Temperature dependence ,conductometric study and antimicrobial assay of six co-ordinate complexes of Fe (III)

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Abstract

Fe (III) complexes have been synthesized by the reaction of iron (III) chloride with 3,5-dichloro-2-hydroxy acetophenone N -4 ethyl thiosemicarbazone in presence of heterocyclic base like pyridine (py), α/β/γ-picoline. Thiosemcarbazone has been characterized by ^{13}C, ^{1}H NMR,ESI-MS as well as IR, electronic spectra.Spectral and magnetic measurements indicated Octahedral geometry for the six coordinate complexes.Conductometric measurement was carried out at different temperatures.The thiosemicarbazone and its Fe (III) complexes have been found antibacterial and showed growth inhibitory activity against bacterial species.

Keywords: Thiosemicarbazone,metal salts,equivalent conductance,antimicrobial activity.

Introduction

Thiosemicarbazone forms complexes with many metals and are of diverse chemical, physical and structural characteristics,they are of interest to coordination chemists [1,2].Thiosemicarbazides and thiosemicarbazones coordinate through the sulfur and one of the hydrazinic nitrogen atoms[3].The thiosemicarbazone moiety without substituents attached to the thione sulfur coordinates as either a neutral or anionic NS bidentate ligand, depending on the method of complex preparation [4], a third coordinating atom often gives ONS (e.g. 2- ydroxybenzaldehyde thiosemicarbazones)[5]orNNS(e.g. 2-acetylpyridine thiosemicarbazones) [6] donor tridentate ligands.In some complexes higher denticity involving one or more thiosemicarbazone moieties, as well as monodentate coordination have been studied [6].Fe (III) complexes of 2 acetyl pyridine thiosemicarbazone,2-dipyridyl ketone thiosemicarbazone,2-formylpyridine thiosemicarbazone and substituted 2-acetypyridine thiosemicarbazone have been reported [7-10].The molecular features essential for activity were 2-pyridylethylidene, thiocarbonylsulfiir, and bulky or cyclic substituents at the terminal N(4)- atom.The most active 2-acetylpyridine thiosemicarbazones were N (4)-phenyl and those with azacyclic substituents.

In the present work the synthesis, spectral characterization temperature dependence condutometric study and biological evaluation of six coordinate complexes of Fe (III) with 5-chloro 2-hydroxy acetophenone N-4 ethyl thisemicarbazone have been reported.

Experimental

Materials and instrumentation

The thiosemicarbazone was synthesized by refluxing 5-chloro 2-hydroxy acetophenone and N-4 ethyl thiosemicarbazide in ethanol in the mole ratio 1:1 for 3 hours. The pale yellow product obtained was filtered and washed with cold ethanol and then diethyl ether. It was recrystalised by hot ethanol and dried over P_2O_5 in vacuum.

SCHEME - I
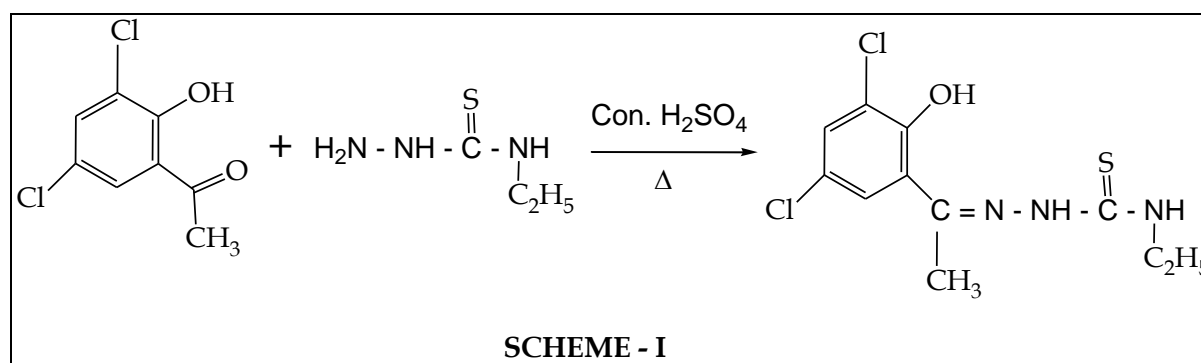
Preparation of complex

$FeCl_3$ salt was dissolved in ethanol.The ethanolic solution of thiosemicarbazone in slight excess over the metal:ligand ratio of 1:1 was added dropwise with constant stirring.The rection mixture was refluxed for three hours.The dark brown product thus obtained was fitered and washed well with cold ethanol and then diethyl ether and dried over P_2O_5 in vacuum.

