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Nickel(II) complexes of m-ethylphenylxanthate with nitrogen donors and their biological screening

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A series of five adducts of m-ethylphenylxanthate of nickel(II) [(m-$C_2H_5C_6H_4OCS_2)_2$Ni] with nitrogen donors have been synthesized in 1:2 molar ratio by the reaction of aqueous solution of $NiCl_2.6H_2O$ with aqueous solution of sodium salt of m-ethylphenylxanthate. These metal complexes are reacted with nitrogen donors to give donor stabilized complex, [(m-$C_2H_5C_6H_4OCS_2)_2(L)_2$Ni] where, L= 2-, 3-, 4-ethylpyridine and 2-, 3-chloropyridine. The adducts have been characterized by elemental analysis, molar conductance and magnetic susceptibility measurements, IR, electronic, mass spectral studies, thermogravimetric analysis, powder X-ray diffraction, biological studies. The spectral studies have revealed the octahedral coordination of ligands around Ni(II) metal ion. The adducts are found to be paramagnetic and non-ionic in nature. Mass studies show the monomeric nature of the adducts. The complexes have depicted potential antifungal activity against *Bipolaris maydis* and *Rhizoctonia solani*. Some of the synthesized Ni(II) xanthate complexes display *in vitro* cytotoxic efficacy against human cancer cell lines.

Keywords: m-Ethylphenylxanthate, Monomeric, Paramagnetic, Pyridine, Thermogravimetric analysis

Xanthates are the ligands containing sulphur and oxygen, which gives diverse and abundant coordination complexes with transition and main group metals.[1] These are known as dithiocarbonates. The chemistry of transition metal xanthates holds much attention due to their importance in the field of metalloenzymes, material precursors, metallurgy and catalysts.[2-4] Metal xanthates are extensively used as fungicides, pesticides, rubber accelerators, corrosion inhibitors, reagents in agriculture and for treating HIV infections.[5-9]. Xanthates are much efficient for removing heavy metals from waste water due to their low solubility products and high stability constants[10]. Xanthates inhibit the replication of both DNA and RNA viruses *in vitro* and therefore, possess enhanced antiviral and antitumor activity[11,12]. The discovery of urease (a nickel containing enzyme) has expanded the significance of nickel in bioinorganic chemistry[13]. Nickel is an essential cofactor of enzymes found in eubacteria, archaebacteria, fungi and plants [14-16]. These enzymes catalyse many redox and non- redox reactions in the living organisms [17]. Nickel(II) complexes are the most promising anticancer drugs in comparison to the traditional cisplatin[18-20]. The present investigation reported the synthesis and characterization of adducts of m-ethylphenylxanthates of nickel(II) with nitrogen donors (substituted pyridines) by various physico-chemical techniques and their biological importance.

Materials and Methods

Toluene and n-hexane were freshly dried over sodium wire. Dichloromethane and methanol were dried over P_2O_5 and $CaCO_3$, respectively. m-ethylphenol was purified by distillation before use. Carbon, hydrogen, nitrogen and sulphur analysis was carried out on elemental analyzer (CHNS-932, LECO Corporation, USA). Molar conductance was measured in DMF (10^{-3}M) at room temperature using a digital conductivity meter "Century CC 601" and a conductivity cell with cell constant 1. Magnetic susceptibility of adducts was recorded at room temperature by VSM method. Infrared (IR) spectra of adducts over the region 4000-400 cm^{-1} was recorded on "Perkin Elmer FTIR spectrophotometer" using KBr pellet. Systronics 119 UV-visible spectrophotometer was used to record electronic spectra in the range of 12500-40000 cm^{-1} and ESI-

MS spectrophotometer was used to record mass spectra of the compounds. Thermogravimetric analysis (TGA/DTA) of complexes was recorded on Linseis STA-PT-thermoanalyzer. Powder X-ray diffraction (XRD) was done on diffractometer system XPERT-PRO. FESEM was carried out at different magnifications on Hitachi-PU 5.0 kV LA30(UL). The antifungal activity of complexes was performed using Poisoned Food Technique and *in vitro* anticancer activity was tested using Sulphorhodamine Blue (SRB) assay

Preparation of sodium salt of m-ethylphenylxanthate

Sodium salt of dithiocarbonate was prepared using standard protocol[21]. Sodium metal (0.74 g, 0.26 mol) was added to a toluene solution of freshly distilled m-ethylphenol (31.6 mL, 0.26 mol). The contents were refluxed for three hours till white precipitates started appearing. When sodium metal was completely dissolved, CS_2 (1.95 mL, 0.26 mol) was added subsequently to the reaction mixture at 15 °C and stirred for 3 h. The compound was isolated by filtration using alkoxy funnel fitted with G-4 sintered disc and dried under reduced pressure in a vacuum pump that lead the formation of m-$C_2H_5C_6H_4OCS_2Na$ as pale yellow solid.

Preparation of Bis(m-ethylphenylxanthato)nickel(II) complex

The aqueous solutions of sodium salt of m-ethylphenylxanthate (4.4 g, 0.02 mol) and $NiCl_2.6H_2O$ (2.37 g, 0.01 mol) were mixed when green coloured precipitates appeared, which were filtered using alkoxy funnel and dried under reduced pressure in a vacuum pump.

