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SYNTHESIS, CHARACTERIZATION AND MICROBIAL ACTIVITIES OF METAL COMPLEXES WITH COUMARINE DERIVATIVES

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Abstract

The metal complexes with Schiff bases derived from the condensation of with ethylenediamine and orthophenylenediameine have gained special interest due to the biological importance of these compounds. When terminal –NH_2 groups of ethylenediamine and orthophenylediamine are condensed with C=O group of 3-acetylcoumarine resulted, Schiff bases such as (2E,3E)-N^1,N^2-bis(1-(2-oxo2H-chromen-3-yl)ethylidene)ethane-1,2-diamine (L^1) and (2E,3E)-N^1,N^2-bis(1-(2-oxo2H-chromen-3-yl)ethylidene)orthophenylenediamine (L^2). These complexes were characterized by elemental analyses, conductance measurements, magnetic susceptibility measurements, IR, ^{1}H NMR, X-ray diffraction and electronic spectral studies. On the basis of magnetic and spectral studies, square planar geometry was assigned for Mn(II), Co(II),Ni(II) and Cu(II) complexes and Zn(II), Cd(II) and Hg(II) complexes are having tetrahedron geometry. These complexes have been screened *in vitro* for their possible antimicrobial activity.

Keywords: Microbial activity, metal complex, coumarine derivatives.

INTRODUCTION

Coordination chemistry has played major role in the medicine and has been used in the treatment, management and diagnosis of diseases[1]. Apart from these, there has been a growing interest in the role of metal ions and their complexes in biological systems[2-3]. Metal complexes have been explored for their catalytic and biological activities[4]. Many enzymes and proteins involving multi-metal systems have been reported[5,6]. Coordination chemistry has now leaped into many areas of science such as analytical chemistry, medicinal chemistry, metallurgy, industrial chemistry, material science etc.

Coumarine and its derivatives have been found to exhibit antibiotic, antibacterial, antifungal, anticoagulating and plant regulating activities[7-11]. Many coumarin compounds, after some suitable structural modification can be used as drugs[12-15]. Chelating ability of coumarin derivatives have been studied to suggest their use as chelating agents[16, 17]. By considering all the above facts, the author intends to discuss the Mn(II), Co(II), Ni(II), Cu(II), Zn(II), Cd(II) and Hg(II) complexes with (2E,3E)-N^1,N^2-bis(1-(2-oxo2H-chromen-3-yl)ethylidene)ethane-1,2-diamine (L^1) and (2E,3E)-N^1, N^2-bis(1-(2-oxo2H-chromen-3-yl)ethylidene)orthophenylenediamine (L^2).

EXPERIMENTAL

All the chemicals and solvents used were of AR grade. Salicylaldehyde was obtained from Sisco-chem.Industries.The metal salts were purchased from commercial sources. Metal contents were estimated using standard methods [18]. IR spectra of the compounds were recorded on a Beckman IR-20 spectrophotometer in the region 4000-250cm^{-1} ^{1}H NMR spectra were recorded on a Perkin-Elmer 90

MHz spectrometer. The electronic spectra were recorded on an Elico SL 159 spectrophotometer in the 200-1000nm ranges in DMF solution (10^{-3}). Elemental analyses were obtained HERAEUS C, H, N-O rapid analyzer. E.S.R. measurements were carried out on a VARAN E-109 GHz. The experiment was carried by taking DPPH as the reference with the field set at 3200 Gauss. Magnetic susceptibilities were determined by the faraday method using a Model 300 Lewis Coil Force Magnetometer of one tesla field strength at room temperature. The instrument being calibrated with Hg $[Co(SCN)_4]$[19]. The single crystal X-ray diffraction data were collected on a Bruker AXS SMART APEX CCD diffractometer at room temperature. The data were collected using graphite monochromated MoK_α radiation. The data were reduced by SAINTPLUS29 and an empirical absorption correction was applied using SADABS29 available in the Bruker software package.

