Global Scientific JOURNALS

GSJ: Volume 9, Issue 11, November 2021, Online: ISSN 2320-9186
www.globalscientificjournal.com

SYNTHESIS, CHARACTERIZATION, AND ANTIMICROBIAL STUDIES OF MIXED LIGAND COMPLEXES OF ACETANILIDE AND AMPICILLIN WITH COBALT (II) AND NICKEL(II) IONS

*OLAGBOYE, Sulaiman. Adeoye and **ADEBAWORE, Adefusisoye Adegalu
*Department of Chemistry, Ekiti State University, Ado-Ekiti, Nigeria.
**Department of Industrial Chemistry, Ekiti State University, Ado-Ekiti, Nigeria.

Corresponding author E-mail: sulaiman.olagboye@eksu.edu.ng

KEYWORDS: *synthesis, acetanilide, ampicillin, Salmonella entrica, Staphylococcus faecalis..*

Abstract

The rise of new infectious diseases, the recovery of several infections that appeared to have been controlled and the increase in bacterial resistance have generated the necessity for studies directed towards the improvement of new antimicrobials. Nickel (II) and Cobalt (II) complexes as well as the mixed ligands of acetanilide and ampicillin in methanol and water medium were synthesized and characterized based on their physical analysis such as color, percentage yield, solubility as well as IR spectroscopic study. The solubility of the complexes was tested using dimethylformamide, carbon tetrachloride, dimethyl sulphate, chloroform, ethylacetate, and methanol. The solubility test showed that the complexes were both polar and non-polar. The coordination of the metal complexes to the ligand was found to be through the nitrogen and oxygen atoms of ampicillin and nitrogen atom of acetanilide The antimicrobial activities of the cobalt (II) ion complexes were evaluated by screening against selected micro-organism, bacteria such as; *Streptococcus faecalis, Xanthomonas axinopodis, Salmonella entrica, Xanthomonas phaseoli and Fungi; Sclerotium rolfsii, Mansourian phomoides, Collectotrichum lindemuthanium. From the findings, t*he result revealed that the active ingredients were not against bacteria but were proactive to fungi.

Introduction

Most transitions that are related to colored metal complexes are either d–d transitions or charge transfer bands. In a d-d transition, an electron in a d-orbital on the metal is excited by a photon to another d orbital of higher energy, therefore d-d transitions occur only for partially-filled d-orbital complexes (d^{1-9}). For complexes having d^0 or d^{10} configurations, charge transfer is still possible even though d–d transitions are not (Harris and Bertolucci, 1989).

According to Claudel (2020), many antimicrobial drugs are upright ligands and there is a possibility that their activity depends on their complexing of metal ions, as well as their effectiveness, is increased when coordinated The improvement of resistance of a microorganism to antibiotics may be due to inherent or natural whereby there is no site for the drugs to impasse there or the permeability against the drug is low, so the drug cannot affect the microorganism, and also, the microorganism acquires resistance to be affected by the drug according to Saga and Yamaguchi (2009).
Kafi-Ahmadia et al., (2018); Abdel-Rahman et al., (2016; 2017; 2019) reported that metal chelators are among materials with antimicrobial activity that is based on chelation theory. The biochemical activity

of bioactive species can be enhanced by chelation also, chelation reduces the polarity of the metal ion due to overlapping of the ligand orbital and partial sharing of the positive charge of the metal ion. Subsequently, the complex may infiltrate the lipid membranes which may disable the enzymes of microorganisms by obstructing their metal-binding sites. Furthermore, such complexes aggravate the respiration of the cell and as a result, the growth of the organism is restricted by upsetting the protein synthesis.

Ampicillin is one of the most widely prescribed antibiotics. Ampicillin is an antibiotic drug used to prevent and treat some bacterial infections, such as respiratory tract infections, urinary tract infections, meningitis, *salmonellosis*, and endocarditis, gastrointestinal infections caused by adulterated water or food (for example, by Salmonella), whooping cough, to prevent and treat secondary infection (middle ear infection) *Sinusitis*. It may also be used to prevent group B *streptococcal* infection in newborns. Like all antibiotics drugs, its functions are limited to the treatment of viral infections (*US National Library of Medicine*).

Ampicillin can penetrates gram-positive and some gram-negative bacteria to inhibit the third and final stage of bacterial cell wall synthesis, which could eventually lead to cell lysis according to Bastug *et al. (*2012). It is considered penicillin and is a close relative of another penicillin, amoxicillin. Unlike penicillin, ampicillin and amoxicillin can insinuate and avert the growth of certain types of bacteria, called gram-negative bacteria. According to My et al., (2011), ampicillin is effective against gram-negative and gram-positive bacteria and is used to treat gonorrhea and infections of the intestinal, urinary, and respiratory tracts.

Acetanilide is an organic compound with formula C_8H_9NO (N-phenylacetamide) and it is produced by reacting acetic anhydride with aniline. Acetanilide is used for the production of 4-acetamido-benzene-sulfonyl chloride, a key intermediate for the manufacture of sulfa drugs. It is also a precursor in the synthesis of penicillin according to Sivakumar and Prema (2015).