Preparation of 1:2 adducts with nitrogen donors

(a) Bis(m-ethylphenylxanthato)bis(2-ethylpyridine)nickel(II)

A weighed amount of [(m-$C_2H_5C_6H_4OCS_2)_2Ni$] (1.18 g, 0.0026 mol) was dissolved in dichloromethane and to this a dichloromethane solution of 2-ethylpyridine (0.59 mL, 0.0052 mol) was added with constant stirring at room temperature. After stirring for 3-4 h, the reaction mixture was refluxed for 15 min for the sake of completion of reaction. The excess of dichloromethane was evaporated in vacuum that lead the formation of the adduct [(m-$C_2H_5C_6H_4OCS_2)_2(C_7H_9N)_2$ Ni] as dark green solid.

(b) Bis(m-ethylphenylxanthato)bis(3-ethylpyridine)nickel(II)

The adduct was prepared by the same procedure as described above in (a), but instead of 2-ethylpyridine, 3-ethylpyridine (0.59 mL, 0.0052 mol) was added. The compound was found to be [(m-$C_2H_5C_6H_4OCS_2)_2(C_7H_9N)_2Ni$] as dark green solid by elemental analysis.

(c) Bis(m-ethylphenylxanthato)bis(4-ethylpyridine)nickel(II)

The adduct was prepared in the same manner as described above, but in this case, 4-ethylpyridine (0.59 mL, 0.0052 mol) was added to the dichloromethane solution of bis(m-ethylphenyldithiocarbonato)nickel(II) with constant stirring at room temperature and then refluxing for 15 min to complete the reaction. Excess of the solvent was evaporated in vacuum, which gives green coloured adduct. The composition of the adduct was found to be [(m-$C_2H_5C_6H_4OCS_2)_2(C_7H_9N)_2Ni$] by elemental analysis.

(d) Bis(m-ethylphenylxanthato)bis(2-chloropyridine)nickel(II)

A weighed amount of [(m-$C_2H_5C_6H_4OCS_2)_2Ni$] (1.18 g, 0.0026 mol) was dissolved in dichloromethane and to this a dichloromethane solution of 2-chloropyridine (0.49 ml, 0.0052 mol) was added with constant stirring at room temperature. After stirring for 3-4 h, the reaction mixture was refluxed for 15 min for the sake of completion of reaction. The excess of dichloromethane was evaporated in vacuum, that results in the formation of the adduct [(m-$C_2H_5C_6H_4OCS_2)_2(C_5H_4NCl)_2Ni$] as dark green solid.

(e) Bis(m-ethylphenylxanthato)bis(3-chloropyridine)nickel(II)

The adduct was prepared in the same manner as described above in (d), but instead of 2-chloropyridine, 3-chloropyridine was added to the dichloromethane solution of bis(m-ethylphenylxanthate)nickel(II) with constant stirring at room temperature and then refluxing for 15 min to complete the reaction. Green coloured adduct was obtained and the composition was found to be [(m-$C_2H_5C_6H_4OCS_2)_2(C_5H_4NCl)_2$ Ni] by elemental analysis.

Biological Studies

Antifungal Studies

Potato dextrose agar (PDA) medium was prepared in a flask and sterilised. The test solutions were prepared by dissolving the compounds in DMSO. The test solutions were mixed in the nutrient medium (PDA) and then discharged in the petridishes inside the laminar flow. After solidification, the petridishes were inoculated (using a cork borer) with 7 days old culture of the fungus *Bipolaris maydis* and

Rhizoctonia solani, separately by placing 2 mm bit in the center of the petridishes. The petridishes were incubated at 27 °C for 4 days. The radial growth of fungus determines the efficiency of each test sample. The linear fungal growth in controlled manner was measured at various concentrations of the test sample. The percent inhibition of the fungus over control was calculated as:

$$\% \text{ Inhibition (I)} = ((C - T)/C) \times 100,$$

where C is the diameter of the fungus colony in the control plate after 4 days and T is the diameter of the fungus colony in the tested plate after 4 days.

Cytotoxic studies

The complexes were subjected to *in vitro* anticancer activity against various human cancer cell lines (Monks et al.)[22]. In brief, the cells were grown in tissue culture flasks in growth medium at 37 °C in an atmosphere of 5% CO_2 and 90% relative humidity in a CO_2 incubator (Hera Cell, Heraeus; Asheville, NCI, USA). The cells at sub-confluent stage were harvested from the flask by treatment with trypsin (0.05% trypsin in PBS containing 0.02% EDTA) and suspended in growth medium. Cells with more than 97% viability (trypan blue exclusion) were used for determination of cytotoxicity. An aliquot of 100 µl of cells (10^5 cells/mL) was transferred to a well of 96-well tissue culture plate. The cells were allowed to grow for 24 h. Extracts (100 µL/well) were then added to the wells and cells were further allowed to grow for another 48 h.The anti-proliferative SRB assay which estimates cell number indirectly by staining total cellular protein with the dye SRB was performed to assess growth inhibition. The SRB staining method is simpler, faster and provides better linearity with cell number. It is less sensitive to environmental fluctuations and does not require a time sensitive measurement of initial reaction velocity (Skehan et al.[23]). The cell growth was stopped by gently layering 50 µl of 50% (ice cold) trichloroacetic acid on the top of growth medium in all the wells. The plates were incubated at 4 °C for 1 h to fix the cells attached to the bottom of the wells. Liquid of all the wells was then gently pipetted out and discarded. The plates were washed five-times with distilled water and air-dried. SRB 100 µL (0.4% in 1% acetic acid) was added to each well and the plates were incubated at room temperature for 30 min. The unbound SRB was quickly removed by washing the cells five-times with 1% acetic acid. Plates were air-dried, tris buffer (100 µL, 0.01 M, pH 10.5) was added to all the wells to solubilize the dye and then plates were gently stirred for 5 min on a mechanical stirrer. The optical density (OD) was recorded on ELISA reader at 540 nm. The growth inhibition of 50% or above was considered active while testing compounds.

