

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Structure, Diagnosis, and in the Vitro Antimicrobial evaluation of 2-amino pyridine-derived Ligand Schiff base and its complexes with Cu (II), Hg (II), Ni (II), Mn (II) and Co (II).

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ABSTRACT

The study given in this paper is concerning the synthesis, diagnosis, and in vitro antimicrobial evaluation of Cu(II), Hg(II), Ni(II), Mn(II) and Co(II) transition metal complexes of Schiff base 2-(phenyl(pyridin-2-ylimino)methyl)benzoic acid derived from 2-amine pyridine and 2-benzoylbenzoic acid. In these complexes amino group available in 2-amine pyridine was allowed to react with 2-benzoylbenzoic acid, to get Schiff base which was, thereafter, let to react with metal chloride $M(II)Cl_2 \cdot nH_2O$ Where (M= Cu(II), Hg(II), Ni(II), Mn(II) and Co(II)) are characterized on the basis of NMR spectroscopy physical properties, FT-IR spectroscopy, conductance measurements, atomic absorption spectroscopy and UV-Visible spectroscopy. Conductance measurements offered that complexes were non-electrolytes and they were set to be ML_2 type. The IR study showed that ligand is tridentate and coordinate to the central metal ion through the azomethine nitrogen - C=N of Schiff base and the nitrogen of pyridine ring and oxygen of carboxylic acid. All the complexes under realisation own antibacterial effectiveness.

Keywords: Structure, Diagnosis, in vitro Antimicrobial evaluation and 2-amino pyridine

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INTRODUCTION

A ligand such as Schiff base is a significant type in the range of coordination chemistry [1]. In two decades ago, great interest has been a push to the chemistry of the metal complexes of Schiff bases forming any donor atom such as nitrogen and other [2-5]. Many Schiff bases and their metal complexes have been establishing to possess important biological and catalytic [6-7]. Schiff bases were used to study of biological and catalytic activity due to their complexation behaviour with metal ions, their great flexibility and diverse structural aspects [8-10]. Also, Schiff bases have analytical applications because they are used as an efficient reagent in trace analysis of some metal cations [11-13]. Lately, there has been great attention in the chemistry of chelating ligands containing O and N, donor atoms [14-16]. They show wide biological efficacy and are of private attention because of the diversity of methods in which they are bonded to metal ions. In this paper, we describe the structure, diagnosis, and in the vitro antimicrobial evaluation of the new Schiff base and its chelation complexes with various metal ions. The growing activity in this scope may be assigned to the noticeable structural characteristics and reported the antimicrobial efficacy of this donor ligand and its complexes. It is known that the existence of metal ions bonded to biologically active compounds may enhance their activities.

EXPERIMENTAL

2-benzoylbenzoic acid and 2-aminopyridine were purchased from sigma Aldrich Co. (China). All reagent and solvents were of high purity (sigma) and were used without further purification. The metal salts used for complexation: Copper (II) chloride dihydrate, Cobalt(II) chloride hexahydrate, Nickel(II) chloride hexahydrate, Manganese (II) chloride tetrahydrate and Mercury (II) chloride were obtained from British Drug House (BDH) chemical limited company.