Preparation of complexes with heterocyclic bases

The complex Fe.L.B (B is heterocyclic base like pyridine, α-picoline, β-picoline,γ-picoline) was synthesized by adding slowly ehanolic solution of $FeCl_3$,heterocyclic base to the hot ehanolic solution of ligand in the ratio 1:1:1and refluxing reaction mixture for three hours. The brown adduct obtained was filtered and washed with hot water, cold ethanol and diethyl ether and dried over P_2O_5 in vacuum.

Physical measurements-

Magnetic measurements were carried out at room temperature by Faraday method. IR spectra were recorded in the range 4000-200 cm^{-1} range.Conductivity measurements were carried out on conductivity Bridge, Systonics conductivity meter-304. Thermo gravimetric analysis was carried out in the temp rnge 30-800ºC.Electronic spectra were measured on Jasco UV-visible double beam spectrophotometer.Metal in the complex and adducts was estimated by standardized xylenol orange as an indicator.Chloride in the complex was estimated by Mohr's method.

Table 1 Physical properties:

Compounds	Colour	Empirical Formula	Magnetic Moment B.M.
L	Yellow	$C_{11}H_{13}N_3OSCl_2$	-
Fe-L.Cl.(H$_2$O)$_2$	Brown	$C_{11}H_{15}N_3O_3SCl_3Fe$	5.84
Fe.L.Py.(H$_2$O)$_2$	Brown	$C_{16}H_{20}N_4O_3SCl_2Fe$	5.87
Fe.α-Pico.(H$_2$O)$_2$	Brown	$C_{17}H_{22}N_4O_3SCl_2Fe$	5.90
Fe.L β-Pico.(H$_2$O)$_2$	Brown	$C_{17}H_{22}N_4O_3SCl_2Fe$	5.88
Fe.L.γ-Pico.(H$_2$O)$_2$	Brown	$C_{17}H_{22}N_4O_3SCl_2Fe$	5.85

Conductivity measurement

The conductivity of complexes was measured and equivalent conductance was calculated. The 0.001 M solution of complexes was prepared in different percentages of DMF-ethanol mixture and the parameter of solution under study was calculated at temperature 298 K,303 Kand 308 K.

Equivalent conductance at 298 K					
DMF-Ethanol mixture	Fe.L.Cl(H$_2$O)$_2$	Fe.L.Py(H$_2$O)$_2$	Fe.L. α-Pico (H$_2$O)$_2$	Fe.L.β-Pico (H$_2$O)$_2$	Fe.L.γ-Pico (H$_2$O)$_2$
75%	40.5	38.3	40.3	41.1	40.4
80%	45.6	46.2	45.6	44.3	45.6
85%	50.2	52.7	51.4	51.4	52.2
90%	54.3	55.3	51.2	52.8	55.3
95%	56.3	60.4	55.9	58.6	58.1

100%	58.2	61.2	58.6	61.0	63.2
Equivalent conductance at 303 K					
DMF-Ethanol mixture	Fe.L.Cl(H_2O)$_2$	Fe.L.Py(H_2O)$_2$	Fe.L. α-Pico (H_2O)$_2$	Fe.L.β-Pico (H_2O)$_2$	Fe.L.γ-Pico (H_2O)$_2$
75%	42.5	40.3	42.3	43.1	43.4
80%	47.6	46.2	46.6	45.0	47.6
85%	51.2	53.7	54.4	53.4	55.2
90%	57.3	58.3	57.2	58.8	58.3
95%	59.3	61.4	62.9	61.6	62.1
100%	63.3	65.4	60.5	62.6	64.7

Equivalent conductance at 308 K					
DMF-Ethanol mixture	Fe.L.Cl(H_2O)$_2$	Fe.L.Py(H_2O)$_2$	Fe.L. α-Pico (H_2O)$_2$	Fe.L.β-Pico (H_2O)$_2$	Fe.L.γ-Pico (H_2O)$_2$
75%	43.5	42.3	43.3	44.1	44.4
80%	48.7	47.2	47.7	46.3	48.3
85%	52.4	54.7	55.4	55.4	56.2
90%	58.3	59.3	58.2	59.8	59.3
95%	60.3	62.4	63.9	63.6	63.1
100%	64.5	66.4	62.3	63.2	65.3

^{1}H-NMR

NMR signals at 12.00 and 2.2 ppm are assigned to – OH and – CH_3 protons respectively. The signals at 2.30, 3.50 correspond to [4]NH and H[4]N-C_2H_5 respectively. Signal at 10.0 ppm corresponds to [2]NH. Aromatic protons show multiplets at 7.0, 7.25, 7.45, ppm.

