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Research Article

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Synthesis, characterization & biological activity of some new thiosemicarbazide derivatives and their transition metal complexes

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ABSTRACT

A synthesis of some new thiosemicarbazide like acetyl hexan thiosemicarbazide by condensation of cyclohexylmethylketone with thiosemicarbazide is carried out. And their metal complexes were synthesized by condensation of acetylhexan thosemiocarbazide and different transition metal chloride salt of Cu(II), Co(II), Ni(II),Cd(II),Zn(II),Hg(II) and Fe(III) their characterization are done by different analytical techniques, such as elemental analysis,FT-IR, ES-Mass .

Key words: Thiosemicarbazide, Metal Complexes, Spectral Characterization.

INTRODUCTION

Coordination compounds have been a challenge to inorganic chemist since they were identified in the 19th century. They defy the usual rules of valence at that time and hence called complexes.

They play vital role in our lives. Transitions metal complexes with soft or hard donor groups have been used extensively in coordination and organometallic chemistry[1].In this context**,** thiosemicarbazones are a class of compounds obtained by condensation of thiosemicarbazide with suitable aldehydes or ketones. In most complexes thiosemicarbazones behave as bidentate ligands because they can bond to metals through sulphur and the hydrazinic nitrogen atoms, although in a few cases they behave as unidentate ligands and bond through only sulphur atom[2]

Thiosemicarbazone derivatives are of special importance because of their versatile biological and pharmacological activities. Thiosemicarbazone derivatives have found application in drug development for the treatment of central nervous system disorders, of bacterial infection, as well as analgesic and antiallergic agent. Thiosemicarbazones are potent intermediates for the synthesis of pharmaceutical and bioactive materials and thus, they are used extensively in the field of medicinal chemistry. Moreover, thiosemicarbazones have found their way into almost every branch of chemistry; commercially they are used as dyes, photographic films, plastic and in textile industry. Over the years, thiosemicarbazone derivatives have demonstrated wide range of biological activity *viz.* antimicrobial[3-10], antitumor[11-12], sodium channel blocker[13], anticancer[14-15], antitubercular[16], antiviral[17]. Keeping mind various biomedical application of these class of compounds, we report the synthesis and characterization of Cu(II), Co(II), Ni(II), Zn(II), Cd(II), Hg(II), Fe(III) complexes of thiosemicarbazide derivative.

EXPERIMENTAL SECTION

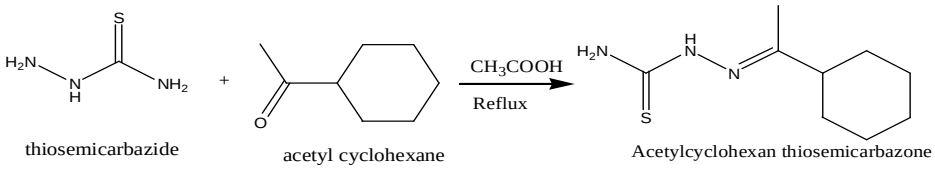
All the chemicals were purchased from Merck and were used as received. Melting point of ligand and metal complexes were taken in open capillary and was incorrected. FT-IR spectra was obtained in KBr pallet in the 4000-400 cm-1 region on a Fourier transform infrared spectrophotometer-8400 Shimandzu, Mass spectra were recorded on a GCMS-QP2010 Shimandzu & micromass Q-T of Micro, elemental analysis was carried out on EURO EA Elemental Analyzer, EA-3000, RS-232.

Synthesis of Acetyl hexane thiosemicarbazone:
An equimolar amount of Cyclohexylmethylketone (0.01 M) and thiosemicarbazide (0.01 M) were dissolved in 20 ml aqeous methanol. The resulting mixture was reflux for 24 hours in the

Presence of catalytic amount of gl.acetic acid. The progress of the reaction and purity of the products were monitored by TLC .After completion of the reaction, reaction mixture was poured into crushed ice. The separated product was filtered wash with cold water, several times and dried at room temperature [18-20]. Physical data of ligand is shown in table **1**.

