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Synthesis, Characterization and Antimicrobial Studies of Copper (II) Complexes of Semicarbazone and Thiosemicarbazone of m- Hydroxy Benzaldehyde and p-Hydroxy Benzaldehyde

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ABSTRACT

We have synthesized Cu(II) complexes with m- hydroxy benzaldehyde semicarbazone (L1 =Hm-HBSC), m-hydroxy benzaldehyde thiosemicarbazone (L2= Hm-HBTSC), p- hydroxyl benzaldehyde semicarbazone (L3= Hp-HBSC) and p-hydroxybenzaldehyde thiosemicarbazone (L4= Hp-HBTSC). These complexes were characterized through elemental analysis, molecular weight, electrical conductance and magnetic susceptibilities at room temperature .The observed magnetic moments of all these complexes are consistent with the presence of a single unpaired electron. On the basis of above observations the complexes were proposed to be octahedral structure. These complexes were screened for anti-bacterial and antifungal properties and have exhibited potential activity.

Key words: m-hydroxybenzaldehyde, p-hydroxybenzaldehyde Semicarbazone, Thiosemicarbazone, Antibacterial Activity, Antifungal Activity etc.

INTRODUCTION

The synthesis of transition metal complexes with thiosemicarbazone ligands have been receiving considerable attention due to the pharmacological properties of both ligands and complexes[1-3].The Chemistry of Thiosemicarbazone has received considerable attention because of their variable bonding modes, promising biological implications, structural diversity, and ion – sensing ability[4-6] .The ligand, based on semicarbazone and pyridoxal moieties(forms found in vitamin B6), has an enormous potential as a biologically active reagent as it has been demonstrated that transition metal complexes incorporating semicarbazones show biological activity. In particular, with regard to biological importance, nickel(II) complexes with semicarbazone ligands show antibacterial acivity[7], and copper(II) complexes containing semicarbazones have also displayed biological properties[8-11]. Additionally, several nickel(II) complexes with octadiensemicarbazones exhibit strong inhibitory activity against Staphylococcus aureus and Eschericia coli[11].In vitro anticancer

studies of several nickel (II) complexes with naphthoquinonesemicarbazone and thiosemicarbazone on MCF – 7 human breast cancer cells reveal that semicarbazone derivative with nickel(II) complexes is more actively inhibiting cell proliferation than thiosemicarbazone analogues[13].

The present work is related to synthesized and characterization of Cu(II) complex of Semicarbazone and Thiosemicarbazone of m-hydroxybenzaldehyde and p-hydroxybenzaldehyde. These were screened antibacterial, and antifungal properties.

EXPERIMENTAL

Materials

All the chemicals used of analytical R grade and procured from sigma- Aldrich and flucka metal salts were purchased from E. Merck and used as received

Synthesis of Ligands(L)

Hot ethanolic solution of m-hydroxybenzaldehyde and p-hydroxybenzaldehyde allowed to react with semicarbazide/thiosemicarbazide. The resulting mixture was heated on water bath for 4-5h. After

Table 1: Analytical, magnetic moment, electronic spectra, decomposition Temperature and Molar conductance data for ligands and their metal complexes

Complexes	MW	μ eff B.M.	Molar Conduc. tance Ω^{-1} cm^2 mol^{-1}	γ_{max} elect. .ronic cm^{-1}	m.p. ^oC	%Analysis found (Cal.)			
						M	C	H	N
(Hm-HBSC) $IL_{1)}$	197.15				170	-	63.10 (63.12)	7.34 (7.32)	23.67 (23.69)
(Hm-HBTSC) (L_2)	195.26				185	-	66.03 (66.05)	6.79 (6.77)	25.38 (25.40)
(Hp-HBSC) (L_3)	196.27				160	-	66.07 (66.06)	6.78 (6.76)	24.65 (24.63)
(Hp-HBTSC) (L_4)	195.26				185	-	66.05 (66.07)	6.25 (6.27)	24.45 (24.47)
$[Cu(L_1)_2]Cl_2$	296	1.86	19	12500 25000	307	16.45 (16.47)	46.05 (46.07)	5.79 (5.77)	22.12 (22.14)
$[Cu(L_2)_2]Cl_2$	312	1.81	20	12620 25000	312	5.33 (5.35)	43.03 (43.05)	14.58 (14.7)	19.37 (19.5)
$[Cu(L_3)_2]Cl_2$	296	1.82	17	12380 26500	293	14.69 (14.71)	42.15 (42.13)	5.50 (5.52)	18.38 (18.40)
$[Cu(L_4)_2]Cl_2$	312	1.83	20	12136 25310	306	16.94 (16.96)	41.05 (41.07)	5.32 (5.34)	19.37 (19.39)
$[Cu(L_1)_2]Br_2$	584	1.97	19	12380 25300	301	14.69 (14.65)	46.05 (46.07)	5.62 (5.64)	19.28 (19.26)
$[Cu(L_2)_2]Br_2$	400	1.87	21	12250 25400	295	14.75 (14.77)	45..11 (45.13)	4.78 (4.80)	16.24 (16.22)
$[Cu(L_3)_2]Br_2$	384	1.92	19	12980 24400	294	14.95 (14.97)	44.11 (44.09)	4.54 (4.52)	16.16 (16.18)
$[Cu(L_4)_2]Br_2$	400	1.95	17	12580 25600	291	14.85 (14.10)	43.12 (43.14)	4.26 (4.23)	18.18 (18.20)