^{13}C-NMR (DMSO-D$_6$): δppm
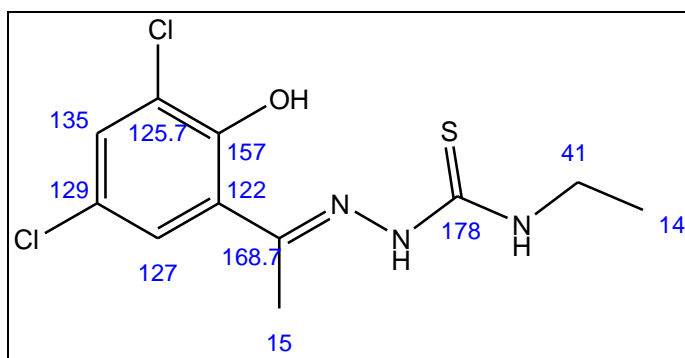
 (Calcd) found ESI-MS m/z, ion M[+]:$C_{11}H_{13}N_3OSCl_2$ (306.19) 306.71,$C_{11}H_{15}N_3O_3SCl_3Fe$ (431.66) 431.02, $C_{16}H_{20}N_4O_3SCl_2Fe$ (475.30) 475.97,$C_{17}H_{22}N_4O_3SCl_2Fe$ (489.33) 489.94,$C_{17}H_{22}N_4O_3SCl_2Fe$ (489.33) 489.76,$C_{17}H_{22}N_4O_3SCl_2Fe$ (489.33) 489.96.

Analytical data

1.**L:** % C 43.74 (43.15),% H 4.72 (4.28),% N 13.18 (13.72),% S 10.81 (10.47)

2.**Fe-L.Cl.(H₂O)₂:** % Fe 12.09 (12.97),%Cl 8.81 (8.21),%C 30.12 (30.61),%H 3.81

  (3.50),%N 9.10 (9.73),%S 7.91 (7.43).

3**. Fe.L.Py.(H₂O)₂ :**% Fe 11.07 (11.78),%C 40.43 (40.12),%H 4.84 (4.24),%N 11.04

  (11.78),%S 6.07 (6.74).

4.**Fe.α-Pico.(H₂O)₂**: % Fe 11.81 (11.44),%C 41.03 (41.69),%H 4.03 (4.53),%N 11.89

  (11.15),%S 7.01 (6.55).

5.**Fe.L β-Pico.(H₂O)₂**: Fe 11.78 (11.44),%C 41.08 (41.69),%H 4.08 (4.53),%N 11.80

  (11.15),%S 7.04 (6.55).

6.**Fe.L.γ-Pico.(H₂O)₂**: Fe 11.82 (11.44),%C 41.10 (41.69),%H 4.05 (4.53),%N 11.78

  (11.15),%S 7.05 (6.55).

Table 2.**Electronic spectral data (cm⁻¹)**

Compound	MLCT	$n \rightarrow \pi^*$	$\pi \rightarrow \pi^*$
L	-	28570	40800
Fe-L.Cl.(H₂O)₂	25625	32450	42880
Fe.L.Py.(H₂O)₂	25744	32577	42850
Fe.α-Pico.(H₂O)₂	25850	32695	42800
Fe.L β-Pico.(H₂O)₂	25686	32755	42862
Fe.L.γ-Pico.(H₂O)₂	25925	32865	42888

Infrared Spectroscopic data (**cm⁻¹**)

1.**L**:ν (- OH) 3200; ν (C = N) 1670; ν (- C = S) 785, 1370 ; ν (N – N) 1050; ν (²N-H) 3250; ν (C – O) 1290.

