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Synthesis, Spectral and Antimicrobial Study of Cd (II) Complexes and Heterocyclic base Adducts Derived from N (4) Phenyl Thiosemicarbazone

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ABSTRACT

The synthesis and characterization, spectroscopic, and biological studies of 5-chloro-2-hydroxy acetophenone N (4) phenyl thiosemicarbazone and its complexes with cadmium (II) chloride are reported here. The thiosemicarbazone was synthesized by condensation of appropriate ketone and N (4) phenyl thiosemicarbazide. The reactions were carried out in the presence of sulfuric acid. The ligand,complex and adducts were characterized by means of Elemental analysis,ESI-MS, Fourier Transform Infrared (FT-IR) spectroscopy, Nuclear Magnetic Resonance (1HNMR and 13CNMR) spectroscopy magnetism and conductivity. The metal complexes and their corresponding thiosemicarbazone were tested against bacterial parasites. It was found that the cadmium complexes synthesized are more biologically active then their corresponding thiosemicarbazone.

Keywords : Metal Salts, Bioactivemetalcomplexes, Antimicrobial Activity, MIC.

I. INTRODUCTION

Thiosemicarbazonesare the compounds containing N,S donor atoms.On complexation with metal ion, they show heterodentate nature [1-6]. Thiosemicarbazones are the compounds having good high biological activity.The biological activity is due to ability to coordinate to metal centres.Thiosemicarbazone derivatives have additional functional groups which coordinate to metal ion and this enhance the biological activity. Thus biologic activity depends on non coordinating group. Cadmium is toxic element and is naturally present in the environment. The analysis shows cadmium ion is a problem due to toxic effect of this metal, associated with Hg and Pbwhich are most toxic environmental pollutants [7-9]. It is rapidly localized intracellular in the liver and then bound to metallothionein forming a complex that is slowly transferred to the blood stream to be deposited in the kidneys. This metal competes with Zn and blocks active sites of metal-enzymes. It removes Zn(II) in cysteine-coordinated zinc compounds or Ca(II) ions in bone cells. The development of chelating agents is essential for the treatment of cadmium in toxicity. The ability to coordinate sulphur is more for cadmium as compared to Zn (II), whose toxic properties is related to strong Cd-S bond [10]. Chelating sulfur donors are under study as antidotes in cadmium(II) poisoning [11,12]. The increase in antitumoractivity of Cd (II) ions reported [13]. Cd (II) has stable filleddsublevel (d^{10})and it shows few characteristics of transition metals. It forms stable complexes with O,N.S donor thiosemicarbzone like other elements . d^{10}configuration has no crystal field stabilization.Hence stereochemistry of a compound depends on the size and polarizing power of the M(II) cation.Zn (II) and Cd(lI) favour 4-co-ordinate tetrahedral complexes though Cd(II), being the larger

one, Cd (II) forms 6-coordinate octahedral complexes more readily than Zn(II)..

In this research work the synthesis, spectral characterization and biological studies of six coordinate complexes of Cd (II) with 5-dichloro 2-hydroxy acetophenone N (4) phenylthisemicarbazone have been reported.