It has been reported by Ogunniran *et al*. (2008) that mixed ligand metal complexes of ampicillin and chloramphenicol with Cu(II), Ni(II), and Fe(III) metal chloride hexahydrates have been prepared, characterized both physically and spectroscopically and the results showed that complexes were effective chemotherapy agents. It has also been reported by Abdulhamid *et al. (*2016) that the ampicillin metal complexes with Co(II) and Cu(II) were synthesized and characterized as well as antimicrobial studies and the results revealed that metal complexes were better antidotes for metal overload or poisoning. Metals not only provide prototypes for synthesis, but they also introduce functionalities that enrich drug delivery vectors (Obaleye *et al*., 2012; Abubakar et al., 2019). Many organic drugs necessitate interaction with metals for action. They interrelate with metals at their target site or during their metabolism or interrupt the balance of metal ion uptake and distribution in cell and tissue. The unique properties of metal complexes tend to offer advantages in the innovation and improvement of new drugs (Obaleye *et al*., 2021).

Materials and Methods

(a) Reagents and Instruments:

All chemicals and solvents used were of analytical grade. Pure sample of Acetanilide, molecular formula C_8H_9NO (N-phenylacetamide) and molecular weight 135, was obtained from Sigma – Aldrick. Ampicillin trihydrate obtained as a gift from Drugfield Pharmaceutical Company, Sango, Lagos, Nigeria. Metal salts $CoCl_2.6H_2O$ and $NiCl_2.6H_2O$ were obtained British Drug Chemical House Limited Co, Poole, England. Analytical Reagent grade hydrated metal chlorides from Bristish Scientific Chemicals were used for the preparation of the complexes. Elemental analysis (C, H, N and O) were carried out using micro analytical technique on C,H,N,S,O Elemental analyzer at Universiti Technologi Petronas (UTP) Malaysia. The melting points were carried out on a Gallenkamp melting point apparatus. Infra-red spectral analyses were recorded using Shimadzu FTIR-8400S (Fourier Transform Infrared Spectrophotometer) in the range 4500 – 300 cm^{-1}. The solid reflectance studies were also determined using a double beam machine scan in the range 200 – 800 nm.

(b) Synthesis

0.012191 mol of Acetanilide, 0.003699 mol were added to the ethanolic solution of Nickel salt metal to the ligand in ratio 1:1 (ML), the reacting mixture was stirred on a magnetic stirrer for 3 hours, a whitish-green mixture was formed then filtered with a sintered glass porosity No:4, washed in methanolic solution and dried in a desiccator containing silica gel for 5days. The residue was weighed until a specific weight was obtained. The ratio 1:2 (ML2) Acetanilide – Nickel complex was synthesized by increasing the concentration of the ligand (acetanilide) to two. Mixed ligand metal complexes of acetanilide were prepared by introducing the Ampicillin in ratio 1:1:1 (MLL1) alongside metal and acetanilide whereas, the 1:2:1 complex was prepared by increasing the concentration of acetanilide ML2L1. The processes of filtrations, washing, drying remain the same as stated in the ratio 1:1 synthesis. Metal complexes residue gave green color with reasonable percentage yields as stated. For cobalt salt, 0.008481 mol of a red wine solution of cobalt (II) chloride to a colorless methanolic solution of (0.003699 mol) acetanilide of the same concentration in a beaker as (ML) in ratio 1:1. The mixture became peach in color and no precipitate formed and stirred for 2hrs:30mins. The mixture was filtered, washed in methanolic solution, using sintered glass with porosity No: 4 then the residue was dried in a desiccator containing silica gel for 4days. The ratio 1:2 (ML2) cobalt-acetanilide complex was synthesized by double the concentration of the ligand. The residue gave red color. Mixed ligand metal complexes were prepared in ratios 1:1:1 and 1:2:1 by adding ampicillin as the secondary ligand. Equimolar concentrations of the cobalt metal, acetanilide, and ampicillin were added independently as (MLL1) but for the ratio 1:2:1 complex. The concentration of acetanilide increased to 2 as (ML2L1). The two mixed ligand metal complexes followed the processes of filtration, washing, drying as in ratio 1:1 and 1:2 metal complexes. Red residues with appreciable yields were obtained.

Antibacterial Activities

The test microorganisms used for screening antimicrobial activities were standard pathogenic stains obtained from the culture collection unit of the Department of Microbiology, Ondo state University Teaching Hospital, Akure, Nigeria. The laboratory tests were carried out at the Pest and Control Section of the Department of Crops and protection, Federal University of Technology, Akure, Nigeria. The antimicrobial activities of newly generated complexes were screened against the following fungi: *Sclerotium roofil, Mansourian phomoides, Collectotrichum lindimuchianum.* Using poisoned food techniques at 0.025g/ml concentration, under sterile culture molten potato dextrose (PDA) and solvent used was dimethylsulphuroxide at 0.025g/ml concentration. A negative control plate (NTR) without any treatment was also set up. The mycelia growth inhibition was calculated in percentage (Singh and Srivastava, 2013). All newly synthesized complexes were tested for their antibacterial activities against *Streptococcus fecalis, Xantomonas axinopolis, Salmonella entrica, Clavibacter michiganense, Xanthomonas phaseoli alongside* with the control (amoxillin), and using Broth Dilution method. At 0.035g/ml concentrations. The MIC (minimal inhibitory concentration) of the control organism is used and read to check the accuracy of the complexes (Konaté et al., 2012). The lowest concentration inhibiting growth of the organism is recorded as the MIC. This result is compared with the control amoxillin. Mycelia growth were measured with the aid of Vernier calipers, mycelia growth inhibition were calculated in percentage using the formula:

$$\%\ \text{ZONE OF INHIBITION} = \frac{NTR - TR}{TR}\ X\ 100$$

Where NTR= Average diameter of fungal colony in negative control sets (plates without any treatment) and TR= Average diameter of fungal colony in treated sets.