Synthesis of 3-acetyl cumarine:

To a cold mixture of salicylaldehyde (0.10mol) and ethylated acetate (0.10mol) was added 1gm piperidine by solid shaking, the solid separated was filtered and washed with ethanol. Crystallization of the solid from water gave pure 3-acetyl caumarine[20]. mp. 119 ^{0}C, (lit., 120^0 C)

(2E,3E)-N^1,N^2-bis(1-(2-oxo2H-chromen-3-yl)ethylidene)ethane-1,2-diamine (L^1) and (2E,3E)-N^1,N^2-bis(1-(2-oxo2H-chromen-3-yl)ethylidene) ortho phenylenediamine (L^2) :

3-acetylcoumarine (0.1mol) and ethylenediamine / orthophenylene diamine (0.5mol) was refluxed with ethanol for four hrs. The solution was concentrated and left overnight. Fine crystals were separated by filtration. Washed with cold ethanol and recrystallized by ethanol. (m.p. 208 °C)

Preparation of metal complexes :

A hot solution of a respective metal chloride (0.001mol) in ethanol was added to a hot solution of (2E,3E)-N^1,N^2-bis(1-(2-oxo 2H-chromen-3-yl)ethylidene)ethane-1,2-diamine**(L^1)** / (2E,3E)-N^1,N^2-bis(1-(2-oxo 2H-chromen-3-yl)ethylidene) orthophenylene diamine **(L^2)** (0.001mol) in ethanol, the reaction mixture was refluxed for 4 to 6 hrs. It was treated with sodium acetate (0.5 g) the resultant reaction mixture was further refluxed for 2 more hrs, and then it was decomposed by pouring to distilled water (80 to 100 mL) with stirring. The separated solid (complex) was allowed to settle and collected by filtration, washed several times with distilled water and then with hot ethanol. The solid complex obtained was dried in desiccators over anhydrous calcium chloride.

The antimicrobial activity of the ligands L^1 and L^2 and their metal complexes were determined by agar cup-plate method. The antibacterial activity against *Escherichia coli* and *Pseudomonas aeroginosa* and antifungal activity against *Aspergillus niger* and *Candida albicans*, were screened by the ligands and their metal complexes. The medium was prepared as per the instructions of the manufacturer of dry Mueller Hinton agar powder (Hi-Media). The test ligands and their metal complexes were dissolved in dimethylsulphoxide (DMSO) at a concentration of 100μg/ml. Ciproflaxacin (100μg/ml) in DMSO was used as reference standard for antibacterial and flucanozole (100μg/ml) in DMSO was used as reference standard for antifungal activity. The solvent control (only DMSO) was also maintained throughout the experiment. The zones of inhibition are reported in Table-4.

RESULTS AND DISCUSSION

The analytical and physical data of the compounds are given in Table-1. The results of elemental analyses of the complexes correspond to stoichiometry for metal:ligand in 1:2 molar ratios. The conductance values of all these complexes in DMF at the concentration 10^{-3} M fall range 85.42 - 98.32 Mho cm^{2}mol^{-1} indicating the electrolytic nature[21-22]. IR spectra of ligands exhibits high intensity bands in the region of 1620-1597 cm^{-1} which are assigned to the $\upsilon_{C=N}$. group in view of the previous assignments. The absence of C = O group at 1695 cm^{-1} and also the absence of 3200cm^{-1} broad band of NH_2 group of diamines. Mark the condensation leading to the formation of Schiff base, which is confirmed by the presence of 1620-1597 cm^{-1} band in the product. The band due to $\upsilon_{(C=N)}$ in these complexes appears around 1600cm^{-1}. A high frequency shift compared with the ligands is suggestive of coordination of the azomethine group to the metal (II) moiety[23]. This results in lowering the bond order of C=N link. The bands due to $\upsilon_{(C=O)}$ around 1535cm^{-1} of the ligands shifted to higher frequency in the complexes, due to coordination through

C=O group of the ligands. The magnetic moment of all manganese, cobalt, nickel and copper complexes are 5.89-5.91, 2.32-2.50, diamagnetic and 1.55-1.65 B.M respectively. The μ_{eff} values are well within the range known for square planar geometry. The electronic spectra of Mn(II) complexes, a strong band appearing at ~29400cm^{-1} may be attributed to the π-π^* transition of the C=N group. The complexes in the visible region show very weak absorptions at ~21700 and ~ 25000 cm^{-1}. Which may be assigned to $^6A_{1g}\rightarrow{}^4E(G)$ and $^6A_1\rightarrow{}^4A_1$ (G) transitions of a square planar special arrangements evidences by earlier reports [24].