cooling, the precipitate was collected and washed thoroughly with water and crystallized twice from ethanol to furnish m-hydroxybenzaldehyde and p-hydroxybenzaldehyde semicarbazone and thiosemicarbazone as long, thick ,whitish yellow and short pale yellow needles.. These ligands are dried over vacuum over P_4O_{10}.

Synthesis of Complex

A general method was used for the synthesis of the complexes. They were prepared by mixing an ethanolic solution (20ml) 0.1 mol of hydrated metal salts and a warm ethanolic solution (20ml) of respective ligand(0.05)mol. The resulting reaction mixture were heated on water bath for 4-5h.They were filtered, washed several times with distilled water and dried over P_4O_{10} .

Analysis

The C, H, and N were recrystalized on Carlo- Erba 1106 elemental analyzer. The nitrogen contents of the complexes was determined using Kjeldahl·s method copper contents of the complexes were estimated complexometrically with EDTA using mercuroxide and erichrome blackT as an indicator after decomposing the complexes with concentrated H_2SO_4 and H_2O_2[14]. The electronic spectra in DMF were recorded on a Toshniwal – CL – 54 spectrophotometer. Molar conductance data were recorded on systronics conductometer model 303 using DMF. The magnetic measurement on powder form of the complexes were carried out at room temperature on Gouy·s balance using anhydrous copper sulphate as calibrant. The infra – red spectra of the complexes were recorded on Perkin Elmer infra- red spectrophotometer model-521 in KBr/CSI in the range 4000-200 cm^{-1} . The analytical data, colour, conductivity measurements, magnetic susceptibility, electronic spectra and decomposition temperature of the complexes shown in Table 1.

Antimicrobial Screening

In vitro antimicrobial screening was performed by agar disc diffusion method[15-16]. All the test organisms were obtained from microbial type culture collection and gene bank [MTCC]. Nutrient agar growth media was prepared according to the instruction of MTCC .

Antibacterial Screening

The antibacterial activity of the ligand and its metal complexes were tested by using paper disc diffusion method[17-19] against *Bacillus macerans* (Gram positive) and *pseudomonas striata* (Gram negative) at concentration of compound 25µg\ml and 50 µg\ml. Twenty five millilitre nutrient agar media was poured in each petriplates. After solidification,0.1 ml of test bacteria spread over the medium using a spreader. The discs of whatman no.1 filter paper having diameter 5.00 mm were placed containing at four equidistant places at a distance of 2 cm from the centre in the inoculated petriplates.. The petriplates were incubated at 37^{0}C for 26 hours. The zone of inhibition was calculated.

Table 2: Infrared spectral data of L_1, L_2,L_3,L_4 and its complexes with Cu(II) metal ions

Compounds	v(OH)	v(NH)	v(C=O)	v(C=N)	v(C=S)	v(M-O)	v(M-S)	v(M-N)
L_1	3335	3400-3100	1630	1460				
L_2	3332	3372-3100		1510	780			
L_3	3436	3270-3100	1630	1490				
L_4	3537	3273-3160		1992	680			
$[Cu(L_1)_2]Cl_2$		3500-3000	1621	1490		435		344
$[Cu(L_2)_2]Cl_2$		3500-3000		1491	740		405	355
$[Cu(L_3)_2]Cl_2$		3500-3000	1619	1493		460		350
$[Cu(L_4)_2]Cl_2$		3500-3000		1587	742		400	340
$[Cu(L_1)_2]Br_2$		3200-3000	1620	1583		465		360
$[Cu(L_2)_2]Br_2$		3270-3001		1584	740		410	350
$[Cu(L_3)_2]Br_2$		3273-3000	1625	1581		462		350
$[Cu(L_4)_2]Br_2$		3271-3000		1502	743		400	340

