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PREPARATION, CHARACTERIZATION, SPECTROPHOTOMETRIC DETERMINATION OF THE FORMULA OF ACOORDINATION COMPLEX AND BIOLOGICAL STUDIES OF SULFAMETHOXAZOLE (ANTIBIOTIC) WITH TIN DICHLORIDE

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ABSTRACT : Sn(II) complex of the type, $[Sn(SMZ)_2]Cl_2$ was synthesized by the interaction of Sulfamethoxazole ligand and Tin Chloride, the complex was confirmed on the basis of results of elemental analyses, FT-IR, UV-Vis, molar conductance ($\ddot{E}_m$). The elemental analysis data, suggests the stoichiometry to be 1:2 (metal: ligand) and determination of the formula of a coordination a complex formed between the Sn(II) ion and the SMZ using Job's method of continuous variations. The study of (Ëm), indicated the electrolytic nature type 1:2. The $[Sn(SMZ)_2]Cl_2$ was screened for antibacterial activity against Gram-ve (*Escherichia coli* and Gram+ve (*Staphylococcus aureus*) and (*Candida albicans*) antifungal. The IR spectral data suggested that the coordination sites of SMZ are the sulfonyl oxygen and SO_2-NH sulfonamide nitrogen as a bidentate ligand.

Key words : Tin complex, spectroscopy, sulfamethoxazole, biological activity.

INTRODUCTION

The coordination chemistry of tin and organotin halides use as supramolecular chemistry have attracted considerable interest due to their biological, industrial and catalytic properties (Arnold and Blok, 2004; Ebrahim *et al*, 2016; Dorosti *et al*, 2015). A series of [tin (II) and tin (IV)]-(salen) complexes synthesized from the corresponding salen ligands and $SnCl_2$ (Jing *et al*, 2015). There have been numerous studies of $SnCl_2$ complexes using conductance, potentiometric, polarography and solubility methods to determinates equilibrium formation constants (Alias *et al*, 2015; Bamigboye *et al*, 2012). Sulfamethoxazole (SMZ) is the most predominant sulfonamide in human medicine.Some sulfa drugs were used in the treatment of malaria, cancer, leprosy and tuberculosis (Trottier *et al*, 1980). Sulfur can coordinate both in terminal and bridging fashion to a metal center (Blasco *et al*, 1996). The presence of donor atoms (N, S, O) at various positions in SMZ enable, it to behave as multidentate ligand and thus form chelates of diverse structural types with a wide range of metal ions (El–Nawawy *et al*, 2011; Yasmi *et al*, 2017). Keeping these facts in view, the present paper describes the Synthesis and characterization of sulfamethoxazole (antibiotic) with Tin ion (II).

MATERIALS AND METHODS

All chemicals were purchased from Aldrich / Merck the reagents were used without further purification. b-Instruments: FT-I.R spectra were recorded as KBr discs using Shimadzu 24 FT-I.R 8400s. Electronic spectra of the prepared complexes were measured in the region (200-1100) nm for 10^{-3} M solutions in (DMSO) by using Shimadzu-U.V-160. An Ultra Violet Visible-Spectrophotometer, while the percentage of the metal in the complex was determined by Atomic A absorption (A.A) Technique using Japan A.A-67G Shimadzu. Electrical conductivity measurements of the compound were recorded at room temperature for 10^{-3} M solutions of the samples in (DMSO) using pw9527 Digital conductivity meter (Philips). Melting points were recorded by using Stuart melting point apparatus. The proposed molecular structure of the complexes were drawing by using chem. office program, 3DX (2016).

Preparation of complex

The $[Sn(SMZ)_2]Cl_2$ complex was prepared by the following general method :

A solution of (sulfamethoxzole) (0.5 gm, 2 mmole) in (50%) (v/v) ethanol-water (20 mL) was add with stirring to Sn (II) chloride (0.22 gm,1 mmole) dissolved in in ethanol: water 50% 20mL in a flask and stirred at room temperature (20ºC) by using the stoichiometric amount (1:2) Metal: ligand molar ratios, the above reaction mixture to raise the pH up to ~6.0 and the mixture was stirred for (20 -30mint). The solid precipitate obtained collected by the filtration and recrystallized from H_2O/ethanol as a light yellow powder; yield 84 % and mp < 260ºC. The complex was analyzed for their metal and chloride contents were determined by standard methods (Yasmi *et al*, 2017; Vogel, 1996).

