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Synthesis, Characterization and Antibacterial Activity of Schiff Base of Cu (II), Ni (II) and Co (II) Complexes

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ABSTRACT

Due to their importance as catalysts in many reactions and their biological activities, an interest in the synthesis and characterization of transition metal complexes containing Schiff bases is increasing. The major aim of this study was to compare the antibacterial activity of the ligands with their metal complexes. We have successfully synthesized Cu (II), Ni (II) and Co (II) complexes of N, N-Bis(vanillinidene)-1,2-phenylenediamine and N,N-Bis(salicylidene)-1,2-phenylenediamine. The Schiff's bases were synthesized by the reaction of o-phenylenediamine with salisaldehyde or o-vanillin and their metal complex were synthesized by the reaction of the ligands with the metal salts. The structure of all the synthesized ligands were confirmed using NMR, IR and UV-Vis spectral analysis and their metal complexes were confirmed using IR and UV-vis spectra. The synthesized ligands and their metal complexes were screened for their antibacterial activities against Escherichia coli, Staphylococcus aureus, and Klebsiella pneumonia bacterial strains by using disc diffusion method. Among the synthesized compounds, the ligand L1 is moderately active against Staphylococcus aureus, K. pneumonia and Escherichia coli bacteria strain, CoL1 exhibited the highest activity, with 22mm zone of inhibition against staphylococcus aureus, compared to standard gentamycin activity, with 21 mm zone of inhibition.

Keywords: o-phenylenediamine; o-vanillin; Salisaldhyde; Schiff base; Transition metal (II) complexes; Antibacterial activity

INTRODUCTION

Schiff's base ligands are usually prepared by condensation between aldehydes and primary amines. They are the most widely studied ligands and are considered as ''privileged ligands'' [1,2] and are able to coordinate many different metals to stabilize them in various oxidation states [3].
Multidentate Schiff bases have been widely used as ligands, because they can be easily attached to metal ions to generate stable complexes. It interacts with most metallic ions and especially with transition ones and have ability to stabilize them in various oxidation states. Schiff bases have played an important role as chelating ligands for a large variety of metal ions.Recently, there has been enhanced interest in the synthesis and characterization of transition metal complexes containing Schiff bases due to their importance as catalysts in many reactions [4-10].

Transitionmetal complexes of Schiff's bases particularly derived from carbonyl compounds based on heterocyclic rings have also received great attention in medicinal and pharmaceutical field, a number of compounds containing Schiff base have been synthesized and tested for their biological activity, because they exhibited broad range of biological activities, such as antibacterial [11-13],anticancer [14-18], anti-inflammatory [19],antioxidant [20-22] etc.

In this paper, we present the synthesis and anti-bacterial activity investigations of N, N-Bis(vanillinidene)-1,2-phenylenediamine and N, N-Bis(salicylidene)-1,2-phenylenediamine and their metal complex against *K. pneumoniae*, *E. coli*, and *S. aureus* bacterial strain. The major aim of this study was to compare the activity of the ligands with their metal complexes.

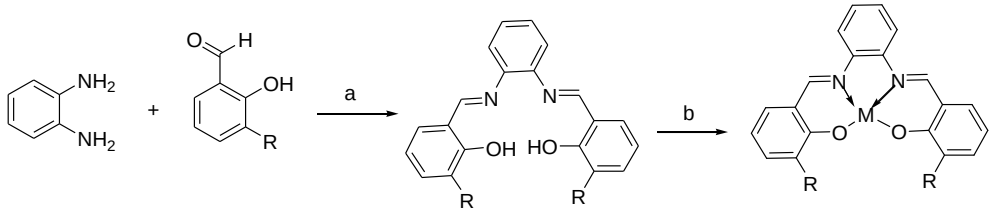
EXPERIMENTAL SECTION

Materials and methods

All chemicals and solvents were analytical grade and used without further purification; the progress of the reaction was monitored by TLC silica gel plates; the purification of the products was performed by column chromatography using silica gel (100–200mesh). Melting points were measured in open capillary tubes and were uncorrected; infrared (IR) spectra were recorded using FT-IR Bruker Alpha spectrometer.NMR spectra were recorded on BrukerAvance NMR spectrometer (400MHz) using TMS as the internal standard.

