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Synthesis, physico-chemical and spectral studies of Hg(II) and Cu(II) complexes with sulfamethoxazole schiff base

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ABSTRACT

Schiff bases derived from sulfa drugs act as good ligand to transition metal ions and they exhibit several coordination modes. The metal complexes of Cu(II) and Hg(II) have been synthesized with Schiff base of sulfamethoxazole [4-amino-N-(5-methyl-3-isoxazolyl) benzenesulfonamide] and salicylaldehyde. Sulfa drugs concentrate in the urine before being excreted and treat urinary tract infections. Conductometric titrations have suggested metal-ligand ratio of 1:2 for both Cu(II) and Hg(II) complexes. The ligand behaves as a bidentate with N, O donor atoms. Complexes have been synthesized and characterized by elemental analysis, IR and NMR spectral studies.

Key words: Complex, Sulfamethoxazole, Schiff base, IR, NMR.

INTRODUCTION

Sulfa drugs had attracted special attention from their therapeutic importance as they were used against a wide spectrum of bacterial ailments [1,2]. Studies on sulfanilamide metal chelates have much physiological and pharmacological relevance because the metal chelates of sulfadrugs have been found to be more bacteriostatic than the drugs themselves [3-6]. Schiff base compounds which contain the azomethine (imine) group (–RC=N–) are usually prepared by the condensation of a primary amine with an active carbonyl compound [7]. It has been often used as chelating agents (ligands) in the field of coordination chemistry and Schiff base metal complexes were of great interest for many years. It is well known that O and N atoms play a key role at the active sites of numerous metallo biomolecules in the coordination with metals [8]. Hg(II) has been used in medicine for many years[9,10] . It has been noticed that Cu(II) complexes as anti-inflammatory drugs are often more active than the parent ligands themselves [11,12].

Here in this paper we are describing synthesis and characterization of Copper(II) and Mercury(II) complexes with Schiff base of sulfamethoxazole [4-amino-N-(5-methyl-3-isoxazolyl) benzenesulfonamide]. (Fig. 1).

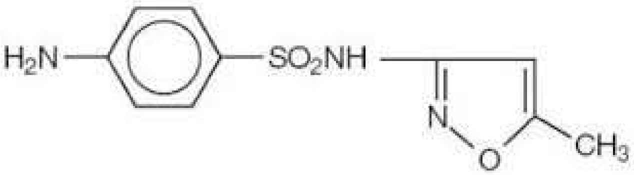


Fig.1.Structure of Sulfamethoxazole

MATERIALS AND METHODS

(a) Reagents and Instruments:

All chemicals and solvents used were of analytical grade. Pure sample of Sulfamethoxazole , molecular formula $C_{10}H_{11}N_3O_3S$ and molecular weight 253.28, was obtained from HiMedia Laboratories Pvt. Ltd. Mumbai. Salicylaldehyde from Central Drug House , New Delhi . Metal salts $HgCl_2$ and $CuCl_2.2H_2O$ were of Merck chemicals.

Elemental analysis (C, H, N and S) were carried out using micro analytical technique on C,H,N,S,O Elemental analyzer at SAIF, CDRI Lucknow. The Infrared spectra of ligand and metal complexes were recorded on KBr pellets in the range 4000-450 cm^{-1} on Perkin Elmer FTIR spectrophotometer. The NMR spectra were recorded on Bruker Avance II 400 FT NMR spectrometer in DMSO using TMS as the internal standard. Melting points were recorded using melting point apparatus and found 180^0C for Schiff base ,199 ^{0}C for Cu(II) complex and 224^0C for Hg(II) complex.

(b) Synthesis of Schiff base:

Equimolar (0.01) solutions of pure drug (0.2532g) and salicylaldehyde (0.12ml) were separately dissolved in methanol water mixture (1:1) and refluxed for for four hours and kept for a day. Pale yellow crystals of sulfamethoxazole Schiff base (SMZ-SD) were formed in the reaction mixture which were filtered and washed thoroughly with 50% methanol–water mixture, dried over vacuum and weighed. Melting point of Schiff base was recorded. (Fig. 2).

