ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Synthesis, Characterization and Antimicrobial Evaluations of Mixed Ligand Complexes of Diphenylamine of Cobalt.

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ABSTRACT

Nove l cobalt(II) diphenylamine complexes have been synthesized in water-methanol medium and characterized on the basis of their elemental analysis, melting points, solubility tests, conductivity tests , UV-Visible and IR spectral studies. The antimicrobial activities of the cobalt (II) complexes were screened against Enterohaemorragic coli, Staphylococcus aureus, Clostridium tetani,Neisseria gonorrheae and Streptococcus pyogeus bacteria and Mucor, Rhizomucor, Aspergillus fumigates, Rhizopus, Sporothrix schenckii, Aspergillus flavus, Aspergillus terreus, Absidia, Aspergillus niger and Candida spp pathogenic fungi. The melting points or decomposition temperatures of the metal complexes fell between 89-101^{0}C . The colors of the metal complexes range from blue to purple. The spectral results suggest the binding of diphenylamine(ligand) through the nitrogen atom to the cobalt(II) ions. The absorption bands observed in the Uv-Visible region are presumed to be due to charge transfer or intra-ligand transitions from the ligands or d-d transition from the metal ions.The metal complexes displayed proactive activities against the tested bacteria and fungi pathogens.
Keywords: Metal complexes, mixed ligand, antimicrobial, diphenylamine

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ISSN: 0975-8585

INTRODUCTION

Metal complexes are one of the most important groups of chemical compounds and they form the basis of coordination chemistry. The chemistry of complexes is dominated by interaction between s and p molecular orbital of the ligands and the d-orbital of the metal ions (Alexandria *et al* ,2003).

Many of the complexes often have spectacular colour caused by electronic transitions by the absorption of light. For this reason, they are often applied as pigments. Most transitions that are related to coloured metal complexes are either d-d transition or charged transfer bond (Harries *et al* ,1998).

Most recently, Co(II) based ligand complexes have been found to posses both antiviral and anti bacterial activities .However, synthesis, characterization and antimicrobial activity of Co(ii) metal complexes against multi drug resistant bacteria have been reported (Sebastian *et al,..* 2008).

Also, synthesis, physico-chemical and antimicrobial properties of Co(II) mixed ligand complexes of dimethyglyoxime had been reported and the complexes showed marked antimicrobial activity against the tested microbes at 10mg per liters (Osunlaja *et al*.,2011).

Some metal complexes have been growing increasing importance in the design of respiratory, slow release of controlled release drugs. Likewise, the efficacy of some therapeutic agents are known to increase upon coordination (Ajibola,1990; Obaleye et al ;1989. Some metal complexes, especially mixed –ligand complexes are known to exhibit remarkable activities (Kudirat et al, 1994;Yeamin et al , 2003; Ogundiran et al;2007, Olagboye et al,2011).

Co(II) complexes containing the rigid bidentate nitrogen ligand 2,6 –di isopropyl-phenyl imino acenaphthene demonstrated potent antibacterial properties against *Staphylococcus aureus* and Escherichia coli. The observed antibacterial activity was highly dependent on the bulkiness of the N-bis imine derivatives which increase the relative lipophilicitiy of the molecule (Salia, et al., 2009).

Diphenylamine an organic compound with the formula $(C_6H_5)_2$ NH , is a colorless solid but often yellow due to oxidized impurities. Diphenylamine is a monodentate ligand having one donating site with lone pair of electron on the nitrogen atom. It is a weak base with K_b of 10-14, reacts with acid and soluble in water (Vogel, *et al* 2005).

Antifungal properties of Co (II) sulfathiazolate complexes and the uncoordinated ligands had been studied and tested on *Aspergillus fumigant* . *Aspergillus flavus* . The achieved difference in activities could be due to the presence of the metal in the complexes, a result of antifungal action by inhibition of enzymes that are involved in the biosynthesis of the cell wall of fungi (Mestrolorenzo et al, 2000).

Antibacterial activities of metal complexes and commercial drugs(ampicillin and streptomycin) were checked against some bacterial pathogens such as *Pseudomonas aeruginosa, Escherichia coli, Klebsiella pneumonia, Staphylococcus aureus, Vibrio cholera* etc. Cobalt complex gave a better result in the form of zone of inhibition in culture plates rather than commercial drug.

