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Synthesis, Spectroscopic Characterisation and Biological Studies of Novel Co (II) Mixed Ligand Complexes of Piperidine Dithiocarbamate and Schiff Bases

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Abstract: Simple mixed ligand complexes of Cobalt(II) with piperidine dithiocarbamate and Schiff Bases derived from vanillin/Salicylaldehyde and amines such as ethylene diamine(en) and diethylenetriamine(dien), viz.salen,vanen and vandien, have been synthesized and characterized by elemental and thermal analysis, IR, UV-Vis and ESR spectral studies, and magnetic susceptibility studies. Antibacterial, Antifungal and Anticancer activities have also been carried out on these complexes, which indicates promising activity.

Keywords: Mixed ligand Cobalt (II) vanen/vandien/salen, Schiff Base, pentamethylene dithiocabamate complexes, anti- bacterial, antifungal activities.

INTRODUCTION

Coordination chemistry of metallo-nitrogen and sulphur compounds is a source of stimulation to many research workers, due to the fact that such complexes possess unique stereochemical, magnetic and spectral properties. Metal complexes of ligands containing nitrogen and sulphur as donor atoms have been reviewed by several authors [1-4]. There has been intense interest in the coordination compounds of unsaturated sulphur donor chelating ligands such as dithiocarbamates, and related molecules from chemists, physicists, biologists and theoreticians alike owing to their interesting chemical properties and possible wide applications[5]and interesting molecular structures Structural investigations and chemical studies of these metal chelates cover a full gamut of areas ranging from general considerations of metal-sulphur bonding and the formation of four membered chelate rings to the employment of these ligands in inorganic qualitative analysis, their practical

application in organic synthesis, medicine, and biology, and their uses as vulcanisation accelerators, floatation agents, fungicides, pesticides, radiation protectors, antioxidants and photostabilisers of polymers[6-9]. Their role in material science has also been quite significant.

Schiff-bases are considered as a very important class of organic compounds, having wide applications in many biological aspects, proteins, visual pigments, enzymic aldolization and decarboxylation reactions. Moreover, some Schiff bases and their metal complexes exhibit antibiotic, antiviral and antitumor activity [10, 11].They are also used as catalysts in polymer and dyes industry, beside some uses as antifertility and enzymatic agents[12]. An interesting application of Schiff bases is their use as an effective corrosion inhibitor, which is based on their ability to spontaneously form a monolayer on the surface to be protected[13]. The wide range of applications exhibited by the above said dithiocarbamate and Schiff base complexes made us curious to synthesize mixed ligand complexes containing both these ligands to check if any synergism results. An extensive search through literature showed that very few mixed ligand dithiocarbamate complexes with Schiff base have been reported [14,15]. Herein we report the synthesis, characterisation and application of mixed ligand complexes of Co (II) containing Schiff Bases (derived from vanillin and Salicylaldehyde with en/dien) and dithiocarbamates (derived from piperidine)

EXPERIMENTAL SECTION

The chemicals employed for the preparation are of Analar grade and hence used without further purification. The Cobalt chloride hexa hydrate and vanillin used for the synthesis are of analytical grade. Piperidine, carbon disulphide, Ethylene diamine, diethylenetriamine, and salicylaladehyde are pure grade chemicals from Merck chemicals. The chloroform used as solvent in all our studies is distilled by standard procedures.

Preparation Of [Co (pmdtc)$_2$(Schiffs base)]

Step 1: Preparation of Pentamethylene dithiocarbamate (pmdtc):

The dithiocarbamate was prepared by adding equi molar volumes of Carbon disulphide to Piperidine and chloroform with constant stirring under ice cold conditions [2-4 ^oC]. To this was added an equi molar solution of NaOH in water, a white precipitate was obtained .The precipitate was washed with ether and filtered over vacuum and dried.