Results and Discussion

The addition complexes of bis(m-ethylphenylxanthato)nickel(II) with nitrogen donors were found microcrystalline solids, green to dark green in colour. These complexes were found soluble in dimethylformamide and dimethylsulfoxide, partially soluble in chloroform, insoluble in acetone, benzene, carbontetrachloride, and water. The yield of adducts and percentage of nickel is given in Table 1. On the basis of elemental analysis (Table 2), the adducts have been assigned the general formula $[(m\text{-}C_6H_4C_2H_5OCS_2)_2(L)_2Ni]$, L= 2-, 3-, 4-ethylpyridine or 2-, 3-chloropyridine.

Molar conductance and magnetic susceptibility measurements

Molar conductance values of the millimolar solutions of adduct in DMF were found in the range of 19.25-24.22 $ohm^{-1}mol^{-1}cm^2$ (Table 2). The values were much smaller than that expected for any uni-univalent electrolyte suggesting that these complexes were neutral and non-ionic in nature[24,25]. The magnetic moment values of these adducts were found in the range of 2.87-3.30 B.M., that are in good agreement with the values observed for octahedral nickel(II) complexes. The magnetic moment values suggested the paramagnetic nature of complexes and the absence of direct magnetic exchange between nickel(II) ions[26] (Table 2).

Table 1 — Adducts of bis(m-ethylphenylxanthato)nickel(II) along with yield and percentage of metal

S. No.	Name of the adduct	Yield (%)	Nickel (%)	
			Calculated	Found
1.	Bis(m-ethylphenylxanthato)bis(2-ethylpyridine)nickel(II)	79	8.80	8.25
2.	Bis(m-ethylphenylxanthato)bis(3-ethylpyridine)nickel(II)	77	8.80	8.39
3.	Bis(m-ethylphenylxanthato)bis(4-ethylpyridine)nickel(II)	79	8.80	8.41
4.	Bis(m-ethylphenylxanthato)bis(2-chloropyridine)nickel(II)	74	8.63	8.20
5.	Bis(m-ethylphenylxanthato)bis(3-chloropyridine)nickel(II)	76	8.63	8.29

Table 2 — Molar conductance, magnetic moments and analytical data of 1:2 adducts of bis(m-ethylphenylxanthato)nickel(II) with substituted pyridines

S. No.	Name of the adduct	Molar conductance ($ohm^{-1}mol^{-1}cm^2$)	μ_{eff} (B.M.) 298 K	Percentage (%) found (calculated)			
				C	H	N	S
1.	Bis(m-ethylphenylxanthato)bis(2-ethylpyridine)nickel(II)	19.25	2.90	56.2 (57.6)	5.1 (5.4)	3.8 (4.2)	18.4 (19.2)
2	Bis(m-ethylphenylxanthato)bis(3-ethylpyridine)nickel(II)	24.22	2.87	56.6 (57.6)	5.0 (5.4)	3.7 (4.2)	18.7 (19.2)
3	Bis(m-ethylphenylxanthato)bis(4-ethylpyridine)nickel(II)	17.25	3.18	57.0 (57.6)	5.2 (5.4)	3.5 (4.2)	18.7 (19.2)
4	Bis(m-ethylphenylxanthato)bis(2-chloropyridine)nickel(II)	20.13	3.30	48.5 (49.4)	3.4 (3.8)	3.6 (4.1)	17.5 (18.8)
5	Bis(m-ethylphenylxanthato)bis (3-chloropyridine)nickel(II)	22.19	3.23	48.8 (49.4)	3.2 (3.8)	3.3 (4.1)	17.6 (18.8)