Results and Discussion

Results

The physical properties of nickel and cobalt (II) were shown in Tables 1 and 2. Tables 3 and 4 shows the ratio of different solvent used for the solubility tests of nickel and cobalt complexes. Tables 5 and 6 redeemed the prominent regions of FTIR spectra of mixed ligand complexes with nickel and cobalt (II) while the evaluation of antifungal activities of Ni^{2+} and Co^{2+} complexes are shown in Tables 7 and 8 respectively. And finally, evaluation of antibacterial screening of Ni^{2+} and Co^{2+}complexes are shown in Table 9 and 10.

Table 1: Physical Properties of Nickel (II) ion complexes

COMPOUND/COMPLEX	RATIO	MEDIUM	% YIELD	COLOR
Ni(acetanilide)$Cl_2.H_2O$	1:1	Meth-H_2O	77	Green
Ni(acetanilide)$_2Cl_2.H_2O$	1:2	Meth-H_2O	63	Green
Ni(acetanilide)(ampicillin)$Cl_2.H_2O$	1:1:1	Meth-H_2O	67	Green
Ni(acetanilide)$_2$(ampicillin)$Cl_2.H_2O$	1:2:1	Meth-H_2O	76	Green
Acetanilide	-	Meth-H_2O		White
Ampicillin	-	Meth-H_2O		White

Table 2: Physical Properties of Cobalt (II) ion complexes

COMPOUND/COMPLEX	RATIO	MEDIUM	% YIELD	COLOR
Co(acetanilide)Cl_2.6H2O	1:1	Meth-H_2O	77	Red
Co(acetanilide)$_2Cl_2$..$6H_2O$	1:2	Meth-H_2O	59	Red
Co(acetanilide)(ampicillin)$Cl_2.6.H_2O$	1:1:1	Meth-H_2O	70	Red
Co(acetanilide)$_2$(ampicillin)$Cl_2.6H_2O$	1:2:1	Meth-H_2O	79	Red
Acetanilide	-	Meth-H_2O		White
Ampicillin	-	Meth-H_2O		White

Table 3: The ratio of different solvent used for the solubility tests of nickel complexes

	1:01	1:02	1:01:01	1:02:01
CHLOROFORM	Soluble	Soluble	Insoluble	Insoluble
ETHYLACETATE	Soluble	Soluble	Insoluble	Insoluble
DMF	Soluble	Soluble	Insoluble	Soluble
CCl_4	Soluble	Insoluble	Insoluble	Insoluble
METHANOL	Insoluble	Soluble	Insoluble	Insoluble
DMSO	Soluble	Insoluble	Insoluble	Insoluble

ACETONE	Insoluble	Soluble	Insoluble	Insoluble

Table 4: The ratio of different solvent used for the solubility tests of cobalt complexes

	1:01	1:02	1:01:01	1:02:01
CHLOROFORM	Soluble	Soluble	Soluble	Soluble
ETHYLACETATE	Soluble	Soluble	Insoluble	Insoluble
DMF	Soluble	Soluble	Soluble	Soluble
CCl_4	Insoluble	Insoluble	Insoluble	Insoluble
METHANOL	Soluble	Soluble	Insoluble	Soluble
DMSO	Insoluble	Soluble	Insoluble	Insoluble
ACETONE	Soluble	Soluble	Insoluble	Insoluble

Table 5: Prominent Regions of FTIR Spectra of Mixed Ligand Complexes with Nickel (II)

Ligand Complexes	Uv-Visble (nm)	vN-H	vC=O	vC=N	COO-	-OH	M-N	M-O
Acetanilide	-	3122	1325	1518	-	-	-	-
Ampicillin	325,229	3027	1309	1507	1707	-	-	-
$Ni(Acet)Cl_2$	720,680	3195	-	1691	-	3446	575	443
$Ni(Acet)_2Cl_2$	720,680	3194	-	1668	-	3575	542	440
$Ni(Act)(Amp)Cl_2$	760,680	3195	-	1668	1775	3527	516	425
$Ni(Acet)_2(Amp)Cl_2$	785,680	3196	1499	1687	1774	3446	522	426

Table 6: Prominent Regions of FTIR Spectra of Mixed Ligand Complexes with Cobalt (II)

Ligand Complexes	Uv-Visble (nm)	vN-H	vC=O	vC=N	COO-	-OH	M-N	M-O
Acetanilide	-	3122	1325	1518	-	-	-	-
Ampicillin	325,229	3107	1309	1507	1707	-	-	--
$Co(Acet)Cl_2$	755,725	3136	-	1664	-	3748	580	455
$Co(Acet)_2Cl_2$	760,725	3195	-	1684	-	3758	566	444
$Co(Acet)(Amp)Cl_2$	755,680	3194	1496	1687	1774	3486	587	456
$Co(Acet)_2(Amp)Cl_2$	680,760	3295	1499	1663	-	3776	589	448

