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Synthesis, Characterization, and the Antimicrobial and Anthelmintic Activities of some Metal Complexes with a New Schiff base 3-[(Z)–5-Amino–1,3,3-Trimethyl Cyclohexylmethylimino]–1,3-Dihydroindol–2-One[1]

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Abstract—The complexes of Co(II), Ni(II), Cu(II), Zn(II), Cd(II), Hg(II), dioxouranium(VI), and Th (IV) with a new Schiff base, 3-[(Z)–5-amino–1,3,3-trimethyl cyclohexylmethylimino]–1,3-dihydroindol–2-one formed by the condensation of isatin (Indole–2.3-dione) with isophoronediamine(5-amino–1,3,3-trimethyl-cyclohexane methylamine) (IPDA) was synthesized and characterized by microanalysis, conductivity, UV-visi-ble, FT-IR, ^{1}H NMR,TGA, and magnetic susceptibility measurements. All the complexes exhibit 1 : 1 metal to ligand ratio except for the dioxouranium(VI) and thorium(IV) complexes, where the metal : ligand stoichiometry is 1 : 2. The spectral data revealed that the ligand acts as monobasic bidentate, coordinating to the metal ion through the azomethine nitrogen and carbonyl oxygen of the isatin moiety. Tetrahedral geometry for Co(II), Ni(II), Zn(II), Cd(II), and Hg(II) complexes, square planar geometry for Cu(II) complexes, and the coordination numbers 6 and 8 for UO_2(VI) and Th(IV) complexes, respectively, are proposed. Both the ligand and the metal complexes were screened for their antibacterial activity against *Bacillus subtilis, Staphylococcus aureus (S. aureus), Escherichia coli (E. coli), and Pseudomonas aeruginosa*, and the complexes are more potent bactericides than the ligand. The anthelmentic activity of the ligand and its complexes against earthworms was also investigated.

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Isatin thiosemicarbazone derivatives exhibit interesting applications as research tools in physiological studies [1]. Many isatin-derived compounds possess a wide spectrum of medicinal properties and, thus, have been studied for activity against tuberculosis [2, 3] and leprosy [4], as well as fungal [5, 6], viral [7], and bacterial infections [8, 9], etc. A survey of the literature reveals that the biological activity of the Schiff base was enhanced by complexation [10]. In continuation of our work to synthesize novel isatin Schiff bases [11, 12], we report in this paper the synthesis and characterization of a novel Schiff base and complexes of Co(II), Ni(II), Cu(II), Zn(II), Cd(II), Hg(II), dioxouranium(VI), and Th(IV).The ligand and its metal complexes were screened for antibacterial activity against *Bacillus subtilis, Staphylococcus aureus (S. aureus), Escherichia coli (E. coli)*, and *Pseudomonas aeruginosa.* Anthelmentic activity of the compounds was tested on earthworms (*Peretima posthuma*).

EXPERIMENTAL

The chemicals employed for the preparation of Schiff bases were of AR or LR grade. All the solvents were purified by standard methods. Isophoronediamine (IPDA) (Aldrich Chemicals) and isatin (S.D Fine chemicals) were used.

Preparation of Schiff Base

The Schiff base was prepared by the reported method [12]. Equimolar ethanolic solution (50 ml each) of isatin and isophoronediamine were mixed and refluxed for about 1 h. The reaction mixture was concentrated to a small volume and allowed to cool. The Schiff base precipitated out as faint pink solid. It was filtered, washed with ethanol and recrystallised from ethanol. The purity of the Schiff base ligand was monitored by TLC using 1 : 1 ethyl acetate and petroleum ether as eluant and separated by column chromatography, m.p: 117°C (Yield 90%).

Preparation of the Complexes

The metal complexes were prepared by adding ethanolic solution (50 ml) of the metal salt to the ligand (100 ml) in 1 : 2 molar ratio and heating under reflux for about 3 h. The reaction mixture was concentrated to a small volume. On cooling, the metal complexes crystal-

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[1] This article was submitted by the authors in English.

lizes out. They were filtered, washed with ethanol and dried in vacuo.