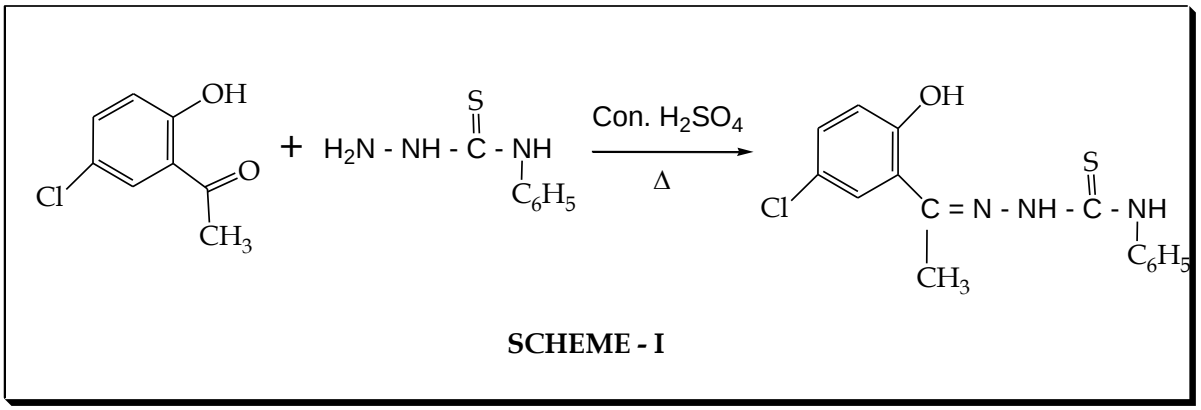
II. MATERIALS AND METHODS

The chemicals used are of A.R.grade.Room temperature magnetic susceptibility measurement was carried out by Faraday method. IR spectra were recorded in solid state in the range 4000-200 cm^{-1} range. NMR spectra were recorded in the mixture of $CDCl_3$ and DMSO-d_6 (1:1 v/v) with a Bruker AC-300F 300MHz spectrometer. The number of water molecules in the complexes were determined by TGA in the temperature range 30-800°C.Metal in the complex and adducts was estimated by standerdized E.D.T.A using xylenolorange as anindicator and PH-10 buffer solution. Chloride in the complex was determined by Mohr's method.

III. EXPERIMENTAL

Synthesis of thiosemicarbazone :

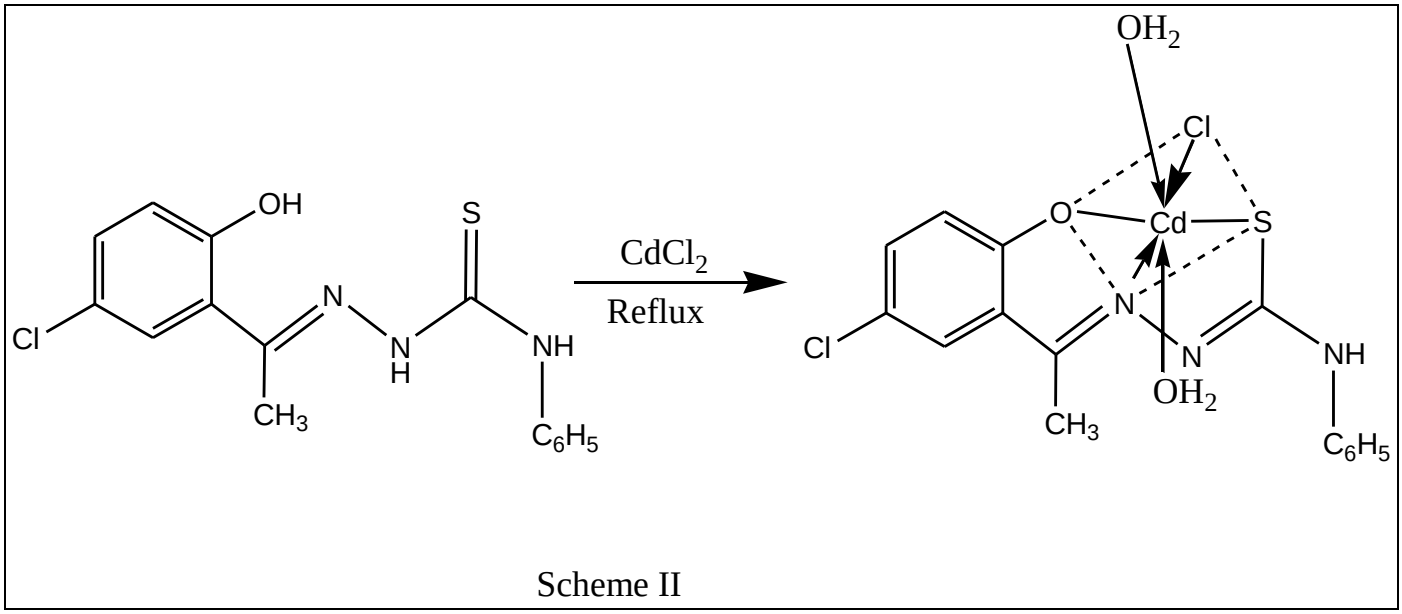
Ethanolic solution of 5-chloro 2-hydroxy acetophenone (0.01 mole) was added to ethanolic solution of N (4) phenylthiosemicarbazide (0.01 mole) in the mole ratio 1:1.The reaction mixture was refluxed for three hours.. The pale yellow product obtained on cooling was filtered and washed with hot water then cold ethanol and finally with ether. The compound was then purified in ethanol and dried in vacuum.



