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Synthesis and pharmacological studies of some bivalent metal complexes with Schiff based ligand derived from xipamide

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ABSTRACT

The Zn(II) and Hg(II) complexes of Schiff base derived from Salicylaldehyde and Xipamide have been synthesized keeping in view that some metal complexes are found to be more potent than their parent drugs. The complexes of the type ML_2 have been synthesized and characterized on the basis of elemental analysis, conductivity, magnetic measurements, IR and electronic spectral studies. The conductivity data of the complexes also suggests their non-electrolytic nature. Comparative antimicrobial behavior and particle size analysis of Schiff base with their complexes has also been studied.

Key words: Ligand, Schiff base, non-electrolytic, conductivity, Xipamide.

INTRODUCTION

Schiff bases are an important class of ligands in coordination chemistry. Preparation of Schiff base containing azomethine group with potential binding ability has drawn a lot of attention in the last few years because of their biocidal properties[1-3]. Schiff base metal chelates have played a central role in the development of coordination chemistry. A detailed survey of literature reveals that biological activity of a ligand can be enhanced on chelation with suitable metal ions[4-6]. In the present communication we report the preparation, spectroscopic and biocidal studies of Zn(II) and Hg(II) complexes with Xipamide, a diuretic drug. The biological activities of ligand and metal complexes have also been studied.

MATERIALS AND METHODS

All the chemicals used were of AR/GR grade. Pure sample of Xipamide drug was obtained from Dishman's pharmaceuticals. Metal salts used were of Merck. Solvents used were methanol, acetone and deionized double distilled water.

Preparation of Schiff base

Equimolar solution of pure drug and salicylaldehyde were separately dissolved in methanol-water mixture (1:1) and refluxed for four hours and kept for a day. Pale yellow crystals of xipamide Schiff base (XM-SA) were formed in the reaction mixture, which were filtered and washed thoroughly with 50% methanol, dried over vacuum and weighed. Melting point of Schiff base was recorded.

Synthesis of Complexes

For the synthesis of complexes, ligand-metal ratio was confirmed by conductometric titration using monovariation method on systronics conductivitymeter using dip-type electrode. Conductometric titration supported 2:1 (L:M) ratio in the complex which was further supported by Job's method[7] of continuous variation modified by Turner & Anderson[8].The stability constants and free energy changes were also calculated.

The metal complexes were prepared by refluxing 60% acetone solution of ligand (0.006M) and metal salt(0.003M) for four hours. The refluxed solutions were kept for some days. Solid crystalline compounds appeared in the solution, which were filtered, washed with 60% acetone and dried over fused $CaCl_2$

Antibacterial Activity

Above synthesized compounds and ligands (Schiff base) were screened against bacteria Escherichia coli by the filter paper disc method at various concentrations using nutrient agar as medium. Sterilized filter paper of 5 mm diameter were soaked in solutions of different concentrations of test samples and introduced on nutrient agar plates. These plates were incubated for 48 hours at 35^0C.

Analytical procedure

The magnetic moments have been obtained by a vibrating sample magnetometer (model 7304 lakeshore with a 735 Controller and 450 Gauss meter). Elemental analyses were carried out on a model 240 Perkin elemental analyzer. Metal contents were determined gravimetrically[9]. The infrared spectra were measured on a Nicolet 400 D FT- IR spectrophotometer in KBr pallets. The electronic spectra of the metal complexes in DMF were recorded on LAMBDA 19 UV/VIS/NIR spectrophotometer. Molar conductance measurements were made in anhydrous DMF on a Systronics (model 305) conductivity bridge. The melting points of the ligand and complexes were recorded in open capillaries on a capillary melting point apparatus. Particle size analysis was carried out at SICART, Gujarat using laser diffraction particle size analyzer.

RESULTS AND DISCUSSION

On the basis of physicochemical characteristics, it has been found that the complexes are non- hygroscopic, stable at room temperature, insoluble in water but fairly soluble in DMSO. According to magnetic moment data Zn (II) and Hg(II) complexes are diamagnetic in nature. The molar conductance values for the complexes in 10^{-3} M DMSO are in the range of 9.5-14 Ω^{-1} cm^2 mol^{-1} suggesting that they are non-electrolytic in nature [10]. Elemental analysis data, formula weights and melting points are given in Table 1.