Chemistry

The free ligands and their metal complexes were prepared as outlined in Scheme 1. The Schiff's bases were synthesized by the reaction of o-phenylenediamine with salisaldehyde or o-vanillin. The product was further purified by column chromatography using mixture of hexane and ethyl acetate as solvents system in different ratio. The ligands were further reacted with copper (II) acetate, nickel (II) acetate and hydrated cobalt (II) chloride. The mixture was refluxed at a temperature of 70-80 ^{o}C and the progress of the reaction was monitored by thin layer chromatography (TLC). The solid product formed was separated by filtration, washed with ethanol and recrystallized from chloroform and dried.



L_1, R = OCH_3, L_2, R = H; M= Cu, Ni or Co

Scheme 1: reagent and condition: a) EtOH, AcOH, reflux; b) metal salt, EtOH, reflux

Synthesis and characterization

General procedure for the Synthesis of N, N-Bis (vanillinidene)-benzene-1, 2-diamine (L_1) and N, N-Bis (salicylidene)-benzene-1, 2-diamine (L_2)

O-phenylenediamine (0.054g, 0.5mmol) was dissolved in 10ml ethanol and a solution of o-vanillin (0.304g, 1mmol) or salisaldehyde (0.244g, 1 mmol) in 20ml ethanol was added to this mixture, 3-5 drops of glacial acetic acid was added and refluxed at 70-80°C for 2 hours.The progress of the reaction was monitored by using TLC. After completion of the reaction, the reaction mixture was cooled and ethanol was removed using rotary evaporator.The solid obtained was further purified by column chromatography using mixture of n-hexane: ethyl acetate solvent system.

Characterization of L_1

Reddish yellow solid, Yield: 75 %, Mp: 161-163^{o}C; ^{1}H NMR (DMSO-d_6, 400MHz): δ_H 13.20(2H, OH), 7.57 (s, 2H, azomethine), 6.69-7.09(m, 10H, aromatic proton), 3.73(s, 6H, methoxy proton). ^{13}C NMR (DMSO-d_6, 100MHz): δ_C 164.1, 152.1, 151.0, 142.5, 128.3, 124.9, 123.7, 122.9, 119.6, 118.7, 56.2

Characterization of L_2

Orange solid, Yield: 68.1 %, Mp: 206-208 ^{o}C; IR(KBr, Cm^{-1}): 3394(-NH), 3240(-OH), 3047(C-H, aromatic), 2854(C-H, methyl), 1593(C=N);^{1}H NMR (DMSO-d_6,400MHz): δ_H 12.9(s, 2H, OH). 8.1(s, *2H*, azomethine proton) 6.96-7.4(m, 12H, aromatic proton); ^{13}C NMR (DMSO-d_6, 100MHz): δ_C 161.2, 160.3, 142.7, 132.5, 130.6, 128.8,1 23, 121.5, 118.5, 116

Synthesis of Cu (II), Ni (II) and Co (II) complexes of ligand L_1

The ligand L_1 (0.224g, 0.5mmol) was dissolved in 10ml of hot ethanol, and mixed with (0.5mmol) of $Cu(CH_3COO)_2.H_2O$,$Ni(CH_3COO)_2.4H_2O$ or $CuCl_2.6H_2O$ dissolved in 5ml of hot ethanol. The reaction mixtures were refluxed for 1 hour. The progress of the reaction was monitored using TLC. After the reaction was completed, the reaction product was cooled in ice water, filtered and washed with ethanol. Finally, the solid was recrystallized from chloroform and dried. The physical characteristics and molar conductance of L_1, L_2 and their metal (II)complexes given in Table 1.

