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Synthesis, Characterization and Biological Activity of Complexes of N-phenyl-N'-(2-pyrimidyl) Thiourea with Pd(II), Pt(II), Ni(II), Co(II),Cu(II), Mn(II), Cd(II) and Zn(II)

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This paper reports the synthesis, characterization and biological activities of Pd(II), Pt(II), Ni(II), Co(II), Cu(II), Mn(II), Cd(II) and Zn(II) complexes with N-phenyl-N'-(2-pyrimidyl) thiourea (PPTU). All the synthesized complexes were characterized by elemental analysis, infrared and electronic spectral data, magnetic susceptibility and molar conductance. The biological activity of the synthesized complexes were tested against *Staphylococcus aures*, *Escherichia coli* and *Pseudomonas aeruginosa* using a well assay method. Dunnett method was used to compare the biological activities of the complexes with the control.

Key Words: Thiourea derivative, Transition metal complexes, Biological activity.

INTRODUCTION

Thioureas are versatile ligands, able to coordinate to a range of metal centres as either neutral ligands[1], monoanions[2] or dianions[3,4]. In addition, the hard nitrogen and soft sulfur donor atoms provide a multitude of bonding possibilities[5]. Thiourea and its derivatives form a variety of complexes of different symmetries with various metal ions like Ni(II), Pd(II) and Co(II)[6]. Extensive work is reported on the complexing behaviour of disubstituted thiourea. In theses complexes it is shown that one of the coordination sites is thiocarbonyl sulfur[7]. Study of the thiourea derivatives has attracted the attention of many research groups due to their interest as selective ligands for the concentration and separation of metal cations[8,9], treatment of lead and mercury poisoning in humans[10] and as highly selective reagents for liquid-liquid extraction[11]. Thioureas have also been shown to possess antibacterial, antifungal, antitubercular, antithyroid and insecticidal properties[12]. Most investigations showed that the complexation between transition metal ions and thiourea derivatives leads to a dramatically increase of biological activity properties[13]. Here the synthesis, characterization and biological activity of Pd(II), Pt(II), Ni(II), Co(II), Cu(II), Mn(II), Cd(II) and Zn(II) complexes of N-phenyl-N'-(2-pyrimidyl) thiourea is reported.

EXPERIMENTAL

Phenylisothiocyanate, 2-aminopyridine, potassium chloride, potassium bromide, $K_2[PtCl_4]$ and $NiCl_2·6H_2O$ were purchased from Fluka AG. Zn(II)chloride and *n*-butanol are Merk products. $PdCl_2$, $CoCl_2·6H_2O$, $CdCl_2·6H_2O$, $HgCl_2$, $CuCl_2·2H_2O$ and $MnCl_2·2H_2O$ were supplied by BDH.

Melting points were measured using Toshinwal Electrothermal melting point apparatus. Electronic spectra of the ligand and the complexes were measured in DMSO using a Jenway 6485 spectrophotometer. The infrared spectra of the ligand and the complexes were recorded on a F.T. Thermo Mattsoin IR 300 spectrometer in the 4000-400 cm^{-1} range using potassium iodide discs. Elemental analyses were performed using a Perkin-Elmer 2400 elemental analyzer. The conductivity measurements of the complexes were made in DMSO using a conductimeter type EC215 Bench Conductivity Meter. Magnetic measurements were recorded on a Bruker BM6 instrument at room temperature following Faraday method.

Preparation of N-phenyl-N'-(2-pyrimidyl) thiourea (PPTU): To a solution of 2-aminopyrimidine (4.755 g, 50 mmol) in 25 cm^3 of benzene, phenylisothiocyanate (6.75 g, 50 mmol) was added with stirring to give a clear solution .The solution was refluxed for 3 h to give a turbid faint yellow solution. Then the solution left to cool in ice-water to give a faint yellow precipitate, which was filtered off, washed with benzene, dried and recrystallized from ethanol (yield *ca.* 43.45 %).

General procedure for the preparation of the PPTU metal complexes: To a hot solution of PPTU (0.3126 mmol) in 20 cm^3 *n*-butanol containing a few drops of DMF, a warm solution of a metal chloride (0.3126 mmol) in 20 cm^3 *n*-butanol was added. The mixture was digested over a water bath for 0.5 h then on a hot-plate for another 0.5 h. A precipitate was separated on cooling. The mixture was filtered and the precipitate was washed with hot *n*-butanol and finally with ether. The precipitate was dried at room temperature over P_2O_5.

Biological activity of the PPTU metal complexes: The agar plates were prepared by striking the plates with bacteria inoculum and drying at room temperature. Then wells of 5-millimeter diameter were cut in the agar plates using a sterilized glass tubes. Finally 0.5 mL solution of each prepared complex (1×10^{-3} M) and the control was added to the labeled wells and the plates were incubated at 37°C for 48 h. The inhibition zones were measured[14] and Dunnett method was used to compare the activities of the prepared complexes with the control.