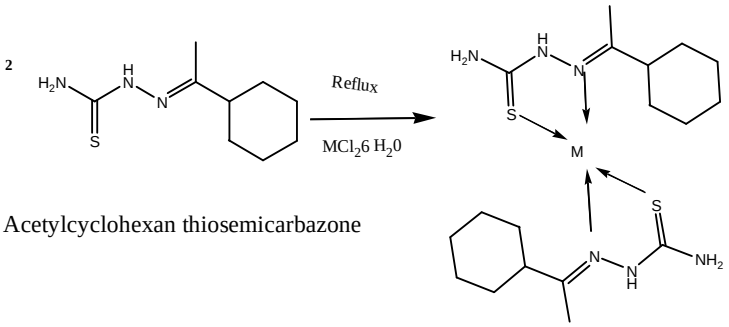
Synthesis of Acetylcyclohexanthiosemicarbazone metal complexes:
Acetylcyclohexanthiosemicarbazide (0.02M) was dissolved in methanol than solid $M \cdot Cl_2 \cdot 6H2O$ (0.01M) (where M = Co, Ni, Zn, Cd, Cu, Hg &Fe) was added to reaction mixture. The resulting reaction mixture was refluxed for 24 hours in the presence catalytic amount of NH_3 with continues stirring. After completion of the reaction the resulting solid was filtered and wash with cold Methanol and dried at room temperature. Physical data of complex is shown in table **1**.

REACTION SCHEME
Step I: Synthesis of acetylhexanethiosemicarbazone:



thiosemicarbazide acetyl cyclohexane Acetylcyclohexan thiosemicarbazone

Step II: Synthesis of Co(II),Ni(II), Zn(II),Cd(II),Cu(II),Hg(II)&Fe(III) metal complexes of thiosemicarbazide derivative



Acetylcyclohexan thiosemicarbazone

M= Co, Ni, Zn,Cd,Cu, Hg & Fe

RESULTS AND DISCUSSION

The Acetylcyclohexanthiosemicarbazide (L) and their metal complexes were subjected to elemental analyses. The results of elemental analyses (C, H, N, S and M) with and melting points are presented in Table (**1)**.The results obtained are in good agreement with those calculated for the suggested formula. The structures of the ligand and metal complexes are also confirmed by IR, MASS, which are discussed below.

Mass spectral data confirm the structure of the ligand and their Co(II),Ni(II), Cu(II),Cd(II),Zn(II),Hg(II),&Fe(III) complexes as indicated by the molecular ion peaks corresponding to their molecular weight (Fig.1, 2, 3,4,5,6&7).

The IR spectrum of the ligand showed (Fig. 4) a strong absorption band at 1594.91cm^{-1} which was assigned to the azomethine group, ν(C=N)[18]. The strong band observed at 1141.86 & 817.39cm^{-1} in the spectrum was due to the ν(C=S) & δ(C=S) [19] .The bands observed at 3420.49 cm^{-1} and 3235.4cm^{-1} were assigned to ν(NH_2) and ν(N–H) vibrations respectively. This further indicates that the ligand remained in the thione form. The diagnostic IR spectral bands of the complexes (Fig.2,3,4,5,6,7,&8) are presented in Table **(2)**, together with their tentative assignments. In the spectra of all the complexes, the band due to the azomethine moiety (C=N) was shifted to a lower or higher frequency, indicating its involvement in coordination with metal ion. The ν(C=S) stretching frequency was lowered in the spectra of the complexes, indicating the involvement of the thioketo sulphur in the coordination.

Table 1: The experimental result and physical data of ligand and its complexes

S.No	Compound	Colour	M.P	Elementary Analysis % calculated (found)					M.wt	Conductance Ohm^{-1}cm^{2}mole^1
				C	H	N	**S**	Metal		
1	Ligand	White	80^{o}c	54.27 (55.01)	5.52 (5.90)	21.10 (21.56)	16.08 (16.75)	- - - -	199	
2	Co-ACHTSC	Brown	200^{0}c	47.27 (47.87)	4.80 (4.99)	18.32 (19.01)	14.05 (15.01)	12.89 (13.05)	456.9	37.6
3	Ni- ACHTSC	Brown	180^{0}c	46.62 (47.01)	4.66 (4.70)	18.13 (18.95)	13.81 (14.12)	12.88 (13.51)	456.6	41.5
4	Zn- ACHTSC	Pale yellow	180^{0}c	46.62 (47.20)	4.74 (4.92)	18.13 (18.90)	13.91 (13.85)	14.11 (14.71)	463.3	31.2
5	Cd- ACHTSC	Pale yellow	158^{0}c	42.31 (43.13)	4.31 (4.56)	16.45 (16.91)	12.53 (13.14)	22.02 (23.11)	510.4	65.3
6	Hg- ACHTSC	White	154^{0}c	33.44 (33.91)	3.67 (4.01)	14.04 (14.75)	10.07 (10.84)	33.44 (33.94)	598	46.1
7	Cu-ACHTSC	Green	162^{0}c	46.80 (47.55)	4.76 (4.83)	18.20 (18.92)	13.86 (13.98)	13.75 (13.92)	461.5	53.5