SCHEME - I

Synthesis of complex M:L:

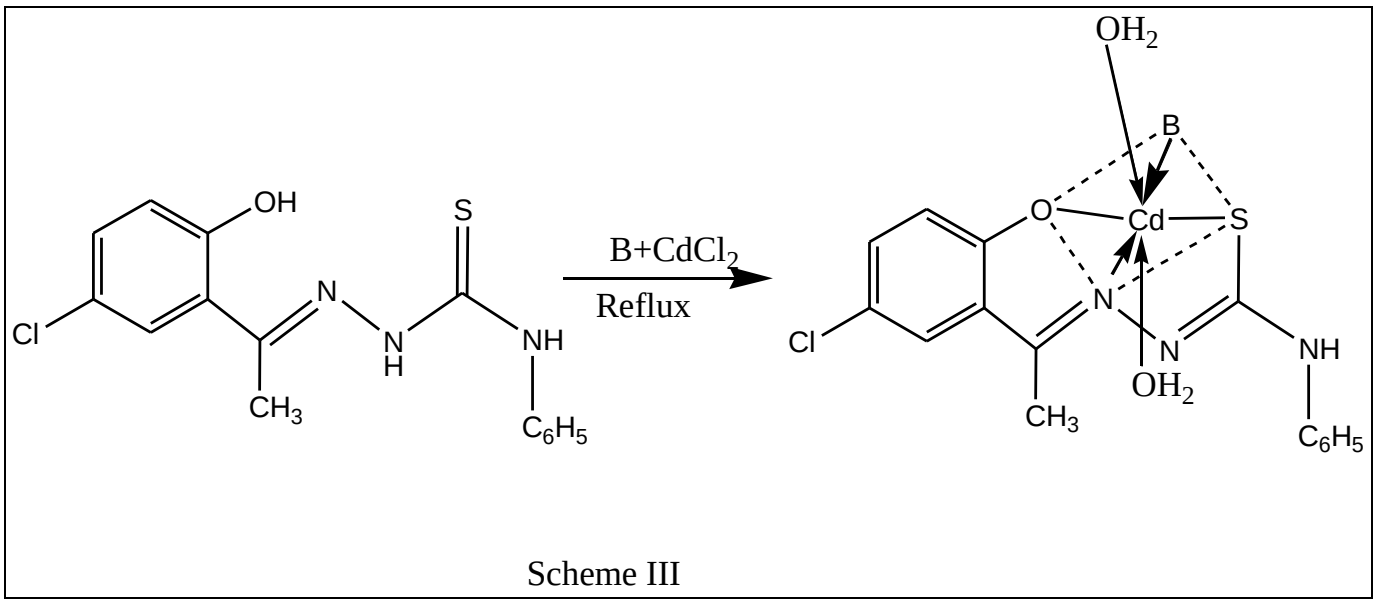
The complex of the type $M.L.Cl.(H_2O)_2$ was synthesized by refluxing ethanolic solutions of thiosemicarbazone (0.01mole), $CdCl_2.2.5\ H_2O$ (0.01 mole) in the mole ratio 1:1 for two hours.The light yellow product obtained was fitered and washed with hot water,cold absolute ethanol and then ether and dried in vacuum.



Scheme II

Synthesis of adducts:

The adducts of the type Cd.L.B (B is heterocyclic base like pyridine, 2-chloro pyridine, , 3-chloro pyridine ,4-chloro pyridine) was synthesized by adding slowly ehanolic solutions of $CdCl_2.2.5H_2O$(0.01 mole) and heterocyclic base (0.01 mole) to the hot ehanolic solution of thiosemicarbazone(0.01 mole) in the ratio 1:1:1 and refluxing reaction mixture for four hour. The yellow adduct obtained was filtered and washed with hot water, cold ethanol and diethyl ether and dried in vacuum.