This paper is aimed at the synthesis, characterization and evaluation of the antimicrobial activities of the novelty Cobalt(II)diphenylamine complexes in water-methanol medium.

MATERIALS AND METHODS

All chemical reagents used were of analytical grades and were used without further purification. The ligand (diphenylamine) and potassium thiocyanate were certified reagents obtained from Hopkin and Williams. Cobalt(II) hexa hydrate and sodium hydroxide were obtained from Sigma.

The metal is analylsed by complexometric methods (Vogel,1989).Sulphur content was analysed using barium chloride method and chloride content was analysed using silver chloride (Mohr's method). Infra red spectroscopic method was used to determine the functional properties of the complexes. The spectra were obtained in the range of 400 – 800 cm^{-1} (Shimadzu) using KBr pellets. Electron transition studies were

conducted using Uv-visible spectrophotometer (Uv-2500PC series) and measurements were taken in the region of 200 – 900 nm.

Electrical conductivity measurement was done using a conductivity metre WPA CM 35 Linton Cambridge ($Ohm^{-1}cm^2\ mol^{-1}$) measurements were taken at Hertz and operating temperature maintained at ± 0.1^0C . A Graffin melting point apparatus was used to measure the melting points / decomposition temperatures. The solubility of the metal complexes was determined in some polar and non –polar solvents. The antimicrobial screening of the metal complexes were performed in the Crops, Soil, Pest and Management Department of the Federal University of Technology. Nigeria using disc diffusion method (Ajayi *et al* ,2008 and Onifade,1998)

Synthesis of Metal Complexes

Equimolar concentrations of the ligand and cobalt (II)hexa hydrate were prepared in 1:1 and 1:2 in methanol medium. A colorless solution of the ligand (diphenylamine) was added to the purple solution of cobalt (II) chloride and this was stirred for 3hrs on a magnetic stirrer with hot plate. The purple mixture was filtered through a sintered glass via suction pump. The purple residue was washed in distilled H_2O followed by washing with diethyl ether and dried over activated silica gel inside a desiccators. The above procedure was also repeated for the 2:1 mixture by increasing the amount of ligand added.

The mixed complexes were also synthesized where ammonium thiocyanate solution was also added to the primary ligand and metal solution in equal proportion 1:1:1 on the other hand, the ligand (diphenylamine) concentration was increased and NH_4SCN) were added to the metal salt of cobalt(II) chloro hexa hydrate in methanol medium in the ratio 1:2:1. The process of filtration, washing, drying and weighing followed the above steps.

Antibacterial Assay

14g powdered Mueller into agar was weighed and dispensed into 400ml of distilled water inside a conical flask was plugged within cotton wool foiled with aluminum foil. The agar was allowed to dissolve and homogenize on hot plate. Homogenized medium was autoclaved at 121^0C for 15 minutes. The agar was allowed to cool and aseptically poured into sterile petri dishes. After solidification, the media / well was made into the agar by means of cork borer. The complexes were dispersed into the well. Amoxicillin antibiotic was used as the control and the plate were incubated at 37^oC for 24hrs. after incubation the zone of inhibition were measured in multi meter.

Anti-fungal Assay

The antifungal assay of the complexes sample was done according to the method of Ajayi et al, (2008). Ten millimeter (10ml) of each of the complexes solution was mixed with 15ml agar to give 25ml per petris dish. The samples were replicated and the control was set up without the complex sample. Comparative study was carried out using ketoconazole (standard fungicide). As soon as the agar-complex solidified, each of the petri dishes were marked at reversed side with two line that cross at the center of the Petri dish to facilitate easy measurement of the mycelia growth.

A 7mm diameter cork borer was used to make a well into the agar. The suspensions of fungi pathogen were introduced into the well by means of Pasteur pipette. All the plates incubated at 25^oC for 7days after which the mycelia growth were observed and measured in millimeter (mm). the % inhibition of each complex concentration was determined as described by Ajayi et al, 2008 and Onifade,1998).

$$\%= \frac{MgC-Mgt}{Mgc} \times 100$$

MgC = mycelia growth of control
Mgt = mycelia growth of test.