Table 7: Evaluation of Antifungal of Ni^{2+} Complexes

COMPLEXES	RATIO	S.R	M.P	C.L
$Ni(acetanilide)Cl_2.H_2O$	1:01	58.5	40	48
$Ni(acetanilide)_2Cl_2.H_2O$	1:02	60	43.9	56.1
$Ni(acetanilide)(ampicillin)Cl_2.H_2O$	1:01:01	66	53.33	75
$Ni(acetanilide)_2(ampicillin)Cl_2.H_2O$	1:02:01	88.04	63.33	78.09
Kocides	-	100	100	100
Ampicillin		18	21	19

S.R - *Sclerotium roofsii;* M.P - *Mansourian phaeoli;* C.L - *Collectotrichum lindimuthianum*

Table 8: Evaluation of Antifungal of Co (II) Complexes

COMPLEXES	RATIO	S.R	M.P	C.L
Co(acetanilide)Cl$_2$.6H2O	1:01	53.85	22.22	43.98
Co(acetanilide)$_2$Cl$_2$.6H2O	1:02	5400	25.5	48
Co(acetanilide)(ampicillin)Cl$_2$.6H2O	1:01:01	64.1	44.44	50.54
Co(acetanilide)$_2$(ampicillin)Cl$_2$.6H2O	1:02:01	69.85	47.78	63.44
Kocides	-	100	100	100
Ampicillin	-	5	2	0

S.R - *Sclerotium roofsii;* M.P - *Mansourian phaeoli;* C.L - *Collectotrichum lindimuthianum*

Table 9: Evaluation of Antibacterial Screening of Ni^{2+} Complexes.

COMPLEX	RATIO	A	B	C	D	E
Ni(acetanilide) Cl$_2$.H$_2$O	1:01	0	12	0	0	0
Ni(acetanilide)$_2$Cl$_2$.H$_2$O	1:02	0	14	0	0	0
Ni(acetanilide)(ampicillin)Cl$_2$.H$_2$O	1:01:01	17	15	22	22	20
Ni(acetanilide)$_2$(ampicillin)Cl$_2$.H$_2$O	1:02:01	16	24	20	20	19
Amoxillinl	-	20	24	20	24	20
Acetanilide	-	-	-	-	-	-
Ampicillin	-	18	21	19	19	14

A - *Streptococcus fecalis; B - Xantomonas axinopolis; C - Salmonella entrica;*
D - Clavibacter michiganense; E - Xanthomonas phaseoli

Table 10: Evaluation of Antibacterial Screening of Co^{2+} Complexes.

COMPLEX	RATIO	A	B	C	D	E
Co(acetanilide)Cl$_2$.6H2O	1:01	0	0	10	0	0
Co(acetanilide)$_2$Cl$_2$,6H$_2$O	1:02	0	0	12	0	0
Co(acetanilide)(ampicillin)Cl$_2$.6H2O	1:01:01	18	18	20	21	28
Co(acetanilide)$_2$(ampicillin)Cl$_2$.6H2O	1:02:01	13	22	18	22	24
Amoxillin	-	20	24	20	24	20
Acetanilide	-	0	0	0	0	0
AMPILLIN	-	18	21	19	19	14

A - *Streptococcus fecalis; B - Xantomonas axinopolis; C - Salmonella entrica;*
D - Clavibacter michiganense; E - Xanthomonas phaseoli

Discussion

Complexes of Nickel (II) and Cobalt (II) with acetanilide and its mixed ligand ampicillin were synthesized at different ratio concentrations in water-methanol medium as shown in Table 1 and 2 respectively. The colors, melting points and percentage yields were also recorded. The percentage yields of the metal complexes are reasonable while, there is no variation in colors obtained, because the ligands have no dominant effects on the metal salt. The variation in colour of the ligands with its corresponding complexes indicates coordination of the ligand acetanilide and with Ampicillin, mixed ligand with the metal ions. The colour of the compounds is ascribed to 'd-d' orbital transition of electron between one energy level to another, by their magnitude of splitting, which in turn relies on the geometry of the complex, the nature of the ligand and charge transfer (Olagboye, 2015).

The decomposition temperatures of the complexes are relatively high and thermally stable. The solubility tests of metal complexes in the available organic solvents clearly showed that they were soluble in most organic solvents as indicated in Tables 3 and 4 respectively. Results from Table 3 shows that others complexes are non-polar in nature as they are insoluble in water. The results of the solubility tests revealed that some metal complexes are soluble in non-polar solvents like chloroform and dimethyl formaldehyde (DMF) while, some are not soluble in water. This indicates that metal complexes are non-electrolytes and non-hygroscopic in characters. The solubility of metal (II) complexes in the common solvents indicated their low polarity which can be used to predict the suitable solvents that could be utilized or employed for subsequent spectroscopic measurements (Jones and Fleming, 2010).