Scheme III

(B= pyridine 2-chloro pyridine,3-chloro pyridine,4-chloro pyridine)

Table 1 Physical Properties

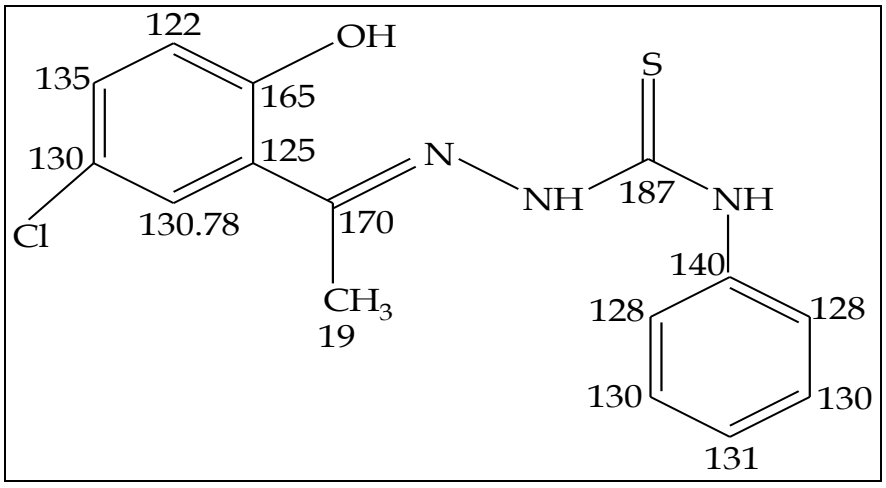
Compounds	Colour	Empirical Formula	Molar conductance $Ohm^{-1}cm^2mole^{-1}$	Magnetic Moment B.M.
L	Yellow	$C_{15}H_{14}ClN_3OS$	-	-
Cd-L.Cl.$(H_2O)_2$	Yellow	$C_{15}H_{116}N_3O_3SCl_2Cd$	45.0	Diamagnetic
Cd.L.Py.$(H_2O)_2$	Yellow	$C_{20}H_{21}N_4O_3SClCd$	40.0	Diamagnetic
Cd.L.2-Cl.py.$(H_2O)_2$	Yellow	$C_{20}H_{20}N_4O_3SCl_2Cd$	42.0	Diamagnetic
Cd.L.3-Cl.py.$(H_2O)_2$	Yellow	$C_{20}H_{20}N_4O_3SCl_2Cd$	47.0	Diamagnetic
Cd.L.4-Cl.py.$(H_2O)_2$	Yellow	$C_{20}H_{20}N_4O_3SCl_2Cd$	46.0	Diamagnetic

^{1}H-NMR

^{1}H-NMR

NMR signals at 13.00 and 3.1 ppm are assigned to – OH and – CH_3 protons respectively. Absence of ^{2}NH proton signal suggests enolisation of ^{2}NH – C = S group to ^{2}N=C-SH. Signal at 3.9 ppm cooresponds to ^{4}NH Aromatic protons show multiples at 6.9, 7.20 , 7.60,7.65,7.77,7.30,6.20,7.29 ppm range.

^{13}C-NMR (DMSO-D_6): δppm122 (C=C), 135 (C=C), 130 (C=C-Cl), 130.78 (C=C), 125(C=C),165 (C=C-OH),170 (C=N),19 (=C-CH_3),187 (C=S),140 (NH-C=C),128 (C=C),130 (C=C),131 (C=C),130 (C=C),128 (C=C).