 2 [Fe-L.Cl.(H₂O)₂]: ν (C = N) 1615; ν (C = N-N=C) 1548, ν (C-S) 715, 1318,ν (N-N) 1125, ν(M - N) 425, ν (M-O) 520, ν (M-S) 320, ν (C - O) 1225, ν(Fe-Cl) 380.
ν(H₂O) 3510,3540.
3.[Fe.L.Py.(H₂O)₂] :ν (C = N) 1582; ν (C = N-N=C) 1545, ν (C-S) 717, 1320; ν (N-N) 1130, ν (M - N) Base 255, ν (M - N) 430, ν (M - O) 525, ν (M-S) 325, ν (C - O) 1228, Band due to HB 1465, ν(H₂O) 3540,3550.
4.Fe.α-Pico.(H₂O)₂ :ν (C = N) 1587; ν (C = N-N=C) 1548, ν (C-S) 720, 1326,ν (N-N) 1132, ν (M - N) Base 260, ν (M - N) 435, ν (M - O) 530, ν (M-S) 330, ν (C - O) 1232, Band due to HB 1464, ν(H₂O) 3548,3560.
5.Fe.L β-Pico.(H₂O)₂ :ν (C = N) 1590; ν (C = N-N=C) 1553, ν (C-S) 725, 1330,ν (N-N) 1140, ν (M - N) Base 265, ν (M - N) 440, ν (M - O) 535, ν (M-S) 334, ν (C - O) 1235, Band due to HB 1470, ν(H₂O) 3553,3572.
6.Fe.L.γ-Pico.(H₂O)₂ :ν (C = N) 1598; ν (C = N-N=C) 1558, ν (C-S) 728, 1336,ν (N-N) 1144, ν (M - N) Base 270, ν (M - N) 450, ν (M - O) 540, ν (M-S) 337, ν (C - O) 1242, Bands due to HB 1474, ν(H₂O) 3557,3583.

TGA analysis data:
The TGA curves of complexes were recorded between the temperatures 30 °C to 800 °C

1.[Fe-L.Cl.(H₂O)₂]: First step, 117.0 °C, Mass loss 9.62 % second step, 135.0 °C, Mass loss, 15.0 % Third Step 245.0 °C, Mass loss, 35.0 % Fourth Step, 370.0 °C, Mass loss 62.0 %, Residue 800 °C, % of Fe₂O₃, 37.70 (37.06).

2.[Fe.L.Py.(H₂O)₂]:First step, 118 °C, Mass loss 6.04 % second step,130.0 °C, Mass loss, 10.0 % Third Step 250 °C, Mass loss, 32.0 % Fourth Step, 369.0°C, Mass loss, 60.0 %, Residue, 793.0 °C, % of Fe₂O₃, 33.92 (33.66).

3.Fe.α-Pico.(H₂O)₂:First step, 115.0 °C, Mass loss 6.06 % second step,   134.0 °C, Mass loss,12.0 % Third Step 252.0 °C, Mass loss, 34.0 % Fourth Step, 370.0°C, Mass loss 62.0 %, Residue 800 °C, % of Fe₂O₃, 32.05 (32.70).

4.Fe.L β-Pico.(H$_2$O)$_2$:First step, 116.0 °C, Mass loss 6.17 % second step, 132.0 °C, Mass loss, 18.0 % Third Step 255.0 °C, Mass loss, 36.02 % Fourth Step, 366.0°C, Mass loss, 65.0 %, Residue, 780.0 °C, % of Fe$_2$O$_3$, 32.33 (32.70).

5.Fe.L.γ-Pico.(H$_2$O)$_2$:First step, 117.0 °C, Mass loss 6.16 % second step, 134.0 °C, Mass loss, 15.0 % Third Step 258.0 °C, Mass loss, 38.0 % Fourth Step, 370.0 °C, Mass loss 64.0 %, Residue 800 °C, % of Fe$_2$O$_3$, 32.38 (32.70).