Synthesis of Cu (II), Ni (II) and Co (II) complexes of ligand L_2

The ligand L2 (0.16 g, 0.5 mmol) was dissolved in 10 ml of hot ethanol, and mixed with (0.5mmol) of $Cu(CH_3COO)2.H_2O$, or $Ni(CH_3COO)2.4H_2O$ dissolved in 5 ml of hot ethanol. The reaction mixtures were refluxed for 1 hour. The progress of the reaction was monitored using TLC. After the reaction was completed, the reaction product was cooled in ice water, filtered and washed with ethanol. Finally, the solid was recrystallized from chloroform and dried .

Table 1: Physical characteristics and molar conductance of L1, L2 and their metal (II) complexes.

No	Compound	Color	% yield	Molar conductance(μ s/cm)
1	L1	Reddishyellow	75	27.1
2	L2	Orange	68.1	25.6
3	Cu (II)L_1	Yellowish brown	79.64	24.6
4	Ni (II)L_1	Black red	74	18.8
5	Co (II)L_1	Brown	42.13	22.4
6	Cu (II)L_2	White brown	59.89	20.5
7	Ni (II)L_2	Black red	80.6	14.14

Uv-vis spectrum of the ligands and their metal (II) complexes

The Uv-visble spectra of the ligand, L_1 and its complexes were recorded in DMSO at room temperature .The observed spectrum of ligand L_1 showed three intense bands around 278 nm, which was assigned to π→π* transition of C=N, 291nm assigned to n→π* transition of C-O methoxy group, 300nm transition of the OH. In complex formation this was shifted to a higher wavelength suggested the coordination of azomethine nitrogen. The UV-Vis spectra of copper complex showed three bands at 301nm assigned to π→π* transition from C=N, 382 nm assigned to n→π* transition from the azomethine nitrogen of ligand to metal charge transfer and 493nm n→π* transition from hydroxyl oxygen of ligand to metal charge transfer. Nickel (II) complexes showed three absorption bands at 301nm π→π* transition of C=N, 382nm n→π* transition from azomethine nitrogen of the ligand to metal charge transfer, 496nm n→π* transition from the hydroxyl of the ligand to metal charge transfer. Cobalt(II) complex of L_1 showed three absorption bands at 301nm π→π* transition of azomethine C=N group, 381nm transition from the azomethine nitrogen of the ligand to metal charge transfer, 496nm transition fromthehydroxyl oxygen of the ligand to metal charge transfer.

The UV-visible spectra of the ligand, L_2 and its metal complexes were recorded in DMSO-d_6 at room temperature. The electronic spectra of ligand L_2 showed two bands at 273nm which is assigned to π→π* transition of C=N group, 333nm n→π* transition from OH. UV of Cu (II) complex showed three bands at 301nm π→π* transition of azomethine group(C=N), 381nm n→π* transition from azomethine nitrogen of the ligand to metal charge transfer and 493nm n→π* transition from the hydroxyl oxygen of the ligand to metal charge transfer. The Ni (II) complex exhibit three bands at 300nm π→π* transition of the azomethine C=N group, 382nm n→π* transition from azomethine nitrogen of the ligand to metal charge transfer and 495nm n→π* transition from the hydroxyl oxygen of the ligand to metal charge transfer.

RESULTS AND DISCUSSIONS

Antibacterial activities

Culture media and disk preparation

Nutrient agar, Muller Hinton agar and Nutrient broth were prepared according to themanufacturer instruction in which the prepared media was autoclaved at 121^{o}C for 15minutes. Then the prepared culture media was checked for the sterility for 24 hours at 37^{o}C. Quality control stains of *Staphylococcus aureus*, *Escherichia coli and Klebsiella pneumonia* known. American type culture collection committee (ATCC) was used to perform theantibacterial activities of the agents. Watman filter paper was used to prepare a disk of 5mm diameter using manual paper punching.

Preparation of chemical solution and media for the antibacterial activity

By using analytical balance, a 500 μ g of each chemical powder was added to 15µl dimethyl sulfoxide (DMSO) and mixed to form a homogenous solution. A 5µl of solution was added to the sterile disk prepared before using sterile micropipette. Quality control strains obtained from Hawassa University College of medicine and health science was inoculated on nutrient agar plate using sterile loop (Table 2).

