



NOVEL SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL ACTIVITIES OF COMPLEXES OF Mn(II), Ni(II) AND Cu(II) WITH 4-HYDROXY ACETOPHENONE THIOSEMICARBAZONE

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Abstract: A series of novel 4-Hydroxyacetothiosemicarbazones complexes with three transition metal i.e. Mn(II), Ni(II) and Cu(II) having the general composition $[Mn(4HAT)_2Cl_2]$, $[Ni(4HAT)_2Cl_2]$ and $[Cu(4HAT)_2Cl_2]$ {where 4HAT= 4-Hydroxyacetophenone thiosemicarbazones, have been synthesized by the reaction of thiosemicarbazide with 4-Hydroxyacetophenone by conventional heating as well as microwave irradiations method followed by complexation with transition metals. The synthesized compounds have been characterised by elemental analysis, melting point determination, FTIR, UV-visible spectral analysis. The synthesized ligands and their new metal complexes have been screened in vitro for antibacterial activity against *Escherichia coli*, *Staphylococcus aureus* and *Bacillus subtilis* bacteria.

Keywords: Thiosemicarbazones, Microwave irradiation, Transition metal complexes.

I. INTRODUCTION

Thiosemicarbazones is an important class of compounds obtained by condensing thiosemicarbazide with suitable aldehydes or ketones [1]. The active group for chelation is Sulphur [2]. In most of the complexes, the thiosemicarbazones coordinate to the metal ion as a bidentate ligand bonding through the sulphur atom and the hydrazino nitrogen atom. In a few cases they behave as unidentate ligands by bonding only through the sulphur atom. In certain cases thiosemicarbazones also act as multidentate ligands if donor groups are also present in the parent aldehyde or ketone moiety [3]. Transition metal complexes with N,N- and N,S-donor ligands have attracted remarkable attention because of their interesting chemical and biological properties [4]. It is well known that N and S atoms play important roles in the coordination of metal ions at active sites of numerous metallobiomolecules [5]. Interest in metal complexes with thiosemicarbazone ligands has been stimulated because biological activities are often enhanced on complexation [6]. Thiosemicarbazones and their metal complexes have received considerable attention because of their antibacterial, antifungal, antitumor, antiamoebic, antimalarial, antiviral, radioprotective, trypanocidal and anti-inflammatory activities [7-22]. With the growing interest of thiosemicarbazones the present work was undertaken in order to investigate the ligational behaviour of the thiosemicarbazone towards transition metal ions as well as their biological activity in inhibiting the growth of some pathogenic bacteria [23].

Aims and Objectives

To carry out Green synthesis and evaluate the biological activity of transition metal thiosemicarbazone complexes.

II. MATERIALS AND METHODS

All the chemicals and solvents used were of AR grade and procured from Sigma-Aldrich and E Merck and used as received. Purity of synthesized compounds has been checked by thin layer chromatography. IR spectra are recorded on Bruker Optic Model Alpha (FT-IR) (Zn-Se Optics, ATR) (4000-500 cm^{-1}) using KBr disc. Magnetic susceptibility



measurements were carried out on the vibrating sample magnetometer (VSM) model 155 at 5500 Gauss field strength. Microwave synthesis was carried out in domestic microwave oven Model KENSTAR-OM20ACF, 2450MHz, 800W and GMBR (Green Microwave Biochemical Reactor) at GCRC, P.G. Dept. of Chemistry, Govt. Dungar College (NAAC-A- Grade) MGS University Bikaner, Rajasthan. ECIL Double Beam UV-Visible Spectrophotometer, model UV 5704SS, with quartz cell of 10 mm light path was used for absorption measurement. All biological activities have been carried out with horizontal laminar at BIFR, Bikaner.

Preparation of Ligands.

Two different routes were used for the synthesis of ligands.

Microwave irradiation synthesis of ligands

Ligand i.e. 4-Hydroxyacetophenone thiosemicarbazone (4HAT), was synthesized by a typical preparation in which water or water alcohol mixture of thiosemicarbazide (0.01mol) and 4-Hydroxyacetophenone were taken in Erlen Meyer flask capped with a funnel and placed in a microwave oven and irradiated at 200 watt for 2-5 minutes. The reaction was monitored by TLC. After completion the reaction, the reaction mixture was allowed to attain room temperature and solid separated was filtered. The crude product was recrystallized from redistilled ethanol.

