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Synthesis and characterization of ternary complexes of copper(II)-, nickel(II)-, zinc(II)- cobalt(II)- and mercury(II)-theophylline with ethylenediamine

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Abstract: Several new ternary complexes of copper(II)-, nickel(II)-, zinc(II)- cobalt(II)- and mercury(II)-theophylline with ethylenediamine have been synthesized and characterized. Various physico-chemical methods including solubility, melting point, metal content estimation, IR and UV-Visible spectra, magnetic moment data, thermogravimetric analysis and differential scanning calorimetric analysis have been employed for their characterization.

Investigation of their melting points, thermogravimetric analysis and differential scanning calorimetry analysis shows that compound **A**, **B**, **C** and **E** exhibit high thermal stability even up to 276^{o}C while compound **D** commence decomposition at very low temperature at about 100^{o}C due to loss of one molecule of water. IR spectral investigation indicates that metal-theophylline bonding occurs through N(7) and O(6) of theophylline. UV-Visible spectral investigation shows that compound **A**, **B**, and **D**, shows d → d transition in the visible region. The absorption spectrum of high spin**D** complex shows two spin-allowed bandswhich are assigned to $\nu_1 = {}^4T_{1g} \rightarrow {}^4A_{2g}and\nu_2 = {}^4T_{1g}(F) \rightarrow {}^4T_{1g}$ (P). The spectrum of the d^8 complex **B** shows three bands which are assigned to $\nu_1 = {}^3A_{2g}(F) \rightarrow {}^3T_{2g}(F)$, $\nu_2 = {}^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)$and $\nu_3 = {}^3A_{2g}(F) \rightarrow {}^3T_{1g}(P)$. In the spectra of**A**complex ${}^2A \leftarrow {}^2E$ transitions is occurred.But other complexes yield bands in UV region due to $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ electronic transition within the ligand.

On the basis of metal contents the studied compounds have been formulated as-

$[Cu(C_7H_7N_4O_2)_2(C_2H_8N_2)]$	**A**
$[Ni(C_7H_7N_4O_2)_2(C_2H_8N_2)]$	**B**
$[Zn(C_7H_7N_4O_7)_2(C_2H_8N_2)]$	**C**
$[Co(C_7H_7N_4O_2)_2(C_2H_8N_2)].H_2O$	**D**
$[Hg(C_7H_7N_4O_7)_2(C_2H_8N_2)]$	**E**

Keywords: Theophylline, Ethylenediamine, IR and UV-Visible spectra,Thermogravimetric and Differential Scanning CalorimetricAnalysis, Melting points andComplex Compounds.

1. Introduction

Theophyllineis a derivative of purine, consisting of a fused pyrimidine-imidazole ring system with conjugated double bonds and it has biological importance which can be used in anticancer drugs[1-4]. The purines including theophylline, theobromine and caffeine, constitute an important class of anti-inflammatory agents[5]. As it is structurally related to nucleic acids components it has tremendous biological importance[6]. Thus it can be used as a drug in pulmonary disease. On the other hand, many metal ions present in small quantities in living organism and play significant roles of extreme biological importance. The metals essential for such diverse intricate functions, beyond certain levels of concentration and in certain chemical forms may bring about adverse effects.

Like other purine derivative theophylline has many pharmacologic properties. Since a few metal-theophylline complexes have shown significant antitumor activity[7], it is very important to know the coordinating behavior of theophylline with transition metal ions.The antibacterial activity of theophylline is wellknown, especially as this alkaloid is present in tealeaves[8].The previous study is mainly focused on preparation and characterization of some complexes of thephylline with metal ions alone. But comparatively little attention has been given in the past to the coordinating behavior of theophylline with the metal ions and ethylenediamineas a mixed ligand. The existing literatures are undoubtedly important but inadequate for a deeper understanding about the extent of theophylline-metal-ethylenediamine interaction.Several earlier investigators[9, 10, 11] claimed that theophylline is deprotonated at N(7). The N(7) and O(6) atom of theophylline acts as donor site. Because of this we became interested in the chemistry of theophylline-metal-ethylenediamine compounds to establish under which