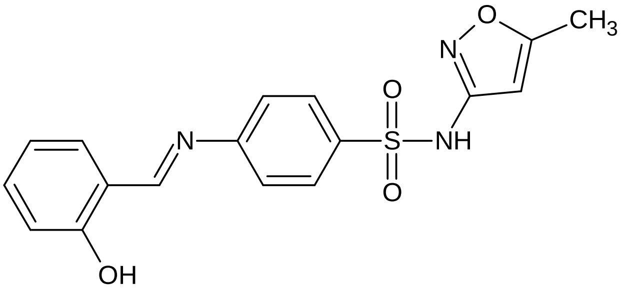


Fig. 2. Structure of Sulfamethoxazole-Salicyladimine (Schiff Base)

(c) Ligand-Metal ratio:

For the synthesis of complexes, we need to confirm metal-ligand ratio by conductometric titration method. 0.01 M solution of Sulfamethoxazole-Salicylaldimine Schiff base was prepared in 60:40 mixture of acetone and distilled water. Similarly, solution of metal salts $HgCl_2$ and $CuCl_2.2H_2O$ were prepared in the same solvent of 0.02 M concentration. 20 ml of ligand solution was diluted to 200 ml. The ligand was titrated against metal salt solutions and conductance was recorded after each addition of metal salt solution. From the graph between corrected conductance and volume of titrant added, it was concluded that the complex formation has taken place in the ratio of 1:2 (metal-ligand).

(d) Synthesis of complex:

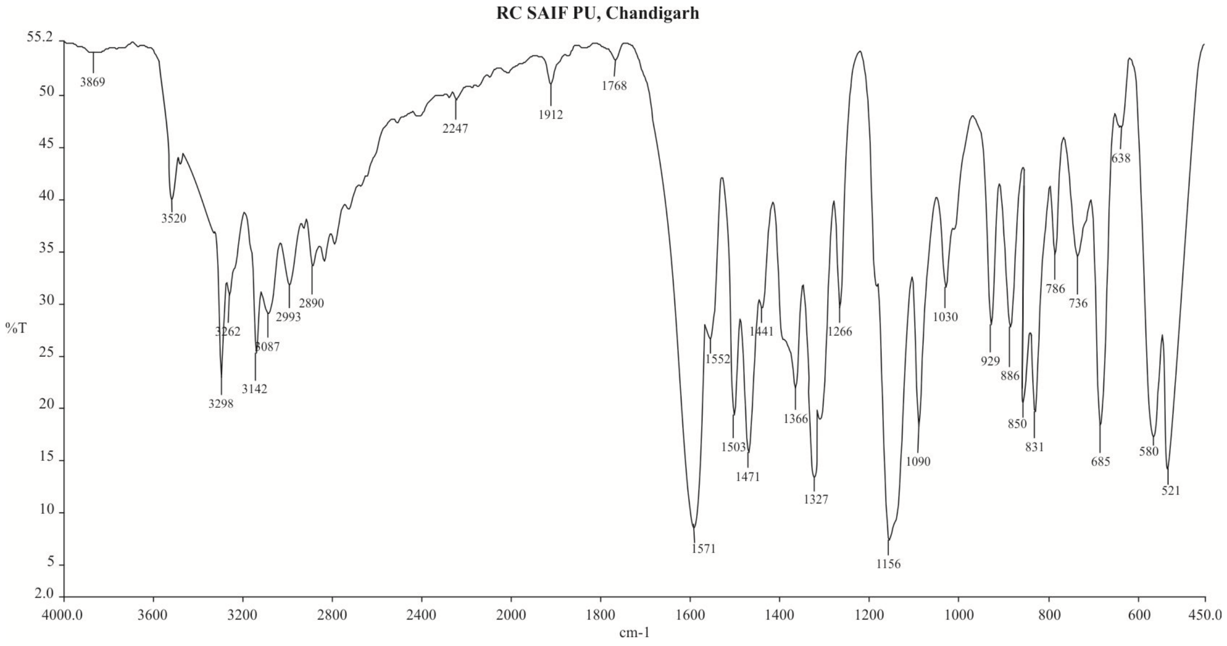
For the synthesis of complexes, 0.02 mol sulfamethoxazole–salicylaldimine (L) solution was prepared in 60% acetone–water solvent and refluxed for four hours with 0.01 mol solution of metal salts separately. The refluxed solutions were kept for some days. Solid crystalline compounds appeared in the solution, which were filtered, washed with 60% acetone–water mixture, dried and weighed. Melting point of the complexes was recorded.