Thermal method

For comparison purposes, the above ligand was also synthesized by the thermal method, where instead of a few drops of alcohol, a hot ethanolic solution (25 mL) of 4-Hydroxyacetophenone (0.01 mol) was mixed to a hot ethanolic refluxing solution (30 mL) of thiosemicarbazide (0.01 mol) in a 1 : 1 molar ratio. The contents were refluxed for about 6-10 hours in a water bath. The solution was then concentrated under reduced pressure, which upon cooling gave crystalline precipitates. The products were washed in alcohol and recrystallized in the same solvent. The structures of ligands are shown in (Fig.1). A comparison between the thermal method and microwave method is given in (Table 1).

Preparation of the complexes

Two different methods were employed for the synthesis of the transition metal complexes with 4HAT. A comparison between the thermal method and microwave method has been given in Table 1.

Microwave method

For the preparation of various complexes, a slurry of ligand (i.e. 4HAT) (0.2mmol) was prepared in water or in water-ethanol mixture. In this, solution of respective transition metals (i.e. Manganese chloride, Nickel chloride and Copper nitrate) (0.01mmol in 30 ml ethanol), was added. The resulting mixture was irradiated in a microwave oven for 2 to 6 minutes at medium power level (600W) maintaining the occasional shaking. The mixture was cooled to room temperature and poured into ice chilled methanol and dried in vacuum over P₂O₅ [24].

Thermal method

The complexes were also synthesized by the thermal method. In this method hot ethanolic solution (20ml) of the 4HAT (0.02mmol) and hot ethanolic solution (20ml) of the respective transition metals (0.01mmol) were mixed with constant stirring. The reaction mixture was refluxed after adding 4-5 drops of glacial acetic acid for 8-10 hours at 80-90° C. On cooling coloured complexes were precipitated out. They were filtered, washed with 50% ethanol and dried in vacuum desiccators and recrystallized in ethanol. The obtained solid metal complexes and their colours are shown in table 1.

III. RESULTS AND DISCUSSION

Ligands and complexes were identified on the basis of elemental analysis and spectral studies. Colour, yield and elemental analysis data are represented in Table 1.

Infrared Spectra

The binding mode of the ligand to metal ions was further elucidated by analysis of the IR spectra of the ligands and metal complexes (table 2). A study and comparison of infrared spectra of free ligand and its metal complexes imply that the ligand behaves as bidentate and the metal ion is coordinated through the azomethine nitrogen and the thione sulphur. A band in the range 1660 - 1600 cm⁻¹ in the IR spectra of the ligand is due to $\nu(\text{C}=\text{N})$ [25]. Coordination of azomethine nitrogen in complexes is suggested by the shift of $\nu(\text{C}=\text{N})$ band to lower frequencies. The absence of a $\nu(\text{S}-\text{H})$ absorption in the region 2700-2500 cm⁻¹ is considered as evidence that the thione form of the ligands exist in the



solid state [26-27]. The intensity of the medium band in the range 1100 – 1060 cm^{-1} assigned for ν (N-N) in spectrum of the ligands is remains unchanged in all the spectra of the complexes however, it shifted to the higher frequency. The strong band observed in the range 880 - 820 cm^{-1} assigned for ν (C=S) in spectrum of the ligand is shifted towards lower frequency and occurred at 830 - 820 cm^{-1} in the corresponding spectra of the metal complexes indicating the coordination of the thione sulphur to metal atom[28-29]. The bands in the range 3200 - 3140 cm^{-1} in ligands are due to NH vibration. In all the complexes, the presence of a band in this region corresponds to NH vibration which indicates that the ligand is coordinated in the neutral form.

Magnetic Moments and Electronic Spectra

The observed magnetic moments for Mn(II), Ni(II) and Cu(II) complexes were found 5.80, 2.84 and 1.82 BM respectively at room temperature. These values are typical of distorted octahedral geometry coordinated around transition metal complexes. The electronic spectra of these complexes have been recorded in DMF are reported in table 3. The electronic spectra of all the Mn(II), Ni(II) and Cu(II) complexes recorded and their band maxima and their assignments are presented in Table 3.