The plate was incubated for 24 hours at 37 ^{o}C. A 3-5 colonies was picked and suspended in 5ml nutrient broth to form agar plate in three directions to form uniform inoculums, then a disk with a control gentamicin and solution impregnated disk was placed on the plate and incubated for 24 hours at 37 ^{o}C. Each disk was labeled with its unique ID number on the back of the Petri dish. After incubation the diameter of the zone of inhibition was measured using ruler. Growth of bacteria pathogens on each concentration was checked to determine the minimum concentration that inhibits the growth of bacteria's. It is evident from table 2 that the minimum concentration value for each ligands and its metal complexes were (500 μ g/5 μ L disc) against *Staphylococcus aureus, Klebsiella pneumonia and Escherichia coli.*

Table 2: In-vitro antibacterial activity values of the synthesized Ligands and their metal (II) complexes

Compound (500 μ g/5 μ L disc)	Inhibition zone(mm)		
	Staphylococcus aureus	Klebsiella pneumonia	Escherichia coli
L1	13	7	9
CuL1	7	5	5
Ni L1	10	5	11
Co L1	22	5	5

L2	11	5	5
CuL2	7	5	5
NiL2	5	5	5
Gentamicin	21	6	21

The antibacterial activity of the ligands and complexes were measured based on zone of inhibition on the grown bacteria on the prepared culture media on petri-dish as shown (Figures 1-3) its inhibition value were measured using ruler.

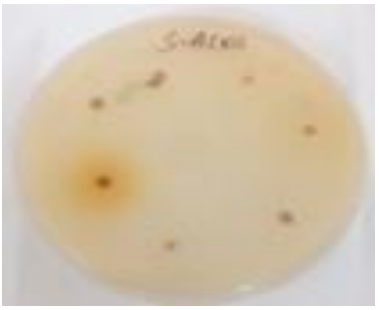


Figure 1: Zone of inhibition for *Staphylococcus aureus*, image of ligands and their complexes.

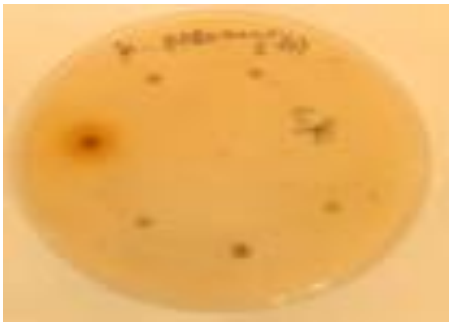


Figure 2: Zone of inhibition for ***Klebsiella pneumonia,*** image of ligands and complexes

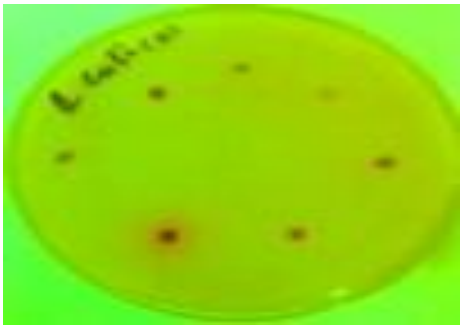


Figure 3: Zone of inhibition for ***Escherichia coli,*** image of ligands and Complexes

CONCLUSION

The antibacterial activity of the ligands and their metal complexes were studied against three pathogenic bacterial strains, one gram positive *(Staphylococcus aureus*) and two gram negative (*Klebsiella pneumonia and Escherichia coli*) Table 2. The ligand L_1 is moderately active against *Staphylococcus aureus, K. pneumonia* and *Escherichia coli* bacteria strain, whereas NiL_1 complex exhibited less activity against those bacteria strain and CoL_1 exhibited the highest activity against *Staphylococcus aureus*. CuL_2 and NiL_2 exhibited no significant activity against all the tested bacterial strain. In general, the ligand L_1 and its metal complexes have higher zone of inhibition than L_2 and its metal complexes. Comparing the two ligands, L_1 showed better activity than L_2, structurally the two ligands differ by the presence of methoxy substituent, the difference in activity may be due to this substituent.

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