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Synthesis, Characterization and Antimicrobial Screening of Mn(II), Ni(II) and Cu(II) Complexes of 3,4,5-Trihydroxy benzoic acid[1-(pyridyl)ethylidene]hydrazone

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In the present study, synthesis of Mn(II), Ni(II) and Cu(II) complexes of 3,4,5-trihydroxy benzoic acid[1-(pyridyl)ethylidene]-hydrazone is reported. The synthesized complexes were characterized by IR, UV-visible, ^{1}H NMR, mass spectroscopy, TGA-DTA, XRD, elemental analysis and conductivity measurements. The spectral studies indicate that the synthesized complexes possess octahedral geometry. These complexes also exhibited the antimicrobial activities.

Keywords: Metal(II) complexes, Antimicrobial, 3,4,5-Trihydroxy benzoic acid[1-(pyridyl)ethylidene]hydrazone.

INTRODUCTION

Schiff bases play an important role in inorganic chemistry as they easily form stable complexes with most of the transition metal ions [1]. Various Schiff base complexes have been widely studied because they have antimicrobial, anticancer, analgesic, anti-inflammatory, and herbicidal applications [2]. Hydrazone containing azomethine -HN-N=CH- moeity constitute an important class of compounds for new drug development as target structures. Many researchers synthesized these target structures and evaluated their biological activity [3]. The most common and oldest method for the synthesis of hydrazones is the reaction of hydrazines with carbonyl compounds [4]. Hydrazone compounds possess diverse biological and pharmacological properties such as antimicrobial, anti-inflammatory, analgesic, antifungal, anti-tubercular, antiviral, anticancer, antiplatelet, antimalarial, anticonvulsant, cardio protective, antihelmintic, antiprotozoal, anti-trypanosomal, antischistosomiasis, *etc*. [5]. Hydrazones are important compounds for drug design, as possible ligands for metal complexes, organocatalysis and also for the syntheses of heterocyclic compounds [6]. The complexes of various hydrazones are also reported to act as inhibitors of enzymes [7].

Hydrazone Schiff bases and their metal complexes have various biological applications. Hydrazone metal complexes are pharmacologically active compounds. The biologically active heterocyclic compounds containing hydrazones are of wide interest because of their assorted biological and clinical applications [8-11]. This led to the synthesis of a wide variety of hydrazone derivatives by many researchers and the synthesized derivatives were also screened for their various biological activities *viz*. antidepressant, antiviral, anticonvulsant, analgesic, antiinflammatory, antiplatelet, antimalarial, antimicrobial, antimycobacterial, antidiabetic, anticancer, vasodialator, antischistosomiasis, anti-HIV, antihelmintic and trypanocidal activities [12-21]. These observations have been steering for the development of new hydrazones that exhibit varied biological activities [22-26].

Keeping in view of wide applications of hydrazone derivatives, the present study was carried out on the synthesis of Mn(II), Ni(II) and Cu(II) complexes of 3,4,5-trihydroxy benzoic acid-[1-(pyridyl)ethylidene]hydrazone. The properties of these newly synthesized metal complexes were investigated by physical and spectroscopic methods.

EXPERIMENTAL

All the chemicals were obtained from commercial sources and were used without further purification. The synthesized complexes were characterized using Elementar Vario EL III in SAIF, IIT, Cochin. The FT-IR spectra were recorded by IR-Affinity-1 SHIMADZU IR spectrophotometer using KBr pellets in the region 4000-400 cm^{-1}. The UV-visible spectra were recorded in DMSO on JASCO UV-Vis NIR in the range of 200-800nm. The NMR spectra were recorded on Bruker-FT-NMR-400 MHZ spectrometer. The mass spectra were recorded using JEOL GC-MATE II HR Mass spectrometer in SAIF, IIT, Chennai, India. The thermal analysis was recorded on Perkin Elmer STA 6000 TGA-DTA. Powder X-Ray Diffraction patterns

were obtained using AXS D8 Advance. Photoelectrochemical measurements were carried out on a CHI608E electro-chemical workstation using a standard three electrode cell with a Pt-wire as counter electrode and Ag/AgCl (in saturated KCl) as reference electrode. A 100 W Xe arc lamp (OSRAM, Germany) was used as the light source. An aqueous solution of 0.1 M Na_2SO_4 was used as electrolyte.