Biological activity

The antibacterial activity of the compounds against *E.coli*, *S.aureus* and *B.subtilis* were carried out using Muller Hinton Agar media (Hi media). The activity was carried out using paper disc method is represented in Table 4 which shows all the Co(II), Ni(II) and Cu(II) complexes have moderate antibacterial activities against these bacteria. Among the various complexes, Cu(II) Complex has been found out to be most effective against these bacteria showing maximum clarity of zones.

IV. CONCLUSION

The thiosemicarbazone ligand 4HAT and its complexes with Mn(II), Ni(II) and Cu(II) were characterized by elemental analysis, spectral studies and magnetic moment measurements. On the basis of above data the thiosemicarbazone ligand 4HAT appear to behave as bidentate ligand coordinating through the azomethine nitrogen and the thione sulphur atom. The results of the above studies suggest that the Mn(II), Ni(II) and Cu(II) complexes probably possess a distorted octahedral geometry. The antibacterial properties of the ligands and its complexes were studied against *E.coli*, *S.aureus* and *B.subtilis* bacteria. The result shows that all the Mn(II), Ni(II) and Cu(II) complexes have moderate antibacterial activities against these bacteria.

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**Table 1. Physico-Chemical Data of 4HAT and Complexes**
(C.M. = Conventional method, M.M. = Microwave method)

S.N	Compound	Colour	Reaction period		Yield %		Elemental Analysis Calculated(Found) %		
			CM (Hrs.)	MM (Min.)	CM	MM	C	H	N
1	4HAT	Yellow	6	4.5	61	74	45.38 (45.19)	4.20 (4.08)	23.53 (23.59)
2	[Mn(4HAT) ₂ Cl ₂]	Yellow	6.5	2.0	54	65	43.03 (43.13)	4.38 (4.23)	16.74 (16.66)
3	[Ni(4HAT) ₂ Cl ₂]	Light Yellow	6.5	4	55	68	32.79 (32.53)	3.04 (3.01)	21.25 (21.05)
4	[Cu(4HAT) ₂ Cl ₂]	Light Pink	8.5	3.30	48	55	35.38 (35.32)	3.28 (3.22)	18.35 (18.30)

Table 2. Significant infrared spectral bands (cm⁻¹) of the ligands and its metal complexes

Compounds	$\nu(\text{C}=\text{N})$	$\nu(\text{N}-\text{N})$	$\nu(\text{C}=\text{S})$	$\nu(\text{N}-\text{H})$	$\nu(\text{M}-\text{N})$	$\nu(\text{M}-\text{S})$
4HAT	1654	1078	830	3198	-	-
[Mn(4HAT) ₂ Cl ₂]	1586	1134	808	3206	459	428
[Ni(4HAT) ₂ Cl ₂]	1585	1103	824	3197	449	413
[Cu(4HAT) ₂ Cl ₂]	1585	1113	827	3197	455	423

Table 3. Magnetic moments and electronic spectral data of complexes

S. N.	Complex	μ_{eff} (BM)	Electronic Spectral bands $\lambda_{\text{max}}(\text{cm}^{-1})$	Tentative assignments	Comments
1	Mn(II)-4HAT	5.80	40650, 33222, 30959, 25974	${}^6\text{A}_{1g} \rightarrow {}^4\text{T}_{1g}$, ${}^6\text{A}_{1g} \rightarrow {}^4\text{T}_{2g}$, ${}^6\text{A}_{1g} \rightarrow {}^4\text{E}_g$, ${}^4\text{A}_{1g}(\text{G})$	Distorted octahedral Mn(II) Geometry
2	Ni(II)-4HAT	2.84	40983, 31545, 24845, 24038, 22548	${}^3\text{A}_{2g}(\text{F}) \rightarrow {}^3\text{T}_{2g}(\text{F})$, ${}^3\text{A}_{2g}(\text{F}) \rightarrow {}^3\text{T}_{1g}(\text{F})$, ${}^3\text{A}_{2g}(\text{F}) \rightarrow {}^3\text{T}_{1g}(\text{P})$	Distorted octahedral Ni(II) Geometry
3	Cu(II)-4HAT	1.82	32728, 28269, 23364, 22296,	${}^2\text{T}_{2g} \leftarrow {}^2\text{E}_g$ ${}^2\text{B}_{1g} \rightarrow {}^2\text{A}_{1g}$	Distorted octahedral Co(II) Geometry