The anti-bacterial activity of the metal complexes studied against three bacterial strains one is a gram positive *psedomonas &* two are gram negative *Escherichia coli, Klebsiella species.* All the compounds showing good bacterial activity but in case of Hg complex only one single organism called *Klebsiella* showing less activity the results are presened in table (**4) &** fig **(1).**

Table 2: IR spectral data (cm-1) of the ligand and their metal complex in KBr pellets

S.NO	**Frequency in cm-1**				
	ν(C=N)	ν/ δ (C=S)	ν(NH)	ν(NH_2)	ν(N-N)
Ligand	1594.91	1141.86/817.39	3235.4	3420.49	1071.72
Co-ACHTSC	1610.77	1145.76/841.02	2852.55	2928.41	1025.70
Ni- ACHTSC	1550.43	1146.43/ 789	3145.78	3423	1029.35
Zn- ACHTSC	1615.24	1235.44 / 791	3183.17	3458	1026
Cd- ACHTSC	1619.14	1162.52/789.81	3170.13	3435.47	1021.09
Hg- ACHTSC	1575.29	1161.30/801.25	3161.46	3447.26	1018.57
Cu-ACHTSC	1613.86	1157.05/790.27	3183.51	3427.83	1026.83

Table 3: Mass spectra of the compounds

	Calculated mass m/Z	**Obtained mass m/Z**
Ligand	199	200.9
Co-ACHTSC	456.9	457.3
Ni- ACHTSC	456.6	456.3
Zn- ACHTSC	463.3	462.4
Cd- ACHTSC	510.41	511.1
Hg- ACHTSC	598	599.4
Cu-ACHTSC	461.5	460.4

The mass spectral data of Schiff base ligand and its metal chelates are given in table-3. Mass spectra of the ligand and its metal chelates show molecular ion peaks, which are in good agreement with the expected values. The mass

spectrum of ligand L gives a peak at 200 m/Z, which is assigned for [L+H] peak. Co, Ni, Zn,Cd, Cu, & Hg, complexes gives molecular ion peak at 457.3,456.3,464.2,511.1,599.4 and 460.4 m/Z respectively and are assigned as [M+1] peak.

Antibacterial activity

Test organisms and culture condition:

A collection of three organisms including Gram-positive and Gram-negative organisms were used for this study of clinical isolates such as *Escherichia coli*, *psedomoas*, *Klebsiella species* were obtained from Microbiology laboratory of Global Hospital, Hyderabad. All strains were tested for purity by standard microbiological methods. The bacterial stock cultures were maintained on Mueller Hinton Agar (MHA) slants and stored at 4°C.

Determination of antibacterial activity:

An agar-well diffusion method was employed for evaluation of antibacterial activity. The bacterial strains were reactivated from stock cultures by transferring into Mueller Hinton Broth (MHB) and incubating at 37°C for 18 h. A final inoculum containing 10^6 colony forming units (1 x 10^6 CFU/ml) was added aseptically to MHA medium and poured into sterile Petri dishes. Different test compounds at a concentration of 0.2mg/50µL were added to wells (8 mm in diameter) punched on agar surface. Plates were incubated overnight at 37°C and diameter of inhibition zone (DIZ) around each well was measured in mm. Experiments were performed in triplicates. Antibiotic such as ciprofloxacin at a concentration of 0.4mg/50µL were used as positive reference to determine sensitivity of microorganisms tested. DMSO was used as a negative control.

