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Novel Mn(II) mixed ligand complexes of pentamethylene dithiocarbamate and schiff base: Synthesis, spectroscopic investigation and biological activity

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ABSTRACT

A new series of binuclear Mn(II) mixed ligand complexes containing pentamethylene dithiocarbamate (pmdtc) and schiff base formed from Salicaldehyde/ Vanillin and diamines such as ethylene diamine and diethylene triamine (salen,vanen,saldien,vandien) have been synthesized and characterized by elemental and thermal analysis, UV-Vis, IR,EPR Spectral studies and magnetic susceptibility studies. In order to evaluate the effect of Mn(II) upon simultaneous chelation to both pmdtc and Schiff base,the complexes have been screened for antibacterial, antifungal and anticancer activities which shows promising activity towards some of the tested microorganisms.

Keywords: Cobalt Mn(II), Pentamethylene dithiocarbamate along with Schiffbase Antibacterial, antifungal, Anticancer activity.

1. INTRODUCTION

The dithiocarbamates and their metal complexes have received much attention due to their diverse applications in material science, medicine and agriculture and also possess interesting structural chemistry that make their study continuously attractive [1-9]. Metal complexes of dithiocarbamates with nitrogenousbase such as piperidine, 1, 10 phenanthroline.picoline, pyridine have been well studied by several researchers[10-18]. However, literature reports on dithiocarbamate complexes containing schiff bases are scarce [19]. Schiff bases are known to have biological activities such as antibacterial, antifungal, antitumour and herbicidal [20-22]. A Wide range of applications of dithiocarbamates and various aspects of bioactivity of Schiff bases prompted us to attempt mixed ligand complexes containing the above two ligands. The present study describes the synthesis, spectroscopic studies, antibacterial, antifungal and anticancer activity of binuclear Mn(II) mixed ligand complexes containing pentamethylane dithiocarbamate and schiff base (derived from from salicaldehyde/vanillin with diamines).

2. EXPERIMENTAL

The chemicals employed for the preparation are of pure grade and used without further purification. The Manganese sulphate used for the synthesis is of analytical grade. piperidine, carbon disulphide, ethylene diamine, diethylenetriamine, salicyaldehyde and vanillin are pure grade chemicals from Merck. The chloroform used as solvent in all our studies is distilled by standard procedures. Preparation of pmdtc: The ligand was prepared as follows: To a solution of piperidine(0.05mol) in chloroform(5ml) constantly stirred in ice added 4ml of sodium hydroxide (10N) and carbon disulphide(3ml,0.05 mol) for about 30 minutes, sodium salt of dithiocarbamate precipitated out. The obtained precipitate was washed with ether and dried in vacuum. Preparation of Schiff base: To 1mmol of diamines added 2mmol of salicyaldehyde/vanillin in 10ml of alcoholic medium, yellow precipitate was obtained which was filtered and dried in oven at 60^{o} C.The complexes were synthesized by mixing aqueous solution of $MnSO_4.H_2O$(1mmol) and aqueous solution of pmdtc (2mmol) to the schiff base in alcohol with continuous stirring for 10 minutes. The formed precipitate was filtered off, washed with water and alcohol several times and dried in vaccum. The synthesized complexes were characterized by elemental analysis (Nitrogen - kjelhdhal's method metal -ICPOES- Inductively Coupled Plasma optical emission spectroscopy-PerkinElmer Optima 5300 spectrometer, Sulphur –gravimetrically by barium sulphate method),thermal analysis-(TGA were recorded in

nitrogen atmosphere using NETZSCH STA 490C/CD thermal analyser with a heating rate of 10° C/min), UV-Visible absorption spectra (as solution in chloroform- a schimadu UV 1600 model spectrometer),Infra spectrum (as KBr disc - schimadzu spectrometer) and EPR Spectra (JES-FA 200 electron spin resonance spectrometer in the region from 1000-8000 guass). Magnetic suspectibility studies were carried out using Vibrating magnetometer Lakeshore VSM 7410. The antibacterial and antifungal studies were carried out by using agar disc diffusion method originally described by Baeur [23]. The invitro cytotoxicity of the prepared complexes were carried out by MTT based assay [24] with cancer cell line, MCF-7(human breast cell line). In parallel the activity was tested on normal cell line VERO (monkey kidney cell line).