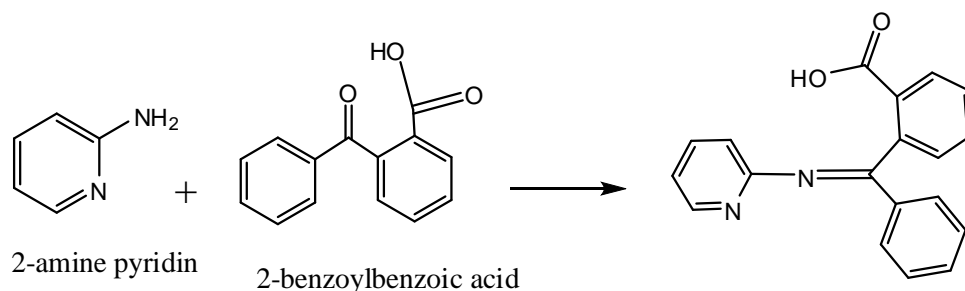
INSTRUMENTS

Melting points were recorded using hot stage Gallenkamp melting point apparatus and were uncorrected. Infrared spectra were recorded using Fourier transform infrared SHIMADZU (8300) (FT-IR) infrared spectrophotometer, KBr disc or thin film was performed by CO.S.Q.C IRAQ. ^1H NMR and ^{13}C - NMR spectra were recorded on Fourier Transform Varian spectrometer, operating at 300 MHz with tetramethylsilane as an internal standard in DMSO, Measurements' were made at Chemistry Department, Al-Bayt University, Jordan. Conductivity measurements were obtained from WTW conductivity meter by using ethanol as a solvent of 10^{-3}M concentration at room temperature. Magnetic susceptibility measurements were obtained at room temperature on the solid state applying Faraday's Method using Bruker BM6 instrument. Metal analyses of complexes were determined by Atomic Absorption (A.A.) Technique. Using a Shimadzu PR-5. GRAPHIC PRINTER atomic absorption spectrophotometer.

Preparation of Schiff base ligand

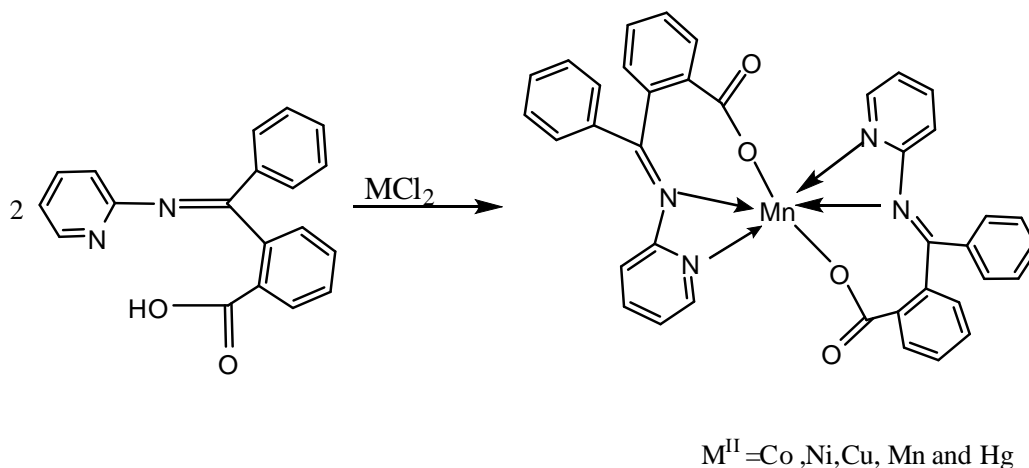
Conventional method Synthesis of 2-(phenyl(pyridin-2-ylimino)methyl)benzoic acid :

The ligand was prepared by the condensation of the equal molar ratio of 2- amine pyridine (9.411 g, 0.1mmol) with 2-benzoylbenzoic acid (2.26g, 0.1mmol) dissolved in ethanol. The resulting was stirred fully, refluxed for 5 hrs. and then allowed to cool overnight. The coloured precipitate of Schiff base got was filtered, washed with hot ethanol many times and dried in air at room temperature and finally stocked in a CaCl_2 desiccator under miniature pressure. The purity of prepared compounds was tested by TLC using silica gel G. Yield: 78%, m.p. 110°C . Characteristic ^1H NMR peaks in ligand Fig(1), are (DMSO- d_6 , TMS, δ /ppm): 2.41, (6H, s, DMSO); 7.17-8.68, (m, 12H, C_6H_5) ; 13.51, (1H, s, $-\text{COOH}$), ^{13}C NMR Fig(2), (DMSO, 75MHZ) δ /ppm: 40.21 (s, DMSO); 117.67-142.82 (m, C_6H_5); 162.23, (s, $\text{C}=\text{N}$)_{pyridine} ; 59.05 (s, COOH); 172.81 (s, $\text{C}=\text{N}$)_{imine}.