Table 4: Antibacterial activity of ligand & their metal complexes

S. No	Name of Compounds	Diameter of inhibition Zone (mm)					
		1mg/250 uL			2mg/250 uL		
		Escherichia coli	*Klebsiella pneumoniae*	*Pseudomonas aeruginosa*	*Escherichia coli*	*Klebsiella pneumoniae*	*Pseudomonas aeruginosa*
1	ACHTSC	-	12	14	-	13	16
2	ZnACHTSC	-	14	14	-	16	16
3	HgACHTSC	-	-	-	-	09	-
4	MnACHTSC	-	-	-	-	-	-
5	CoACHTSC	12	09	-	14	-	-
6	FeACHTSC	14	11	-	15	15	14
7	NiACHTSC	14	17	-	18	20	20
8	CuACHTSC	23	23	16	17	20	18
9	Ciprofloxacin	46	55	45	47	55	53

Figure1: Antibacterial activity of the Schiff base complexes against bacterial organisms

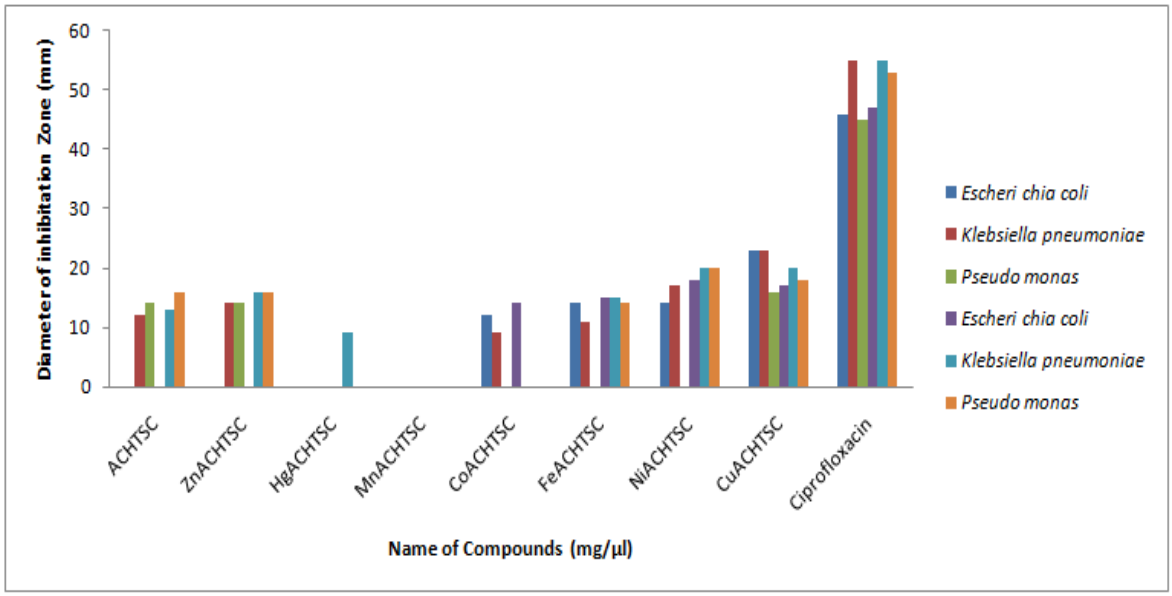


Figure 2: IR Spectrum of acetyl cyclohexane thiosemicarbazone

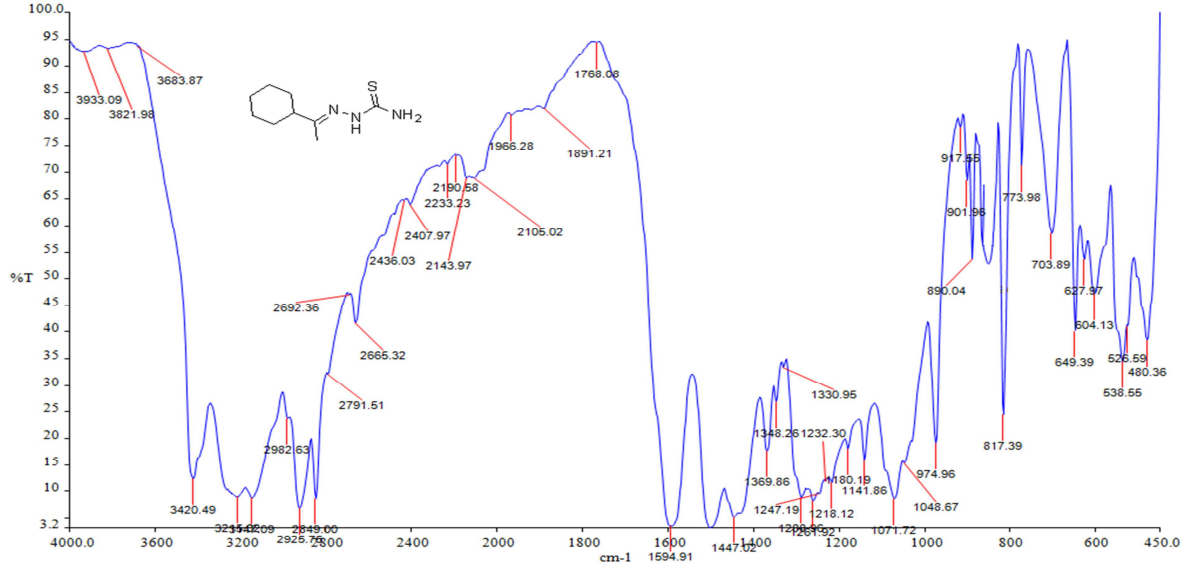


Figure 3:IR Spectrum of Co-complex of acetyl cyclohexane thiosemicarbazone