ISSN: 0975-8585

RESULTS AND DISCUSSION

Table 1: Physical Characterization

Complexes/formula	Ratio	Colour	%yield	Conductivity	Melting point
$[CoLCl(H_2O)_2]H_2O$	1:1	Blue	51.57	70.4	89 -91
$[CoL_2Cl\ H_2O]H_2O$	1:2	Pink	56.12	70.1	91-92
$[CoLSCNClH_2O]H_2O$	1:1:1	Purple	67.1	56.8	99-100
$[CoL_2SCN\ Cl]H_2O]H_2O$	1:2:1	Purple	66.6	46.8	99-101

Ligand
L= $C_6H_5)_2NH$

Table 2: Element Analysis of metal complexes Calculated and (Experimental).

Proposed formula	Ratio	M/wt	M	Cl	S
$CoLCl(H_2O)_2]H_2O$	1:1	297.5	19.49 (19.51)	11.93 (11.89)	-
$[CoL_2ClH_2O]H_2O$	1:2	447.5	12.96 (12.99)	7.93 (8.00)	-
$[CoLSCNClH_2O]H_2O$	1:1:1	337.5	17.18 (17.23)	10.45 (10.49)	9.45 (9,53)
$[CoL_2SCNClH_2O]H_2O$	1:2:1	505.5	11.47 (11.49)	7.02 (7.07)	6.33 (6.36)

L= $(C_6H_5)_2$ NH

Table3: Spectroscopic studies of metal complexes

Complexes	UV	IR
$CoLCl(H_2O)_2]H_2O$	313	686(Co-Cl) 742(H_2O) 873(Co-L) 1640(-C=N) 1528(C_6H_5) 3041 (Co-Ni) 3604(-OH).
$[CoL_2ClH_2O]H_2O$	314	690(Co-Cl) 742(H_2O) 873(Co-L) 1646(-C=N) 3041(Co-N) 3446(-OH).
$[CoLSCNClH_2O]H_2O$	311	685(Co-Cl) 742(H_2O) 873(Co-L) 1588(-C=N) 3041(Co-N) 2100(-SCN) 3446(-OH).
$[Co[L_2SCNClH_2O]H2O$	313	692(Co-Cl) 738(H_2O) 838(Co-L) 1600(-C=N) 3036(Co-N) 2091(-SCN) 3545(-OH).
Ligand		794, 994, 1528(C_6H_5), 1640, 2968 (C-H),3165, 3254(-NH)

Table 4: Antimicrobial Activities Of Diphenylamine Cobalt(Ii)Complexes

Complexes	*Enteroheammorragic. Coli*	*Staphylococcus aureus*	*Clostridium tetani*	*Neisseria gonorrhea*	*Streptococcus pyogenes*
$[CoLCl(H_2O)_2]H_2O$	25	20	*0*	6	20
$[CoL_2ClH_2O]H_2O$	20	25	20	20	20
$[CoLSCNClH_2O]H_2O$	6	20	15	0	15
$[CoL_2SCNClH_2O]H_2O$	20	20	20	20	18
Control	15	20	15	0	20

Table 5: % sensitivity of the complexes against the test organisms

Test sample	No of Pathogen tested	No. sensitive	% sensitive
$[CoLCl(H_2O)_2]H_2O$	5	3	60
$[CoL_2ClH_2O]H_2O$	5	5	100
$[CoLSCNClH_2O]H_2O$	5	5	100
$[Co[L_2SCNClH_2O]H_2O$	5	4	80
Control	5	5	100

Note: 10mm zone of inhibition is sensitive according to Bethy et al 2007.

Tables 6 - 9: % INHIBITION OF METAL COMPLEXES AT DIFFERENT CONCENTRATIONS AGAINST THE FUNGI PATHOGENS.

Table 6 : % Inhibition of the Metal Complexes at 1mg/L Concentration

Complexes	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
$[CoLCl(H_2O)_2]H_2O$	16	18	34	23	27	10	11	13	23	10
$[CoL_2ClH_2O]H_2O$	20	25	30	31	30	17	22	25	23	15
$[CoLSCNClH_2O]H_2O$	26	31	30	35	33	20	30	20	30	34
$[Co[L_2SCNClH_2O]H_2O$	30	33	38	38	39	26	31	25	32	38
Ligand	10	12	10	10	11	08	10	05	10	10
Control (3mg/l)	39	33	44	45	48	40	36	38	39	40