Antimicrobial Assay(Agar plate diffusion method)
  Table.3 Absorbance of the L , Fe (III) complexes and standered

Compounds	Staphylococcus aureu		Bacilus subtilis		Escherichia Coli		Peudomonas aeruginosa	
	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	0.72	0.36	0.70	0.40	0.71	0.40	0.72	0.42
Fe-L.Cl.(H$_2$O)$_2$	0.66	0.37	0.68	0.25	0.66	0.27	0.69	0.28
Fe.L.Py.(H$_2$O)$_2$	0.63	0.34	0.64	0.23	0.63	0.24	0.64	0.25
Fe.α-Pico.(H$_2$O)$_2$	0.61	0.32	0.62	0.21	0.61	0.22	0.62	0.23
Fe.Lβ-ico.(H$_2$O)$_2$	0.62	0.33	0.63	0.22	0.62	0.23	0.63	0.24
Fe.L.γ-co.(H$_2$O)$_2$	0.63	0.34	0.64	0.23	0.63	0.24	0.64	0.25
Standered	0.16	0.11	0.13	0.12	0.12	0.11	0.15	0.11
FeCl$_3$	0.50	0.20	0.19	0.19	0.14	0.19	0.30	0.17

(Standered -Cefodoxine,Fluconazole)

Fig 1 Antimicrobial Assay
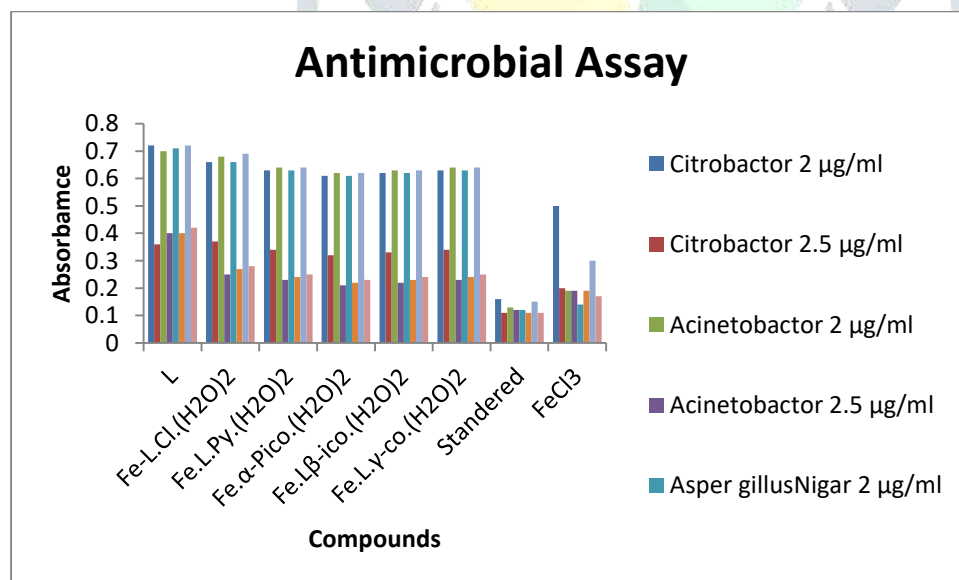
Results and discussion

Physical data of thiosemicarbazone and its complexes are presented in Table 1.Elemental analysis data confirmed with 1:1 ratio of metal ion, thiosemicarbazone for complex and 1:1:1 ratio for metal,thiosemicarbazone and heterocyclic base for all adducts.The complexes are soluble in DMF in which conductivity measurements were made.

The equivalent conductance of electrolyte solution varies with the concentration of the electrolyte.The equivalent conductance of an electrolyte increases with decrease in concentration or increase in dilution. It is observed that all complexes show increasing value of conductance with increase in the dilution at 298 K, 303K,308 K.Equivalent conductance varies with respect to solvent

used. The equivalent conductance of electrolyte solution varies with the concentration of the electrolyte.The conductivity of an electrolyte depends upon the temperature.The conductivity of an electrolyte increases with increase in temperature.This may be due to at higher temperature the mobility of ions is more and hence more conductivity is observed.

The ground term is ^6S in high-spin complexes.For the ^6A_1g ground term in an octahedral; field there is no reduction of the moment below the spin-only value by spin -orbit coupling with higher liquid field terms.The magnetic moments are found to be very close to the spin-only value of 5.92 B.M.and to be independent of temperature.In the octahedral complexes with $^6A_1$ ground term also shows the similar behavior.A comparison of the variation of moment with temperature gives an estimation of the extent of electron delocalization and the magnitude of the low symmetry liquid field component.The magnetic susceptibility data of the Fe (III) complexes of ligands studied in the present work are listed in Table No.1

Mass spectral data confirmed the structure of the thiosemicarbazone as indicated by molecular ion peak (M + 1) corresponding to their molecular weights.