RESULTS AND DISCUSSION

The analytical data of the complexes are given in Table 1. All these complexes are analyzed for 1:2 stoichiometry of the type ML2. On the basis of these characterizations it has been found that all the complexes are non-hygroscopic, stable at room temperature, insoluble in water but fairly soluble in DMSO.

(a) Infrared Spectral studies:

The relevant spectral bands and their assignments are recorded. The IR spectra [13,14] of the complexes indicate that the ligand behaves as bidentate and the metal coordinates via azomethine nitrogen and phenolic –OH groups. The shift of vC,=N to lower wave number by 30–40 cm^{-1} in the complexes indicates that these groups are involved in complexation [15]. The ligand shows strong band at 3430 cm^{-1} due to phenolic –OH group [16]. This band is absent in all the metal complexes indicating the involvement of this group in complex formation [17]. Moreover, the shift of the vC–O phenolic bands from 1282 cm^{-1} in ligand to 1292–1327 cm^{-1} in the spectra of metal complexes supports the coordination of the phenolic oxygen atom to the metal ion [18]. The Cu(II),complex shows a broad band in the region 3520 cm^{-1} suggesting the presence of coordinated water [19,20]. The bands for vM–O mode [21] appeared in the range of 570–580 cm^{-1} in both the complexes. The presence of sharp band in the region 514–521 cm^{-1} in the spectra of the complexes assigned to vM–N mode [22], further support the involvement of nitrogen atom in coordination. (Fig. 3 & 4).



Spectrum Name: Neha Bhopal-13.sp Description: SMZ-SD-Cu

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Fig. 3. IR Spectra of SMZ-SD-Cu