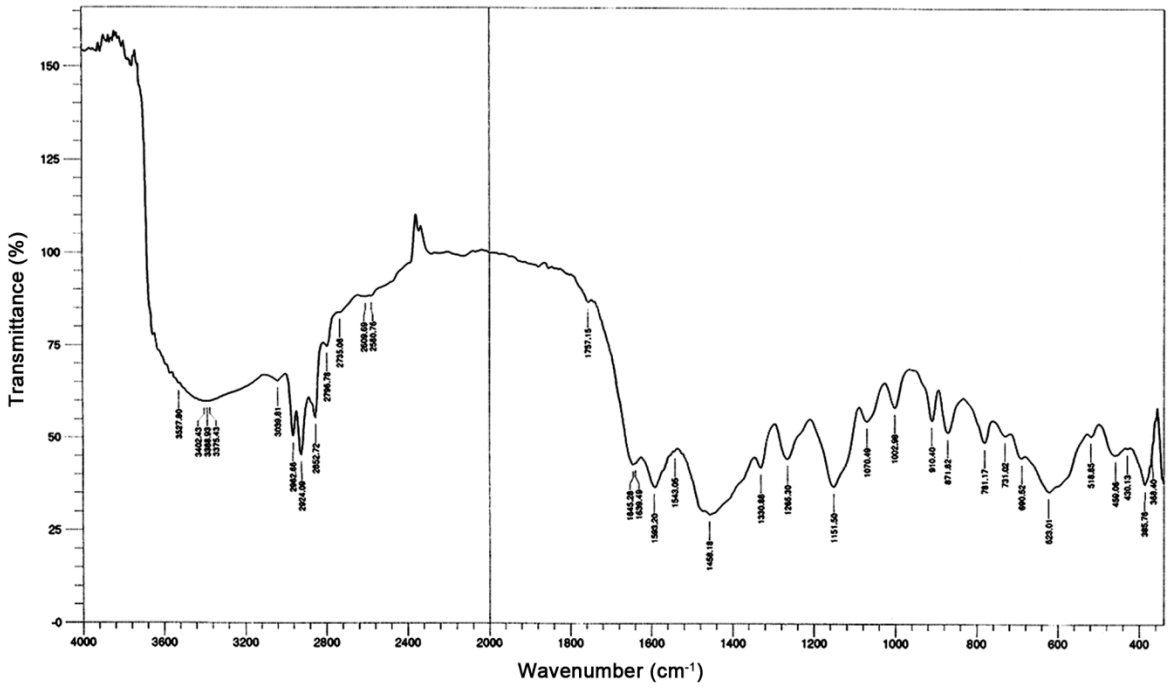

Fig. 1 — IR spectrum of Bis(m-ethylphenylxanthato)bis(2-chloropyridine)nickel(II)

Infrared spectra

The IR spectrum of Bis(m-ethylphenylxanthato) bis(2-chloropyridine)nickel(II) is shown in Fig. 1. It exhibits absorption bands for xanthate ligands at 1270-1210 cm^{-1} and 1140 cm^{-1} which are assigned to ν_{as}(C-O-C) and ν_s(C-O-C) vibrations while the bands at 1030-1040 cm^{-1} and 614-644 cm^{-1} belongs to the ν(C-S) vibrations[27,28]. Presently, there is an intense band corresponding to ν(C-S) vibrations in the range 1014-1062 cm^{-1} observed for all the adducts which suggested xanthate as a symmetrical bidentate chelating ligand[29,30]. The characteristic bands corresponding to ν_{as}(C-O-C) and ν_s(C-O-C) vibrations were observed in the range of 1216-1190 cm^{-1} and 1125-1155 cm^{-1}, respectively. In all the complexes, the bands occurring below 400 cm^{-1} have been assigned to ν(Ni-S) stretching modes[31,32] (Table 3). In free bases, the characteristic bands corresponding to C-N stretching vibrations were observed in the region 1440-1460 cm^{-1}. However, on coordination with metal ion, these bands undergo blue shift and new bands appeared in the region 1480-1495 cm^{-1}. The blue shift is due to back-bonding from metal to the ring through extensive π-bonding. This clearly established the coordination of substituted pyridines with nickel(II) ion through ring nitrogen atom. In the

Table 3 — Infrared spectral data of 1:2 adducts of bis(m-ethylphenylxanthato)nickel(II) with substituted pyridines

S. No.	Name of the adduct	ν(C-O-C)	ν(C-S)	Aromatic stretching		ν(Ni-S)
				ν(C-H)	ν(C-C)	
1	Bis(m-ethylphenylxanthato)bis(2-ethylpyridine)nickel(II)	1151	1030	3039	1543	368
2	Bis(m-ethylphenylxanthato)bis(3-ethylpyridine)nickel(II)	1240	1019	3037	1595	340
3	Bis(m-ethylphenylxanthato)bis(4-ethylpyridine)nickel(II)	1147	1062	3024	1604	389
4	Bis(m-ethylphenylxanthato)bis(2-chloropyridine)nickel(II)	1216	1014	3017	1598	339
5	Bis(m-ethylphenylxanthato)bis(3-chloropyridine)nickel(II)	1242	1056	3022	1602	387

Table 4 — Electronic spectral data of 1:2 adducts of bis(m-ethylphenylxanthato)nickel(II) with substituted pyridines

S. No.	Name of the adduct	ν_1 (cm^{-1})	ν_2 (cm^{-1})	ν_3 (cm^{-1})
1	Bis(m-ethylphenylxanthato)bis(2-ethylpyridine)nickel(II)	15587	19859	24875
2	Bis(m-ethylphenylxanthato)bis(3-ethylpyridine)nickel(II)	14590	20678	25768
3	Bis(m-ethylphenylxanthato)bis(4-ethylpyridine)nickel(II)	16687	19770	26960
4	Bis(m-ethylphenylxanthato)bis(2-chloropyridine)nickel(II)	17488	19990	24980
5	Bis(m-ethylphenylxanthato)bis(3-chloropyridine)nickel(II)	16895	22592	26422

adducts of bis(m-ethylphenylxanthato)nickel(II) with chloropyridines, a strong band due to C-Cl stretching vibration was observed in the range of 630-669 cm^{-1}.

Electronic spectra

The electronic spectra of 1:2 adducts of bis (m-ethylphenylxanthato)nickel(II) with substituted pyridines showed three bands in the range 14590-17488 cm^{-1}, 19770-22592 cm^{-1} and 24875-26960 cm^{-1} which were assigned to d-d transitions:$^3A_{2g} \rightarrow {}^3T_{2g}(F)(\nu_1)$, $^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)(\nu_2)$ and $^3A_{2g}(F) \rightarrow {}^3T_{1g}(P)(\nu_3)$, respectively (Table 4). The electronic spectra spectra of Bis(m-ethylphenylxanthato)bis(3-ethylpyridine)nickel(II) is shown in Fig. 2. The appearance of these bands along with shoulders revealed that the adducts synthesized have distorted octahedral geometry around Ni(II) metal ion[33,34]. In addition to these low intensity bands, M → L charge transfer transitions were also seen as intense bands above 30000 cm^{-1}.