The ligand 3,4,5-trihydroxy benzoic acid[1-(pyridyl)-ethylidene]hydrazone was prepared using reported methods [27,28]. The antimicrobial activity of the ligand and its metal complexes were tested using agar-well diffusion diffusion method against Gram positive *Bacillus subtilis, Streptococcus Faecalis, Staphylococcus epidermis, Salmonella typhi-A, Staphylococcus aureus*, Gram negative *Proteus vulgaris, Escherichia coli, Klebsiella pneumoniae, Vibrio cholera, Shigella dysentriae* and Fungi *Candida albicans, Aspergillus flavus, Aspergillus niger*.

General procedure for synthesis of metal complexes: One equivalent of the corresponding metal acetate solution was prepared in ethanol. It was further treated with one equivalent of ethanolic ligand solution. The resulting mixed solution was added with 4 drops of triethylamine and was refluxed for 6 h where coloured complex precipitated out. The precipitate was filtered, washed with acetone and dried.

RESULTS AND DISCUSSION

The metal complexes were synthesized by easy and efficient method. All the metal complexes were formed of different colour and are thermally stable. They were insoluble in most of the organic solvents like acetone, benzene, ethanol, methanol and chloroform but soluble in DMSO. The elemental analysis and mass spectral data are in good agreement with the molecular formula of the metal complexes. The physical and analytical data of ligand and its metal complexes are presented in Table-1. The analytical data suggested the metal-ligand stoichiometry is 1:1 for all the metal complexes.

The significant bands in the IR spectra of ligand and its metal complexes are given in Table-2. The IR spectral band of ν(Ph-OH) of the ligand appeared at 3390 cm^{-1} is shifted towards higher wavenumbers in the case of the metal complexes. The peak appeared at 1616 cm^{-1} is due to ν(C=O) group in the IR spectrum of ligand, which is shifted towards lower wave numbers ranging from 1568-1566 cm^{-1} in the metal complexes. The IR spectrum of the ligand shows a strong band at 1375 cm^{-1} due to the azomethine (C=N) group. This band is shifted to higher frequencies during the formation of the metal complexes. The N-N bond observed at 1053 cm^{-1} in the ligand is shifted to higher frequencies after complex formation. The metal complexes showing weak bands in the range of 665-619 cm^{-1} are due to ν(M-O). This indicates that acetate group is coordinated with metal ions in the complexes through oxygen. The complexes showing peaks in the range of 1117-1105 cm^{-1} are due to ν(C-O). The peaks appearing in the range of 3749-3746 cm^{-1} may be due to the coordinated water molecules that are present in the metal complexes.

The UV-visible spectra of the solution of known concentration of (1×10^{-4} M) of ligand and its metal complexes prepared in DMSO were recorded in the range 200-800 nm. The ligand shows absorption bands at 324 and 249 nm due to n-π^* and π-π^* transitions. The metal complexes exhibit absorption bands in the region 260-290 nm attributed to π–π^* transitions.

^{1}H NMR spectra of metal complexes were recorded in DMSO as solvent and TMS as internal standard. The signals appearing at 3.5 ppm are due to acetyl methyl groups in metal complexes. The signals appeared at 1.1-1.2 ppm are due to the presence of methyl protons and the signals appeared at 8.3 ppm are due to the presence of phenolic OH groups.

Thermal study of the metal complexes has been carried out using TGA and DTA analysis. The thermograms of complexes indicate the loss of coordinated water molecules at around 110-120 ºC. Further increase in temperature, the metal complexes were found to decompose slowly in the temperature range 250 to 450 ºC giving residue of corresponding metal oxides. The DTA curves of metal complexes showing endothermic peaks at different temperatures support the degradation processes observed in thermogravimetric curves.