Antibacterial and Anthelmentic Activity Measurements

The ligand and its complexes with Cu(II), Co(II), Ni(II), Zn(II), Cd(II), and Hg(II) were screened for antibacterial activity against *Bacillus subtilis, Staphylococcus aureus (S. aureus), Escherichia coli (E. coli)*, and *Pseudomonas aeruginosa* at a concentration of 1 mg/0.02 mL in DMF by the cup plate method [13]. Anthelmentic activity of the compounds was measured on earthworms (*Peretima posthuma*) by the reported method [14].

Analysis and Physical Measurements

The microanalysis of the samples was carried using Carlo Ebra analyser.The metals were estimated by the standard methods [15]. The conductivity measurements were made on a Systronics Conductivity Meter 304 with a dip type conductivity cell with a cell constant of 1 unit. The magnetic susceptibility measurements were carried out at room temperature using the Faraday balance. Electronic spectra were recorded in DMF in the range 350–900 nm using a Shimadzu UV–3101 PC UV-VIS-NIR scanning spectrophotometer. ^{1}H NMR spectra of the ligand and its complexes were obtained using a Bruker AMX 400 MHz FT NMR spectrometer. IR spectra of samples in KBr pellets were recorded in the region 4000–600 cm^{-1} with a Nicolet Impact 400-D FT-IR spectrometer. The far IR spectra of the complexes in the region 600–250 cm^{-1} were recorded using a Perkin Elmer Instruments, Spectrum one FT-IR spectrometer. The mass Spectrum of the ligand was recorded using an ESI-MS Bruker Daltronics mass spectrometer. TGA studies of the complexes were carried out using a Perkin–Elmer Thermogravimetric analyser TGA 7 with a scan rate of 10°C per minute in nitrogen atmosphere.

RESULTS AND DISCUSSION

All the metal complexes are either colored or colorless solids and are stable towards air and have high melting points (above 300°C). Analytical data of the complexes suggest that the metal to ligand composition is 1 : 1 for Co(II), Ni(II), Cu(II), Zn(II), Cd(II), and Hg(II) complexes and 1 : 2 for UO_2(VI) and Th(IV) complexes. The complexes have the general formula $[MLCl \cdot H_2O]$ where M = Co(II), Ni(II), Zn(II), Cd(II), or Hg(II), while the Cu(II) salt yields complexes of the type $[CuL \cdot 2H_2O]Cl$; with UO_2(VI) and Th(IV) salts complexes of the type $[UO_2L_2] \cdot H_2O$ and $[ThL_2(NO_3) \cdot 2H_2O]\ NO_3$, respectively, were obtained. The complexes are insoluble in water and common organic solvents but have partial solubility in DMF and DMSO. Hence, molecular weights could not be determined.

Conductivity Measurements

The conductivity for 10^{-3} M solutions of the complexes (Table 1) in DMF show Cu(II) and Th(IV) complexes to be 1 : 1 electrolytes; the other complexes show non-electrolytic behavior.

IR Spectra

The IR spectrum of the free ligand is characterized mainly by strong bands at 3220, 1717, and 1618 cm^{-1}, which are attributed to the stretching frequencies of NH, C=O, and C=N [16] respectively. Upon complexation with the metal ion, the bands due to C=O and NH disappear with the simultaneous appearance of band at 1280–1310 cm^{-1}, which may be assigned to C–O, suggesting deprotonation of the NH group via the carbonyl oxygen atom of the isatin moiety through its lactam–lactim tautomerism [16]. The band at 1618 cm^{-1} due to C=N group stretching vibration in the spectrum of the free Schiff-base ligand shifts, with splitting to lower wave numbers in all the metal complexes (1590–1615 cm^{-1}), indicating that the azomethine nitrogen atom is coordinated to the central metal ion [16]. The bands observed in the region 3150–3200 cm^{-1} attributed to symmetric modes of the NH_2 group remain at nearly the same position in the spectra of the complexes, indicating the non-participation of this group in coordination. Further, these chelate spectra exhibit new bands at 520 cm^{-1}, 420–410 cm^{-1}, and 332 cm^{-1}, which may be assigned to M–O, M–N, and M–Cl stretching modes respectively in all the complexes [10]. The IR spectra of UO_2(VI) complex showed no absorption bands either due to free or coordinated nitrate groups. On the other hand, the spectra of Th(IV) complex showed an absorption band at 1380 cm^{-1}, where the free nitrate is known to absorb [17]. The complex exhibited bands at 1512, 1290, 1028, 809, 745, and 720 cm^{-1} corresponding to the bidentate nitrate groups [17]. The IR spectra of all the metal complexes under study exhibit a broad band in the 3380–3550 cm^{-1} region, which can be attributed to the OH stretching vibration of water [16, 17], as expected from elemental analysis.