condition the theophylline molecules are linked to N(7) and O(6) and ethylenediamine molecule is linked to two N atom of NH_2- groups. We started a systematic study of such materials because of their extreme biological significance. Moreover, in the literature there are only a few metal compounds with theophylline and ethylenediamine as a mixed ligand. Under these circumstances the first attempt of our investigation that is described in this report comprises preparation, properties and structural characterization of compounds of some metal ions Cu(II), Ni(II), Co(II), Zn(II) and Hg(II) are presented with theophylene-ethylenediamine.Mixed ligand complexes of Cu(II), Ni(II), Co(II), Zn(II) and Hg(II) with theophylline as primary ligand and ethylenediamineas secondary ligand were synthesized by adopting simple procedures using water as the solvent.The complexation behavior of theophyllinewas intensely studied for modelling metal interactions with the guanine baseof nucleic acids [12]. In this report we describe the synthesis, characterization and various properties of copper(II), nickel(II), cobalt(II), zinc(II) and mercury(II) compounds of theophylline and ethylenediamine.

2. Materials and Methods

Theophylline was procured from FlukaBiochemika (Switzerland), and ethylenediamine from Riedel-de Haen (Germany).Copper(II) chloride, nickel(II) chloride, zinc(II) sulphate, cobalt(II) acetate, mercury(II) acetate, nitric acid, sulphuric acid and organic solvents etc., used in all synthetic and analytical work were analar grade, either Aldrich (U.S.A.), E. Merck (Germany) or E. Merck (India).

Melting points of complexes were recorded with Stuart SPM-11 (UK) melting point apparatus. The metal content of the compound was determined complexometrically[13] using Na_2EDTA solution as the titrating agent.FTIR (Fourier Transform Spectrophotometer) spectra were recorded with FTIR 8400S Shimadzu (Japan) Spectrophotometer in the range of 400-4000 cm^{-1} using appropriate quantity of KBr and sample (in the ratio 100:3). The UV-visible spectra (electronic spectra) were recorded using UV-visible recording Spectrometer, Model UV-1800, Shimadzu (Japan), in the wavelength range, 200 -1100 nm. Magnetic susceptibility of the complexes was determined by the SHERWOOD SCIENTIFIC Magnetic Susceptibility Balance (M.S.B.), Cambridge, England, Model: Magway MSB Mk1. The thermogravimetric analysis (TGA) of the complexes was carried out with TGA-50 analyzer, Shimadzu (Japan). The Differential Scanning Calorimetry (DSC) was performed by using a Shimadzu Thermal Analyzer DT-40.

2.1. Preparation of Complexes

Mono(ethylenediamine)bis(theophyllinato)copper(II) A.

0.1705g (1.0 mmol) of $CuCl_2.2H_2O$ was dissolved into 5 ml of distilled water and added to an aqueous solution of 15 ml theophylline (0.1802g). The resultant blue colored solution was treated with 7 drops of ethylenediamine and it was allowed to stand at room temperate for crystallization. Deep blue crystals were formed at 24 hours. The crystals was filtered, washed with hot water and dried over silica gel.

Mono(ethylenediamine)bis(theophyllinato)nickel(II) B

Aqueous solutions of $NiCl_2.6H_2O$ (0.2400g in 5 ml water) and theophylline (0.1822g in 15 ml water) were mixed together and 6 drops of ethylenediamine was added to it. Then it was refluxed about 3 hours and it was allowed to stand at room temperate for crystallization. Next day violet colored crystals of $[Ni(C_7H_7N_4O_2)_2(C_2H_8N_2)]$ were found. The crystals were filtered, washed with hot water, dried in air first and then over silica gel.

Mono(ethylenediamine)bis(theophyllinato)Zinc(II) C

In aqueous solutions of$ZnSO_4.7H_2O$ (0.2901g in 5 ml water) 2 drops of ethylenediamine was added. This resultant solution is trated with 15 ml aqeous solution of theophylline (0.1822g) and instantly jelly like precipitate was found then it was stored. The powdery crystals were filtered, washed with hot water, dried in air first and then over silica gel.