For Co(II) complexes, square planar Co(II) complexes exhibit two bands around 15500cm^{-1}and another broad band near 20000cm^{-1} corresponding to the transitions $^2A_{2g}\rightarrow{}^2B_{1g}$ and $^2A_{1g}\rightarrow{}^2E_g$ respectively[25] and Ni(II) complexes exhibit a medium intensity board band in the region 15800-16500cm^{-1} and this may be regarded as due to the $^1A_{1g}\rightarrow{}^1A_{2g}$ transitions. The band due to the M-L charge transfer band. These observations indicate that the isolated Ni(II) complexes have square-planar configuration. The band maxima observed in present study for Cu(II) complexes in DMF falls in the region 16120 – 16570 cm^{-1}**.** The nature and shape of the band maxima can very well established square planar Cu(II) complexes[27]. These observations suggest that the Cu(II) complexes are having square-planar geometries. Various ligand field parameters have been evaluated for cobalt and nickel complexes (Table3).The nephelauxetic parameter, β is readily obtained using the relation β=B(complex)/B(free ion), indicate that complex under study have appreciable covalent character. The value of D_q could be evaluated with the help of the curve transition energies versus D_q by Orgel using the energy level due to transitions $^4T_{1g}(F)\rightarrow{}^4A_{2g}(F)$ and $^3A_{2g}\rightarrow{}^3T_{1g}(P)$ respectively. The parameter B was evaluated by using the methods reported earlier [28].

The ^{1}H NMR spectrum of these ligands (2E,3E)-N^1,N^2-bis(1-(2-oxo2H-chromen-3-yl)ethyledene)ethane-1,2-diamine L^1 and (2E,3E)-N^1,N^2-bis(1-(2-oxo2H-chromen-3-yl)ethyledene)orthophenylene diamine L^2 in DMSO –d$_6$ solvent gave well-resolved multiplets at 7.20δ–7.85δ corresponding to five aromatic protons. In the complexes, these signals were shifted to lower field were observed at 7.30-7.77 δ due to complexation. In the complexes we observe the signals at 3.64-4.20δ (ppm) assigned to the protons of CH**2** - group. These signals are shifted to down field, because of coordination through oxygen of C=O (lactone) and nitrogen of azomethine (C=N) group to the metal ions respectively [29-31]. The ESR spectra of the copper complexes as polycrystalline sample have been recorded at room temperature, (ESR chart was calibrated with DPPH). The polycrystalline samples gives one broad isotropic signal centered approximately at 2.023 and 2.040 for the complex Cu (L$_1$). The observed g values of the Cu (L^1) complex as follows $g_{||}$ =2.058, $g_\perp$ =2.014, g_{av} =2.028 and G = 4.19. While for Cu (L^2), $g_{||}$ = 2.052 $g_\perp$ = 2.024 g_{av} = 2.030 and G = 4.22. G = $(g_{||}-2)/(g_\perp-2)$ which measures the exchange interaction between copper centers in a polycrystalline solid has been calculated. According the Hathaway[32] if the G value is greater than 4, the exchange interaction is negligible, while a value of G less than 4 indicates a considerable exchange in the solid complexes. As G=4.13 and G= 4.20 for [Cu(L^1)]Cl$_2$and [Cu(L^2)]Cl$_2$ respectively, indicates the exchange interaction is negligible.

In addition, we have carried out powder X-ray diffraction studies of complex. Powder XRD pattern of [Cu(L^1)]Cl$_2$consists of 7 reflections in the range 5-50^o (2θ) The inter planar spacing (d) has been calculated from the positions of intense peaks using Bragg's relationship. The 2θ values with maximum intensity of the peak for ligand was found to be 5.709 (2θ) which corresponds to d=15.4539. All the important peaks have been indexed and the observed values of inter planar distance were compared with the calculated ones. It was found that there is good agreement between the calculated and observed values[33]. The $(h^2+k^2+l^2)$ values are 1,5,27,32,58,72 and 74. The presence of forbidden number confirms the tetragonal systems.

