keys: L- Schiff base of P-nitroaniline benzaldehyde, L-Ni-Schiff base of P-nitroaniline benzaldehyde Nickel (II) metal complex, L-Co-Schiff base of P-nitroaniline benzaldehyde Cobalt (II) metal complex

Table 2.0: Solubility Test

Compound	H_2O	DMSO	Methanol	Chloroform	Ethylacetate	Acetone	Ethanol
L	IS	S	S	SS	S	S	S
L-Ni	IS	S	S	IS	S	S	S
L-Co	IS	S	S	IS	S	S	S

Keys : S-Soluble , IS-Insoluble , SS- Slightly Soluble

Table 3.0: Melting Point/ Decomposition Temperature

Compound	Melting point (°C)	Decomposition temperature (°C)
L	147.8	-
L-Ni	-	157.9
L-Co	-	158.8

Table 4.0: UV-visible absorption of the synthesized compound

Compound	L	L-Co	L-Ni
λmax (nm)	414	385	352

Table 5.0: IR-Vibrational Frequencies Of The Ligand And The Complex

Ligand And Ligand Complex	IR Vmax(cm)
L	3358.3(NH-Stretch), 3082.5(CH-Stretch) and 1628.8(C=N)
L-Co	3354.6(NH-Strech), 3082.5(CH-Stretch) and 1623.8(C=N)
L-Ni	3354.6(NH-Stretch), 3082.5(CH-Stetch) and 1626.8(C=N)

Table 6: Antimicrobial Screening of Schiff Base and Its Nickel and Cobalt Metal Complex Zone of Inhibition

Test microbes		CONCONCENTRATION OF COMPOUNDS IN(μg) AND ZONE IN mm															CONTROL	
		L					L-Ni					L-Co						
		200	100	50	25	12.5	200	100	50	25	12.5	200	100	50	25	12.5	CPX	FLU
Staphylococusaureus		13	08	00	00	00	00	00	00	00	00	14	10	00	00	00	28	-
Escherichia coli		17	14	10	00	00	20	17	10	11	08	22	19	17	14	10	30	-
Candida albicaus(fungus)		15	12	09	00	00	20	16	13	09	00	21	18	15	13	09	-	33

Keys: CPX—Ciprofloxacin , Flu—Fluoconazole

Table 7.0: Minimum Inhibitory Concentration Of The Compounds(MIC)

Test microbes	CONCONCENTRATION OF COMPOUNDS IN(μg) AND ZONE INmm														
	L					L-Ni					L-Co				
	200	100	50	25	12.5	200	100	50	25	12.5	200	100	50	25	12.5
Staphylococus Aureus	–	+	+ +	+ + +	+ + + +	ND	ND	ND	ND	ND	–	+	+ +	+ + +	+ + + +
Escherichiacoli	–	–	+	+ +	+ + +	–	–	–	+	+ +	–	–	–	–	+
Candidaalbicaus(fungus)	–	+	+ +	+ + +	+ + + +	–	+	+ +	+ + +	+ + + +	–	–	–	–	+

Keys: ND—not determined, –→no turbidity, +→ mild turbidity, ++→ moderate turbidity, + + +→ high turbidity, + + ++→ very high turbidity.

Table 8.0: Minimum Bactericidal/ Fungicidal Concentration (MBC/MFC)

Test microbes	CONCONCENTRATION OF COMPOUNDS IN(μg) AND ZONE IN mm														
	L					L-Ni					L-Co				
	200	100	50	25	12.5	200	100	50	25	12.5	200	100	50	25	12.5
Staphylococus aureus	–	+	+ +	+ + +	+ + + +	ND	ND	ND	ND	ND	–	+	+ +	+ + +	+ + + +
Escherichiacoli	–	+	+ +	+ + +	+ + + +	–	–	+	+ + +	+ + + +	–	–	–	+	+ +
Candidaalbicaus(fungus)	–	+	+ +	+ + +	+ + + +	–	+	+ +	+ + +	+ + + +	–	–	–	+	+ +

Keys: ND—not determined, –→no growth, +→ mild growth, ++→ moderate growth, + + +→ high growth, + + ++→ very high growth.