Step2: Preparation of the complex [Co (pmdtc)$_2$(Schiff Base)]

To one equivalent of the Diammine added two equivalent of vanillin/salicylaldehyde in alcohol and stirred. A yellow precipitate was obtained. This was filtered, dried and recrystallized from alcohol and used for further reaction. To one equivalent of the metal in water added the same equivalent of Vanillin/salicylaldehyde- amine (en/dien) Schiff base in alcohol. To this added, two equivalent of pmdtc and stirred .A green precipitate was obtained. This was then filtered and dried over vacuum.Our attempt to prepare the (Saldien), analogue resulted in the formation of a resinous mass, which might be due to the polymeric nature of the product. Hence, we have not considered it for this discussion.

The Cobalt present in the complex was estimated using ICP-OES- Inductively Coupled Plasma optical emission spectroscopy- PerkinElmer Optima 5300 spectrometer. The nitrogen and sulphur were estimated by Kjelhdhal's method and barium sulphate method respectively.TG were recorded in NETZSCH STA 449F3 thermal analyser with a heating rate of 10^o/min. Magnetic susceptibility studies were carried out using Vibrating sample magnetometer Lakeshore VSM 7410. UV-Visible absorption spectra were recorded using a Shimadzu UV 1600 model spectrometer. The IR spectrums

of the complexes were recorded as KBr disc using Shimadzu Spectrometer. The EPR spectra of the complexes were recorded using JES-FA200 EPR spectrometer in the region from 1000-8000 gauss. The bactericidal and fungicidal activities of the complexes were studied by agar disc diffusion method[16]. The anti-cancer activities were studied using the MTT assay method[17].

RESULTS AND DISCUSSION

The elemental analysis on the complexes (Table-1) confirm the proposed mplecular formula assigned to the complexes via: [Co (pmdtc) $_2$(vanen], [Co (pmdtc) $_2$(vandien], [Co (pmdtc) $_2$(salen]. All the complexes are green in colour and are completely soluble in chloroform, partially soluble in DMSO and alcohol, and insoluble in water. The electrical molar conductance of the complexes at a concentration of about 10^{-3} M in chloroformic solution was found to be 5-10 $Ohm^{-1}mol^{-1}$ cm^2 indicating the non-electrolytic nature of the complexes[18]. The thermo gravimetric analysis data on the complexes is furnished in Table -I.

Table-I: Elemental Composition and Electronic Spectral Data

Complexes	%N (theo) exp	%S (theo) exp	%Co (theo) exp	Λmax(nm)	Residue% TGA (theo) exp
[Co (vanen)(pmdtc)$_2$]	(7.31) 7.88	(16.72) 17.05	(7.70) 7.54	636,480, 356	(11.88) 11.1
[Co (vandien)(pmdtc)$_2$]	(8.22) 8.31	(15.0) 14.19	(6.92) 6.82	639,480, 330	(10.68) 7.74
[Co (salen)(pmdtc)$_2$]	(11.27) 10.96	(17.18) 17.37	(7.91) 7.45	641,480 370	(12.2) 12.98

The thermo grams were run up to 1000^{o}C.The residual mass corresponds to CoS in case of Vanen and salen complexes whereas it was the metal in case of vandien complex. This complex forms CoS at around 900^{o}C which on further heating decomposes to Co at 1000^{o}C. The UV-Vis spectrum shows bands at the region around 640nm, 480nm an 330-390nm indicating that the ligands are arranged in octahedral geometry around Co^{2+}.The IR spectrum(Table-II) shows bands around 2950$cm^{-1}$and 2850cm^{-1}affirms the presence of piperidine and aliphatic C-H of amines . The presence of a band in the region 1360cm^{-1} indicates the presence of C-N bonds in the complexes. The band in the region 1625cm^{-1}, which is the characteristic feature of Schiff bases, is found in all the complexes[19]. The two bands around 890-1010 cm^{-1} indicated the coordination of the dithiocarbamate moiety occurred in bidentate fashion and that the dithiocarbamate was monoionic [20].The g values calculated from the ESR spectra for the complexes (vanen=2.003,vandien=2.004,salen=2.004) indicated an isotropic environment around the Co(II) ion. The magnetic susceptibility studies of these complexes show an increase in mass in the presence of the magnetic field and the VSM plot of magnetic moment Vs field shows hysteresis loop indicating Ferro magnetism. Observation of loop with a negligible height and the coercivity suggest that in these complexes particles have significantly small size and the complexes are magnetically significant too.