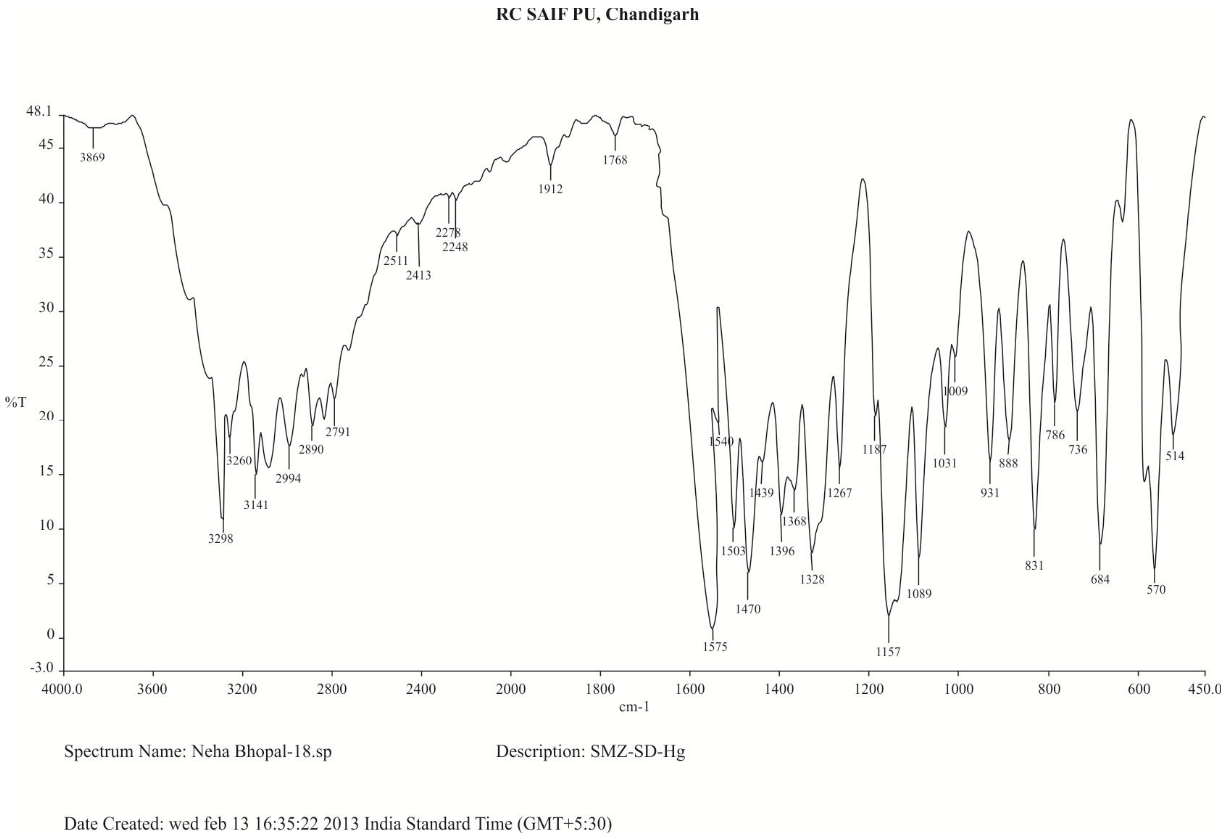


Fig. 4. IR Spectra of SMZ-SD-Hg

(b) NMR Spectral studies:

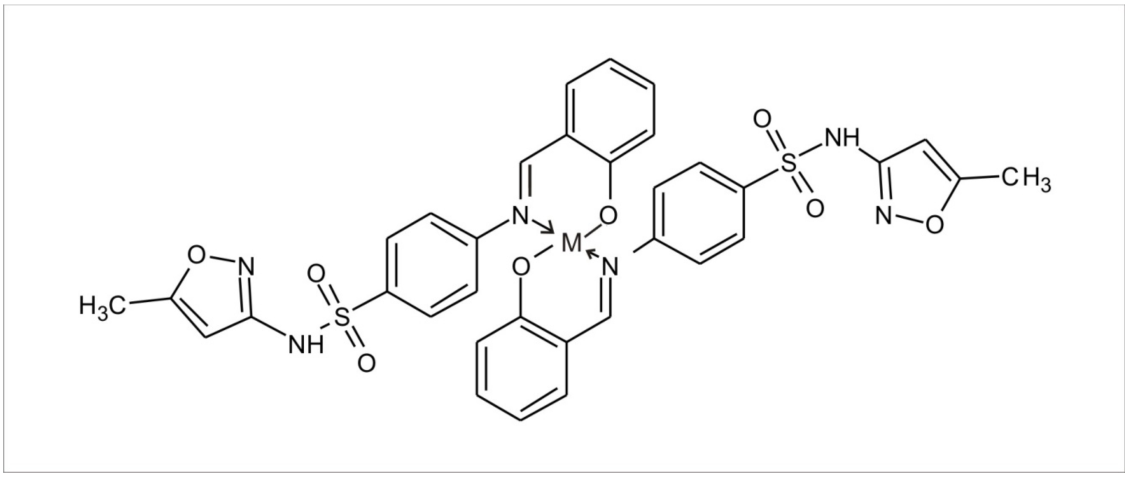
The 1H NMR spectra of the ligand has the expected characteristic signals. The CH$_3$ proton shows singlet at δ 2.29-2.53 and isoxazole proton at δ 6.05 ppm . In addition a multiplet peak at δ 6.59-7.49 may be due to aromatic protons and peak at δ10.59 ppm may be due to NH proton. The OH proton of salicylaldehyde moiety resonates as a singlet at δ12.10 ppm in case of ligand [23] disappears in the complexex indicating the involvement of phenolic oxygen in the coordination via deprotonation [24]. Signals observed in the ligand at region of δ 8.15 ppm due to azomethine proton shows downfield shift of 0.06 ppm and appears at δ 8.08 ppm indicating the coordination of azomethine nitrogen with metal ions [25].These observations support the following assigned structure to the complex.