IV. DISCUSSION

Physical properties of ligand and complex

The physical properties of the Schiff base, its Cobalt (II) and Nickel(II) complex were analyzed accordingly.The melting point of temperature of the Schiff base was determined to be 147.8^{o}C and the decomposition temperature of its Co(II) and Ni(II) complex were found to be158.8^{o}C and 157.8^{o}C respectively which indicate higher thermal stability of the compound after binding with the metal.

Solubility test of the Ligand and Complex

The Schiff base ligand and its Cobalt(II) and Nickel (II) complexes were analyzed to be soluble in most of the polar organic solvent tested. They were tested with ethanol, methanol, ethylacetate, water, chloroform, and acetone.

UV-VIS spectra

UV-Visible spectra of ligand and its Co(II) and Ni(II)metal complex were recorded in ethanol. λmax for ligand and its Cobalt (II) and Nickel (II) complex are 414 nm ,385 nm, 352 nm respectively. It confirms complex formation

IR spectra

The ligand shows a sharp absorption band at 1628.8 cm^{-1} corresponding to C=N frequency, and the presence of band in the region 1600- 1690 cm^{-1}supports the existence of C=N stretching in the metal complexes. On coordination of the azomethine nitrogen, the IR stretching frequency of C=N shows a shift and is observed in the region 1600-1690 cm^{-1}in synthesized Schiff base metal complexes. The appearance of the band around 1500-1600 cm^{-1}corresponds to N-O stretching frequency both in ligand and in metal complexes.

The ligand show a sharp absorbtion at 3358.3 cm^{-1} which corresponds to N-H frequency, and the slight shift in the absorption band of the Co(II) and Ni(II) metal complex which were 3354.6cm^{-1} and 3354.8cm^{-1} respectively confirmed complexation. (infra-red spectroscopy absorption table)

Antimicrobial Activity

The antimicrobial activity of the synthesized Schiff base and its Cobalt(II) and Nickel(II) metal complexes were tested against bacterial species *Staphylococcus aureus*, *Escherichia coli*, and its antifungal activity against *Candida albicans* were carried out. The potency of the synthesized ligand and its metal complexes as antimicrobial agents were screened in addition to evaluation of some known antibiotics using ciprofloxacin and fluconazole as standard or reference. The result showed that the ligand and its cobalt complex were found to be mildly active against *Staphylococcus aureus* while its Ni(II) complex showed no activity towards *S.aureus*. The synthesized ligand, its nickel and cobalt metal complex was found to be active against *Escherichia coli* and*Candida albicans*. The synthesized Schiff base metal complexes were found to have a higher antimicrobial activity than its synthesized Schiff base against the tested organisms but less active when compared with the standard drug. The increased activity of these complexes can be explained on the basis of chelation theory, which states that; the chelation tends to make the complex to acts as more powerful and potent bactericidal or bacteriostatic agent than the ligand (Sengupta *et al*., 1998). It is observed that, in a complex, the positive charge of a metal is partially shared with the donor atoms present in the ligand, and there may be π-electron delocalization over the whole chelating system (Sengupta *et al*., 1998). This increases the lipophilicity character of the metal chelate and favors its permeation through the lipid layer of the bacterial membranes. There are also other factors which increase the activity, namely solubility, conductivity and bond length between the metal and the ligand (Chohan *et al*., 2003). Which was in line with the work done on benzaldehyde and nitroaniline by Jadhav S. P. and Kapadnis K. H., (2018)

V. CONCLUSION

The Benzaldehyde and p-nitroaniline Schiff base ligand and its Cobalt(II) and Nickel(II) metal complexes were successfully synthesized and confirmed/ characterized by melting point/decomposition temperature, solubility test, UV-visible spectroscopy and infra-red spectroscopy. The complexes and the ligand were subjected to antimicrobial activity, where they were found to be sensitive against the tested bacteria and fungal isolates studied but for L-Ni which was found to be inactive against S.aureus. The complexes exhibited better activity than Schiff base but less active compared to the standard drugs (control).

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