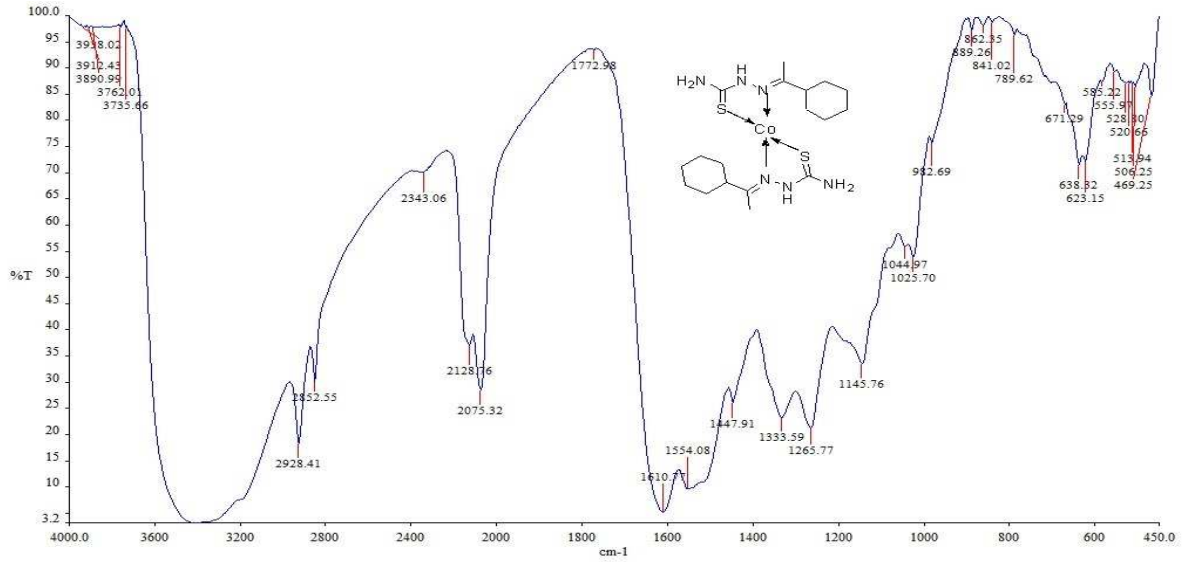


Figure 4: IR Spectrum of Ni-complex of acetyl cyclohexane thiosemicarbazone

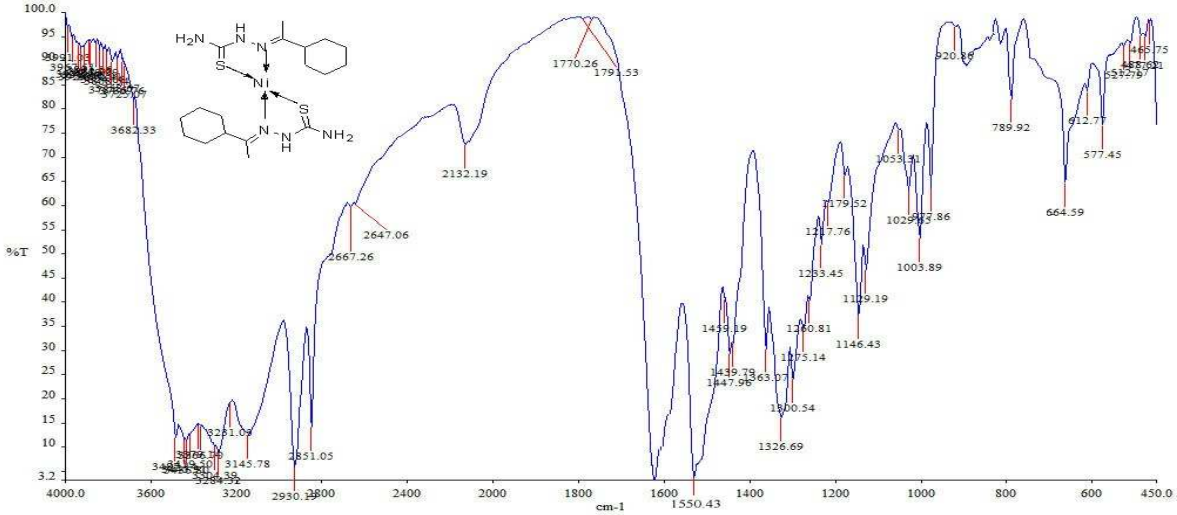


Figure 5:IR Spectrum of Zn-complex of acetyl cyclohexane thiosemicarbazone

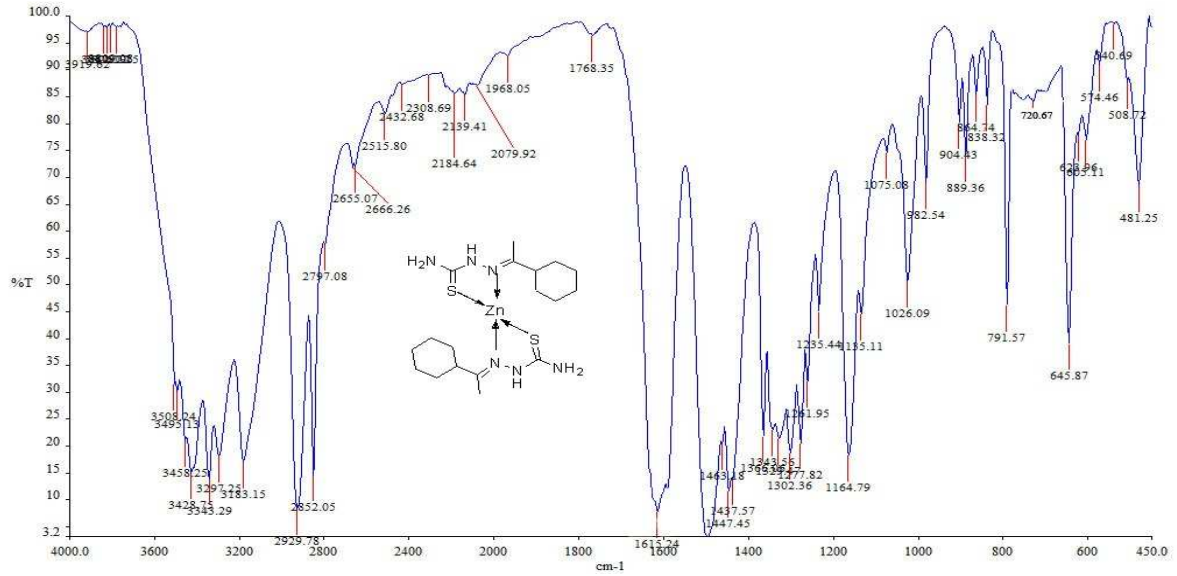


Figure 6: IR Spectrum of Cd-complex acetyl cyclohexane thiosemicarbazone

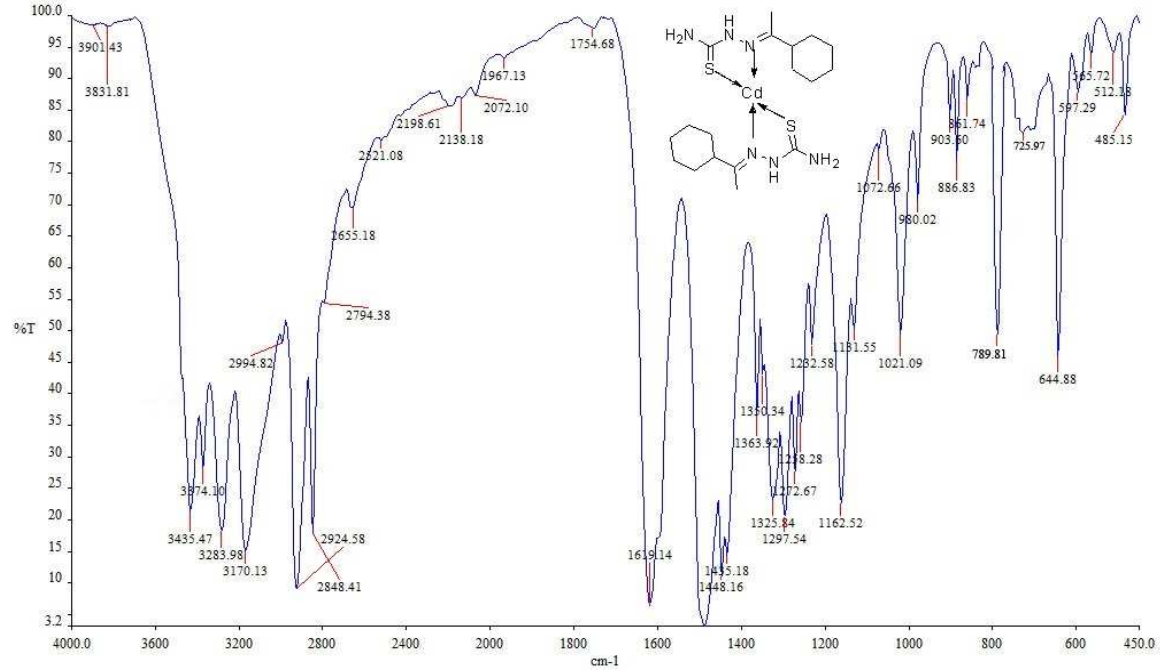