The UV-Visible spectrophotometer was used to measure and examine the level of conjugations and unsaturation of metal complexes. Ni (II) ion complexes show bands around (680-760 nm) as shown in the Table 5 while Co (II) ion complexes show bands between (305-760nm) as shown in the Table 6. The UV-visible spectroscopic studies of the ligands demonstrated absorption bands at (229 - 325) nm which belongs to π-π* and n-π* bands found within the Uv-region due to carbonyl and benzene ring in the ligands. The UV-visible spectroscopic studies of the ligands demonstrated absorption bands at (250-285) nm which belongs to π-π* and n-π* bands found within the Uv-region and it is also demonstrated absorption bands at (680-760) nm which implies that d-d transition takes place and shows only weak absorptions. The intense absorption in the UV region at around (229-325) nm is a characteristics of metal charge 3d - 4s transition at respectively high energies and assigned to charge transfer from π orbital of the donor ligand to the orbital of the metal, d-π* and inter ligand to the d orbital of the metal, n-π* transitions (Naeimi and Moradian, 2009). A shift was observed generally for all the complexes, indicating coordination. (725-755) nm shows that the complexes contain inner water. The intense absorption in the UV region at around (250-285) nm is a characteristics of ligand charge transfer as a result of delocalization of π-electrons in the benzene ring in the ligand. However, absorption bands at (680-765) nm in both the single ligand and the mixed ligand is an indication of d-d transition takes place in the visible region also weak absorptions (720-755) nm show that the complexes contain inner water (Waziri *et al*., 2014). The electronic spectra of the nickel complexes at different ratios displayed two prominent bands at 680 – 765nm may be attributed to $^1A_{1g} \rightarrow {}^1A_{2g}$ and $^1A_{1g} \rightarrow {}^2B_{2g}$ transition (Cotton et al, 1999; Aiyelabola et al., 2012), demonstrating a distorted square-planar geometry as supported by the magnetic moment of d^8 configuration with two unpaired electrons according to the Crystal field theory (CFT) $t_{2g}^6\ e_g^2$ which can be either of these geometries $d(x^2 - y^2)^1$ and $(dz^2)^1$ or $d(x^2 - y^2)^2$ and $(dz^2)^0$ (Ahmed *et al.*, 2011; Beyrambadi *et al*., 2011). The prominent bands at 3122cm^{-1} and 3027cm^{-1} ascribed to a protonated v(NH$_2$) V(NH) in both acetanilide and ampicillin with a bathochromic shift or higher shift to 3194 – 3196 cm^{-1} regions in acetanilide and ampicillin mixed ligand (Chang *et al.*, 2010).

This is evident of coordination of metal to the ligand (M – L) through the nitrogen atoms of nitro group. However, broad bands found at 1325 and 1309cm^{-1} in acetanilide and ampicillin respectively were assigned to their carbonyl groups (C = O), not found in the metal complexes but with a shift to 1499cm^{-1} in the mixed ligand (1:2:1), is an indication of carbonyl group involvement in the complex formations (Khan and Asnani, 2011; Gulcan *et al.*,2012). The broad band found around 3446 – 3575 cm^{-1} in the metal complexes were attributed to v(OH) of the non- coordinated water in the outer sphere (Osowole *et al*., 2015). On the other hand, the new bands in the range 516 – 522 cm^{-1}, 425 – 443cm^{-1} and 316 – 342 cm^{-1} in the spectra of the metal complexes are traceable to (M – N), (M – O) and (M – Cl) respectively. However, these bands could not found in the spectra of acetanilide and ampicillin, this confirms the coordination. Co(II) complexes exhibited two major shoulder bands at 725nm and 750nm which are assigned to $^2A_{2g} \rightarrow {}^2B_{1g}$ and $^2A_{1g} \rightarrow {}^2E_{1g}$ transitions typically a paramagnetic d^7 configuration (Nakamoto, 2009; Konstantinovic *et al.*, 2003). The infra-red spectroscopic studies of cobalt (II) ion complexes demonstrated different bands between the ligands and metal complexes as shown in table 8 the bands found around 3027 – 3122cm^{-1} in the spectra of the ligand but shifted to 3132 – 3295cm^{-1} in the metal complexes were assigned to V(NH) group. This confirms the coordination of metal to the ligand through the nitrogen atom. Furthermore, the bands occurred at 1322 and 1309cm^{-1} in acetanilide and ampicillin (ligands) that were attributed to carbonyl group , with no absorbance in acetanilide – cobalt complexes but with shift to longer wavelengths or bands in the mixed ligand ampicillin to 1496cm^{-1} and 1499cm^{-1} Another band found at 1707cm^{-1} in ampicillin mixed ascribed to β - lactun carbonyl group but shifted to 1774cm^{-1}, a bathochromic shift which disappeared in 1:2:1 complexes. This may due to degradation or partial conversion of ampicillin to ampicillonic acid (carboxyclic acid), showing that C=O probably from carboxylic acid involvement in the coordination (Pranay, 2009). Likewise, The presence of v(OH) group is evident in the sharp bands at 3486 – 3776cm^{-1} also strong bands found in the metal complexes between 566 - 589cm^{-1}, 444 – 456cm^{-1} and 323- 328cm^{-1} regions were assigned to M–N, M-O and M-Cl respectively, this further buttresses their involvement in the coordination (Ogunniran *et al.*, 2008) and shows the presence of chloride ions from the cobalt (II) salt found in the inner coordination sphere (Olagboye, 2015) and (M–O), implying that coordination of the central metal atom is through the oxygen atom of the ligand (Nakamoto, 2009).