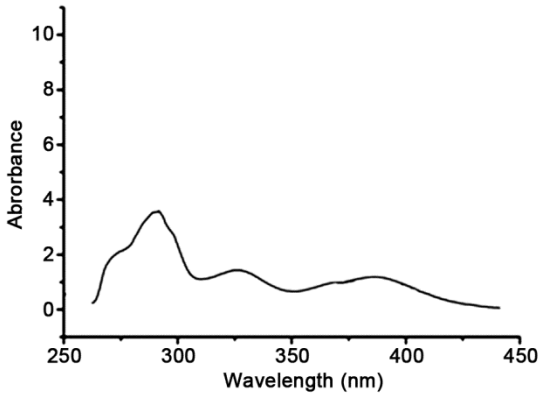

Fig. 2 — Electronic spectrum of Bis(m-ethylphenylxanthato)-bis(3-ethylpyridine)nickel(II)

Mass spectra

The mass spectrum of the adduct [Ni(m-$C_2H_5C_6H_4OCS_2)_2$ (3-ethylpyridine)$_2$] (m/z =666.6) showed a weak molecular ion peak at m/z 666 and a base peak at 452.6, which was highly intense and corresponds to a fragment $[Ni(S_2COC_6H_4C_2H_5)_2]^+$. The mass spectra of [Ni(m-$C_2H_5C_6H_4OCS_2)_2$(2-chloropyridine)$_2$] showed a weak molecular ion peak at m/z 679.6 and a high intensity base peak at m/z 452.2 which corresponds to a stable fragment $[Ni(S_2COC_6H_4C_2H_5)_2]^+$ (Fig. 3). Besides these two peaks, many other peaks were observed with different m/z values in the mass spectra of the complexes. The occurrence of molecular ion peak at this value indicated the monomeric nature of the adducts. The elemental analysis values agreed well with the values calculated from the molecular formulae assigned to these complexes which are further supported by ESI-mass studies.

Thermogravimetric analysis

The complexes were subjected to thermo-gravimetric analysis from 30-1000 °C in nitrogen atmosphere. The TG curve of the adduct [Ni(m-$C_6H_4C_2H_5OCS_2)_2$(2-ethylpyridine)$_2$] showed an initial loss in weight of 20% at 289.3 °C (calculated= 16%) due to loss of one molecule of 2-ethylpyridine. Another loss of pyridine molecule was observed

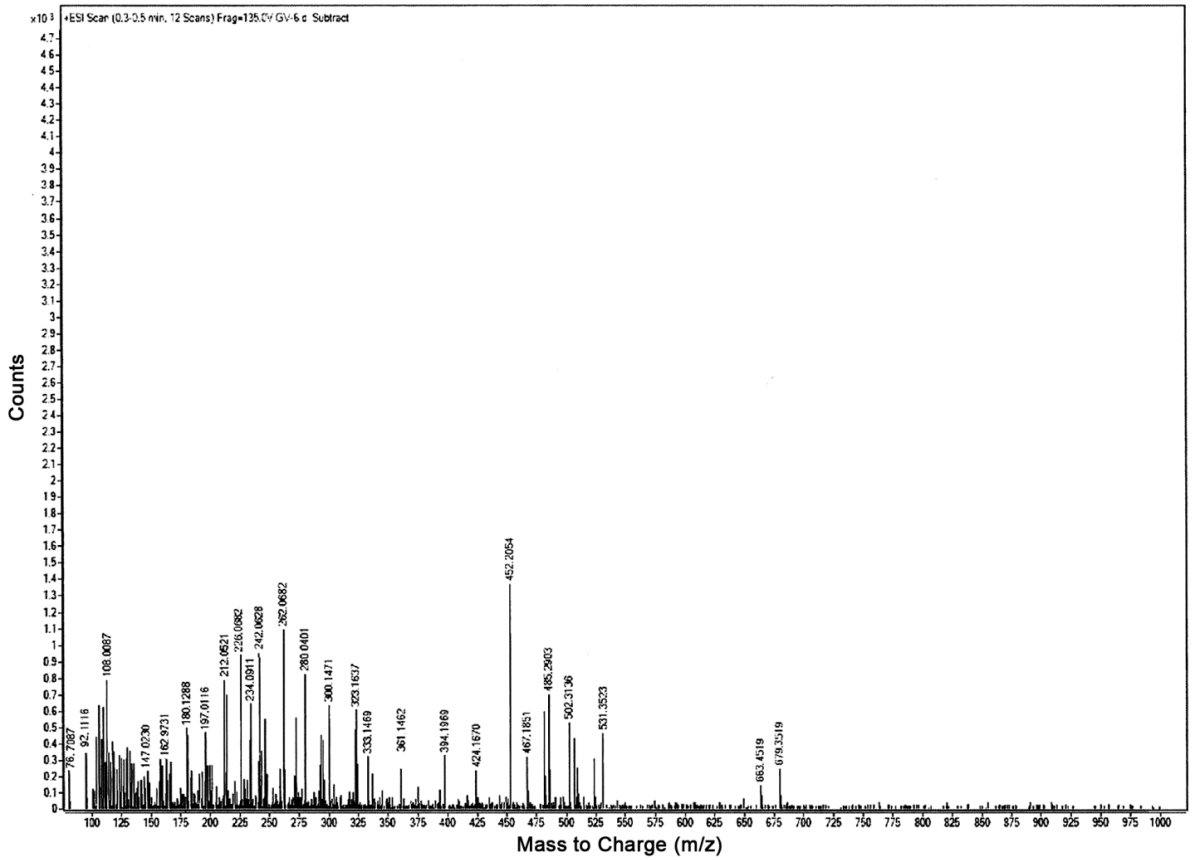

Fig. 3 — Mass spectrum of Bis(m-ethylphenylxanthato)bis(2-chloropyridine)nickel(II)

at 393.5 °C (found = 39.5%, calculated = 32.1%). A significant loss in mass of 57.2% was found at 512.5 °C (calculated =59%) due to loss of dithiocarbonate moiety. A gradual loss in weight on further heating leads to a stable sulphide, NiS as end product at 900 °C (Fig. 4).