Mono(ethylenediamine)bis(theophyllinato)Cobalt(II). Monohydrate D

Aqueous solutions of cobalt acetate (0.1769 g in 5 ml water) and theophylline (0.1804 g in 15 ml water) were mixed together and 1 drop of ethylenediamine was added to it. Then light pinkish cloudy state was formed so it was filtered to get a clear solution. The volume of the solution was reduced to get a saturated solution for the crystallization and kept at room temperature. After two days pink crystals of $[Co(C_7H_7N_4O_2)_2(C_2H_8N_2)].H_2O$ were found. The crystals were collected by filtration, washed with hot water, dried in air first and then over silica gel.

Mono(ethylenediamine)bis(theophyllinato)Mercury(II) E

2 drops of ethylenediamine was added in a beaker to the aqueous solution of mercury acetate (0.319 g in 5 ml of water). Aqueous solution of theophylline (0.1809 g in 15 ml of water) was prepared in another beaker and

these two solutions were mixed together then white precipitate of $[Hg(C_7H_7N_4O_2)_2(C_2H_8N_2)]$ was found.The crystals were collected, washed with hot water and dried in air first then over silica gel.

3. Result and Discussion

Satisfactory results of solubility, melting point, metal content estimation, IR and UV-Visible spectra, magnetic moment data, thermogravimetric analysis, differential scanning calorimetric analysis, elemental analysis and spectral studies reveal that the complexes areof good purity.

Table 1: Melting points, Solubility and Metal content of Compounds A-E

Compounds	Melting points	Metal content		Solubility									
		Found (%)	Calculated (%)	Water		Methanol		Ethanol		Acetone		n-Hexane	
				Hot	Cold	Hot	Cold	Hot	Cold	Hot	Cold	Hot	Cold
A	> 250(d)	13.15	13.18	sls	ins	sls	ins	ins	ins	ins	ins	ins	ins
B	137	10.67	12.30	s	ins	S	ins	s	ins	ins	ins	ins	ins
C	> 250(d)	13.39	13.52	sls	ins	ins	ins	ins	ins	ins	ins	ins	ins
D	> 250(d)	11.68	11.85	sls	ins	ins	ins	ins	ins	ins	ins	ins	ins
E	> 250(d)	31.71	32.41	s	ins	ins	ins	sls	ins	ins	ins	ins	ins

s=soluble, sls=slightly soluble, ins=insoluble

Investigation of their melting points indicates that cobalt(II) complex melt at relatively lower temperature than other complexes. While the complexes of copper(II), nickel(II), zinc(II) and mercury(II) melts at a higher temperature, above 250 ^oC. Solubility data show that copper(II), cobalt(II) and zinc(II) complexes are sparingly soluble in hot water and are insoluble in other studied solvents. Whereas the nickel(II) and mercury(II) complex is soluble in hot water. Results of the metal analysis of the complexes are in good agreement with the theoretically calculated values. The metal contents are estimated by complexometric method following standard procedures.

IR and UV-Visible spectra of the complexes are discussed with tabulations and tentative assignments of their characteristic bands. The peaks of various important vibrational modes observed in the spectra of the complexes are listed in Table 2 for comparative study.

Table 2: IR and UV of the complex compounds

Compounds		Infrared band						UV	
	υ(O-H) and/or υ(N-H)/ υ(C-H), aro	□(C=), sym	□(C=), asym	□(C=N)	□(C-N), asym	M-N	M-O	λ_{max} (nm)	Abs
	cm^{-1}	cm^{-1}	cm^{-1}	cm^{-1}	cm^{-1}	cm^{-1}	cm^{-1}		
theo	3380-2888	1713	1666	1561	1244	-	-		
en	3500-3250	-	-	-	1316	-	-		
A	3227-2882	1694	1642	1532	1253	645	548	261	2.861
								379	2.725
B	3295-2884	1686	1640	1526	1224	658	580	275	2.631
								356	2.471
C	3329-2949	1691	1640	1587	1265	681	647	261	2.868
								500	2.349
D	3447-3000	1655	1610	1534	1230	682	655	263	2.643
								295	2.611
E	-	1639	-	1534	1282	652	-	259	2.946

Where, theo = theophylline and en = ethylenediamine.