General experimental procedure for the synthesis of metal complexes (Scheme-2)

The ligand (0.02 mole) and the appropriate metal chloride (0.01 mole) in 50 ml ethanol (60°C) was refluxed for 2 hours. In all the cases the ligand concentration was a slight excess of 1:2 metal :ligand molar ratios. After refluxing the solid mass separated filtered through a sintered glass crucible (G4) and the residue was washed with a (1:1) (ethanol-water mixture) and diethyl ether finally dried under vacuum desiccators over fused calcium chloride. The Yield, colour, % of element content and elemental analysis and melting point of the prepared complexes are given in Table



RESULTS AND DISCUSSION

Characterization of metal complexes

The complexes of tridentate Schiff bases were prepared by the reaction of 1:2 molar ratio of metal ions (chloride salt of metals) and the Schiff base solutions in the ethanolic medium. The ligand acted as uninegative tridentate anion on the removal of the one proton from which $[M(L)_2]$ type complexes were obtained. Most of the complexes are insoluble in acetone, alcohol and ether. Some of them are moderately soluble in chloroform. But most of the complexes are highly soluble in DMSO and DMF. All the prepared complexes are described by the following values. Based on the proportion of different elements and micro-analysis the structure of metal complexes assists to formulate the complexes. Molar conductance data were obtained in the reign of $40-60 \text{ohm}^{-1} \text{cm}^2 \text{mol}^{-1}$, which points that the complexes are (1:0 type) non-electrolyte. All compounds are stable and have sharp melting points that indicate the purity of all the compounds. The elemental analyses of the compounds are co-operating with the composition suggested for the compounds.

Infrared

The IR of ligand compound, Fig(3) confirms the formation of imine bond ($-C=N$) at (1629cm^{-1}) and absence of the original aldehydic bond ($-C=O$). A band at $1616-1623 \text{cm}^{-1}$ is assigned to stretching vibration of the imine group $\nu(C=N)_{\text{imine}}$. All the compounds displayed a band at $1270-1288 \text{cm}^{-1}$ which are assigned to $\nu(C=N)$ stretching

vibration of the pyridine, respectively. The spectra of the free ligand showed the band at $(3319)\text{cm}^{-1}$ due to $\nu(\text{O-H})$ of 2-benzoyl benzoic acid. Deprotonation of all carboxylic functions is confirmed by the lack of O-H stretching bands in the IR region $3400\text{--}3300\text{ cm}^{-1}$ for all complexes Fig(4). In all the complexes additional bands are also shown in the region $\sim 434\text{--}454$ and $527\text{--}562\text{ cm}^{-1}$. These vibrations have been ascribed to $\nu\text{ M-O}$ and $\nu\text{ M-N}$ respectively, indicating coordination. (Table-2)

Table 1: Some physical properties of prepared ligand (HL) and its complexes

compounds	Formula	Molecular Weight	Colour	Yield%	M.P.	%Elemental Analysis Found % (Calculated)			
						C	H	N	M
HL	$\text{C}_{19}\text{H}_{14}\text{N}_2\text{O}_2$	302.33	Light brown	61	131	75.14 (75.48)	4.21 (4.67)	9.08 (9.27)	-
$[\text{Co}(\text{L})_2]$	$\text{C}_{38}\text{H}_{26}\text{CoN}_4\text{O}_4$	661.57	Brown	70	222	68.66 (68.99)	3.42 (3.96)	8.15 (8.47)	8.71 (8.91)
$[\text{Ni}(\text{L})_2]$	$\text{C}_{38}\text{H}_{26}\text{N}_4\text{NiO}_4$	661.33	Brown	71	236	68.79 (69.01)	3.24 (3.96)	8.31 (8.47)	8.38 (8.88)
$[\text{Mn}(\text{L})_2]$	$\text{C}_{38}\text{H}_{26}\text{MnN}_4\text{O}_4$	657.58	Deep brown	76	247	69.26 (69.41)	3.43 (3.99)	4.54 (4.78)	8.14 (8.35)
$[\text{Cu}(\text{L})_2]$	$\text{C}_{38}\text{H}_{26}\text{CuN}_4\text{O}_4$	666.18	Dark Brown	73	253	69.10 (69.41)	3.33 (3.93)	8.29 (8.52)	9.32 (8.35)
$[\text{Hg}(\text{L})_2]$	$\text{C}_{38}\text{H}_{26}\text{HgN}_4\text{O}_4$	803.23	Off-White	68	243	56.52 (56.82)	3.03 (3.26)	6.71 (6.98)	24.13 (24.97)