Table-1. Analytical data of the ligand and complex

S. No.	Composition of ligand /complexes (m.wt.)	Color	Yield (%)	m.p. (^{0}C)	Elemental analyses(%):found (calcd)				
					C	H	N	S	M
1.	$C_{17}H_{15}N_3O_4S$	Pale yellow	68	180	56.43 (57.13)	4.13 (4.23)	11.50 (11.76)	8.91 (8.97)	–
2.	$C_{34}H_{32}N_6O_{10}S_2Cu$	Green	62	199	51.12 (51.27)	3.01 (3.97)	10.02 (10.35)	8.03 (7.89)	7.48 (7.82)
3.	$C_{34}H_{28}N_6O_8S_2Hg$	Off white	51	224	44.47 (44.71)	3.11 (3.09)	9.16 (9.20)	6.77 (7.02)	21.68 (21.96)

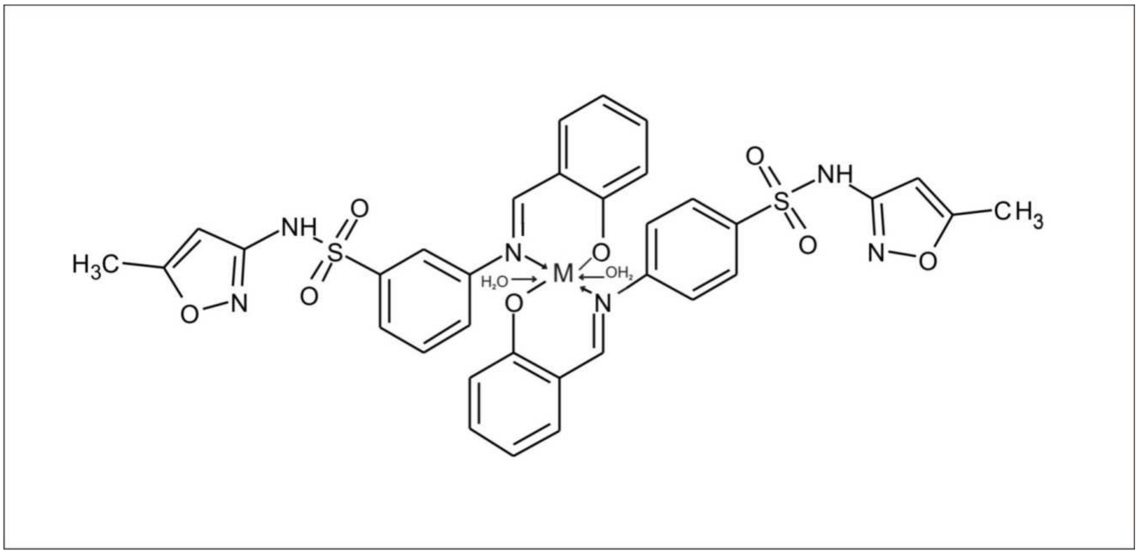
CONCLUSION

From the analytical and spectral data, it can be concluded that the synthesized complexes are stable with probably following structures. (Fig. 5 & 6).



[M=Hg]

Fig. 5. Structure of SMZ-SD-Hg complex



[M=Cu]

Fig. 6. Structure of SMZ-SD-Cu complex

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