ESI-MS m/z, ion M^+(Calcd) found

$C_{15}H_{14}$ N_3OSCl (319.79) 319.11, $C_{15}H_{16}N_3O_3SCl_2Cd$(501.26) 501.91, $C_{20}H_{21}N_4O_3SClCd$ (544.90) 544.17, $C_{20}H_{20}N_4O_3SCl_2Cd$ (581.14) 581.92, $C_{20}H_{20}N_4O_3SCl_2Cd$ (581.14) 581.90. $C_{20}H_{20}N_4O_3SCl_2Cd$ (581.14) 581.82

III ANALYTICAL DATA

1.**L:**% C 56.33 (56.90),% H 4.82 (4.41),% N 13.83 (13.14), % O 6.06 (6.57)% S 13.71 (13.16)

2. **Cd-L.Cl.$(H_2O)_2$:** % Cd 22.84 (22.34), %Cl 7.92 (7.07), %C 35.12 (35.94), %H 3.72

(3.22), %N 8.90 (8.38), % O 9.79 (9.58) %S 6.01 (6.40).

3. **Cd.L.Py.(H_2O)$_2$:** % Cd 20.93 (20.55), %C 44.82 (44.08), %H 3.16 (3.88), %N 10.72

(10.28), % O 822 (8.81) %S 5.09 (5.88).

4. **Cd.2-Cl.py.(H_2O)$_2$**: % Cd 19.87 (19.27), %C 41.81 (41.64), %H 3.97 (3.47), %N 11.71

(9.64), % O 8.71 (8.26) %S 5.04 (5.52).

5. **Cd.3-Cl.py.(H_2O)$_2$**% Cd 19.87 (19.27), %C 41.81 (41.64), %H 3.97 (3.47), %N 11.71

(9.64), % O 8.71 (8.26) %S 5.04 (5.52).

6. **Cd.4-Cl.py.(H_2O)$_2$**: % Cd 19.87 (19.27), %C 41.81 (41.64), %H 3.97 (3.47), %N 11.71

(9.64), % O 8.71 (8.26) %S 5.04 (5.52).

IV **INFRARED SPECTROSCOPIC DATA** (**cm^{-1}**)

1.L: ν (- OH) 3340; ν (C = N) 1678; ν (- C = S) 790, 1375 ; ν (N – N) 1075; ν (^{2}N-H) 3240; ν (C – O) 1285.

2 Cd-L.Cl.(H_2O)$_2$:ν (C = N) 1554; ν (C = N-N=C) 1519, ν (C-S) 705, 1307,ν (N-N) 1151, ν(M - N) 461, ν (M-O) 531, ν (M-S) 330, ν (C - O) 1211, ν(H_2O) 3419,3539.

3 Cd.L.Py.(H_2O)$_2$: ν (C = N) 1561; ν (C = N-N=C) 1531, ν (C-S) 709, 1306; ν (N-N) 1153, ν (M - N) Base 258, ν (M - N) 459, ν (M - O) 531, ν (M-S) 333, ν (C - O) 1213, Band due to HB 1421, ν(H_2O) 3449,3521.

4. Cd.2-Cl.py.(H_2O)$_2$: ν (C = N) 1565; ν (C = N-N=C) 1532, ν (C-S) 715, 1316, ν (N-N) 1161, ν (M - N) Base 261, ν (M - N) 472, ν (M - O) 544, ν (M-S) 341, ν (C - O) 1228, Band due to HB 1425, ν(H_2O) 3459,3532.

5. Cd.3-Cl.py.(H_2O)$_2$:ν (C = N) 1576; ν (C = N-N=C) 1547, ν (C-S) 721, 1325,ν (N-N) 1171, ν (M - N) Base 274, ν (M - N) 469, ν (M - O) 552, ν (M-S) 351, ν (C - O) 1235, Band due to HB 1437, ν(H_2O) 3469,3541.

6. Cd.4-Cl.py.(H_2O)$_2$: ν (C = N) 1591; ν (C = N-N=C) 1558, ν (C-S) 732, 1337,ν (N-N) 1187, ν (M - N) Base 275, ν (M - N) 481, ν (M - O) 565, ν (M-S) 364, ν (C - O) 1245, Bands due to HB 1443, ν(H_2O) 3479,3554.

V TGA ANALYSIS DATA:

1.**Cd-L.Cl.(H_2O)$_2$**: First step, 118 °C, Mass loss 7.86 % second step, 210 °C, Mass loss, 24.23 % Third Step 355 °C, Mass loss, 50.22 % Fourth Step, 670°C, Mass loss 65.5 %, Residue 782 °C, % of CdO, 25.86 (25.54).