The measured zone of inhibition of the complexes as well as the ligands against *Sclerotium roofil*, *Mansourian phomoides*, *Collectotrichum lindimuchianum* were presented in Table 7 and 8. The comparison of the biological activity of the *Sclerotium roofil,* shows moderate sign of inhibition at (1:2 and 1:1:1) and *Mansourian phomoide* at (1:1:1 and 1:2:1) while for *Collectotrichum lindimuchianum* the percentage of inhibition is commendable and appreciable with Ni^{2+} metal complexes. But for Co^{2+}, all the metal complexes of the *Sclerotium roofil and Mansourian phomoides* shows sign of inhibition that are not good enough with little resistance. Whereas, the inhibition signs are moderate for *Collectotrichum lindimuchianum*. However, antifungal properties so far displayed by the metal complexes against the selected pathogens are not from the metals and the ligands alone but are collective and intricate blend of other factors like solubility, melting point and solvents or media and the environment at which the complexes were prepared. All the organisms under test are susceptible to the threat of the metal complexes, including the control but ampicillin is not known for antifungal properties but a well-known antibacterial agent. However, many metallic elements have been observed to inhibit the growth of microorganisms by deactivating the enzyme, denaturing proteins of the target cells through binding to the active or reactive groups, this results in their precipitation and inactivation. The high affinity of cellular proteins for the metallic ions results in the death of the cell (Benson, 2002). The antifungal properties so far displayed by the metal complexes against the selected pathogens are not from the metals and the ligands alone but are collective and intricate blend of other factors like solubility, melting point and solvents or media and the environment at which the complexes were prepared. It was recommended that the ligands with nitrogen and oxygen donor systems inhibit enzyme activity (Fayad *et al*., 2012). Coordination diminishes the polarity of the metal ion mainly because of the partial sharing of its positive charge with donor groups within the chelate ring system as propounded by Raja *et al.* (2011). The increase in the antibacterial activities of the complexes as compared to the free ligands may be owing to the electropositive nature of metals, which will finally enhancing their antibacterial (Nazir *et al*., 2013). It is substantial from the above data presented in the Tables above that the antibacterial activity significantly increased on coordination.

Tables 9 and 10 presented the zones of inhibition of the samples against one selected pathogenic organism after 24hours of incubation at 37^{o}C. The complexes were tested against selected bacterial species and the results revealed that with acetanilide there is no inhibiting effect against A B C D and E while compared to ampicillin which have inhibiting effect on bacterial. For A, 1:1 and 1:2 did not show inhibition while for B, only 1:2:1 show high inhibition with the same strength as the control drug but moderate with rest pathogens. Mixed ligand complexes showed moderate inhibitions against the pathogenic organisms C, D and E while parent drug complexes displayed no sign of inhibition compared to the results of antibacterial testing of the metal complexes which shows that most of the metal complexes of cobalt (II) ion were not active against micro-bacteria organisms (Table 10). C display high inhibition with metal complexes, perhaps, it is a gram negative bacteria; for D and E, only 1:1:1 and 1:2:1 show inhibition others did not show inhibition. Some organisms are resistant towards the metal complexes this may due to degradation of antibacterial drugs, alteration of bacterial protein sites and modification of membrane permeability of antibiotic metal complexes (Dever and Dermogy, 1991).

Conclusion

Having studied the synthesis, characterization, and antimicrobial activities of nickel (II) ion complexes and cobalt (II) ion complexes with acetanilide and ampicillin mixed ligand at different ratio concentrations. The solubility tests of the metal complexes in some organic solvents confirmed that they are non-polar and non-electrolyte in nature. The IR spectroscopic characterization revealed the position of attachment of the cobalt(II) ion and nickel(II) ion to the ligands (acetanilide and ampicillin) was through the oxygen atom of the carbonyl group (C=O) and the nitrogen atom of N-H. The antimicrobial activities of cobalt (II) ion and nickel (II) ion revealed the bioactivity of the complexes, and they were better inhibitors of fungi and bacteria.

Coordination of metal-ligand reduces the polarity of the metal ion mainly because of the partial sharing of its positive charge with donor groups within the chelate ring system. The increase in the antibacterial activities of the complexes compared to the free ligands may be due to the electropositive nature of metals, ultimately enhancing their antibacterial.