Table 1: Physico-chemical and Analytical data of complexes

Sl. no.	Ligand/ Complexes	Elemental analysis (%): Found (Calcd.)				M.p. (^{o}C)	Color	Molar Conductance $\Omega^{-1}cm^2mol^{-1}$
1	L	56.87 (57.57)	5.84 (5.96)	6.91 (6.97)	----	250	Peach	----
2	HgL_2	47.08 (47.32)	4.97 (5.01)	5.48 (5.73)	17.70 (17.98)	241	Off-White	13.2
3	ZnL_2	53.48 (53.85)	5.64 (5.71)	6.38 (6.52)	6.51 (6.67)	218	White	12.8

Infrared Spectra

The IR spectra of the complexes indicate that the ligand behaves as bidentate and the metal coordinates via azomethine nitrogen and phenolic –OH groups. The IR spectra of ligand shows a sharp band near 1638 cm^{-1} which may be due to azomethine linkage and shows lowering in frequency in metal complexes indicating the coordination of metal ions through azomethine linkage[11]. The ligand shows strong band at 3386 cm^{-1} due to phenolic –OH group. This band is absent in complexes supports the involvement of this group in complex formation[12]. Strong bands observed at 1623 cm^{-1} and 1598 cm^{-1} indicates the presence of (CH=N) bonds in complexes[13]. Bands observed near 1163 cm^{-1} in ligand and complexes is characteristics of SO_2-N linkage. The appearance of the M-O bands at 580 cm^{-1}, 607 cm^{-1} and M-N bands at 514 cm^{-1} and 520 cm^{-1} in Zn(II) and Hg(II)complexes respectively, indicates that XM-SA is coordinated through O & N atom[14,15].

Table 2: IR spectral data (cm^{-1}) of ligand and its complexes

Sl.no	Ligand/Complexes	V_{N-H}	$\nu_{C=N}$	V_{C-O}	$\nu_{C=O}$	ν_{M-N}	ν_{M-O}
1	$C_{22}H_{19}N_2O_5ClS$	3302	1639	1282	1671	----	-----
2	$C_{44}H_{36}N_4O_{10}Cl_2S_2Hg$	3301	1598	1312	1669	514	615
3	$C_{44}H_{36}N_4O_{10}Cl_2S_2Zn$	3300	1623	1282	1681	514	580

Antibacterial Activity

The zone of inhibition based upon size around the disc was measured. Inhibition zone percentages are recorded in Table 3. The percentage inhibition of growth by an inhibitor at different dilutions is determined as 100 x (C-T)/C (where C=diameter of microbial colony in control plate, T=diameter of bacterial colony in the test plate). From the results it is observed that both the complexes show greater activity against Escherichia coli as compared to the ligand and better results were obtained at high concentration. This indicates that chelation increases the antibacterial activity[16,17].

Table 3: Antibacterial activity of Schiff base and complexes

Compounds	% of inhibition zone	
	Escherichia coli	
	Concentration in ppm	
	500	1000
XM-SA	-	40
$(XM-SA)_2Zn$	44	98
$(XM-SA)_2Hg$	57	89
Streptomycin	68	87

Particle size analysis

To find out the maximum efficiency of the drugs and their metal complexes, studies on the particle size analysis are being considered very helpful [18]. Smaller particle size of the complexes is responsible for the enhanced solubility of the drug [19]. The results of the particle size analysis carried out for the pure drug, ligand and its Hg(II) and Zn(IV) complexes have been recorded in Table 4. These results reveal that on complexation, the size of the ligand and complexes got reduced too much extent as compared to their parent drug xipamide (XM). Thus, we conclude from our result that complexation enhanced the absorption and potency of the drug [20-21].

Table 4: Particle size measurement of pure drug, ligand and its complexes

S. No.	Sample Code	Particle Size (µm)
1	XM	112
2	L	95.6
3	HgL_2	67.5
4	ZnL_2	53.5

CONCLUSION

Hence on the basis of elemental analysis, IR spectra, NMR spectra, magnetic moment data and conductivity measurement, complexes are found to be diamagnetic as expected for d^{10} systems with tetrahedral geometry and following tentative structure is produced for complexes.

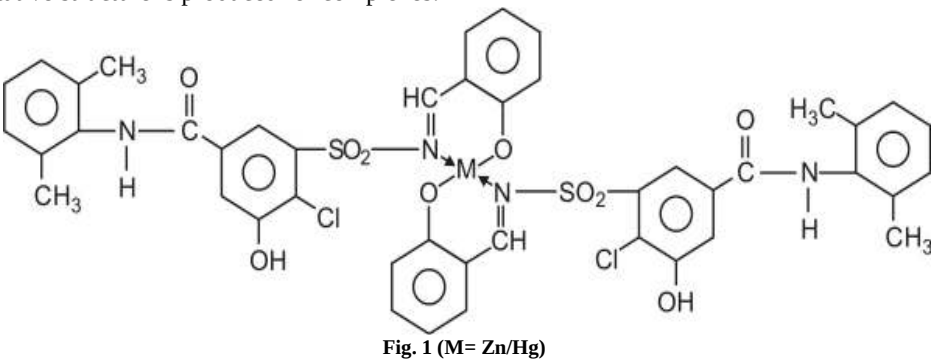

Fig. 1 (M= Zn/Hg)

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