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Synthesis, Characterisationand Study Of Biological Application Of Simple Mixed Ligand Complexes Of Nickel (II) With morpholine dithiocarbamate and Amines Such as Ethylene Diamine, Diethylenetriamine and Triethylenetetramine.

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ABSTRACT

Simple mixed ligand complexes of nickel(II) with morpholinedithiocarbamate and aminessuch asethylene diamine(en),diethylenetriamine(dien), and triethylenetetramine(trien) have been synthesized and characterized by elemental and thermal analysis, IR, UV-Vis and ESRspectral studies, and magnetic susceptibility studies.Antibacterial, and Antifungal and activities have also been carried out on these complexes. All the complexes have shown reasonable activity.

Keywords : Mixed ligand nickel(II) en/dien/trien - morpholinedithiocabamate complexes, anti bacterial, antifungal activities .

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INTRODUCTION

The coordination chemistry of dithiocarbamates has been a major subject of great research interest for a number of years [1-6] .Organic dithiocarbamates are valuable synthetic intermediates[7], which are ubiquitously found in variety of biologically active compounds. Dithiocarbamates and their metal complexes have invited much research attention due to their diverse applications and interesting biological, structural, magnetic, electrochemical and thermal properties[8-14]. Dithiocarbamates are a class of metal- chelating ,antioxidant compounds with various applications in medicines for the treatment of bacterial, fungal infections[15] and even as a possible treatment for AIDS.They are used as accelerators in vulcanization, as high-pressure lubricants, in agricultural field as pesticides, analytical and organic chemistry fields[16-25]. While dithiocarbamates have been known for over a century now, with many thousands having been prepared ,the vast majority of these contain only simple alkyl substituents. A developing interest in the area of dithiocarbamate chemistry is the functionalization of backbone such that new applications and interactions can be developed . This area is still in its early stages but already interesting applications have been done including the functionalisationof gold particles , the stepwise build up of multi- metallic arrays , the synthesis of dithiocarbamate-containing supramolecular systems which can be used for anion binding , the development of technetium radiopharmaceuticals , etc[26-28].

Experimental Section

The chemicals employed for the preparation are of very pure grade and usedwithout further purification. The Nickel chloride used for the synthesis is of analytical grade . Morpholine , carbon disulphide, Ethylene diamine, diethylenetriamine, triethylenetetraamine are pure grade chemicals from Merck chemicals . The chloroform used as solvent in all our studies is distilled by standard procedures. The complexes [Ni(amine)(Morpdtc)$_2$] Where amine stands for en/dien/trienwere prepared by adding equi molar volumes of carbon disulphide to Morpholine and chloroform with constant stirring under ice cold conditions[2^o-4^{o}C] which is added to an equi molar solution of NaOH in water. A white solid obtained. Then half the molar quantity of Nickel chloride in water in the presence of same molar quantity of amine (en/dien/trien) were added to Morpholinedithiocarbamate with constant stirring. A green precipitate was formed which was filtered and dried in an air oven at 60^{o}C and recrystallised from chloroform.The nickel present in the complex was estimated gravimetrically as [Ni(DMG)$_2$] where DMG is dimethyl glyoxime. The nitrogen and sulphur was estimated by Kjelhdhal's method and bariumsulphate method respectively.TG/DSC were recorded in NETZSCH STA 449F3 thermal analyser with a heating rate of 10^0/min Magnetic susceptibility studies were carried out using Vibrating magnetometer Lakeshore VSM 7410.UV-Visible absorption spectra wererecored using a Shimadzu UV 1600 model spectrometer. The IR spectrum of the complexes were recorded asKBr disc using SCHIMADZU Spectrometer. The EPR spectra of the en complex was recorded using JES-FA200 electron spin resonance spectrometer in the region from 1000-8000 gauss.The anti-bacterial activities of the complexes were studied by agar disc diffusion method[29].

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RESULTS AND DISCUSSION

TABLE-I Elemental composistion and Electronic spectral data

Complexes	%N (theo) exp	%s (theo) exp	%Ni (theo) exp	Λ_{max}(nm)
$[Ni^{II}(en)(Morpdtc)_2]$	(12.64) 13.01	(28.89) 28.60	(13.25) 13.20	359,401,425,446
$[Ni^{II}(dien)(Morpdtc)_2]$	(14.40) 14.88	(26.34) 26.57	(12.08) 13.09	386,398,428
$[Ni^{II}(trien)(Morpdtc)_2]$	(15.88) 15.23	(24.19) 24.87	(11.09) 11.70	380,398,431