Table 2: Infrared spectral data (wave number ν') cm^{-1} for the ligand(HL) and its complexes

Compound	$\nu(\text{OH})$	$\nu(\text{C=N})_{\text{pyridine}}$	$\nu(\text{C=N})_{\text{imine}}$	$\nu_{\text{assy}}(\text{COO})^-$	$\nu_{\text{ssy}}(\text{COO})^-$	$\Delta\nu = \nu_{\text{assy}} - \nu_{\text{ssy}}(\text{COO})^-$	$\nu(\text{M-N})$ $\nu(\text{M-O})$
HL	3319	1657	1629	1521	1369	152	-
$[\text{Co}(\text{L})_2]$	-	1644	1621	1522	1382	140	551 454
$[\text{Ni}(\text{L})_2]$	-	1646	1618	1530	1364	166	541 451
$[\text{Cu}(\text{L})_2]$	-	1637	1616	1537	1369	168	562 450
$[\text{Mn}(\text{L})_2]$	-	1640	1620	1542	1383	159	545 434
$[\text{Hg}(\text{L})_2]$	-	1635	1623	1554	1397	157	527 443

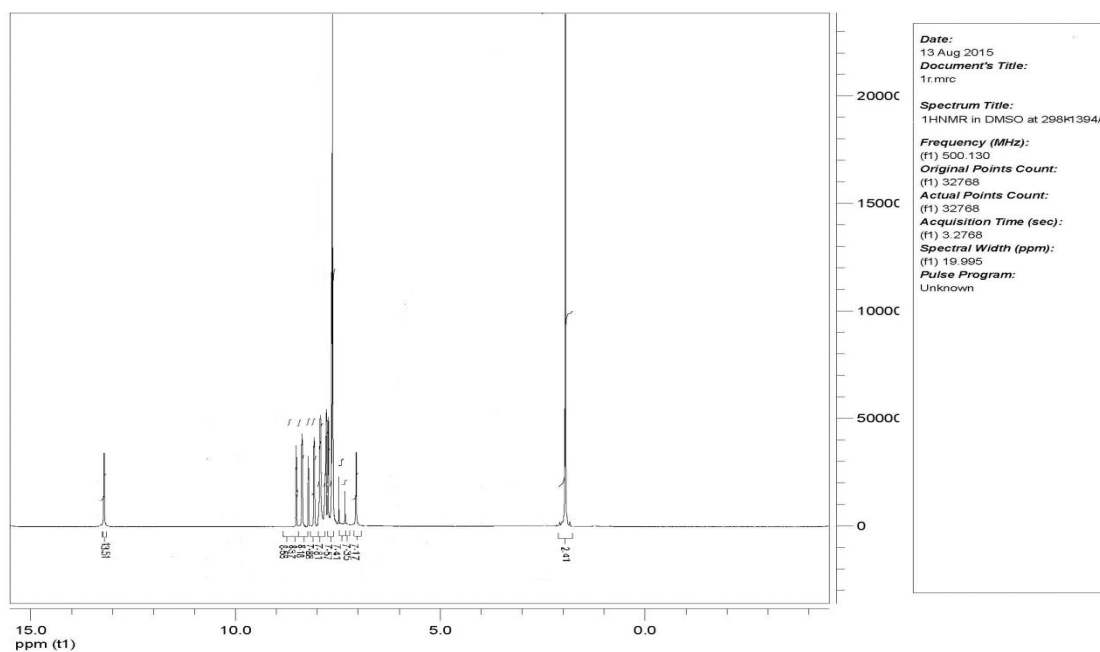
Table 3: Electronic absorption spectral data of the compounds