1mg/l

ISSN: 0975-8585

Table 7: % inhibition of the Metal Complexes at 1.2mg/L Concentration

Complexes	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
$[CoLCl(H_2O)_2]H_2O$	26	20	28	37	33	23	22	20	43	13
$[CoL_2ClH_2O]H_2O$	30	22	30	41	47	28	23	30	48	20
$[CoLSCNClH_2O]H_2O$	43	33	40	45	40	33	36	35	61	30
$[CoL_2SCNClH_2O]H_2O$	46	37	44	48	42	36	38	42	65	36
Ligand	16	12	14	16	20	10	13	10	25	12
Control (3mg/l)	49	40	48	52	50	42	40	48	50	40

Table 8: % Inhibition of the Metal Complexes at 1.5mg/L

Complexes	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
$[CoLCl(H_2O)_2]H_2O$	34	25	36	40	39	27	30	25	50	40
$[CoL_2ClH_2O]H_2O$	38	37	40	54	51	33	35	38	55	45
$[CoLSCNClH_2O]H_2O$	54	37	44	62	57	38	44	53	60	50
$[CoL_2SCNClH_2O]H_2O$	58	42	50	65	60	43	49	57	65	55
Control (3mg/l)	52	49	59	70	69	52	50	67	70	66
Ligand	23	16	20	24	23	20	24	26	25	20

Table 9: % Inhibition of Metal Complexes at 3mg/L

Compounds/Complexes	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
$[CoLCl(H_2O)_2]H_2O$	50	47	50	71	54	53	49	48	60	58
$[CoL_2ClH_2O]H_2O$	66	53	64	79	66	60	55	56	66	60
$[CoLSCNClH_2O]H_2O$	76	60	70	57	64	60	58	57	75	66
$[Co[L_2SCNCl]H_2O]H_2O$	78	70	78	71	74	66	64	63	80	70
Ligand	26	24	26	20	33	22	30	23	31	24
Control (3mg/l)	90	75	89	88	83	70	69	69	95	76

KEY : F1 = *Mucor* *F2 = Rhizomucor* *F3 = Aspergillus fumigates*
F4 =Rhizopus *F5 =Sporothritix schenckii* *F6 =Aspergillus flavus*
F7 =Aspergillus terreus *F8= Absidia* *F9 =Aspergillus niger*
F10 = Candida spp

DISCUSSION

Different metal complexes of Co(II) with diphenylamine and thiocyanate ion in aqueous medium were synthesized and characterized, the colours of the metal complexes range from blue to purple, showing that ligands have more effects on the colour of the metal complexes, the percentage yield was reasonably high ranging from 51.57-67.1 % , the conductivity of metal complexes is relatively small, an indication of poor electrolytic nature of the metal complexes. The results of the elemental analysis for experimental values are very close to the theoretical values. The melting points of the metal complexes were found 89-101^{o}C and mixed ligand metal complexes being the highest.

IR-spectra result showed some prominent bands at different wavelengths. The prominent bands displayed by the ligand are 794, 994, 1528cm^{-1} but experienced a shift by the metal complexes 686, 690, 865, 692cm^{-1} attributed to Co-Cl, while at 873, 873, 838, 873 confirmed to have caused by (Co-L) bond (M-N) respectively). Another prominent bands that was common to the ligand and the metal complexes are 1640, 1646, 1585 cm^{-1} and 1600cm^{-1} which are assigned to –C=N while other bands that also common to both the ligand and metal complexes are 1528, 1515, 1574, 1515cm^{-1} are also attributed to the phenyl rings. The anode group that served as the coordinating sites for the metal complexes had absorbed strong at 3165 but have a shift in bands in all the metal complexes at 3041, 3040, 3041, 3036cm^{-1}, all these bands showing the coordination of (Co-N) of cobalt to the nitrogen atom of the diphenylamine.

However, other distinct bands found in complexes $[CoLSCNCl]H_2O$ and $[Co[L_2SCNCl]H_2O$ but not found in the metal complexes including the ligand are characteristic features of the secondary mixed ligand due to the presence of thiocyanate ions (SCN^-) which showed strong bands at 2100.67 and 2091cm^{-1} respectively (Joseph and Herbert ,1987).

Furthermore, bands at 3565cm^{-1} for the ligand and other metals complexes which also absorbed at 3604, 3546, , 3647 and 3545cm^{-1} are due to the presence of free water molecules. These likely come from the water of crystallization of the cobalt salt.