Powder X-Ray Diffraction

The powder XRD of the adduct [Ni(m-$C_2H_5C_6H_4OCS_2)_2$(2- chloropyridine)$_2$] was done with the help of X- ray diffractometer (XPERT-PRO) with Cu as anode material, Kα (Å) =1.5406 and the generator settings 40 mA, 45 kV.The diffraction pattern was recorded between 2θ ranging from 10° to 90°. The recorded PXRD pattern of Cu(II) complex is shown in Fig. 5. The XRD pattern of the complex showed maximum intensity peak at 31.682 (2θ) which corresponds to the interplanar spacing (d) = 2.821 Å. The PXRD peak list of the complex along with the corresponding full width at half maximum (FWHM), relative intensities and d-spacing are given in Table 5. The peaks in the diffraction pattern reveal that the complex is crystalline in nature. The Scherrer equation in X-ray diffraction and crystallography relates the size of particles or crystallites in a solid to

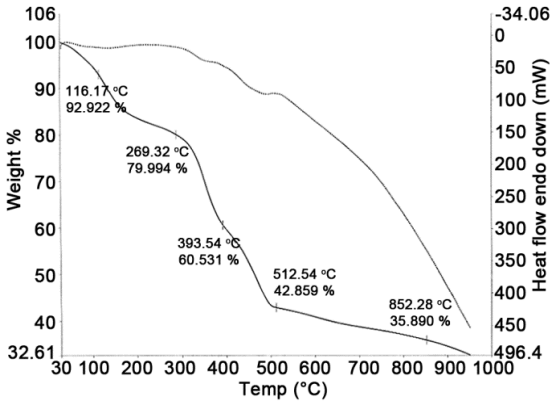

Fig. 4 — TGA plot of bis(m-ethylphenylxanthato)bis(2-ethylpyridine)nickel(II)

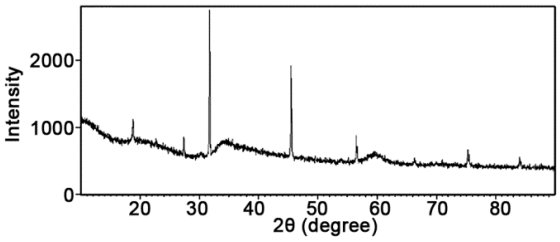

Fig. 5 — Powder XRD of Bis(m-ethylphenylxanthato)bis(2-chloropyridine)nickel(II)

Table 5 — PXRD data of adduct Bis(m-ethylphenyldithiocarbonato)bis(2-chloropyridine)nickel(II)

Position [°2θ]	FWHM Total [°2θ]	d-spacing [Å]	Rel. Int. [%]	Area [cts*°2θ]
18.7638	0.1802	4.72534	11.32	59.42
27.3513	0.0714	3.25811	5.99	8.27
31.6825	0.0950	2.82189	100.00	197.46
45.4242	0.0893	1.99507	70.07	161.29
56.4479	0.0950	1.62882	19.25	42.03
62.0836	0.0340	1.49380	5.88	3.87
75.2765	0.1369	1.26139	13.00	39.34
83.9786	0.1279	1.15143	8.20	30.32

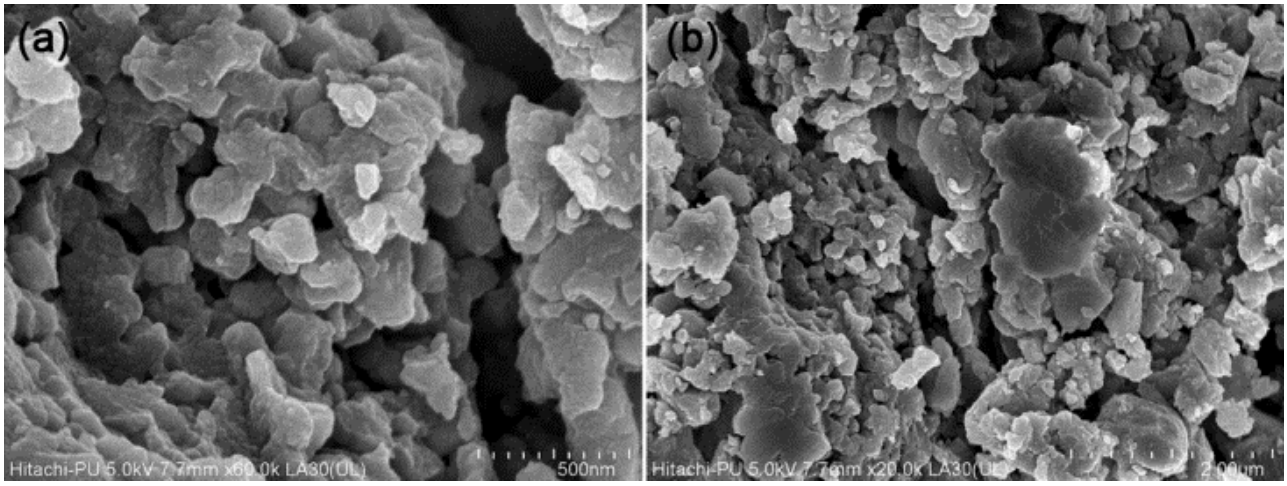

Fig. 6 — FESEM images of nickel(II) complex of m-ethylphenylxanthate with 2-ethylpyridine

the broadening of a peak in a diffraction pattern[35,36]. The Debye-Scherrer equation is $D = k\lambda/\beta \cos \theta$, where β = full width at half maximum height (0.001657 radians), k = constant taken as 0.9, λ = wavelength of X-ray radiation (Cu Kα =1.5406 Å), D = size of crystallite, θ = angle of diffraction (31.6825°). The crystallite size of the Ni(II) complex with 2-chloropyridine was found to be 86.9 nm.