RESULTS AND DISCUSSION

The synthesis complex may be according to the following proposed equation:

$$2\ SMZ + SnCl_2.2H_2O \rightarrow [Sn(SMZ)_2]Cl_2 + 2H_2O$$

SMZ = Sulfamethoxazole

$[Sn(SMZ)_2]Cl_2$ complex was dissolved in various solvents and HCl.

The complex was soluble in DMSO, DMF, H_2O, Hexanol and HCl, while partially soluble in Benzene and acetone.

Conductance data of Sn(II) complex refer that two of chloride ions presence outside of the coordination sphere. The obtained results were strongly matched with the (C.H.N) analysis data, where Cl^- ions are detected after the degradation of this complex by using nitric acid (HNO_3) then precipitation of chloride ions using ($AgNO_3$) solution (Vogel, 1996) color, light yellow; mp, <260^{0}C and elemental analysis (%), calcd. For $C_{20}H_{22}Cl_2N_6O_5$: C, 39.43; H, 3.64; N, 13.79; Sn, 19.48 found, C: 39.95; H, 3.86; N, 14.67, Sn, 22.08. The conductivity value 73$Ù^{-1}$ $cm^2\ mol^{-1}$ in DMSO imply the presence of electrolyte type 1:2.

In conclusion, our investigation suggests that the Sulfamethoxazole coordinates with Sn (II) forming tetrahedral geometry. The coordination sites and the binding properties of (SMZ) were determined by using FT.IR spectroscopy. Bands of IR spectra for selected ligand and its ion metal complexes are represented in Table 1 and Fig. 1. ä (N–H) vibrations (aromatic sec. amine) of $–NH_2$ occur at [3468 and 3378] cm^{-1} for free (SMZ) due to υ [a symmetric and symmetric] NH_2, respectively. The hypochromic effect (decreasing in the intensity of υ (NH) vibrations in case of complex rather than (SMZ) alone as well as the blue-shifted in the wavenumbers from 3299 cm^{-1} (Al-barki *et al*, 2016; Taghreed *et al*, 2014).

More evidence new bands appeared in [(567) and (451)] cm^{-1} due to the stretching frequencies of (Sn-O) and (Sn-N) bonds, respectively (Raheem *et al*, 2014). The absorption band at 567cm^{-1} corresponds to the stretching vibration of the Sn-O group, in good agreement with literature data for related complexes (Silverstein *et al*, 1980).

The UV-Vis spectrum of the (SMZ) in (DMSO)