Table-II: IR Spectral data on Schiff Base complexes(cm^{-1})

Complexes	νC-O	νC-H (pip)	νC-H amine	νC=S (asy)	νN-C	νC-S (sym)	νC=N
[Co (vanen)(pmdtc)$_2$]	1111	. 2926	2862	1244	1359	1006, 873	1625
[Co (vandien)(pmdtc)$_2$]	1124	2929	2854	1238	1354	1004, 871	1620
[Co (salen)(pmdtc)$_2$]	1130	2964	2850	1232	1359	1018, 880	1613

Antimicrobial Activities: The data showing diameter of inhibitory zone from anti-bacterial and anti-fungal studies performed by the disc diffusion method are furnished in **Table III and IV.**

Table -III: Anti-bacterial studies of the Schiff base complexes:

Complex	Bacteria	Zone of Inhibition(mm) Concentration(µg/ml)			Antibiotic (1mg/ml)
		1000	750	500	
[Co (vanen)(pmdtc)2]	Staphylococcus aureus	12	10	-	14
	E.coli	12	10	-	14
	Pseudomonas aeruginosa	12	10	-	12
	Aeromonas hydrophila	12	10	-	14
	Vibrio spp.	14	12	-	16
[Co (vandien)(pmdtc)2]	Staphylococcus aureus	14	12	10	14
	E.coli	12	10	-	14
	Pseudomonas aeruginosa	12	-	-	12
	Aeromonas hydrophila	14	12	-	14
	Vibrio spp.	14	12	10	16
[Co (salen)(pmdtc)2]	Staphylococcus aureus	14	-	-	14
	E.coli	14	-	-	12
	Pseudomonas aeruginosa	12	8	-	12
	Aeromonas hydrophila	14	-	-	14
	Vibrio spp.	12	-	-	16

These compounds are found to possess reasonable antibacterial and antifungal activity against Staphylococcus aureus, E.coli, Aeromonas hydrophila, pseudomonas aeruginosa and Vibrio spp.The complexes are found to show no activity against all the bacteriae at lower concentrations whereas the vandien complex shows an activity even at 500µg against Staphylococcus aureus and vibrio spy. The fungicidal activity data on the complexes furnished in Table-IV.

Table IV: Anti-Fungal Studies of schiff base complexes

Complexes	Fungi	Zone of Inhibition(mm) Concentration(µg/ml)			Antibiotic (1mg/ml)
		1000	750	500	
[Co_{ii}(vanen)(pmdtc)2]	Candida albicans	-	-	-	7
	Aspergillus niger	7	4	6	8
	Rhizopus spp.	7	6	5	8
[Co_{ii}(vandien)(pmdtc)2]	Candida albicans	7	6	5	7
	Aspergillus niger	-	-	-	8
	Rhizopus spp.	8	-	-	9
[Co_{ii}(salen)(pmdtc)2]	Candida albicans	9	8	7	8
	Aspergillus niger	14	12	11	13
	Rhizopus spp.	9	8	7	8

indicate that the salen complex possesses excellent fungicidal activity against all the three fungi among the three complexes The vanen complex was found to be inactive against Candida albicans .Similarly the vandien complex was found to be inactive against Aspergilus Niger .The vanen and vandien are found to be more selective in their activity.

Anticancer Activity: The anticancer activities of these complexes were studied using MTT assay on MCF-7 cell line (Breast Cancer). In parallel the activity was studied in VERO cell line (normal cell line .The selectivity index of all the complexes were found to be 8 for vanen and vandien and it was found to be 4 for Salen complexes, indicating the fact that the vanen and vandien can act as better anticancer agents when compared to salen analogue [Selectivity index =IC50 for norml cell line /IC50 for cancerous cell line], indicating considerable activity of the complexes as anticancer agents.