Field emission scanning electron microscope:

FESEM of one of the adducts at different magnifications was done which clearly showed the homogeneous appearance of the microcrystals. These are irregular granular shaped in the form of clusters with rough texture (Fig. 6).

Biological Studies

Antifungal Studies

The antifungal data for *Bipolaris maydis*is reported in Table 6, according to which complex (a) showed large % inhibition in growth of fungus than complex (b) and (c). The antifungal results of *Rhizoctonia solani* are given in Table 7, which showed that complex (c) has high antifungal activity in comparison to (a) and (b). Therefore, the fungal colony diameter decreased, on increasing the complex concentration, which means percent inhibition of fungus increases. This enhanced activity is due to the reason that metal complexes diffused through the cell membrane, disturbed the respiration process of the cell and blocked the formation of proteins that inhibited the fungal growth. This can be more clearly explained in the light of Overtone's concept and Tweedy's chelation theory[37].

Cytotoxic Studies

The results regarding the *in vitro* cytotoxic effect of nickel(II) complexes against various human cancer cell lines are given in Table 8. The complex No. 1 showed striking observations as the complex suppressed the proliferation of five tested human cancer cell lines in the range of 70-99%. Maximum growth inhibition *i.e.,* 99% was observed against PC-3, a cancer cell line from prostate origin. The complex showed 98% growth inhibition against colon cancer cell line (HCT-116) and 97% growth inhibition against lung cancer cell line (A-549). 84% and 70% growth inhibition was again observed against colon

Table 6 — *In vitro* antifungal activity of complexes of bis(m-ethylphenylxanthato)nickel(II) with nitrogen donors against *Bipolaris maydis*

S. No.	Name of the adduct	Concentration (ppm)	Colony diameter (T) (mm)	% inhibition I= [(C-T)/C] X 100
(a)	Bis(m-ethylphenylxanthato)bis(2-ethylpyridine)nickel(II)	50	65.7	27
		100	49.3	45.2
		150	36.8	59.1
		200	29.4	67.3
		250	22.2	75.3
(b)	Bis(m-ethylphenylxanthato)bis(4-ethylpyridine)nickel(II)	50	69.5	22.7
		100	50	44.4
		150	38.5	57.2
		200	31.7	64.7
		250	26.5	70.5
(c)	Bis(m-ethylphenylxanthato)bis(3-chloropyridine)nickel(II)	50	72.6	19.3
		100	55.5	38.3
		150	50.9	43.4
		200	42.8	52.4
		250	36.3	59.6

Table 7 — *In vitro* antifungal activity of complexes of bis(m-ethylphenylxanthato)nickel(II) with nitrogen donors against *Rhizoctonia solani*

S. No.	Name of the adduct	Concentration (ppm)	Colony diameter (T) (mm)	% inhibition I= [(C-T)/C] X 100
(a)	Bis(m-ethylphenylxanthato)bis(2-ethylpyridine)nickel(II)	50	77.8	13.5
		100	63.2	29.7
		150	60.0	33.3
		200	51.5	42.7
		250	42.8	52.4
(b)	Bis(m-ethylphenylxanthato)bis(3-ethylpyridine)nickel(II)	50	74.5	17.2
		100	65.6	27.1
		150	58.7	34.7
		200	51.3	43.0
		250	44.0	51.1
(c)	Bis(m-ethylphenylxanthato)bis(2-chloropyridine)nickel(II)	50	71.4	20.6
		100	56.6	37.1
		150	49.7	44.7
		200	43.6	51.5
		250	31.2	65.3

Table 8 — Growth inhibitory effect of Nickel(II)xanthate complexes along with positive controls against human cancer cell lines

S. No.	Nickel (II) complexes of m-ethylphenylxanthate with substituted pyridines	Conc. (µg/mL)	Human cancer cell lines from six different tissues						
			Breast	Colon	Colon	Colon	Lung	Ovary	Prostate
			MCF-7	HT-29	HCT-116	SW-620	A-549	OVCAR-5	PC-3
			Growth inhibition (%)						
1	[Ni(m-$C_2H_5C_6H_4OCS_2$)$_2$ (2-C_5H_4NCl)$_2$]	100	11	70	98	84	97	07	99
2	[Ni(m-$C_2H_5C_6H_4OCS_2$)$_2$ (3-C_7H_9N)$_2$]	100	19	50	09	52	74	11	00
3	[Ni(m-$C_2H_5C_6H_4OCS_2$)$_2$ (4-C_7H_9N)$_2$]	100	22	56	12	61	52	34	00
Positive controls (standard drugs)		Conc. (µM)	Growth inhibition (%)						
5-Fluorouracil		20	-	72	65	68	-	-	-
Mitomycin-C		1	-	-	-	-	-	-	69
Paclitaxel		1	77	-	-	-	71	84	-

Growth inhibition of 50% or more has been indicated in bold numbers
Mark (-) indicates that particular human cancer cell line was not treated with that particular positive control

cancer cell lines namely SW-620 and HT-29, respectively. The Complex No. 2 was found active against lung cancer cell line (A-549, GI 74%) and colon cancer cell lines (HT-29, GI 52% and SW-620, GI 50%). Similarly, the Complex No. 3 showed *in vitro* cytotoxic effect against lung cancer cell line (A-549) and growth inhibition was 52%. The complex suppressed 61% and 56% proliferation of colon cancer cells - SW-620 and HT-29, respectively.