Compound	$\lambda\text{ nm}$	ABS	$\nu\text{ cm}^{-1}$	ϵ_{max} ($\text{molar}^{-1}\cdot\text{cm}^{-1}$)	Assignments	μ_{eff} (BM)	geometry
HL	271 338	0.876 0.098	36101 30303	876 98	$\pi \rightarrow \pi^*$ $n \rightarrow \pi^*$	-	-
$[\text{Co}(\text{L})_2]$	274 361 908	1.467 0.385 0.075	37037 27700 11013	1523 385 75	L.F C.T ${}^5\text{T}_{2g} \rightarrow {}^5\text{E}_g$	4.82	Distorted Octahedral
$[\text{Ni}(\text{L})_2]$	276 349 992	1.927 0.311 0.021	36231 28653 10080	1927 311 21	L.F C.T ${}^4\text{T}_{1g}(\text{F}) \rightarrow {}^4\text{T}_{2g}(\text{F})$	4.62	Octahedral

[Mn(L) ₂]	278	1.476	35971	1476	L.F	5.73	Octahedral
	351	0.339	27248	351	C.T		
	590	0.026	16750	26	³ A _{2g} (F) → ³ T _{2g} (F)		
	777	0.019	12804	19	³ A _{2g} (F) → ³ T _{1g} (F)		
	828	0.013	12019	13	³ A _{2g} (F) → ³ T _{1g} (P)		
[Cu(L) ₂]	281	2.200	36363	2200	L.F	1.85	Distorted Octahedral
	356	0.367	28089	367	C.T		
	817	0.041	12239	41	² E _g → ² T _{2g}		
[Hg(L) ₂]	283	2.284	35335	2284	L.F	0.0	Octahedral
	366	0.782	27322	782	C.T		

Table 4: Diameter of zone of inhibition (mm) of HL

Compound	HL	[Co(L) ₂]	[Mn(L) ₂]	[Ni(L) ₂]	[Cu(L) ₂]	[Hg(L) ₂]
<i>Escherichia. Coli</i>	3	9	12	10	11	10
<i>Staphylococcus aureus</i>	4	14	7	14	-	8
<i>Bacillus</i>	-	8	9	15	6	-
<i>Pseudomonas</i>	2	11	15	13	8	5


 Fig 1: The ¹H-NMR spectrum of the ligand (HL)