^{1}H NMR Spectra

The ^{1}H NMR spectrum of the ligand and its diamagnetic Zn(II), Cd(II), Hg(II), U(VI), and Th(IV) complexes were recorded in DMSO-d_6. The ^{1}H NMR spectral data are reported in Table 2. The spectrum of the Schiff base ligand shows bands in four distinct regions (singlet at δ10.5, multiplet at 6.8–7.5, multiplet at 2.4,

Table 1. Analytical and physical data of the complexes

Compound	Yield %	Color	(%) Found (Calcd.)				Mol. cond. S cm^2 mol^{-1}	μ_{eff}, μ_B
			C	H	N	M		
HIsIPD (L)	90	Pale pink	71.95 (72.14)	8.33 (8.35)	13.98 (14.03)	–	–	–
[CuL · 2H_2O]Cl	85	Light green	49.34 (49.71)	6.57 (6.67)	9.52 (9.66)	14.70 (14.72)	95	1.87
[CoLCl · H_2O]	85	Brown	52.55 (52.49)	6.51 (6.56)	10.11 (10.20)	14.35 (14.33)	12	4.54
[NiLCl · H_2O]	80	Brown	52.48 (52.53)	6.62 (6.56)	10.45 (10.41)	14.20 (14.27)	24	3.70
[ZnLCl · H_2O]	74	Brown	52.01 (51.81)	6.21 (6.24)	10.10 (10.07)	15.62 (15.68)	14	–
[CdLCl · H_2O]	78	Reddish	46.50 (46.55)	5.61 (5.60)	8.98 (9.05)	24.31 (24.23)	07	–
[HgLCl · H_2O]	80	Light white	39.68 (39.13)	4.55 (4.71)	7.54 (7.61)	36.38 (36.33)	12	–
[UO_2L_2] · H_2O	90	Yellow	48.80 (48.75)	5.92 (5.87)	9.44 (9.48)	26.84 (26.86)	16	–
[$ThL_2(NO_3)$ · 2H_2O] NO_3	92	Chilly Red	43.45 (43.70)	5.63 (5.50)	11.58 (11.44)	23.63 (23.41)	96	–

Table 2. ^{1}H NMR Chemical Shifts (δ ppm) for the Schiff base and its complexes

Ligand/Complex	Isatin ring		Side Chain	
	N–H	Aromatic protons	NH_2	Aliphatic protons
HIsIPD (L)	10.5 (1H, s)	7.5–6.8 (4H, m)	2.4 (2H, m)	1.5–0.65 (18H, m)
($C_{18}H_{24}N_3O$)				
[ZnLCl · H_2O]	–	7.85–6.9 (4H, m)	2.4 (2H, m)	1.5–0.65 (18H, m)
[CdLCl · H_2O]	–	7.6–6.8 (4H, m)	2.38 (2H, m)	1.5–0.65 (18H, m)
[HgLCl · H_2O]	–	7.85–6.9 (4H, m)	2.38 (2H, m)	1.5–0.65 (18H, m)
[UO_2L_2] · H_2O	–	7.85–6.9 (4H, m)	2.4 (2H, m)	1.5–0.65 (18H, m)
[$ThL_2(NO_3)$ · 2H_2O]NO_3	–	7.85–6.9 (4H, m)	2.42 (2H, m)	1.5–0.65 (18H, m)

t – triplet, m – multiplet, s – singlet, br – broad.