Antimicrobial Activity:

From the Table-4, it is clear that all the ligands (L^1 and L^2) show moderate activity against all the antibacterial and antifungal microorganisms[34]. But all the metal complexes show moderate to high active against all the organisms. Among the complexes, all copper complexes [Cu(L^1)]Cl$_2$ and [Cu(L^2)]Cl$_2$ were found to be most active against all the microbes tested, as compared to their ligands, which due to the faster diffusion of the Cu(II) complexes. Even though the test compounds are less active with reference to the standarad drug *ciproflaxacin* and *flucanozole*, the data reported in this article may be a helpful guide for the medicinal chemists who are working in the area.

Table-1: Analytical, magnetic and conductance data of Mn(II), Co(II), Ni(II), Cu(II), Zn(II), Cd(II) and Hg(II) complexes with (2E,3E)-N[1],N[2]-bis(1-(2-oxo2H-chromen-3-yl)ethylidene)ethane-1,2-diamine. [a]All the ligands and their complexes showed satisfactory C, H and N analysis.

Comp. code	**Complexes/ Abbreviations[a].**	**Found(calcd%)**			**μ_{eff} BM**	**Mol.cond. λm. MhoCm^{2}mol^{-1}**
		M	**N**	**Cl**		
C_1	$[Mn(C_{24}H_{20}N_2O_4)]Cl_2$ $[Mn(L^1)]Cl_2$	10.39 (10.42)	5.32 (5.36)	13.53 (13.50)	5.89	95.90
C_2	$[Co(C_{24}H_{20}N_2O_4)]Cl_2$ $[Co(L^1)]Cl_2$	11.12 (11.05)	5.28 (5.32)	13.41 (13.36)	2.32	85.50
C_3	$[Ni(C_{24}H_{20}N_2O_4)]Cl_2$ $[Ni(L^1)]Cl_2$	11.05 (11.10)	5.29 (5.25)	13.62 (13.65)	Dia.	88.40
C_4	$[Cu(C_{24}H_{20}N_2O_4)]Cl_2$ $[Cu(L^1)]Cl_2$	11.88 (11.96)	5.24 (5.18)	13.30 (13.38)	1.55	89.30
C_5	$[Zn(C_{24}H_{20}N_2O_4)]Cl_2$ $[Zn(L^1)]Cl_2$	12.18 (12.12)	5.22 (5.25)	13.25 (13.31)	--	87.00
C_6	$[Cd(C_{24}H_{20}N_2O_4)]Cl_2$ $[Cd(L^1)]Cl_2$	19.26 (19.20)	4.79 (4.85)	12.18 (12.20)	--	97.35
C_7	$[Hg(C_{24}H_{20}N_2O_4)]Cl_2[Hg(L^1)]Cl_2$	29.86 (29.82)	4.16 (4.20)	10.58 (10.52)	--	90.30

Table-2: Analytical, magnetic and conductance data of Mn(II), Co(II), Ni(II), Cu(II), Zn(II), Cd(II) and Hg(II) complexes with (2E,3E)-N[1],N[2]-bis(1-(2-oxo2H-chromen-3-yl)ethylidene) orthophenylenediamine.