3. RESULTS AND DISCUSSION

The complexes are stable, non-hygroscopic and brown colored solids. All the complexes were found to be completely soluble in chloroform, partially soluble in DMSO and DMF and insoluble in alcohol and 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 [25]. The elemental analysis data of the complexes given in table 1 confirm the proposed composition of the complexes. $[Mn_2(pmdtc)_2$(Salen/Saldien,Vanen/Vandien) $_2(H_2O)_2 SO_4]$. The thermal analysis data from TGA for the four complexes are furnished in table-1.The thermograms were run upto 1000° C and final residue corresponds to manganese sulphide. The relevant bands in the Infra-Red spectra of the mixed ligand complexes are given in table 2. The bands which appear in the region 1654 -1615 cm-1 was assigned to ν N=C and it is a characteristic feature of schiff base whereas ν O-H(broad) of water molecules appears around 3400cm-1.The aliphatic C-H of amine appears around 2860 cm-1.The bands around 970cm^{-1} which is assigned to ν C-S of dithiocarbamate moiety and indicates the ligand is bidendate and monoionic [26].The bands in the region 1250-1350cm^{-1} is assigned to ν N-C stretching vibration, whereas bridging SO_4 appears as three bands in the region 1010-1138cm^{-1} [27]. The two bands in the region between 410 and 520 cm^{-1} are associated with νM-S and ν M-N vibrations respectively. This may be considered as an evidence for the coordination of metal to sulphur [28]. The electronic spectra of the complexes shown in table 1. The peaks in the region at 390-520 nm corresponds to the presence of an octahedral environment of the ligands around the Mn(II) [29].

Table - 1: Elemental composition, Thermal analysis and electronic absorption spectral data

Complexes	% Nitrogen (theo) exp	% inorg Sulphur (theo) exp	% org Sulphur (theo) exp	% metal (theo) exp	% of Residue TGA (theo) Exp	λmax (nm)
$[Mn_2(pmdtc)_2(Vanen)_2(H_2O)_2.SO_4]$	(6.68) 6.23	(2.62) 2.32	(10.48) 10.25	(9.00) 8.73	(14.24), 14.32	385, 490
$[Mn_2(pmdtc)_2(Vandien)_2(H_2O)_2.SO_4]$	(8.57) 7.96	(2.45) 2.32	(9.80) 8.99	(8.41) 8.23	(13.30) 13.27	485, 530
$[Mn_2(pmdtc)_2(Salen)_2(H_2O)_2.SO_4]$	(7.63) 7.35	(2.91) 2.13	(11.63) 11.23	(9.98) 9.34	(15.80) 15.30	436
$[Mn_2(pmdtc)_2(Saldien)_2(H_2O)_2.SO_4]$	(9.44) 9.25	(2.70) 1.99	(10.78) 10.05	(9.26) 9.12	(14.65) 14.32	430, 520

Table - 2: IR Spectral data (νcm^{-1})

Complexes	νO-H	νN=C	νN-C	νC-S	Bridging SO_4 units	νM-S	νM-N
$[Mn_2(pmdtc)_2(Vanen)_2(H_2O)_2.SO_4]$	3402	1654	1336	954	1122,1138,1010	459	513
$[Mn_2(pmdtc)_2(Vandien)_2(H_2O)_2.SO_4]$	3415	1654	1334	952	1163,1120,1012	434	530
$[Mn_2(pmdtc)_2(Salen)_2(H_2O)_2.SO_4]$	3446	1631	1332	960	1141,1114,1010	464	501
$[Mn_2(pmdtc)_2(Saldien)_2(H_2O)_2.SO_4]$	3390	1616	1350	960	1138,1116, 1010	462	514

All the complexes give a single peak in the EPR spectrum and the g value was calculated to be around 2.0 confirming the presence of high spin d^5 system of Mn (II).The magnetic suspectibility studies shows an increase in mass in the presence of magnetic field. The VSM plot of magnetic moment in emu vs. field shows hysteresis loop indicating ferromagnetism and negligible height loops and the coercivity suggest that these complexes have significantly small size.

Table - 3: Anticancer activity in MCF-7 cell line

Complexes	Concentration (µg/ml)	Absorbance (O.D)	cell viability (%)
$[Mn_2(pmdtc)_2(Vanen)_2(H_2O)_2.SO_4]$	1000	0.05	9.25
	500	0.07	12.96
	250	0.1	18.51
	125	0.12	22.22
	62.5	0.15	27.77
	31.2	0.19	35.18
	15.6	0.21	38.88
	7.8	0.23	42.59
	Control	0.54	100
$[Mn_2(pmdtc)_2(Vandien)_2(H_2O)_2.SO_4]$	1000	0.02	3.7
	500	0.04	7.4
	250	0.06	11.11
	125	0.09	16.66
	62.5	0.11	20.37
	31.2	0.13	24.07
	15.6	0.18	33.33
	7.8	0.22	40.74
	Control	0.54	100
$[Mn_2(pmdtc)_2(Salen)_2(H_2O)_2.SO_4]$	1000	0.03	5.55
	500	0.08	14.81
	250	0.14	25.92
	125	0.16	29.62
	62.5	0.2	37.03
	31.2	0.24	44.44
	15.6	0.26	48.14
	7.8	0.28	51.85
	Control	0.54	100
$[Mn_2(pmdtc)_2(Saldien)_2(H_2O)_2.SO_4]$	1000	0.04	7.4
	500	0.06	11.11
	250	0.09	16.66
	125	0.12	22.22
	62.5	0.16	29.62
	31.2	0.2	37.03
	15.6	0.25	46.29
	7.8	0.29	53.7
	Control	0.54	100