Figure 7: IR Spectrum of Cd-complex of acetyl cyclohexane thiosemicarbazone

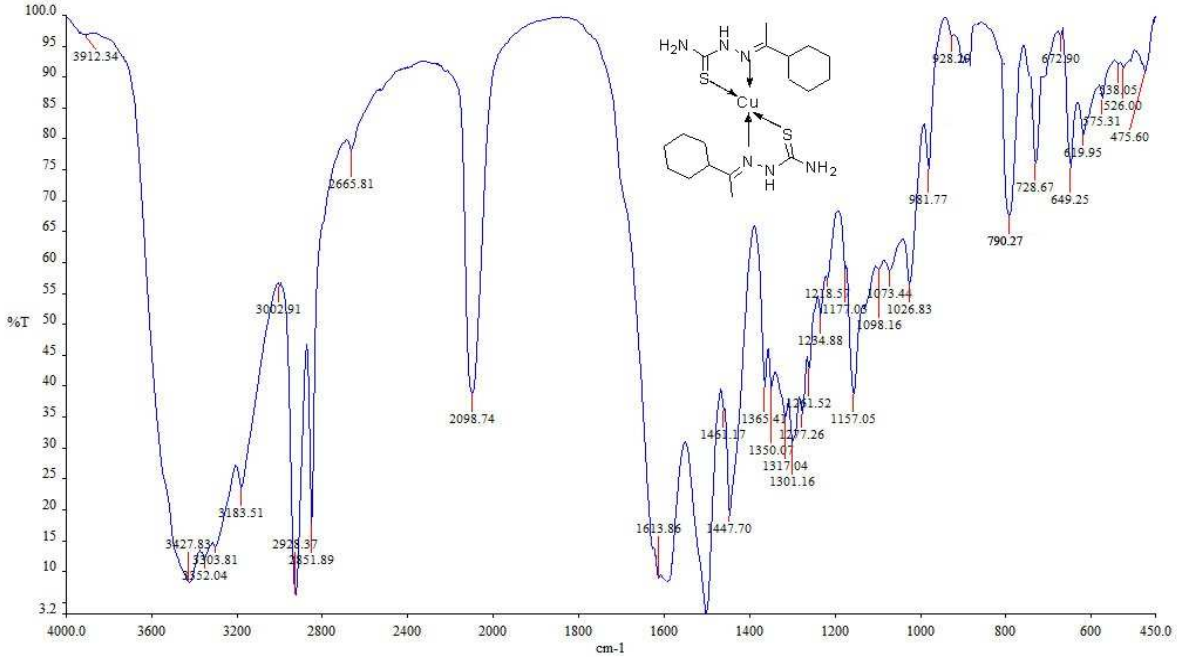
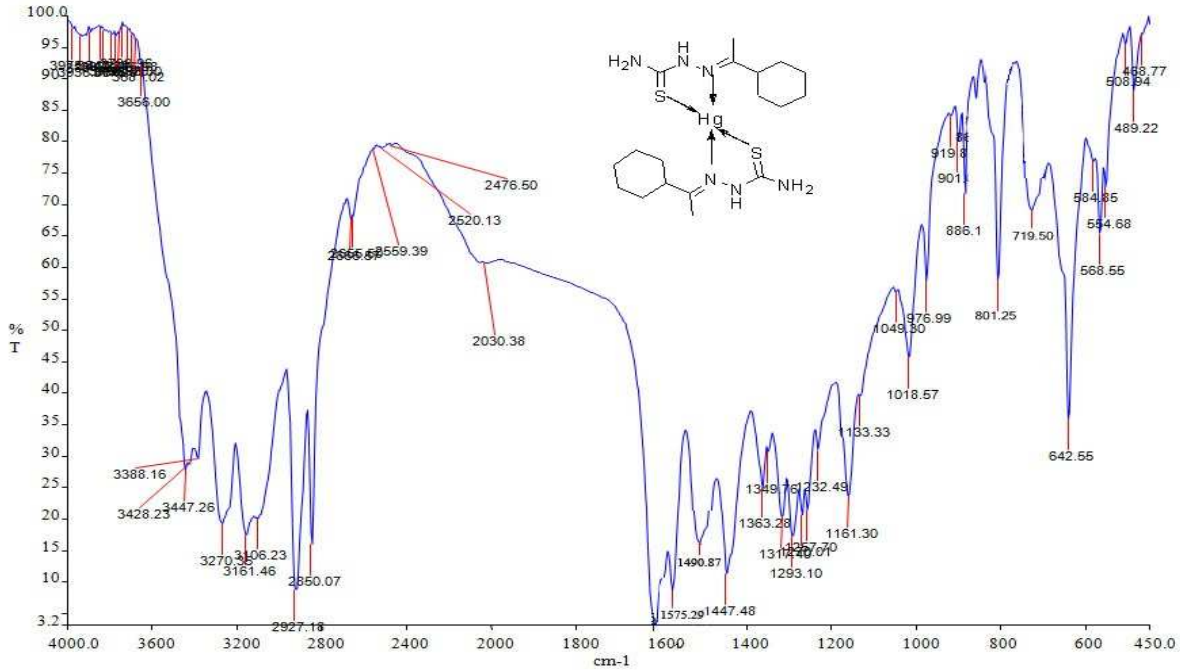


Figure 8: IR Spectrum of Hg-complex of acetyl cyclohexane thiosemicarbazone



CONCLUSION

In this paper we have reported the synthesis of Schiff base ligands derived from thiosemicarbazone with cyclo hexyl methyl ketone & metal complexes have been synthesized using the Schiff base ligands. The ligand and complexes were characterized by spectral and analytical data. On the basis of studies perform the Co, Ni, Zn, Cd, Hg &Cu complexes have been assigned square planner geometry. The anti-bacterial studies carried out with the complexes confirm that they are good antibacterial agents .

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