Table.3: Antibacterial activity of the Complexs

Complexes / Compounds	Inhibition of *B.macerans* Conc.(µg/ml)		Inhibition *P.striata* Conc.(µg/ml)	
	25 µg/ml	50µg/ml	25 µg/ml	50µg/ml
$[Cu(Hm\text{-}HBSC)_2]Cl_2$	11	9	10	9
$[Cu(Hm\text{-}HBTSC)_2]Cl_2$	13	15	14	12
$[Cu(Hp\text{-}HBSC)_2]Cl_2$	-	6	5	-
$[Cu(Hp\text{-}HBTSC)_2]Cl_2$	17	11	16	18
Ciprofloxacin	-	22	-	21

Table 4: Antifungal activity of the Complexs

Complexes / Compounds	Inhibition of *C.albicans* Conc.(µg/ml)		Inhibition *A.niger* Conc.(µg/ml)	
	25 µg/ml	50µg/ml	25 µg/ml	50µg/ml
$[Cu(Hm\text{-}HBSC)_2]Cl_2$	10	9	8	7
$[Cu(Hm\text{-}HBTSC)_2]Cl_2$	16	11	16	14
$[Cu\ (Hp\text{-}HBSC)_2]Cl_2$	7	-	6	5
$[Cu(Hp\text{-}HBTSC)_2]Cl_2$	17	18	15	19
Nystatin	-	22	21	-

Antifungal Screening

The antifungal activity of ligand and its metal complexes were tested against two pathogenic fungi, *Candida albicans* and *Aspergillus niger*. The compounds having concentration 25µg/ml and 50µg/ml were poured in petridishes and Similar experiment were repeated and zones of inhibition formed were measured and compared with that of DMF to evaluate the zone of inhibition due to test compound.

RESULTS AND DISCUSSION

The IR spectrum of ligand L_1 (Hm-HBSC) and L_3 (Hp-HBSC) exhibits a band at 1630 cm^{-1} which may be assigned[20-26] due to $V_{C=O}$ group of semicarbazone moiety.This band is shifted to higher frequency region with decreased sharpness and intensity in the complexes indicating the participitation of carbonyl oxygen of semicarbazone in the coordination conqfirmed by the appearance of a band in the far IR region at the region 450-465 cm^{-1} in the complexes may be assigned [20-26] to v_{M-O} .

The other Ir band of structural significance in the ligand L_1 L_2, L_3,L_4 appears v 1460 cm^{-1} which may be assignable to $V_{C=N}$ [19-28].These band also shifted to higher wave number an complexation which suggest involvement of azomethine N in bonding with metal ions confirmed by appearance a new band in the far infra-red region at 350-365cm-1 in complexes[21-27] to $V_{M-N.}$The next IR for L^2 and L^4[Hm-HBTSC] and [Hp-HBTSC] show medium bands on the range [19-23] 650-780 cm^{-1} to $v_{C=S}$.These band is shifted in the complexes indicating coordination of thiosulpur atom by appearance a new band in far region at 395-415cm^{-1} in the complexes assignable[21-24, 27, 30, 31] to V_{M-S}.These results are in agreement with other thiosemicarbazone compound . The vibrational frequencies of $–NH_2$ group remain unchanged for both the ligands and the complexs.This evidence indicates the non-coordination of $–NH_2$ group to metal ion.

The band at 3335 cm-1 in the spectrum of L^1, L^2,L^3,L^4 which is absent in the spectra of

complexes, is ascribed to free hydroxyl group.The decreasing v(OH) wave number in the ligand compared to free v(OH) group 3700-3500 cm^{-1} seems to suggest the participation of these groups in intermolecular and intramolecular hydrogen bonding[31-33]Table 2.

Electronic Spectra

The electronic spectra of Cu(II) complexes display bands in the ranges of 15432-14727 cm^{-1} and 25575-25380 cm^{-1}.These bands correspond to the transition $^2B_{1g}$- $^2A_{1g}$, $^2B_{1g}$ – $^2B_{2g}$ and third band $^2B_{1g}$ – E_g in range of 33670 – 32570 cm^{-1} may be due to charge transfer. But generally such complexes exhibit a broad structure less bond with or without shoulder between 1400-1800 cm^{-1} depending upon the strength of in plane and axial ligands. The spectra of these complexes show octahedral geometry.

In view of biological relevance the ligand (Hm-HBSC) /(Hp-HBSC) and their metal complexes of Cu(II) were screened at a concentration of 25µg/ml and 50µg/ml were checked against Gram positive bacteria (*bacillus macerans*) and Gram negative (*pseudomonas striata)* and were screened for their antifungal activities against two fungi *(A .niger and C.albicans)*.(Table 3,4).The results have been compared with known drug Ciproflaxin against bacteria and standard drug Nystatin against fungi.The complexes of Thiosemicarbazone were found to be more effective than semicarbazone and free ligands.

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