From the above table it is seen that all compounds show two bands in the region 1610-1694 cm^{-1}due to υ(>C=O). The downward shifting of the carbonyl absorption compared to that observed in the free theophylline molecule (at 1713cm^{-1} and 1633 cm^{-1}) can be explained on the basis of the greater involvement of the >C=O group in bonding. Thus in the complex the metal ion is bonded to theophylline through O(6). In free theophylline υ(C-N) vibration occur at 1244 cm^{-1}. Shifting to the lower frequency of the υ(C-N) absorption compared to that observed in the free theophylline molecule is an indication that imidazole ring nitrogen N(7) of theophylline is deprotonated and N(7) atom of the imidazole ring is coordinated to the metal ion. A broad band in the region 3347 cm^{-1} in the cobalt(II) complex indicates the presence of one H_2O molecule.

From UV-Visible spectral data of the complexes Cobalt(II) complex shows two bands at 38,314.17 cm^{-1} and 20,000 cm^{-1}. These transitions may be assigned to the $^4A_{2g}(F) \leftarrow {}^4T_{1g}(P)$ and $^4T_g(P) \leftarrow {}^4T_{1g}(F)$. In the spectra of copper(II) complex we were observed two bands at 261 nm and 379 nm. The band appears at 379 nm may be assigned to the $^2A \leftarrow {}^2E$ and 261 nm may be assigned as charge-transfer (CT) transition**[14].** The spectrum of the d^8 complex $[Ni(C_7H_7N_4O_2)_2(C_2H_8N_2)]$shows three bands at 275,356 and 556 nm respectively, which are assigned as follows,

$\nu_1 = {}^3A_{2g}(F) \rightarrow {}^3T_{2g}(F) =$ 556 nm,

$\nu_2 = {}^3A_{2g}(F) \rightarrow {}^3T_{1g}(F) =$ 356 nm and

$\nu_3 = {}^3A_{2g}(F) \rightarrow {}^3T_{1g}(P) =$ 275 nm.

The mass susceptibilities of compounds under study were measured and the results are summarized in Table 3.

Table 3: Mass susceptibilities of metal compounds of theophylline and ethylenediamineunder study at 31 ºC

Compound	C_{Bal}	l, cm	m, g	R	R_o	χ_g, C.G.S. unit	T, K	μ_{eff} BM
A	0.9882	2.10	0.1497	132	-32	2.26×10^{-6}	295	1.6029
B	0.9945	2.4	0.1530	281	-30	4.85×10^{-6}	295	2.3369
C	1.0168	2.1	0.1453	-63	-32	-4.56×10^{-7}	302	-
D	1.0177	2.1	0.1532	1154	-33	1.66×10^{-5}	302	4.4602
E	1.0168	2.5	0.1401	-55	-33	-3.99×10^{-7}	302	-

From the magnetic susceptibility data it was found that Co(II), Ni(II) and Cu(II) complexes are paramagnetic and their magnetic moment corresponds to the presence of 3, 2 and1unpaired electron respectively in their 3d orbitals.This observation demonstrates thatCo(II) and Ni(II) compounds possesses octahedral and Cu(II) compounds have tetragonally distorted octahedral geometry. The magnetic susceptibility values of zinc (II) and mercury (II) compounds are negative due to their diamagnetic properties. It implies that Zn(II) and Hg(II) ions have d^{10} electronic configuration in which all the electrons in t_{2g} and e_g levels are paired.

The thermograms obtained from the thermogravimetric analysis of the compounds are plotted in Fig. 3.1-3.5 for comparative study.