References

Abdel-Rahman, L. H., Abu-Dief,A. M., Aboelez, M. O., Hassan, N. A. and AbdelMawgoud, A. A. (2017). DNA interaction, antimicrobial, anticancer activities and molecular docking study of some new VO(II), Cr(III), Mn(II) and Ni(II) mononuclear chelates encompassing quaridentate imine ligand. J Photochem Photobiol B Biol 170:271–285. https://doi.org/10.1016/j.jphotobiol.2017.04.003

Abdel-Rahman, L. H., Abu-Dief, A. M., Ismael, M., Mohamed, M. A. A and, Hashem, N. A. (2016). Synthesis, structure elucidation, biological screening, molecular modeling and DNA binding of some Cu(II) chelates incorporating imines derived from amino acids. J Mol Struct 1103:232–244. https://doi.org/10.1016/j.molst ruc.2015.09.039

Abdel-Rahman, L. H., Abu-Dief, A. M., Shehata, M. R., Atlam, F. M. and AbdelMawgoud, A. A. H. (2019). Some new Ag(I), VO(II) and Pd(II) chelates incorporating tridentate imine ligand: design, synthesis, structure elucidation, density functional theory calculations for DNA interaction, antimicrobial and anticancer activities and molecular docking studies. Appl Organomet Chem 33:e4699. https://doi.org/10.1002/aoc.4699

Abdulhamid, D., Adamu, S. A. and Abba Tijani, M, Manniru, A. A. (2016). Synthesis,characterization and antimicrobial studies of ampicillin complexes. *American Chemical Science Journal*, 12(4): 1-5.

Abubakar, U. A. Birnin-Yauri, U. A., Muhammad, C., Amali, M. A. and Ahmed, A. B. (2019). Synthesis, Characterization and Antibacterial Activity of Co2+ and Ni2+ Mixed Drug Metal (II) Complexes of Sulfamethoxazole and Ampicillin Trihydrate. International Journal of Advanced Research in Chemical Science (IJARCS) 6(7): 10-13 ISSN No. (Online) 2349-0403 DOI: http://dx.doi.org/10.20431/2349-0403.0607002 www.arcjournals.org

Ahmed, E. M., Marzouk, N. A., Hessein, S. A. and Ali, A. M. (2011). Synthesis, Reactions and Antimicrobial activity of some new thienopyridine and thienopyrimidine derivatives. *World Journal of Chemistry*, 6:25-31.

Aiyelabola, T., Ojo, I and Akinkunmi, O. (2012). Structural and Antimicrobial Studies of Coordination Compounds of Phenylalanine and Glycine. *International Journal of Chemistry*, (4)2: 49-59.

Bastug, A., Yilmaz, G. R., Kayaaslan, B., Akinci, E. and Bodur, H. (2012). Risk factors for mortality in patients with nosocomial Staphylococcus aureus bacteremia. Turk. J. Med. Sci., 42, 1222–1229.

Benson, H. J. (2002). Microbiological applications: Laboratory manual in general microbiology. 8th edition.84, McGraw Hill,New York.

Beyrambadi, S. A., Hoseini, H. E., Housaindokht, M. R. and Morsali, A. (2011). Synthesis, experimental and theoretical characterization of Cu (II) complex of @-chloropyrimidine. *Science Research Essentials*, 6(20): 4341-4346.

Chang, E., Simmers, C. and Knight, A. (2010). Cobalt complexes as antiviral and antibacterial agents. *Pharmaceuticals*, **3**, 1711-1728.

Claudel, M., Schwarte, J. V. and Fromm, K. M. (2020). New Antimicrobial Strategies Based on Metal Complexes, *Chemistry* MDPI *2*(4), 849-899; **https://doi.org/10.3390/chemistry2040056**

Cotton, F. A., Wilkinson, G. and Murillo, C. A. (1999). Advanced Inorganic Chemistry, 6th ed. New York Wiley Interscience, 420, 638-648, 1355-1375.

Cox, P. A. (2005). Instant Notes Inorganic Chemistry. 2nd ed. New York: BIOS Scientific Publishers, 237:1001-2299.

Dever, L. A and Dermady, T. S. (1991). Mechanism of bacterial resistance to antibiotics. *Arch. Intern. Med.* 151(5):886 – 893

Fayad, N. K., Taghreed, H. A. and Ghanim, F. H. (2012). Synthesis, Characterization and Antibacterial Activities of Mixed Ligand Complexes of some Metals with 1-nitroso-2-naphthol and L-phenylalanine. *Chemistry and Matrials Research*, **2**(5): 18-29.

Gulcan, M., Sonmeez, M. and Berber, I. (2012). Synthesis, Characterization and antimicrobial of a new pyrimidine Schiff base and its Cu(II), Ni(II), Co(II), Pt(II) and Pd(II) complexes. *Turkey Journal of Chemistry*, 36:189.

Harris, D. and Bertolucci, M. (1989). Symmentry and spectroscopy.Dodver publication. Page 669 673.

Igwo-Ezikpe, M. N., Imaga, N. O. A., Ogbunugafor, H. A., Osuntoki, A. A., Adeleye, S., Ipadeola, A. O. (2013). Antimicrobial effect of Zingiber officinale rhizomes extracts on selected pathogenic clinical isolates. The Bioscientist.1, 73-79.

Johari, R., Kumar, D. and Singh, S. (2009). Synthesis and antibacterial activity of Mn(II) Schiff – base complex. *Journal of the Indian Chemistry Council*, 26:23 – 27.

Jones, M. and Fleming, S. A. (2010). Organic Chemistry (4th ed) USA: Nortown company Inc., 14-16.

Kafi-Ahmadia, L., Marjanib A. P. and Pakdaman-Azaria, M. (2018). Synthesis, Characterization and Antibacterial Properties of N,N’-Bis(4-dimethylaminobenzylidene)benzene-1,3-diamine as New Schiff Base Ligand and its Binuclear Zn(II), Cd(II) Complexes. S. Afr. J. Chem., 71, 155–159.