Uv - visble spectroscopic studies revealed a charge transfer bond which entails the promotion of an electron form a metal-based orbital into an empty ligand orbital (metal to ligand charge transfer), the metal complexes show bands 313, 314, 311, 313 nm respectively (Williams and Fleming, 1989).

The antibacterial screening carried out on the tested organisms as shown in data tables 4 - 5 revealed that the activities of $[CoLCl(H_2O)_2]$ recorded the highest inhibition against *Enterohaemorragic E. coli* with 25mm zone of inhibition showing better activities than the amoxicillin (commercial antibacterial drug) with 15mm inhibition zone. It also showed a good inhibition against *Streptococcus pyogenes* and *Staphylococcus aureus* with 20mm zone of inhibition each. Its effect against *Neisseria gonorrhea* and *Clostridium tetani* which are respectively 6mm and 13mm as compared to that of the control. Sample $[CoL_2ClH_2O]H_2O$ and $[CoLCl(H_2O)_2]H_2O$ proved to be active against all the tested organisms with at least 20mm inhibition against all the bacteria. $[CoLSCNClH_2O]H_2O$ showed a remarkable inhibition against *Staphylococcus aureus* with (30mm) *Clostridium tetani and Streptococcus pyogene* (15mm) respectively while inhibition is very poor on *Enteroheammorragic coli* is the sign of resistant (table4).

In term of sensitivity of the metal complexes against the tested organism, all the metal complexes have a minimum of 60% inhibition, showing that metal complexes of diphenylamine in methanol medium are good antibacterial agents and could be effectively used as the preventive measures for the treatment of most diseases caused by the tested organisms. The result for $[CoL_2ClH_2O]H_2O$ complex with increased concentration gave the highest inhibitory activity. The test metal complexes also showed appreciable inhibition because of the combination effect of the mixed ligand (Olagboye et al, 2011, Petal et al.2010). The activities of these complexes may be due to the presence of sulphur in thiocyanate, another donor atom, apart from the nitrogen atom in the ligand that serves as the coordination site for metals cobalt ions (table5).

Metal complexes were also screened against ten different fungi pathogens at different concentrations ranging from 1-3mg/l as well as the ligand (diphenylamine) and the controls. The results obtained so far have indicated that the metal complexes were good anti fungi agents for the tested organisms. Although, ligand showed some potency against most organisms, it is evident that the coordination of the ligand to the cobalt metal ion has somewhat increased its antifungal activities. As seen in the tables 6 - 9.

The results from findings of the antifungal assay show that the fungi used in the present studies recorded different susceptibility at different concentrations of the metal complexes. The metal complexes of $[CoL_2ClH_2O]H_2O$, $[CoLSCNClH_2O]H_2O$ and $[CoL_2SCNClH_2O]H_2O$ recorded better inhibition against most organisms while the remaining complex $[CoLClH_2O]H_2O$ displayed moderate inhibition.

Tables 5 - 9 show the results obtained for the antifungal screening of complexes at different concentrations. The cobalt complexes have good antifungal activities against some of the tested pathogens or species suggesting that they can be used as antifungal drugs for the treatment of diseases caused by the organisms such as *Aspergilluosis*, a disease majorly caused by *Aspergillus* species, *Mucomycosis*, problem associated with *Mucor and Rhizomucor; Candidiasis and Sporotrichosis* diseases caused by *Candida* species and *Sporothrix schenckii* respectively.(Betty et al,2007).

Furthemore, the results in the tables 5-8 also revealed that antifungal susceptibility of cobalt (II) complexes is concentration dependent since the highest inhibition was recorded at 3.0 mg/l and the lowest inhibition at 1 mg/l. Likewise, ligand (Diphenylamine) had shown little inhibitory effect on the organisms and therefore, evident that, the coordination of the ligand through to the cobalt metal has somewhat increased its antifungal activities. On the other hand, *Ketoconazole* (control) showed an appreciable inhibition. This agrees with the observations of Srivastava,(1981),and Saeed, 2009).

CONCLUSION

Metal complexes of *Cobalt*(II)diphehlamine have been synthesized and characterized. The results revealed that the coordination of cobalt ions to the ligand was through amine group-NH by replacing the

hydrogen ion of the ligand as shown by the spectroscopic studies. The antimicrobial studies confirmed that the cobalt complexes were more proactive than the ligand and the controls and the anti-pathogenic activity of the cobalt complexes is concentration dependent.

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