TABLE-II Thermal decomposistion studies data

Complexes	Residue% TGA (theo)exp	Point of inflection DTG (^{0}C)	DSCdata(temp^{0}C)enthalpychange(j/g)
$[Ni^{II}(en)(Morpdtc)_2]$	(20.47) 22.75	375.5,743.0	376.5(84.36) 774.4(451.5)
$[Ni^{II}(dien)(Morpdtc)_2]$	(18.6) 18.75	371.1,742.6	372.9(57.17) 770.7(391.9)
$[Ni^{II}(trien)(Morpdtc)_2]$	(17.14) 18.0	181.5,240.5,273.5	179.7(64.56) 234.5(150.3) 782.5(138.2)

TABLE-III IR spectral data

Complexes	ν_{N-H}	$\nu_{C-H(morpholine)}$	$\nu_{C-H(amine)}$	$\nu_{C=s}$	ν_{N-C}	ν_{C-S}
$[Ni^{II}(en)(Morpdtc)_2]$	3437	2966.	2914, 2854	1641.,1492. 1487	1355, 1301,1265	1018
$[Ni^{II}(dien)(Morpdtc)_2]$	3419	2929	2877	1479	1332	1002
$[Ni^{II}(trien)(Morpdtc)_2]$	3431	2964	2910, 2854.	1635,1585.,1492	1357, 1307	1014

Table IV: Antibacterial studies

Complexes	ORGANISM	Zone of Inhibition Concentration(µg/ml)			Anibiotic (1mg/ml)
		1000	750	500	
$[Ni^{II}(en)(Morpdtc)_2]$	E. coli	7mm	5mm	2mm	10mm
	Pseudomonas aeruginosa	9mm	7mm	6mm	11mm
	Staphylococcus aureus	9mm	7mm	7mm	15mm
	Bacillus spp	7mm	7mm	6mm	15mm
	Vibrio parahaemolytics	6mm	5mm	3mm	11mm
$Ni^{II}(dien)(Morpdtc)_2]$	E. coli	7mm	6mm	5mm	10mm
	Pseudomonas aeruginosa	7mm	4mm	2mm	11mm
	Staphylococcus aureus	9mm	7mm	6mm	13mm
	Bacillus spp	9mm	7mm	5mm	14mm
	Vibrio parahaemolytics	6mm	4mm	3mm	10mm
$[Ni^{II}(trien)(Morpdtc)_2]$	E. coli	6mm	5mm	3mm	10mm
	Pseudomonas aeruginosa	9mm	7mm	6mm	12mm
	Staphylococcus aureus	11mm	9mm	6mm	10mm
	Bacillus spp	8mm	7mm	6mm	15mm
	Vibrio parahaemolytics.	6mm	5mm	3mm	10mm

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Table V: Antifungal studies

Complexes	ORGANISM	Zone of Inhibition Concentration(µg/ml)			Anibiotic (1mg/ml)
		1000	750	500	
$[Ni^{II}(en)(Morpdtc)_2]$	Candida albicans	6mm	5mm	5mm	6mm
	Aspergillusflavours	8mm	7mm	5mm	9mm
	Pencillium spp.	8mm	7mm	5mm	10mm
	Aspergillusniger	3mm	2mm	1mm	6mm
	Trichophyton	7mm	6mm	5mm	8mm
$Ni^{II}(dien)(Morpdtc)_2]$	Candida albicans	5mm	5mm	2mm	6mm
	Aspergillusflavours	8mm	7mm	5mm	9mm
	Pencillium spp.	8mm	7mm	5mm	10mm
	Aspergillusniger	3mm	2mm	1mm	6mm
	Trichophyton	7mm	6mm	5mm	8mm
$[Ni^{II}(trien)(Morpdtc)_2]$	Candida albicans	5mm	5mm	2mm	6mm
	Aspergillusflavours	6mm	5mm	4mm	9mm
	Pencillium spp.	7mm	6mm	6mm	10mm
	Aspergillusniger	3mm	2mm	1mm	5mm
	Trichophyton	6mm	5mm	5mm	7mm