Khan, F. R. and Asnani, A. J. (2011). Synthesis, antiulcer and anti-secretory activity of some new substituted 2 (pyrimidylsulfinyl) Benzamidazoles Derivatives. *International Journal of Research in Pharmaceutical and Biomedical Sciences*, **2**(2):695-700.

Konaté, K., Mavoungou, J. F. and Lepengué, A. N. (2012). Antibacterial activity against β-lactamase producing Methicillin and Ampicillin-resistants *Staphylococcus aureus*: Fractional Inhibitory Concentration Index (FICI) determination. *Ann. Clin. Microbiol. Antimicrob.* 11:18

Konstantinovic, S., Radovanovic, C., Cakic, Z. and Vasic, V. (2003). Synthesis and characterization of Ci(II), Ni(II), Cu(II) and Zn(II) complexes with 3-salicylidenehydrazono-2-indolinone. Journal of Serbian Chemical Society, 68(8/9), 641-647. http://dx.doi.org/10.2298/JSC0309641K

Kunkely, H and Vogler, A. (2006). Photoproperties of silver sulfadiazine. Inorganic Chem.Commum.10:156 – 228).

My, N.H., Hirao, H., Van, D.U. and Morokuma, K. (2011). Computational studies of bacterial resistance to beta-lactam antibiotics: Mechanism of covalent inhibition of the penicillin-binding protein 2a (PBP2a). J. Chem. Inf. Model. 51, 3226–3234

Naeimi, H and Moradian, M. (2009). Synthesis and characterization of nitro-sciff bases derived from 5 – nitro – salicylaldehyde and various diamines and their complexes of Co (II). J. Coord. Chem, 62: 156 – 166.

Nazir, F., Bukhari, I. H., Arif, M., Riaz, M., Raza, S. A. Bokari T. H. and Jamal, M. A. (2013). Antibacterial Studies and Schiff bases metal complexes with some novel antibiotics. *International Journal of Current Pharmaceutical Research*, **5**(3):40-46.

Nyawade1, E. A., Onani, M. O., Meyer, S. and Dube, P. (2020). Synthesis, characterization and antibacterial activity studies of new 2-pyrral-L-amino acid Schiff base palladium (II) complexes. Springer. 1-12.

Obaleye, J. A., Aliyu, A. A., Rajee, A. O. and Bello, K. E. (2021). Synthesis, Characterization, In-Vitro Anti-Inflammatory and Antimicrobial Screening of Metal(II) Mixed Diclofenac and Acetaminophen Complexes.Bull. Chem. Soc. Ethiop. 2021, 35(1), 77-86.

Obaleye, J. A., Tella, A. C. and Bamigboye, M. O. (2012). Metal complexes as prospective Antibacterial Agents In: B. Valprassad ed. 2012. A Search for Antibacterial Agent. Rijeka: InTech. Rijeka, Croatia, 197-219.

Ogunniran, K. O., Ajanaku, K. O., James, O. O., Ajani, O. O. and Adekoya, J. A. (2008). Synthesis, characterization,antimicrobial activity and toxicology study of some metal complexes of mixed antibiotics. *African Journal of Pure and Applied Chemistry*. 2 (7), 69 – 74.

Olagboye S. A. (2015). Mixed Ligand Complexes of Cobalt (II) Barbitone in Aqueous Medium and their Biological Activities. Chemistry and Materials .Research www.iiste.orgISSN 2224-3224 (Print) ISSN 2225-0956 (Online).Vol.7, Pg**.** 129-133.

Osowole, A. A., Sherifah, M. W. and Alaoluwa, K. A. (2015). Synthesis, Characterization and Antimicrobial Activity of Some Mixed Trimethoprim -Sulfamethoxazole Metal drug Complexes. *World Applied Sciences Journal,* **33**(2):336-342.

Pranay, G. (2009). Studies of two complexes with Ampicillin. *International Journal od Chem. Tech. Research*, (CODEN). 1 (3). 461 – 463.

Raja, S. R., Jisha, J. and Mary, N. L. (2011). Antibacterial Studies of Schiff Base Complexes and Polymer supported Schiff Base Complexes. *International Journal of Institute Pharmaceutical Life Sciences*, **1**(2):49-56.

Saga, T. and Yamaguchi, K. (2009). History of Antimicrobial Agents and Resistant Bacteria settingsJMAJ 52(2): 103–108.

Singh, P. and Srivastava, D. (2013). Phytochemical screening and in vitro antifungal investigation of Parthenium hysterophorus extracts against A. alternata. International Research Journal of Pharmacy. 4:190-193.

Sivakumar, K. and Prema, D. (2015). *"Inclusion Complexation of Acetanilide into the β-Cyclodextrin Nanocavity: A Computational Approach"*, Procedia Materials Science, 10: 467–475, doi: 10.1016/j.mspro.2015.06.083

Waziri, I., Ndahi, N. P., Mala, G. A. and Fugu, M. B. (2014). Synthesis, Spectroscopic and Biological Studies of Cobalt(II), Nickel(II) and Iron(III) mixed antibiotic metal complexes. *Scholars Research Library*, **6**(5):118-122.