Table 4. Antibacterial activity of synthesized compounds

S. N.	Compounds (100ppm)	Zone of inhibition (in mm)		
		<i>E. coli</i>	<i>S. aureus</i>	<i>B. subtilis</i>
1	4HAT	0.5	0.5	0.5
5	[Mn(4HAT) ₂ Cl ₂]	1.0	3.0	0.5
6	[Ni(4HAT) ₂ Cl ₂]	0.5	2.5	0.5
7	[Cu(4HAT) ₂ Cl ₂]	2.	3.0	1.0

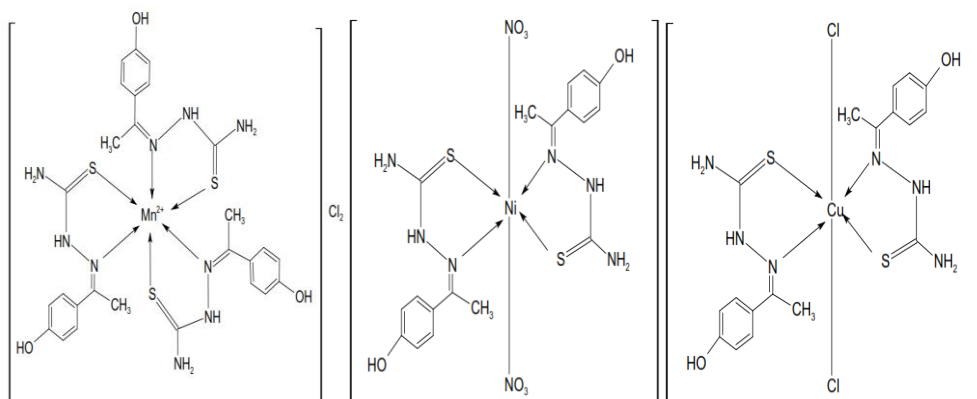


Fig. 2. Tentative Structures of Complexes

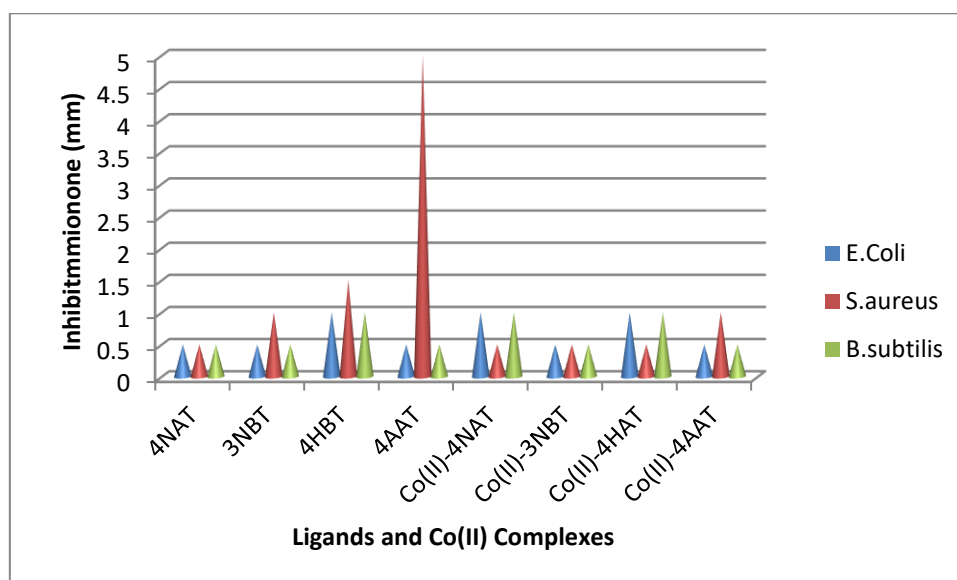


Fig. 4. Graphical Presentation of Biological Activity