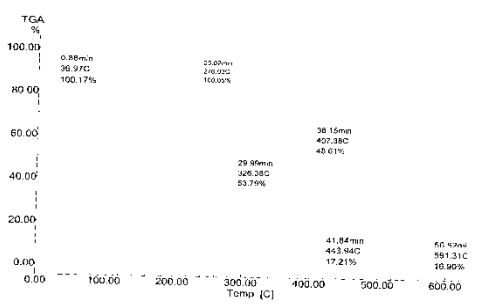

Fig. 3.1 QSTG graph of copper(II) complex

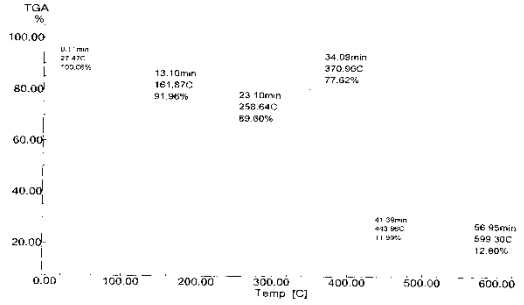

Fig. 3.2 QSTG graph of nickel(II) complex

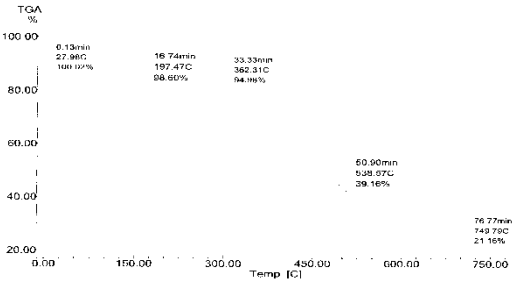

Fig. 3.3 QSTG graph of zinc(II) complex

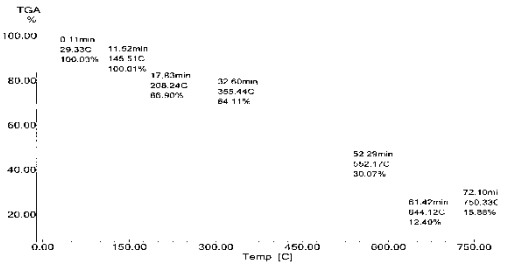

Fig. 3.4 QSTG graph of cobalt(II) complex

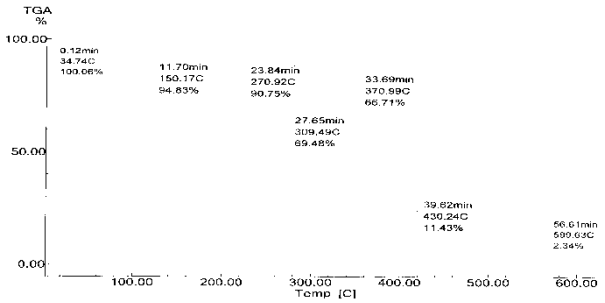

Fig. 3.5 QSTG graph of mercury(II) complex

From the thermal analysis it was observed that Cu(II) and Zn(II) compounds exhibit high thermal stability even up to 276^0C while compounds Co(II) complex commence decomposition at very low temperature at about 100^oC due to loss of one molecule of water of crystallization. After several steps of decomposition Ni(II) compound is converted to their corresponding metal oxides. The Hg(II) compound also shows thermal stability up to 270^0C then starts decomposition and sublimes off.

Table 4: Differential scanning calorimetric analysis data of the compounds

Compounds	Thermal stability (^{0}C)	Melting point (^{0}C)	Endothermic peak(^{0}C)	Changeof enthalpy(^{0}C)
A	280	302.85	302	106.03
B	376	380-420	380-420	248.10
C	370	396	396	116.13
D	104	110-210	110-210	228.79

From the Differential scanning calorimetric analysis the melting point of pure theophylline is 273 ^{o}C but the melting points of the prepared complexes are not similar with the melting point of the theophylline so it concludes that the Cu(II), Ni(II), Zn(II) and Co(II) ion interacts strongly with theophylene under the experimental condition.On the basis of thermal stability the compounds under study are arranged in the following order:

C>A>E> B>D

4. Conclusion

Comparison of solubility, melting point, metal content estimation, IR and UV-Visible spectra, magnetic moment data, thermogravimetric analysis and differential scanning calorimetric analysisof compounds **A**-**E**and their parent substancesgave indication on formation of new molecular compounds and the ligands must satisfy the coordination number as well as the metal ion. Combination of TG mass losses with the results of elemental analysis helped us to determine the composition of **A**-**E**. Actual form of the compounds were established according to FTIR spectra and UV-Visiblepectra. Thermal stability of the five studied compounds seemed to corroborate mainly with the thermal behaviour of the guest molecules.

5. References

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