Conclusions

To conclude, the study confirms the formation of nickel(II)xanthate adducts with nitrogen donor ligands as indicated from elemental analysis, molar measurements, magnetic measurements, spectral analysis, powder XRD, FESEM and TGA. So, it is proposed that Ni(II) ion has a distorted octahedral coordination of ligands around it. The complexes show antifungal activities. The *in vitro* cytotoxic effect of these nickel(II) complexes against various human cancer cell lines were studied.

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References

1 Ghoshal S & Jain V K, *J Chem Sci*, 119 (2007) 583.
2 Chaudhari S & Tare V, *J Appl Polym Sci*, 71 (1999) 1325.
3 Winter G, *Rev Inorg Chem*, 2 (1980) 253.
4 Burns R P, Mccullough F P & Mcauliffe C A, *Adv Inorg Chem Radiochem*, 23 (1980) 211.
5 Victoriano L I & Cortes H B, *J Coord Chem*, 39 (1996) 231.
6 Scendo M, *Corros Sci*, 47 (2005) 1738.
7 Orts W J, Sojka R E & Glenn G M, *Agro Food Industry Hi-Tech*, 13 (2002) 37.
8 Görgülü O A, Arslan M & Çil E, *J Coord Chem*, 59 (2006) 637.
9 Larsson A C & Oberg S, *J Phys Chem A*, 115 (2011) 1396.
10 Gorgulu A O, Arslan M & Cil E, *J Coord Chem*, 58 (2005) 1225.
11 Amtmann E, *Drug Exp Clin Res*, 22 (1996) 287.
12 Perluigi M, Joshi G & Sultana R, *Neuroscience*, 138 (2006) 1161.
13 Dixon N E, Gazzola C, Blakeley R L & Zerner B, *J Am Chem Soc*, 97 (1975) 4131.
14 Musiani F, Bertosa B, Magistrato A, Zambelli B, Turano P, Lossaso V, Michelette C, Ciurli S & Carloni P, *J Chem Theo Comput*, 6 (2010) 3503.
15 Li Y & Zamble D B, *Chem Rev*, 109 (2009) 4617.
16 Muyssen B T A, Brix K V, Defores D K & Janseen C R, *Environ Rev*, 12 (2004) 113.
17 Ragsdale S W, *J Bio Chem*, 284 (2009) 18571.
18 Lee S Y, Hille A, Frias C, Kater B, Bonitzki B, Wolfl S, Scheffler H, Prokop A & Gust R, *J Med Chem*, 53 (2010) 6064.
19 Pradeepa S M, Naik H S B, Kumar B V & Priyadarsini K I, *Spectrochim Acta Part A*, 101 (2013) 132.
20 Sathisha M P, Shetti U N, Revankar V K, Pai K S R, *Eur J Med Chem*, 43 (2008) 2338.
21 Gupta B, Kalgotra N, Andotra S & Pandey S K, *Monatsh Chem*, 143 (2012) 1087.
22 Monks A, Scudiero D, Skehan P, Shoemaker R, Paull K, Vistica D, Hose C, Langley J, Cronise P, Vaigro-Wolff A, Gray-Goodrich M, Campbell H, Mayo J &Boyd M, *J Natl Cancer Inst*, 83 (1991) 57.
23 Skehan P, Storeng R, Scudiero D, Monks A, McMohan J, Vistica D, Warren J T, Bokesch H, Kenney S & Boyd M R, *J Natl Cancer Inst*, 82 (1990) 1107 .
24 Vinayak M N, Kuchinad G T, Patil S K & Mallur N B, *Der Pharma Chem*, 5 (2013) 43.
25 Uivarosi V, Barbuceanu S F, Aldea V, Badea M, Olar R & Marinescu D, *Molecules*, 15 (2010) 1578.
26 Ovcharenko V I, Romanenko G V, Korobkov I V, Ikorskii V N, Ovcharenko I V, Musin R N, Vostrikova K E, Podoplelov A V, Shishkin O V & Struchkov Y T, *J Struct Chem*, 5 (1998) 734.
27 Travnicek Z & Sindelar M, *Transit Met Chem*, 24 (1999) 156.
28 Travnicek Z, Walla J, Kvitek L, Sindelar Z & Biler M, *Transit Met Chem*, 24 (1999) 633.
29 Krueger A G & Winter G, *Aust J Chem*, 24 (2001) 161.
30 Ballester L, Gutierrez A & Perpinan M F, *Polyhedron*, 15 (1996) 1103.
31 Coucouvanis D & Fackler J P, *J Inorg Chem*, 6 (1967) 2047.
32 Watt G W & McCormick B J, *Spectrochim Acta*, 21 (1965) 553.
33 Lever A B P, *Inorganic Electronic Spectroscopy*, 2nd Edn, (Elsevier, Amsterdam) 1984.
34 Bulut I, Ibrahim U C & Kazak C, *Turk J Chem*, 33 (2009) 347.
35 Scherrer P, *Nachrichten von der Gesellschaft der Wissenschaften zu Göttingen, Mathematisch-Physikalische Klasse*, 2 (1918) 98.
36 Patterson A L, *Phys Rev*, 56 (1939) 978.
37 Tweedy B G & Loeppky C, *Phytopathology*, 58 (1968) 1522.