Electronic spectra of solid complexes are presented in Table no.2 The thiosemicarbazone exhibited π- π^*band [11-13] at 40,800 cm-1 and n- π^*[14,15] at 28,570 cm^{-1}.These bands are slightly shifted to higher energy side in complexes.The π-π^*absorption bands are shifted to longer wavelength in complexes due to the weakening of the C=S bond system gets enhanced on complexation [16,17].The reduction in intensity of n- π^*bands in the complexes is due to transfer of lone pair of electrons to the metal and coordination of azomethine nitrogen.The charge transfer bands are broad in the complexes and observed in the region 25000-26000 cm^{-1} which are assignable to Fe→S transitions.

Coordination through azomethine nitrogen shifts ν C=N frequency to the lower side [18].A band in the range 425-450 cm^{-1} confirms the coordination of azomethine nitrogen [19,20].The increase in frequency of νN-N may be due to the increase in double bond character off-sets the loss of electron density via donation to the metal.This confirms the coordination of thiosemicarbazone through the azomethine nitrogen atom.The νN-H of thiosemicarbazone disappears in the complexes indicating the deprotonation.A thioamide band in thiosemicarbazone is shifted to lower side in complexes indicating coordination through thiolate sulfur [21].Bands in 320-340 range due to Fe-S confirms involvement of sulfur coordination.The phenolic oxygen occupies the third coordination on loss of OH protons.This causes shifting of ν(C-O) to lower side in the complexes.Bands due to Fe-O in complexes in the range 520-540 cm^{-1} confirm coordination through oxygen.The heterocyclic base nitrogen atom occupies fourth coordination site.The band is assigned for ν (Fe-N) due to heterocyclic base in 255-270 cm^{-1} range in the spectra of all complexes.The characteristics bands due to coordinated heterocyclic bases are also observed in IR spectra of all complexes[22-24].

The TGA curves of Fe (III) complexes were recorded within a temperature range 30-800^{0}C.The decomposition of complex proceeded in steps.Hydrated molecules of water were lost in between 30-110^{0}C.Then two coordinated water molecules were lost in the temperature range 114-116^{0}C.Mass lost at this stage is about 6-10 %. No change observed ~ 130-135^{0}C after that break observed in the curves due to removal of part of thiosemicarbazone molecule.The remaining part of thiosemicarbazone removed from the coordination sphere at ~ 600^{0}C.The metal oxides were formed above 600^{0}C.The decomposition was complete at ~ 800^{0}C.Fe (III) complexes are thermally stable up to 120^{0}Cand decomposition started at this temperature.The complexes prepared with different metals decompose in steps.It is concluded that the thermal stability of the complexesis due to the coordination of metal ion to thiosemicarbazone [25].

The antibacterial assay was carried out by the agar plate diffusion method.The minimum inhibitory concentration was determined by liquid dilution method [26].The absorbance of the turbid solutions was measured at 520 nm.The same method was used for standard [27]. The thiosemicarbazone was found less active than its iron complexes.This might be due to chelation which reduces the polarity of the central metal atom because of the partial sharing of its positive charge with donor groups and possible π-electron delocalisation within the whole chelating ring.So the lipophilic nature of the central metal atom increases, which favours the permeation of the solution of complexes through the lipid layer of the cell membrane[28].It is found that complexes containing heterocyclic bases show better activity than the thiosemicarbazone and the complex.The absorbance is more at 2µg/ml and less 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 thiosemicarbazone and complexes.

The chelation theory explains the reason behind the better activity of these thiosemicarbazone complexes[29].The polarity of the metal ion is minimized to an advanced level, due to the ligand and positive charge of the metal ion with donor groups especially with sulfur-nitrogen donors.

CONCLUSION

Thiosemicabazone is tridentate ONS donor.The spectral data indicates octahedral geometry for complexes.The complexes are paramagnetic.Two coordinated water molecules were found.The complexes found thermally stable.The complex and adducts showed growth inhibitory activity against gram +ve bacterial species.Finally,antibacterial activity for all compounds is in the order of Standered >metal salt>Fe.α-Pico.(H₂O)₂> Fe.Lβ-ico.(H₂O)₂> Fe.L.γ-co.(H₂O)₂=Fe.L.Py.(H₂O)₂> Fe-L.Cl.(H₂O)₂>L.**The**

minimum inhibitory concentration is 2.5 µg/ml. The equivalent conductance increases on dilution.The equivalent conductance increases with increase in temperature.

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