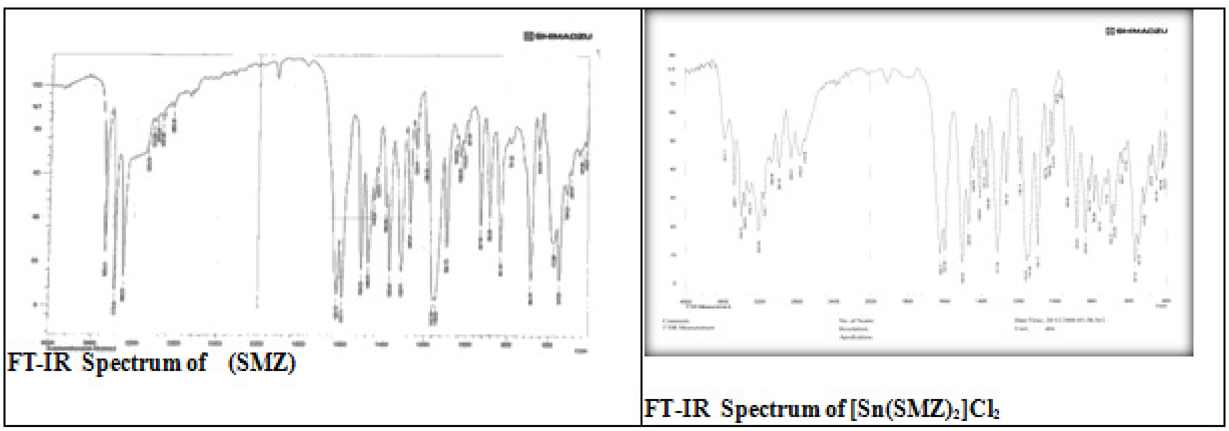


Fig. 1 : FTIR Spectra of compounds.

Table 1 : FT-R spectral data of SMZ and $[Sn(SMZ)_2]Cl_2$.

	vas NH):NH₂ vs (NH):NH2	as (NH): And vs (NH): sulfonam ide group	υ (C–H) Aliph and Arom.	δ(NH₂)	ν(C=C): phenyl ring	υSO₂ asy	υ C–N	υ (C–O)	υ (SO₂) sy	υ (C-S)	Sn-O	Sn-N
SMZ	3468 s 3378s	3372 3300	2929 w, 2831	1622	1597 vs 1504	1365 s	1311s	1267 ms	1157 1143	831 vs	-	-
Sn Com.	3468 υas 3384υs	3360 3140	2981 w 2858	1620	1597 vs 1504 vs	1377s	1309	1261ms	1153 1141	833	567	451

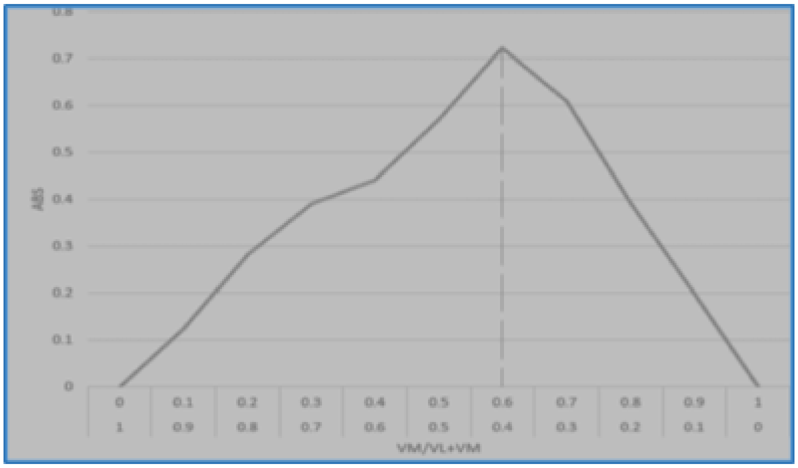
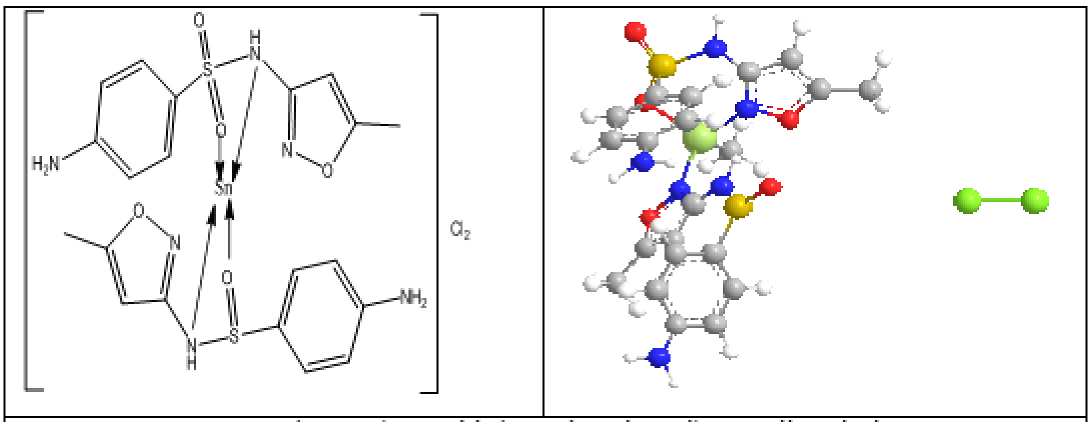


Fig. 2 : Mole ratio (M:2L) by continues variation method.