2.**Cd.L.Py.(H_2O)$_2$:**First step, 115 °C, Mass loss 6.07 % second step,220 °C, Mass loss, 22.32 % Third Step 355 °C, Mass loss, 77.02 % Fourth Step, 669 °C, Mass loss, 62.00 %, Residue, 779 °C, % of ZnO, 23.96 (23.49).

3. **Cd.2-Cl.py.(H_2O)$_2$:** First step, 113 °C, Mass loss 6.88 % second step,230 °C, Mass loss, 27 % Third Step 365 °C, Mass loss, 48.40 % Fourth Step, 660 °C, Mass loss 62.5 %, Residue 778 °C, % of ZnO, 22.79 (22.03).

4 **Cd.3-Cl.py.(H_2O)$_2$:**First step, 116 °C, Mass loss 6.90 % second step, 235 °C, Mass loss, 28.25 % Third Step 360 °C, Mass loss, 49.02 % Fourth Step, 666 °C, Mass loss, 63.27 %, Residue, 779 °C, % of ZnO, 22.90 (22.03).

5 **Cd.4-Cl.py.(H_2O)$_2$:**First step, 117 °C, Mass loss 6.91 % second step, 240 °C, Mass loss, 28 % Third Step 365 °C, Mass loss, 48.28 % Fourth Step, 669 °C, Mass loss 62.70 %, Residue 800 °C, % of ZnO, 22.82 (22.03).

IV. BIOLOGICAL ACTIVITY (AGAR PLATE DIFFUSION METHOD)

Table. 4. Minimum Inhibitory concentration L, Cd (II) complexes and stande red

Compound	*Staphylococcus aureu*		*Bacilus subtilis*		*Escherichia Coli*		*Peudomonas aeruginosa*	
	Gram positive				Gram negative			
	2 µg/ml	2.5 µg/ml	2 µg/ml	2.5 µg/ml	2 µg/ml	2.5 µg/ml	2 µg/ml	2.5 µg/ml
L	0.70	0.365	0.72	0.42	0.72	0.41	0.74	0.41
Cd-L.$(H_2O)_3$	0.62	0.33	0.64	0.22	0.64	0.23	0.67	0.24
Cd-L.Py.$(H_2O)_2$	0.62	0.32	0.64	0.26	0.65	0.22	0.64	0.25
Cd-2-Cl.py.$(H_2O)_2$	0.67	0.33	0.64	0.23	0.67	0.25	0.69	0.27
Cd-3-Cl py.$(H_2O)_2$	0.68	0.35	0.68	0.24	0.70	0.24	0.68	0.26
Cd-4-Cl py.$(H_2O)_2$	0.61	0.32	0.62	0.24	0.63	0.22	0.66	0.23
$CdCl_2.2.5H_2O$	0.21	0.16	0.23	0.18	0.15	0.24	0.13	0.26
Standard	0.13	0.11	0.14	0.12	0.23	0.12	0.14	0.11

(Std-Amphiciline)