Table 3. TGA data of the complexes

Complex	Stage	Temp. °C	Weight loss % Found (% Calc.)	Species lost	Residue
$[CuL \cdot 2H_2O]Cl$	1	150–200	15.2(16.5)	Coordinated $H_2O + Cl$	CuO
	2	370	66.0(68.7)	Ligand	
$[CoLCl \cdot H_2O]$	1	220–280	11.5(13.1)	Coordinated $H_2O + Cl$	Co_2O_3
	2	370	70.0(72.6)	Ligand	
$[NiLCl \cdot H_2O]$	1	220–270	12.7(13.6)	Coordinated $H_2O + Cl$	NiO
	2	350	69.9(70.6)	Ligand	
$[ZnLCl \cdot H_2O]$	1	200–260	11.8(12.8)	Coordinated $H_2O + Cl$	ZnO
	2	330–350	69.2(71.5)	Ligand	
$[CdLCl \cdot H_2O]$	1	180–250	10.8(11.6)	Coordinated $H_2O + Cl$	CdO
	2	360	62.7(64.2)	Ligand	
$[HgLCl \cdot H_2O]$	1	180–250	10.5(9.7)	Coordinated $H_2O + Cl$	HgO
	2	350	52.9(54.0)	Ligand	
$[UO_2L_2] \cdot H_2O$	1	120	1.9(2.0)	Uncoordinated H_2O	U_3O_8
	2	360	65.0(67.5)	Ligand	
$[ThL_2(NO_3) \cdot 2H_2O]NO_3$	1	180	5.8(6.3)	Uncoordinated NO_3	ThO_2
	2	200–250	8.9(9.9)	Coordinated $H_2O + NO_3$	
	3	330	58.2(60.3)	Ligand	

and multiplet at 0.65–1.5 ppm) corresponding to the protons of the aromatic NH, aromatic protons of isatin moiety, NH_2 protons of isophoronediamine, and aliphatic protons of the amine, respectively. These protons are shifted downfield due to coordination to the metal ions [18]. The absence of the peak due to the NH group in the ^1H NMR spectra of the Zn(II), Cd(II), Hg(II), UO_2(VI), and Th(IV) complexes support the deprotonation of this group upon complexation with a metal ion. Due to limited solubility in DMSO, the ^{13}C NMR spectra of the complexes could not be measured.

UV-Visible and Magnetic Susceptibility Measurements

The electronic spectral data of complexes in DMF are included in Table 1. The electronic spectrum of Cu (II) complex in solution exhibits a broad band at 14790 cm^{-1}, which can be assigned to a $^2B_{1g} \longrightarrow {}^2A_{1g}$ transition. This transition, along with the magnetic moment value (μ = 1.88 BM), supports a square planar geometry [19, 20]. The electronic absorption spectrum of Co(II) complex is characterized by the highest energy $^4A_2 \longrightarrow {}^4T_2$ (p) transition at 15170 cm^{-1}, which is typical for tetrahedral Co(II) complexes; the magnetic moment (μ = 4.57 BM) also suggests tetrahedral geometry [21]. The electronic absorption spectrum of Ni(II) complex exhibits two bands at 10 640 cm^{-1} and 17540 cm^{-1} which can be assigned to the allowed transitions $^3T_{2g}(F) \longrightarrow {}^3T_{1g}(P)$ and $^3T_{1g}(F) \longrightarrow {}^3A_{2g}(F)$, respectively. The magnetic moment (μ = 3.70 BM) along with spectral data suggests tetrahedral geometry [22]. The electronic

Table 4. Results of antibacterial activity of the Schiff base and its complexes

Compound 1 mg/0.02 mL	Zone of inhibition (in mm)			
	Bacillus subtilis	*S. aureus*	*E. coli*	*Pseudomonas aeruginosa*
DMF(control)*	–	–	–	–
HIsIPDA (L)	14	6	4	2
$[CuL \cdot 2H_2O]Cl$	18	4	4	7
$[CoLCl \cdot H_2O]$	28	11	4	9
$[NiLCl \cdot H_2O]$	22	10	5	8
$[ZnLCl \cdot H_2O]$	13	8	4	4
$[CdLCl \cdot H_2O]$	13	10	4	7
$[HgLCl \cdot H_2O]$	16	12	9	3