The elemental analysis data on the complexes Table-I confirm the proposed composition$[Ni(en)(morphdtc)_2]$,$[Ni(dien)(morphdtc)_2]$, $[Ni(trien)(morphdtc)_2]$ .All the complexes were found to be completely soluble in chloroform,partially soluble in DMSO and DMF and insoluble in alcohol and water . The thermal analysis data from TGA/DSC on the three complexes are furnished in Table-II . Thethermograms were run upto 1000^0C.The complex starts decomposing around 60^oC indicating less thermal stability.The final product of decomposition corresponded to Nickel Sulphide. The IR spectral data on the complexes are given in Table -III.The bands around 3400cm^{-1} is assigned to υ_{N-H}.The bands around 3000cm^{-1}corresponds to υ_{C-H} of the Morpholine ring while the aliphatic C-H of the amine part appear around 2800cm^{-1} and 2900cm^{-1}.The bands in the region 1480-1680cm^{-1} corresponds to C=S stretching.The bands around 1000cm^{-1} corresponds to υ_{C-S}.The bands in the region 1250-1350cm^{-1} corresponds to N-C stretching. The electronic spectral data are presented in Table I. The spectra of the complexes show two peaks in the regions 395-425nm and 425-450nm. As the complexes are ferromagneticand EPR active, these values must correspond to strong field distorted octahedral Ni(II) . The peak in the region around 380nm is assigned to Metal to Ligand charge transfer[31].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 in emu Vs field shows hysteresis loop indicating Ferro magnetism.As the electronic spectral studies indicate near octahedral environment, a dimeric or polymeric structure through the C=S sulphur of the dithiocarbamate moiety[31] is expected.The EPR spectrum of the complex,Figure-1, of $[Ni^{II}(en)(Morpdtc)_2]$ showed two signals corresponding to $g_\perp$at 2.012 and $g_\parallel$ at 1.948.It is evident from the perpendicular signal that there is coupling with two nitrogen atoms which resulted in the quintet in the ratio 1:2:3:2:1. This perhaps proves the point that Nickel is Octahedrally surrounded by two dithiocarbamate ligands and one ethylene diamine. All the complexes thus have a near Oh arrangement about Ni(II) with two chelated morpholinedtc units and an amine coordinating through two NH_2 Nitrogen atoms.

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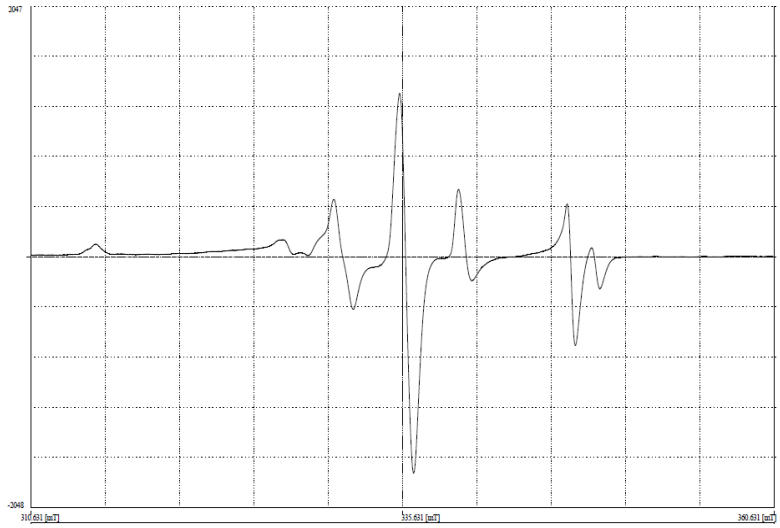
FIGURE 1 EPR Spectrum of $[Ni^{II}(en)(Morpdtc)_2]$



Biological Studies

Antibacterial studies of all the three complexes studied using the disc diffusion method indicated that the complexes are highly active against all the five bacteriastudied namely Staphylococcus aureus, Salmonella subtilis, Bacillus subtilis, E. coli and Pseudomonas aeruginosa compared to the standard antibioticampicillin. The diameter of the inhibitory zone from anti bacterial studies are presented in Table IV.As the concentration of the complex increases, the diameter of the inhibitory zone also increases indicating that the complexes are active. In fact the trien complex shows better activity against staphylococcus aureus compared to the standard antibiotic.Antifungal activities of all the three complexes show good activity against the fungus namely Candida albicans, Aspergillus flavors, Pencillium Spp. Aspergillusniger, Trichophyton. The diameter of the inhibitory zone from antifungal studies are presented in the Table V.As the concentration of the complex increases, the diameter of the inhibitory zone also increases indicating an increased activity.In fact the en complex shows equal activity as standard (Amphotericin B) against Candida albicans.

CONCLUSION

Extensive biological application of dithiocarbamate complexes such as antibacterial, antiviral, antifungal etc have made study on dithiocarbamate complexes highly sought after by chemist. The dithiocarbamate complexes reported here are found to be equally outstanding.The need for such studies leading to the development of new therapeutic strategies against bacterial infection becomes more significant and need of the hour,as bacterial drug resistance to currently administered treatments is ever increasing. We need to venture into complexes of better activity by cautious choice of metal/ligands which will lead us to a better future.

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