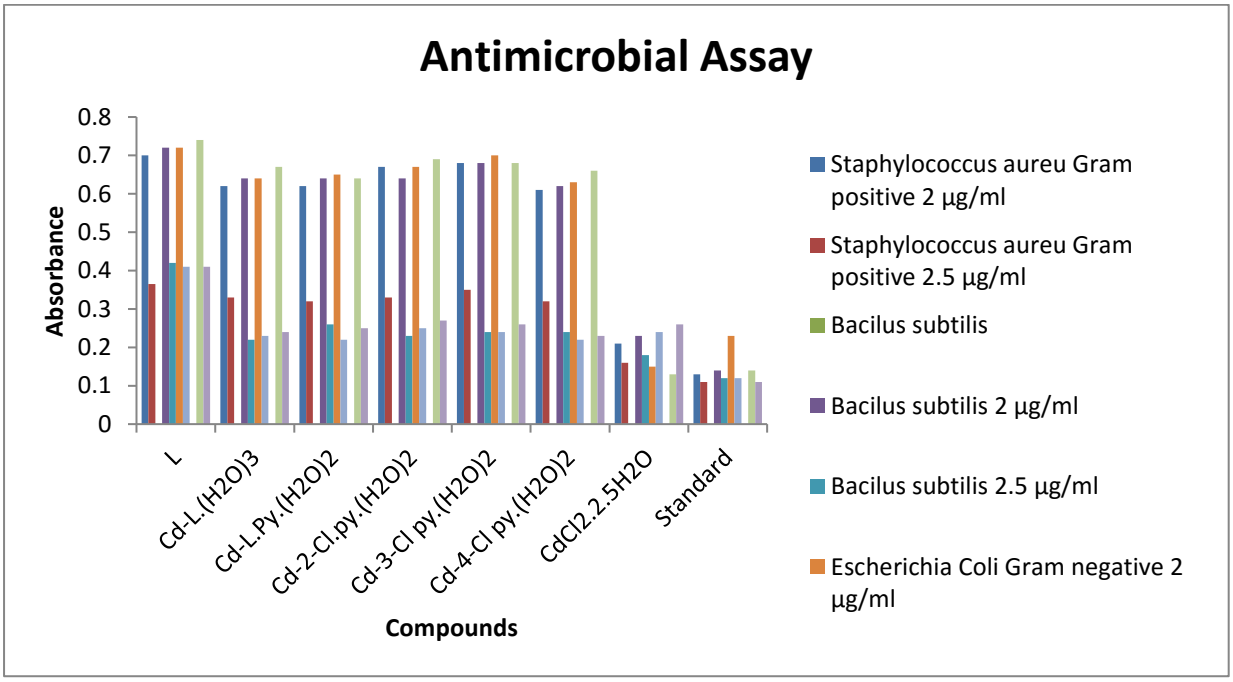


Figure 1

Result and discussion

Physical data of thiosemicarbazone and its complexes is presented in Table 1. The complex and all adducts are in soluble in ethanol and soluble in DMF in which conductivity measurements were carried out (25^{0}C), showing all complexes are non electrolyte in nature [14].The magnetic moment measurement was carried out at room temperature by Faraday method showed diamagnetic behavior expected for d^{10} configuration. Mass spectral data confirmed the structure of the thiosemicarbazone and complexes as indicated by molecular ion peak (M + 1) corresponding to their molecular weights. The calculated and experimental percentages are matched and confirmed 1:1 mole ratio

of metal ion, thiosemicarbazone for complex and 1:1:1 mole ratio for metal ion, thiosemicarbazone and heterocyclic base for all adducts.

The band due to ν(N—H) appears at 3240 cm^{-1} for thiosemicarbazone and disappeared in the spectra of all the complexes. The band at 1678 cm^{-1} due to ν (C = N) in thiosemicarbazone shifted to lower side upon coordination suggest bonding through azomethine nitrogen. The coordination throughazomethine nitrogen is confirmed by a band in the range 459-481cm^{-1}, assignable to ν (Cd-N) for the complexes. A shift in the ν (N- N) bands from 1075 cm^{-1} to higher region is due to the increase in double bond character off-setting the loss of electron density via donation to the metal. Thisalso confirms thecoordination through azomethinenitrogen. The coordination through thiolate sulfur is indicated by decrease in ν (C=S). The bands at 330-364 cm^{-1} assignable to ν (Cd-S) in the complexes confirm sulfur coordination.There is no band in the region 2600-2800 cm^{-1} suggests the coordination through thiolate sulphur. The new peaks observed in the range 531-565 cm^{-1} are due to the Cd-O (phenolic) bond .This is indicated by decrease in ν (C-O).

The water molecules in hydrated layer was removed below 102^0C.The two coordinated water molecules were eliminated in the complexes at relatively temperature less than120^0C.The two coordinated water molecules in complex and adducts were removed in one step at less than 120 °C The decomposition proceeded in several steps. The compounds were stable up to about 260^0C.It is seen adducts are more stable than complex. This may be due to heterocyclic bases in coordination. There are three steps after the removal of water molecules in complex and adducts. In the second step the loss is about 25%.The organic molecule was lost upto650^0C.The mass lost corresponding to this step is about 60%. The decomposition was complete and metal oxide was formed at a temperature about 780 °C.The stability of thiosemicarbazone increases on complexation. The metal complexes are more stable than thiosemicarbazone.