Comp. code	**Complexes/ Abbreviations[a].**	**Found(calcd%)**			**μ_{eff} BM**	**Mol.cond. λm. MhoCm^{2}mol^{-1}**
		M	**N**	**Cl**		
C_8	$[Mn(C_{28}H_{20}N_2O_4)]Cl_2$ $[Mn(L^2)]Cl_2$	9.57 (9.51)	4.88 (4.84)	12.39 (12.34)	5.89	96.85
C_9	$[Co(C_{28}H_{20}N_2O_4)]Cl_2$ $[Co(L^2)]Cl_2$	10.19 (10.22)	4.84 (4.79)	12.30 (12.24)	2.50	88.56
C_{10}	$[Ni(C_{28}H_{20}N_2O_4)]Cl_2$ $[Ni(L^2)]Cl_2$	10.15 (10.21)	4.85 (4.91)	12.30 (12.35)	Dia.	89.36
C_{11}	$[Cu(C_{28}H_{20}N_2O_4)]Cl_2$ $[Cu(L^2)]Cl_2$	10.90 (10.95)	4.80 (4.89)	12.20 (12.26)	1.65	96.68
C_{12}	$[Zn(C_{28}H_{20}N_2O_4)]Cl_2$ $[Zn(L^2)]Cl_2$	11.18 (11.23)	4.79 (4.82)	12.16 (12.12)	--	85.42
C_{13}	$[Cd(C_{28}H_{20}N_2O_4)]Cl_2$ $[Cd(L^2)]Cl_2$	17.19 (17.20)	4.43 (4.45)	12.26 (12.20)	--	85.55
C_{14}	$[Hg(C_{28}H_{20}N_2O_4)]Cl_2$ $[Hg(L^2)]Cl_2$	27.87 (27.82)	3.89 (3.92)	9.88 (9.84)	--	98.32

[a] All the ligands and their complexes showed satisfactory C, H and N analysis.

Table-3: Electronic spectra and ligand field parameters of complexes

Complexes	ν_1 **(cm^{-1})**	ν_2 **(cm^{-1})**	ν_3 **(cm^{-1})**	**Dq (cm^{-1})**	**B` (cm^{-1})**	β	**LFSE**
$[Co(L^1)]Cl_2$	15873	20833	27777	496	2248.66	2.32	14.17
$[Co(L^2)]Cl_2$	15748	21276	26315	553	2066.07	2.12	15.80
$[Ni(L^1)]Cl_2$	16125	20000	26667	387	2336.93	2.24	11.06
$[Ni(L^2)]Cl_2$	16528	20408	27027	388	2386.33	2.29	11.08

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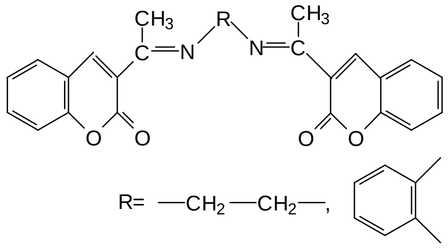

L^1 , L^2

Fig.-1:Schiff bases derived Coumarine derivatives

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Table-4: Antibacterial and antifungal activity data of the ligands and their complexes (Zone of inhibition in mm*)

Ligands/ Complexes	**Antibacterial**		**Antifungal**	
	E.coli	***P.aeroginosa***	***A.niger***	***C.albicans***
L^1	12	14	11	09
$[Mn(L^1)]Cl_2$	14	17	13	12
$[Co(L^1)]Cl_2$	15	18	14	12
$[Ni(L^1)]Cl_2$	20	19	18	16
$[Cu(L^1)]Cl_2$	11	13	10	10
$[Zn(L^1)]Cl_2$	14	16	14	13
$[Cd(L^1)]Cl_2$	14	17	13	14
$[Hg(L^1)]Cl_2$	21	22	17	17
L^2	12	14	12	01
$[Mn(L^2)]Cl_2$	13	16	14	13
$[Co(L^2)]Cl_2$	15	15	14	15
$[Ni(L^2)]Cl_2$	16	17	18	18
$[Cu(L^2)]Cl_2$	23	24	15	14
$[Zn(L^2)]Cl_2$	17	14	12	13
$[Cd(L^2)]Cl_2$	18	17	16	15
$[Hg(L^2)]Cl_2$	17	15	14	17
Ciproflaxacin	27	30	__	__
Flucanozole	__	__	24	23
DMSO	00	00	00	00

*Diameter of cup is 6 mm:, *E.coli*: *Escherichia coli*, *P.aeroginosa*: *Pseudomonas aeroginosa*, *A.niger*: *Aspergillus nige*, *C.albicans*: *Candida albicans*.

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