IUPAC NAME:(2S,2'R)-2,2'-bis(4-aminophenyl)-7,7'-dimethyl-1H,1'H-2'l4,3l3,3'l3,5l4,5'l4-4,4'-spirobi[isoxazolo[3,2- d][1,2,3,5,6]oxathiadiazastannine] 2-oxide dichlorine

Fig. 3 : Probable 3-D structure of the $[Sn(SMZ)_2]Cl_2$.

solvent appeared a high intense absorption band due to the C=N chromophore at 275nm (36363cm^{-1}).

(ð-ð* transition) shifts to a higher wavelength in thespectrum of $[Sn(SMZ)]Cl_2$ complex and appears at 286 nm (34965 cm^{-1}) in the complex (Sutton *et al*, 1968). This indicates the coordination of C=N nitrogen to the metal atom. The complex also shows one week [Taghreed *et al*, 2014, 16) band 834 nm (11990 cm^{-1}) may be assigned as charge transfer bands. It has been reported that the metal is capable of forming dð–pð* bonds with ligands containing nitrogen or oxygen as the donor atom. The Tin atom has its d orbital completely vacant and hence í (Sn ← N) or í(Sn ← O) bonding can take place by the acceptance of the lone pair of electrons from the nitrogen or the oxygen of the (SMZ) (Silverstein *et al*, 1980; Sutton, 1968).

Continuous-Variations method (CVM)

When a colorless aqueous a solution of $SnCl_2$ is treated with SMZ solution color changes light yellow. Stoichiometry of the complex formed by Sn(II) and sulfamethoxazole is determined using the Job's (CVM), spectrophotometry is based on the measurement of a series of different solutions such as those shown in Table 2 in which the molar concentrations of two reactants differ but their sum is constant (1x10^{-3} M). Ten clean 100-mL volumetric flasks were labeled 1 to 10. The mole fraction of SMZ and Sn in the solution at a suitable wavelength (408 nm) was calculated using distilled water as a reference (Table 2). After 5 minutes the absorbance (A) of each solution was measured at 408 nm. The mole fraction of each component in the solution was calculated and plotted against absorbance using distilled H_2O as reference. The experimental results of the stoichiometry (Fig. 3) of the complex of Sn (II) and sulfamethoxazole is 1:2 (Badriah *et al*, 2019; Naggara *et al*, 2016).

The mole a fraction in which the number of moles of Sn^{2+} and SMZ is in the stoichiometric ratio since the sum of mole fractions in a mixture always = 1.

Table 2 : Data for (CVM)of determining Stoichiometry of complex.

Volumes of flask 1mL sulfamethoxazole sol'nligand $1x10^{-3\,M}$	Volumes of Flask 2 mL Sn sol'nmetal $1x10^{-3M}$	Mole Fraction		
		Ligand	Metal	ABS
10	0	1.0	0	0
9	1	0.9	0.1	0.123
8	2	0,8	0.2	0.283
7	3	0.7	0.3	0.392
6	4	0,6	0.4	0.441
5	5	0.5	0.5	0.571
4	6	0.4	0.6	0.723
3	7	0.3	0.7	0.610
2	8	0.2	0.8	0.392
1	9	0.1	0.9	0.201
0	10	0	0.1	0