The bacterial assay was carried out by the agar plate diffusion method. Activity was measured by measuring the absorbance. As compared to complex and thiosemicabazone, adducts showed good activity against bacterial species than free ligand. The minimum inhibitory concentration was determined by liquid dilution method [15].The solutions of thiosemicarbazone and complexes with 2 μg/ml,2.5 μg/ml and 3 μg/ml concentrations were prepared in the solvent DMF. The solutions of standard drug ampicilin and metal salt were also prepared in the same concentration. Inoculums of the overnight culture were prepared.0.2 ml of the inoculums was added to the test tubes containing the solutions of the compounds of different concentrations. After the addition of sterile water to each of the test tubes, these were incubated for 24 hours and observed for turbidity.The absorbance of the turbid solutions was measured at 520 nm.The same method was used for standard [16].It was observed that at 2μg/ml the absorbance is more. Less absorbance at 2.5 μg/ml and no absorbance observed at 3μg/ml. The inhibition is more at 2.5 μg/ml.The metal salt solution showed better inhibition than ligand and complexes. The inhibitory concentration is 2.5 μg/ml. Thus increase in coordination number in coordination and coordination of metal ion to ligand enhances microbial activity. The free metal ion was found more effective than thiosemicarbazone and complexes.

V. CONCLUSION

The synthesized thiosemicabazone is tridentate ONS donor. The spectral data indicates octahedral geometry for complexes and adducts. The complex and adducts are diamagnetic. Two coordinated water molecules were found. The compounds found thermally stable. The decomposition proceded in several steps.The complex and adducts showed growth inhibitory activity against gram +ve bacterial species.The absorbances are found more at 2 μg/ml concentration than 2.5μg/ml .This suggested increase

in concentration increase the activity The metal salts showed more inhibitory activity.

VI. REFERENCES

[1]. LobanaT.S.,Sharma R.,BawaG.,Khanna S.Coord.Chem.Rev.253 2009 933.

[2]. Garg B.S.,KurupM.R.P.,Jain S.K.,BhoonY.K.Trans.Metal Chem.13 1988 92.

[3]. John R.P.,Shreekant A.,kurup M.R.P.,MobinS.M.Polyhedron21 2002 2515.

[4]. Seena E.B.,Beesy Raj B.N,Kurup M.R.P. SreshE.J.Chem.Cryst 36 2006 189.

[5]. Philip V.,Suni V.,Kurup M.R.P.,NethajiM.Polyhedron 23 2004 1225

[6]. Metasanz A.I.,ParezJ.M.,NavarroP.,Moreno J.M.,ColacoiE.,SouzaP.J.Inorga.Biochem 76 1999 29.

[7]. Munno G.D,. Mauro S,.Pizzino T, Viterbo D, J. Chem. Soc., Da1ton Trans. 1993 l113.

[8]. Srivastava H.P.. Tiwari D, J. Indian Chem. Soc. 70 1993 499.

[9]. Walker M.D,. Williams D.R, J. Chem. Soc., Dalton Trans. 1974 1186.

[10]. Farag1ia G,. Graziani R,.Guo Z,.Casellato U, Sitran S., Inorg. Chim. Acta 192 1992 17.

[11]. Casas l.S, Sanchez A.,. Bravo 1,. Garcia-Fontan v, Castellano E.E,.lones M.M, Inorg. Chim. Acta 158 1989 119.

[12]. Romero-Molina M.A,.Gutirrez-Valuro M.D,. Lopez-Garzon R,. Salas-Peregrin J.M,.Arriortua M J,.Zufiiga F.J, Inorg. Chim. Acta 136 1987 87.

[13]. Atassi G,. Dumont P,.Harteel J.C, Eur. J. Cancer 15 (1979) 451.

[14]. Geary W.J., Coord. Chem. Rev, 1971, 7, 81.

[15]. SalmonS.A,WattsJ.L,Cheryal A.J.Clin.Microbial,1995,2435.

[16]. Shankar K.,Muralidhar Reddy P,RohiniR,VaddeRavindraDerPharmacia Letter;1,2009,97