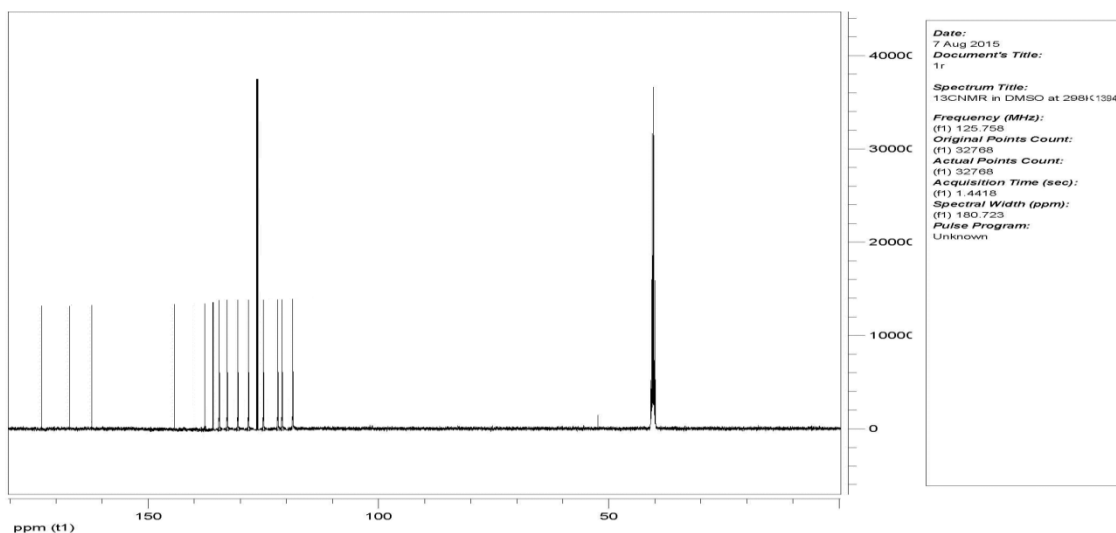


Fig 2: The ¹³C-NMR spectrum of the ligand (HL)

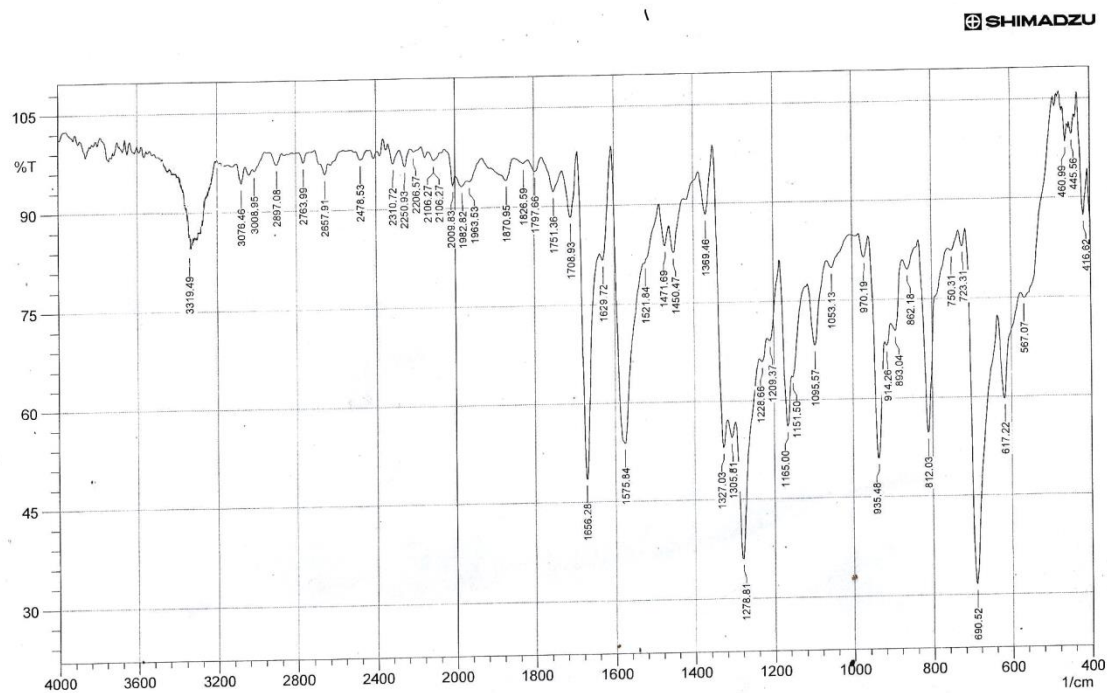


Fig 3: The IR spectrum of the ligand (HL)