The formation constant K_f (or equilibrium constant) for the reaction can be calculated once the equilibrium concentrations are known:

$$K_f = \frac{[M \times Ln]}{[M]^x.[L]^n}$$

$$K_f = \frac{[Sn(SMZ)]}{[Sn].[(SMZ)]^2}$$

ligand concertation [L] = metal concentration $[M]=1\times10^{-3}M$

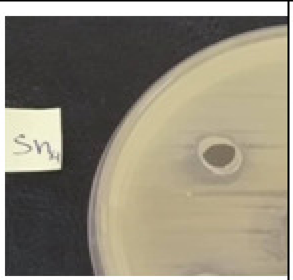
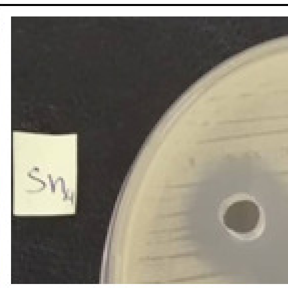
Beer's law gives the relationship between concentration: C^o and absorbance A using quartz cell of (1.0) cm length with concentration (1×10^{-3}) mole L^{-1} solution in concentration at 25±1°C.

$\Delta G = -2.3$ R.T. LogK (Gibs free energy)

Table 3 : Results of continues variation method.

ABS* low concentration for metal	ABS* low concentration for ligand	$å_1$ $å_2 å_{ava}$ metal ligand average			C_o primary concentration for matel or ligand	Kf $L.mol^{-1}$	LogKf	ÄGK cal/mol
		$\varepsilon = \frac{ABs * S}{bc}$ $(L.mol^{-1}.cm^{-1})$						
0.123	0.201	1230	2010	1620	0.00026	3.52×10^5	5.546	-7576

Table 4 : Biological activity (SMZ)and $[Sn(SMZ)_2]Cl_2$ (Diameter of inhibition zone in mm).

	Antibacterial		*Antifungal*
Compound	*Acineto (-)*	*Staphylococcus (+)*	*Candida albicans*
Control (DMSO)	0	0	0
(SMZ)	15	17	9
$[Sn(SMZ)_2]$ Cl_2 Sn4	11	20	6
			

The stability of the complex in solution were investigation by evaluation of (K_f) (stability formation constants or (stability Constant) (K) according to the following equation (Irving *et al*, 1953).

$xM + nL \rightarrow M_X L_n$

Sn +2 (SMZ) → [Sn $(SMZ)^2$]

The stability constants of the complex containing SMZ were calculated from Eqs. below

Sn (SMZ) ↔ Sn(SMZ)

The composition and the stability constant evaluated the mole ratio methods (Fig. 2 and Table 3). The method showed that the molar ratio of Sn(II) is 1:2 (metal : ligand). The stability constant is found to be (3.52×10^5) $L.mol^{-1}$. and -7576 Kcal/mol Gibs free energy.

According to their results and discussed through different techniques the, tetrahedral geometry has been proposed for the resulting tin(II) complex as shown in Fig. 3.

Biological activities

In vitro, the biological activities of the (SMZ).ligand and $[Sn(SMZ)_2]Cl_2$ the complex was screened for antibacterial against *Staphylococcus*(+) and *Acineto* (-) and for antifungal against *Candida albicans* using agar well diffusion method at 37°C. In order to ensure that no effect of solvent a control test was performed with DMSO and found inactive in the culture medium. The results of the biological activities all tested bacterial and fungal strains are shown in Table 4.

From Table 4, it is clear that the inhibition zone of the $[Sn(SMZ)_2]Cl_2$ is lower than that of the free ligand (SMZ). From the biological data it is clearly shown that the $[Sn(SMZ)_2]Cl_2$ is highly active against the gram-positive and lower gram-negative bacterial species and, *Acineto*(-) and *Staphylococcus* (+) bacteria and *Candida albicans* fungal, respectively. The increased activity of the metal complex can be explained in Tweedy's chelation theory (Tweedy, 1964). Overlap of the ligand orbital and partial sharing of the positive charge (+2) of the metal ion with the donor, groups enhance the lipophilic ties of the complex and delocalization of π-electrons over the whole chelates ring (Cappuccino *et al*, 2002).

CONCLUSION

Sulfamethoxazole (SMX) drug complex formulas with Sn (II) was prepared and characterized by molar conductance, elemental analysis, FT-IR and UV-vis_spectroscopy. The data corroborated tetrahedral geometry for the complex.

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