The XRD patterns of metal complexes were obtained in solid form. The X-ray diffractogram of metal complexes showed sharp peaks indicating their crystalline nature. The electrical conductivity (σ) is calculated using the equation $\sigma = t/(R_bA)$. The electrical conductivities of the metal complexes lie in the range of 2.29×10^{-5} to 2.599×10^{-5} S/cm.

The antimicrobial activity of ligand and its metal complexes were tested using agar-well diffusion diffusion method against

TABLE-1
PHYSICAL AND ANALYTICAL DATA OF LIGAND AND ITS METAL COMPLEXES

Compound	Yield (%)	Colour	m.p. (°C)	m.w. (amu): Found (calcd.)	Elemental analysis (%): Found (calcd.)		
					C	H	N
$C_{14}H_{13}O_4N_3$ (L)	64	Black	332	287.02 (287.27)	32.75 (58.53)	4.23 (4.56)	9.61 (14.63)
[MnL(OAc)(H_2O)]	64	Light brown	315	419.41 (419.31)	34.16 (35.83)	4.23 (4.33)	6.67 (10.02)
[NiL(OAc)(H_2O)]	68	Light brown	333	423.00 (423.02)	32.06 (45.43)	4.32 (4.32)	6.69 (9.93)
[CuL(OAc)(H_2O)]	61	Dark green	400	428.01 (427.87)	31.98 (44.91)	4.67 (4.24)	6.40 (9.82)

TABLE-2
FT-IR (cm^{-1}) SPECTRAL DATA OF FREE LIGAND AND ITS METAL COMPLEXES

Compounds	Ph-OH	ν(C=O)	ν(-C=N-)	ν(N-N)	H_2O	ν(M-O)	ν(C-O)
$C_{14}H_{13}O_4N_3$ (L)	3390	1616	1375	1053	–	–	–
[MnL(OAc)(H_2O)]	3397	1566	1417	1055	3745	665	1117
[NiL(OAc)(H_2O)]	3393	1568	1415	1051	3745	619	1112
[CuL(OAc)(H_2O)]	3393	1568	1417	1057	3747	624	1105

TABLE-3
ANTIMICROBIAL ACTIVITIES OF LIGAND AND ITS METAL COMPLEXES

Compounds	Zones of inhibition (mm)												
	Gram-positive bacteriae					Gram-negative bacteriae					Fungi		
	B.S	S.F	S.E	S.T-A	S.A	P.V	E.C	K.P	V.C	S.D	C.A	A.F	A.N
$C_{14}H_{13}N_3O_4$ (L)	4	5	4	5	–	9	13	8	19	4	6	7	4
[MnL(OAc)(H_2O)]	10	5	6	25	11	7	6	8	8	8	8	8	6
[NiL(OAc)(H_2O)]	11	10	9	15	9	13	8	13	13	10	5	11	7
[CuL(OAc)(H_2O)]	13	4	11	4	5	8	12	10	8	6	–	–	6
Ciproflaxin/Ketoconazole	37	35	37	27	32	21	24	31	32	35	16	22	15

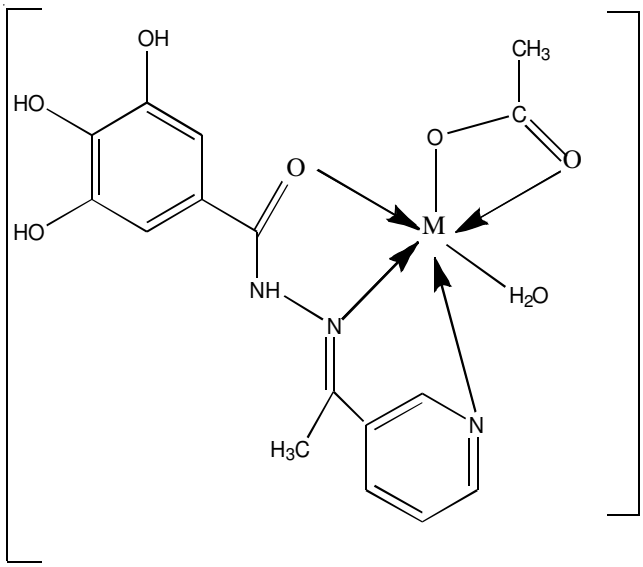
B.S = *Bacillus subtilis*, S.F = *Streptococcus faecalis*, S.E = *Staphylococcus epidermis*, S.T-A = *Salmonella typhi*-A, S.A = *Staphylococcus aureus*, P.V = *Proteus vulgaris*, E.C = *Escherichia coli*, K.P = *Klebsiella pneumonae,* V.C = *Vibrio cholera*, S.D = *Shigella dysentriae*, C.A = *Candida albicans*, A.F = *Aspergillus flavus*, A.N = *Aspergillus niger*