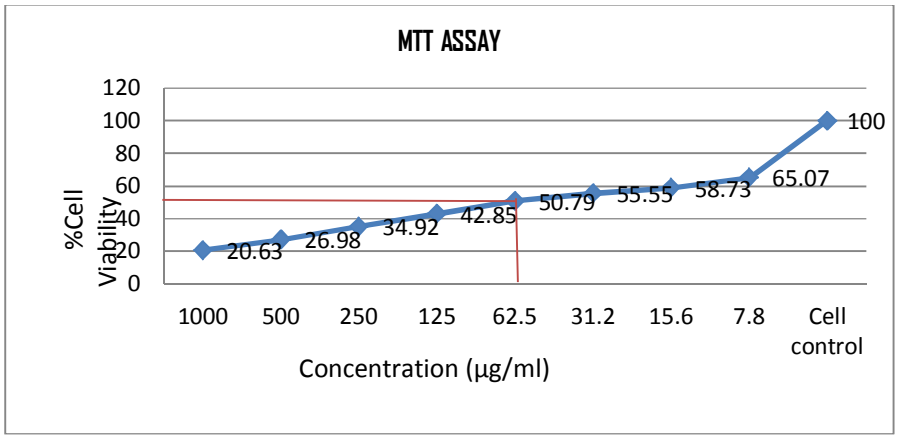

Fig.1: Anticancer activity of Vanen

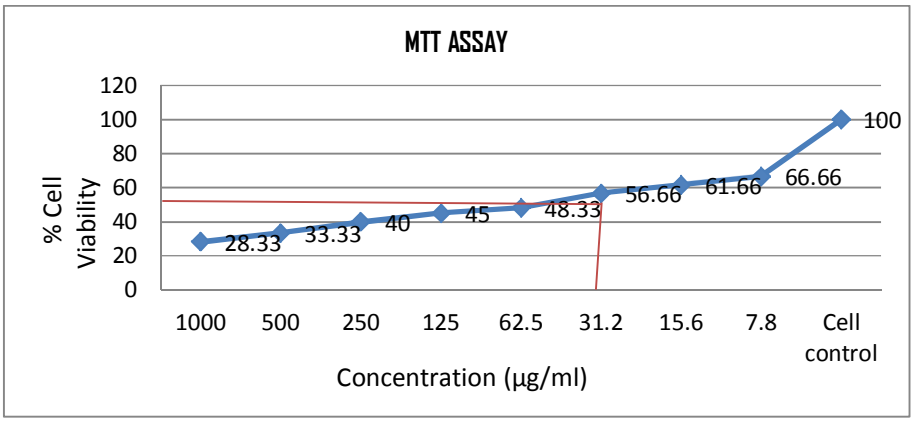

Fig.2: Anticancer activity of vandien

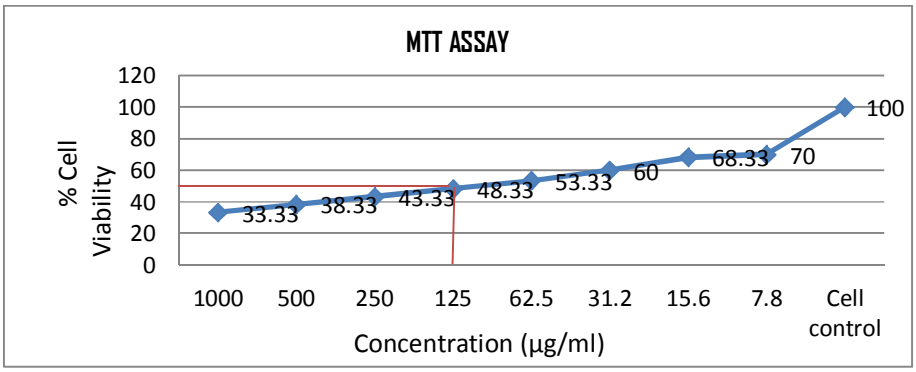

Fig.3: Anticancer activity of Salen

CONCLUSION

The complex from the above elemental and spectral analysis, is proposed to have an octahedral geometry with two dithiocarbamate ligands coordinating in a bidentate fashion through the sulphur atoms and one Schiff base ligand coordinating through the nitrogen atoms. . The antimicrobial studies and the anticancer studies shows promising applications in the field of medicines.

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