3.1. BIOLOGICAL STUDIES

3.1.1. Anticancer property

The invitro cytotoxicity activity of Mn (II) mixed ligand complexes of dithiocarbamate with schiff base formed from vanen/vandien/salen/saldien was performed against MCF-7 cell line(Breast cancer cell line) and was compared against the VERO cell line (normal cell line) (Figure 1-4) (Table 3). All the four complexes show moderate activity against the cancer cells but seems to have less toxicity towards normal cells. The selectivity index of all the complexes was found to be 8. [Selectivity index= IC_{50} of the normal cell line /$IC_{50}$of the cancerous cell line]. This is indicative of the fact that all the complexes show considerable activity with less side effects.

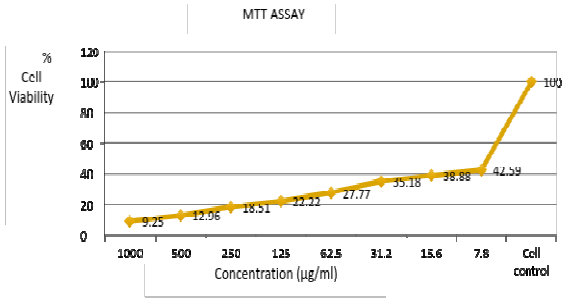

Figure - 1: Anticancer activity of MCF-7 on $[Mn_2(pmdtc)_2(Vanen)_2(H_2O)_2.SO_4]$.

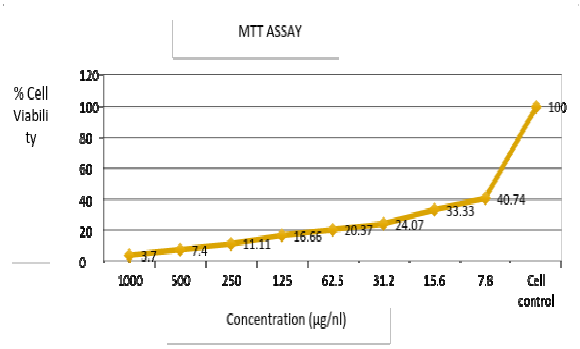

Figure - 2: Anticancer activity of MCF-7 on $[Mn_2(pmdtc)_2(Vandien)_2(H_2O)_2.SO_4]$.

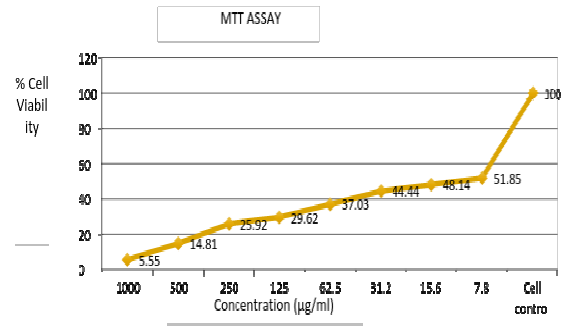

Figure - 3: Anticancer activity of MCF-7 on $[Mn_2(pmdtc)_2(salen)_2(H_2O)_2.SO_4]$.

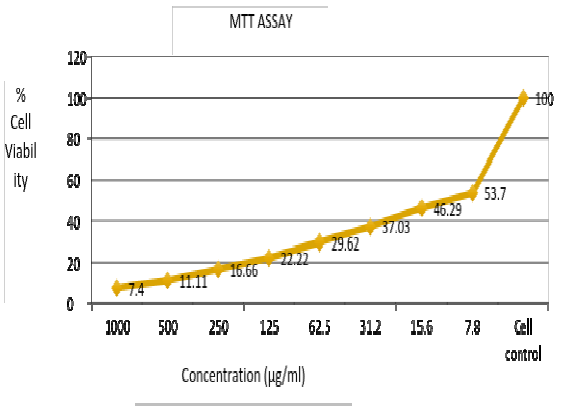

Figure - 4: Anticancer activity of MCF-7 on $[Mn_2(pmdtc)_2(Saldien)_2(H_2O)_2.SO_4]$.