Table 5. Anthelmentic activity of the Schiff base and its complexes

Ligand/Complex	Time taken for paralysis and death of worms	
	Paralysis (min)	Death (min)
Blank (normal saline)	No effect for 10 h	
Standard (piperazine citrate)	10	16
HIsIPDA (L)	12	20
$[CuL \cdot 2H_2O]Cl$	5	7
$[CoLCl \cdot H_2O]$	9	10
$[NiLCl \cdot H_2O]$	12	14
$[ZnLC \cdot H_2O]$	4	6
$[CdLCl \cdot H_2O]$	6	8
$[HgLCl \cdot H_2O]$	4	6

spectra of the U(VI) and Th(IV) complexes in DMF solution gave no bands in the 330–750 nm region. The absorption bands obtained below 330 nm correspond to the ligand $\pi \longrightarrow \pi^*$ transitions and are not much help in determining the geometry around the central uranium and thorium ions. The Zn(II), Cd(II), and Hg(II) complexes do not exhibit d–d electronic transitions due to the completely filled d-orbital. The magnetic susceptibility measurements reveal that all these complexes are diamagnetic as generally expected.

Thermogravimetric Studies

TGA studies of the complexes were carried out in nitrogen atmosphere at a rate of 10° per minute up to 700°C. In the thermal decomposition studies of the complexes of Co(II), Ni(II), Cu(II), Zn(II), Cd(II), Hg(II), UO_2(VI), and Th(IV), a general pattern is observed where the water of hydration is lost followed by the loss of uncoordinated chloride/nitrate, coordinated chloride/nitrate, ligand molecules, and the decomposition of the complex to finally give the respective oxides at higher temperatures.

Antibacterial Activity

The ligand and the metal complexes have been screened for their antibacterial activity and the results obtained are presented in Table 4. It is observed that all the metal complexes are more potent bactericides than the ligand. This enhancement in the activity can be explained on the basis of chelation theory [23, 24].

Anthelmentic Activity (in vitro)

The anthelmentic activity was tested on earthworms (*Pheretima Posthuma*).The Schiff base exhibits high activity and increases upon complexation with Cu(II) and Co(II) ions (Table 5).

CONCLUSIONS

The Schiff base ligand acts as bidentate monobasic with azomethine nitrogen and negatively charged oxygen atom as donors. The probable structures are shown below in Figs. 1–4. The antibacterial activity of the isatin Schiff base is greatly enhanced upon complexation with metal ions, particularly the Co(II) complex.

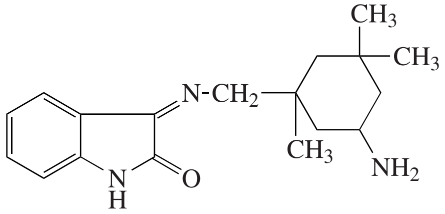

Fig. 1. Structure of the Schiff base ligand.

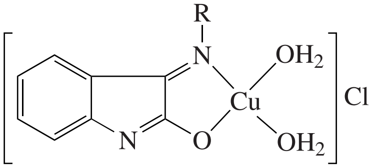

Fig. 2. Tentative structure of the Cu(II) complex.

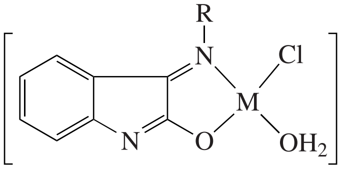

Fig. 3. Tentative structure of the Co(II), Ni(II), Zn(II), Cd(II) and Hg(II) complexes.

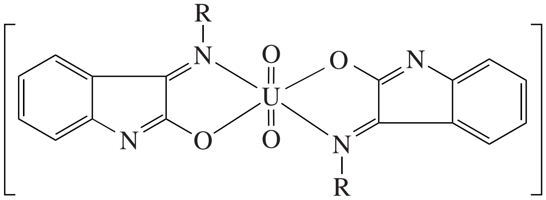

Fig. 4. Tentative structure of the UO_2^{+2} (II) complex.