Gram positive *Bacillus subtilis, Streptococcus Faecalis, Staphylococcus epidermis, Salmonella typhi-A, Staphylococcus aureus*, Gram negative *Proteus vulgaris, Escherichia coli, Klebsiella pneumoniae, Vibrio cholera, Shigella dysentriae* and Fungi *Candida albicans, Aspergillus flavus, Aspergillus niger*. Each antimicrobial isolate was suspended in Mueller Hinton Agar (M-H) for performing antibiotic susceptibility tests and diluted to approximately 10^5 colony forming unit (CFC) per mL. They were flood-inoculated onto the surface of (M-H) agar and then dried. 5 mm diameter wells were cut from agar using a sterile cork-borer and 30 µL of the sample solution were poured into the wells and the plates were incubated for 18 h at 37 ºC. Table-3 shows the antimicrobial activity data evaluated by measuring the diameter of the zone of inhibition in mm against the tested microorganisms. The solvent DMSO was used as negative control and ciprofloxacin was used as the reference for bacterial strains, Ketoconazole was used as the reference for fungal strains.

The ligand shows high sensitivity towards *Escherichia coli* (13 mm) and *Vibrio cholera* (19 mm), moderate sensitivity against *Proteus vulgaris* (9 mm) and least sensitivity towards other bacterial strains. The [MnL(OAc)(H_2O)] complex shows greater activity against *Salmonella typhi-A* (25 mm), which is almost equivalent to the standard. It is moderately sensitive towards *Staphyloccus aureus* (11 mm) and *Bacillus subtilis* (10 mm) and is less active against other bacterial strains. The [NiL(OAc)(H_2O)] complex exhibits high sensitivity towards *Salmonella typhi-A* (15 mm), *Proteus vulgaris* (13 mm), *Vibrio cholera* (13 mm), *Klebsiella pneumonae* (13 mm) and shows moderate activity against other bacterial strains. The copper complex is highly sensitive towards *Bacillus subtilis* (13 mm) and *Escherichia coli* (12 mm). It shows moderate activity against *Staphylococcus epidermis* (11 mm) and *Klebsiella pneumonae* (10 mm) and it is less sensitive towards other bacterial strains. The ligand and [MnL(OAc)(H_2O)] complex show less sensitivity against all the fungal strains. Nickel complex shows moderate sensitivity against *Aspergillus flavus* (11 mm) and least sensitivity against *Candida albicans* and *Aspergillus niger*. The copper complex is less sensitive against *Aspergillus niger* and does not show any activity against *Candida albicans* and *Aspergillus flavus*.

Conclusion

The ligand 3,4,5-trihydroxybenzoic acid [1-(pyridyl)-ethylidene]hydrazone and its Mn(II), Ni(II) and Cu(II) complexes were synthesized and characterized. The spectral studies indicated that the synthesized complexes possess octahedral geometry as given below:



where M = Mn(II), Ni(II) and Cu(II)

The molecular weight of the synthesized compounds are confirmed by *m/z* values of the molecular ion peaks obtained in the mass spectra of these compounds. The TGA-DTA of the synthesized compounds shows different decomposition temperatures depending on the nature of the compounds. The TGA-DTA indicates that the ligand is thermally stable up to the temperature of 322 ºC and its metal complexes' thermal stability ranges from 314 to 428 ºC. These novel compounds have also shown moderate biological activity.

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