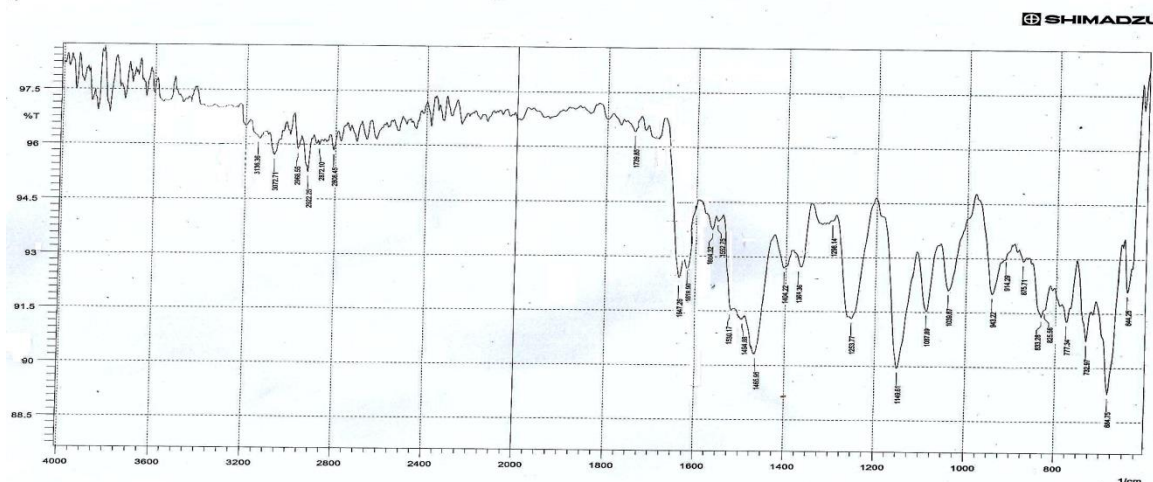
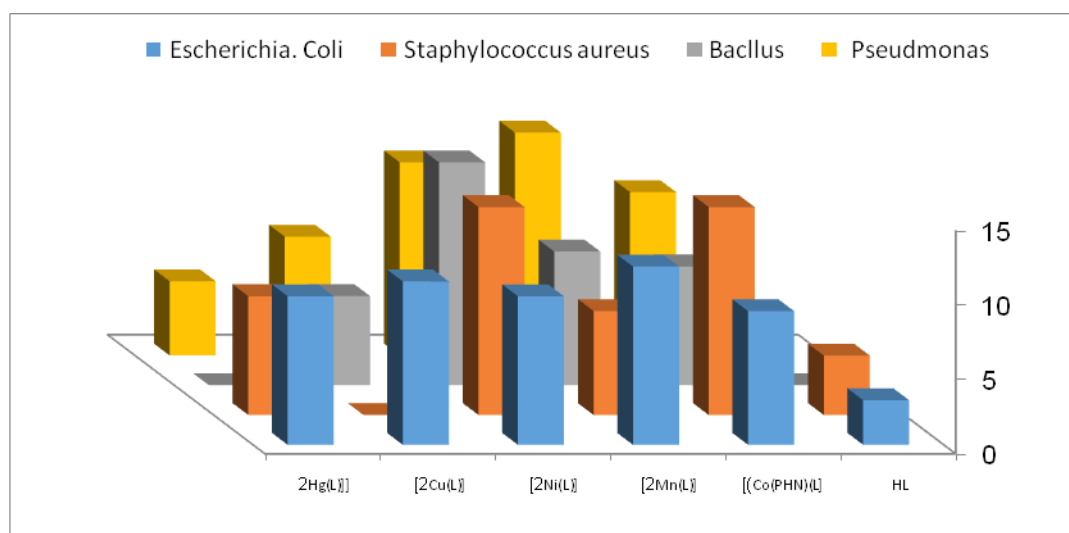

 Fig 4: IR spectrum of $[Ni(L)_2]$ complex


Fig 5: Difference between the antimicrobial activity of ligand(HL)& metal complexes