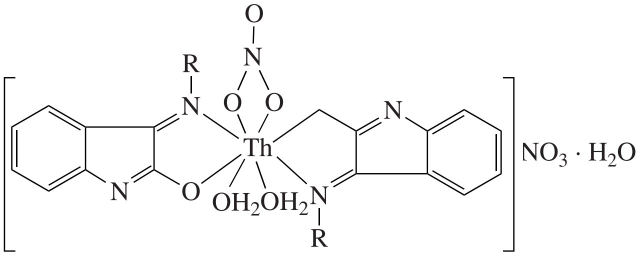

Fig. 5. Tentative structure of the Th(IV) complex.

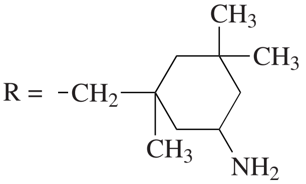

Fig. 6. Structure of the side chain in the complexes.

The anthelmentic activity of the Schiff base was enhanced upon complexation with metal ions.

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REFERENCES

1. D. Singh and R. V. J. Singh, Inorg. Biochem. **15**, 227 (1993).
2. R. Protivinsky, Antibiot. Chemother. **17**, 101 (1971).
3. K. C. Joshi, V. N. Pathak, and S. K. Jain, Pharmazie **35** (11), 677 (1980).
4. R. G. Shepherd, in *Medicinal Chemistry*, Ed. by A. Burger (Wiley, New York, 1970).
5. S. P. Sing, S. K. Shukla, and L. P. Awasthi, Curr. Sci. **52**, 766 (1983).
6. A. Danda, V. Kaur, P. Singh, and J. Indian, Pharm. Sci. **55**, 129 (1993).
7. J. C. Logan, M. P. Fox, J. H. Morgan, et al., J. Gen. Virol. **28**, 271 (1975).
8. A. Omar, M. E. Mohsen, H. Nabil, and M. Hassan, Arch. Pharm. **317** (8), 668 (1984).
9. D. Singh and R. V. J. Singh, Inorg. Biochem. **15**, 227 (1993).
10. K. Rama Krishna Reddy, K. Madhusudan Reddy, and K. N. Mahendra, Ind. J. of Chem., A **45**, 377 (2006).
11. K. Rama Krishna Reddy and K. N. Mahendra, Molbank **M516** (2006).
12. K. Rama Krishna Reddy and K. N. Mahendra, Molbank **M517** (2006).
13. H. W. Seeky and V. Dermak, Microbes in Action (W. H. Freeman, San Francisco, 1972).
14. K. N. Gaind, R. N. Das, B. N. Chopra, and R. N. Kaul, *Indian J. Farm*. **27**, 198 (1963).
15. A. I. Vogel, *A Textbook of Quantitative Inorganic Analysis* (ELBS and Longman's Green, London, 1962).
16. M. A. Hassan and K. Shehata, Synt. React. Inorg. Met-Org.Chem. **23** (5), 815 (1993).

17. K. Nakamoto, *Infrared Spectra of Inorganic and Coordination Compounds 2^nd^ edition* (Wiley, 1963).
18. H. Chohan, A. Pervez Rauf, M. Khan, and T. Supuran, J. Enzyme Inhibition Med. Chem. **19** (5), 417 (2004).
19. R. S. Joseyphus, C. J. Dhanaraj, and M. S. Nair, Trans. Met. Chem. **31**, 699 (2006).
20. E. A. Canpolat Yazici and M. Kaya, Trans. Met. Chem. **31**, 653 (2006).
21. S. Konstantinovic, C. Radovanovic, Z. Capic, and V. J. Basic, Serb. Chem. Soc. **68** (8–9), 641 (2003).
22. P. P. Hankare, L. V. Gavali, V. M. Bhuse, et al., Ind. J. Chem., A **43**, 2578 (2004).
23. K. N. Thimmaiah, W. D. Lloyd, and G. T. Chandrappa, Inorg. Chim. Acta **106**, 81 (1985).
24. W. Levingson, P. Mikeleus, J. Jackson, and W. Kaska, *Inorganic and Nutritional Aspects of Cancer*, Ed. by G.N. Schranzer *Plenum*, New York, 1978).