3.1.2. Antimicrobial studies

Antimicrobial studies was performed on five bacterial species namely Bacillius subtilis, Staphylococcus auerus, Escherichia coli, Aeromonas Spp and Vibrio Parahemolyticus and three fungus namely Candida albicans, Trichoderma viride and Aspergillus niger. The results for the complexes and commercial antibiotics used as positive control are listed in table 4 and 5. With increasing concentration of the complexes, an increase in the diameter of the zone of inhibition was observed indicating the complexes show better antibacterial and antifungal activity. The vanen and vandien complexes were found to be inactive against E.coli. Vandien and Saldien were found to be inactive against Vibrio parahemolyticus even at high concentrations. In case of antifungal studies, vanen and saldien complex do not show any activity towards *Aspergillus niger* even at higher concentrations.

Table - 4: Antibacterial studies

Complexes	Organisms	Zone of inhibition			Antibiotic
	Concentration (µg/mL)	1000	750	500	(1mg/mL)
$[Mn_2(pmdtc)_2(Vanen)_2(H_2O)_2.SO_4]$	*E.coli*	-	-	-	12mm
	Aeromonas Spp	-	-	-	10mm
	Staphylococcus aureus	8mm	6mm	-	17mm
	Vibrio Parahemolyticus	9mm	8mm	5mm	16mm
	Bacillus Subtilis	10mm	7mm	6mm	18mm
$[Mn_2(pmdtc)_2(Vandien)_2(H_2O)_2.SO_4]$	*E.coli*	-	-	-	10mm
	Aeromonas Spp	9mm	7mm	6mm	12mm
	Staphylococcus aureus	7mm	6mm	5mm	15mm
	Vibrio Parahemolyticus	-	-	-	11mm
	Bacillus Subtilis	10mm	8mm	6mm	17mm
$[Mn_2(pmdtc)_2(Salen)_2(H_2O)_2.SO_4]$	*E.coli*	7mm	6mm	5mm	9mm
	Aeromonas Spp	9mm	8mm	7mm	11mm
	Staphylococcus aureus	10mm	9mm	7mm	15mm
	Vibrio Parahemolyticus	7mm	6mm	5mm	16mm
	Bacillus Subtilis	8mm	7mm	5mm	15mm
$[Mn_2(pmdtc)_2(Vandien)_2(H_2O)_2.SO_4]$	*E.coli*	8mm	7mm	6mm	10mm
	Aeromonas Spp	9mm	8mm	7mm	11mm
	Staphylococcus aureus	10mm	8mm	7mm	15mm
	Vibrio Parahemolyticus	-	-	-	12mm
	Bacillus Subtilis	8mm	7mm	6mm	15mm

Table - 5: Antifungal studies

Complexes	Organisms	Zone of inhibition			Antiobiotic
	Concentration (µg/mL)	1000	750	500	(1mg/mL)
$[Mn_2(pmdtc)_2(Vanen)_2(H_2O)_2.SO_4]$	Candida albicians	8mm	7mm	6mm	10mm
	Trichoderma Viridi	9mm	8mm	7mm	11mm
	Aspergillus niger	-	-	-	7mm
$[Mn_2(pmdtc)_2(Vandien)_2(H_2O)_2.SO_4]$	Candida albicians	10mm	9mm	7mm	12mm
	Trichoderma Viridi	12mm	11mm	10mm	14mm
	Aspergillus niger	8mm	7mm	6mm	9mm
$[Mn_2(pmdtc)_2(Salen)_2(H_2O)_2.SO_4]$	Candida albicians	8mm	7mm	-	11mm
	Trichoderma Viridi	10mm	8mm	6mm	13mm
	Aspergillus niger	10mm	8mm	7mm	12mm
$[Mn_2(pmdtc)_2(Saldien)_2(H_2O)_2.SO_4]$	Candida albicians	10mm	9mm	7mm	12mm
	Trichoderma Viridi	12mm	11mm	10mm	14mm
	Aspergillus niger	8mm	7mm	6mm	9mm

4. CONCLUSION

From the above data and various spectral studies, it was concluded that the complexes contain two Mn(II) linked by a bridging sulphate molecule.The two Mn(II) in the complexes have an octahedral environment with the dithiocarbamate in bidentate fashion through two sulphur ,one aquo ligand and one schiff base , coordinating through two nitrogen atoms . The

investigations revealed that the complexes acts as better antimicrobial and anticancer agents towards the tested organisms and cell lines.

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