Electronic spectra and magnetic moment measurements

Electronic spectra provide the most detailed information about the electronic structure. The UV-Vis spectrum of the Schiff base ligand (H_2L) exhibits two charge transfer (CT) bands at (271nm)(36101 cm^{-1}) and (338 nm) ($30303cm^{-1}$) attributed to $\pi-\pi^*$ and $n-\pi^*$ transition within the Schiff base ligand. In the spectrum of the complexes, the CT band at (260 nm) remains as such, in agreement with the $\pi-\pi^*$ transition of the Schiff base ligand. The band observed at (325 nm) observed in the spectrum of the free ligand (H_2L) is red-shifted to (349-361 nm) in complexes in the form of ligand to metal charge transfer (LMCT) transition. Similarly, much weaker and less well defined broad bands are found in the spectrum of the complexes at (520-650 nm) which are assigned to the d-d transitions. The absorption spectrum of copper complexes shows a broad band at about (817nm) ($12239cm^{-1}$) attributed to ${}^2E_g \rightarrow {}^2T_{2g}$ transition which is well within the range of 610-555 nm expected for octahedral $[Cu(L)_2]$. The magnetic moment (μ_{eff}) for this complex was found to be 1.85 B.M. per Cu ion which was in usual range for octahedral copper complexes [12]. The electronic spectra of $[Ni(L)_2]$ complexes show only one band in addition to the intense charge transfer band in the (992 nm) ($10080cm^{-1}$) region owing to the ${}^4T_{1g(F)} \rightarrow {}^4T_{2g(F)}$ transition, indicating a octahedral environment around the nickel(II) metal ions [13] which are confirmed by the magnetic moment (μ_{eff}) for this complex was found to be 4.62 B.M. per Ni ion. The $[Mn(L)_2]$ complex exhibits the peaks at (590 nm) ($16750 cm^{-1}$), (777nm) ($12804cm^{-1}$) and (828 nm) ($12019cm^{-1}$), which may be assigned to ${}^3A_{2g(F)} \rightarrow {}^3T_{2g(F)}$, ${}^3A_{2g(F)} \rightarrow {}^3T_{1g(F)}$ and ${}^3A_{2g(F)} \rightarrow {}^3T_{1g(P)}$ respectively are characteristic of four coordinated octahedral Mn(II) complex [15]. The magnetic moment of manganese (II) complex is 5.73 B.M. which suggest that the complex is four coordinated. The cobalt (II)

complex shows one weak band from d-d transition was observed at (908nm)(11013cm⁻¹) which may be assigned to ⁴T_{2(F)}→⁵E_{g(F)} correspond to the octahedral environment around the Co²⁺ ion. The magnetic moment of Co(II) complex was found to be 4.82 B.M. which is at the lower end of magnetic moments expected for distorted octahedral Co(II) complex suggest the dimeric nature of the complex [16]. From the interpretation of elemental analysis, infrared, electronic spectra, magnetic measurements and molar conductivity, it is possible to draw up the tentative structures of the transition metal complexes. Fig. 4 depicts the representative structure of the metal complexes.

Biological Activity

The in-vitro antimicrobial activity of the scrutinised ligand and its metal complexes was tested against the bacteria *Escherichia coli* and *Staphylococcus usurius* by disc diffusion method using nutrient agar as a medium. The stock solution was prepared by dissolving the compounds in DMSO. In a typical procedure, a well was made on agar medium inoculated with the microorganism. The well was filled with the test solution using a micropipette and the plate was incubated 24 h for bacteria at 37 °C and 72 h for fungi at 30 °C. After incubation, the diameter of the clear zone of inhibition surrounding the sample is taken as a measure of the inhibitory power of the sample against the particular test organism. This may be due to that the chelation considerably reduces the polarity of the metal ion mainly because of partial sharing of its positive charge with the donor groups and possible electron delocalization over the whole created ring such, chelation could also enhance the lipophilic character of the central metal atom, which subsequently favors its permeation through the lipid layer of the cell membrane Fig(5).

CONCLUSION

The Schiff base type N₂O₂ ligand is synthesised from 2-amine pyridine and 2-benzoylbenzoic acid. It considers tridentate ligand and composited mixed complexes with Co^(II), Mn^(II) Cu^(II), Hg^(II) and Ni^(II) transition ions with 1,10-phenanthroline. The ligands and its mixed complexes are recognised utilising analytical values and spectra. The electronic spectra supported by magnetic moments and UV- Visible revealed octahedral geometry for Cu^(II), Mn^(II), Ni^(II), Co^(II) and Hg^(II) complexes. All the mixed complexes have higher antimicrobial activity than the Schiff base ligand.

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