RESULTS AND DISCUSSION

The prepared complexes are soluble in DMSO but insoluble in water, methanol, ethanol and diethyl ether. The elemental analysis data (Table-1), of the prepared complexes are consistent with the suggested stoichiometries; Pd(II), Ni(II), Cu(II), Pt(II) and Cd(II) form complexes of the type [M(PPTU)Cl_2], Co(II) and Zn(II) form [M$(PPTU)_2$] and Mn(II) forms [M$(PPTU)_2Cl_2$].

TABLE-1
PHYSICAL PROPERTIES OF THE PREPARED COMPLEXES AND THE LIGAND PPTU

Complexes	Colour (m.p.) (°C)	Yield (%)	Found (Calcd.) (%)			Δ_m (Ω^{-1} cm^2 mol^{-1})
			C	H	N	
PPTU	Off-White (117-119)	44	56.4 (57.31)	5.31 (4.34)	24.1 (24.31)	–
[Pd(PPTU)Cl_2]	Brown (240- 242)	48	31.71 (32.28)	2.55 (2.45)	13.21 (13.73)	2.50
[Ni(PPTU)Cl_2]	Yellowish-green (> 360)	24	35.97 (36.67)	3.10 (2.77)	14.14 (13.56)	3.06
[Pt(PPTU)Cl_2]	Yellowish-brown (280-282)	48	26.90 (26.59)	2.31 (2.01)	12.04 (11.28)	5.90
[Cu(PPTU)Cl_2]	Grass-green (264-266)	71	35.89 (36.19)	1.99 (2.74)	14.85 (15.35)	1.78
[Cd(PPTU)Cl_2]	Light-yellow (> 360)	71	32.02 (31.91)	22.61 (2.41)	13.25 (13.53)	7.00
[Mn$(PPTU)_2Cl_2$]	White (360 d)	42	44.83 (45.10)	3.61 (3.41)	19.10 (19.09)	2.92
[Co$(PPTU)_2$]	Greenish-blue (194-196)	30	50.66 (50.81)	4.17 (3.84)	21.77 (21.55)	2.15
[Zn$(PPTU)_2$]	White (202-204)	36	50.10 (50.19)	3.77 (3.80)	21.54 (21.29)	1.90

The molar conductivities of the complexes in DMSO are low, suggesting that they are non-electrolytes (Table-1)[15,16].

The infrared spectra of the ligand and the complexes are recorded and the frequencies of the characteristic bands are listed in Table-2.

The observed bands of the complexes in the range 1646-1595 cm^{-1} which are attributed to the ν(C=N) + ν(C=C) were shifted to higher frequency or in some complexes splitted with increasing intensity are indications that the nitrogen atom of the ligand is coordinated to the metals[17].The thioamide bands (I) and (II) of the complexes were shifted to higher or lower frequencies or their intensities were reduced relative to those of the free ligand are indications of the coordination of the ligand to the metal ions[18,19]. The thioamide bands (III) and (IV) at the range 1222-1081 cm^{-1}

and 709-696 cm^{-1}, respectively were shifted to lower frequencies or splitted or both or with reducing intensity suggesting the linkage of the ligand sulfur atom to the metal ions[11,20].

TABLE-2
INFRARED SPECTRAL BANDS OF THE PREPARED THIOUREA DERIVATIVE COMPLEXES AND THE LIGAND (PPTU)

Complexes	ν(NH)	ν(C= C) + ν(C= N)	ν(N-C=S) Thioamide Band (I)	ν(NH) + ν(N-C= S) band (II)	ν(N-C= S) + ν(C= S) band (III)	ν(C= S) band(IV)
PPTU	3431 br	1607 s	1428 s 1453 m	1261w	1081 m	709 s
[Pd(PPTU)Cl$_2$]	3431 br	1646 vs	1428 s 1505 w	1274w	1120w 1184s	709vs
[Ni(PPTU)Cl$_2$]	3443 br	1646 vs	1453 vs 1505 s	1287 w	1222 m	709 w
[Pt(PPTU)Cl$_2$]	3431 br	1633 m	1428 s 1458 s	1261 s	1120 w	709 w
[Cu(PPTU)Cl$_2$]	3443 br	1620 s	1428 vs 1453 s	1299 w	1081 w	734 vs
[Cd(PPTU)Cl$_2$]	3456 br	1582 m	1428 s 1453 m	1248 m	1120 w 1094 m	696 s
[Mn(PPTU)$_2$Cl$_2$]	3456 br	1595 s	1428 s 1453 vs	1261 s	1094 w	696 vs
[Co(PPTU)$_2$]	3456 br	1650 vw	1428 vs 1530 s	1261s	1094 m	709 vs
[Zn(PPTU)$_2$]	3418 br	1607 vs	1415 vs 1453 m	1261 s	1094 m	709 vs

The electronic spectra of the ligand and its metal complexes are measured in DMSO at room temperature in the ultraviolet and visible region, Fig. 1 and the bands are arranged in Table-3. The UV-visible absorption spectra of Pd(II), Pt(II), Ni(II) and Cu(II) complexes are typical of square planar complexes of these metal ions[21,22].

The electronic spectrum of the Mn(II) complex shows two bands at 30769 and 13158 cm^{-1} which are assigned to the transitions $^6A_{1g} \rightarrow {}^4T_{1g(D)}$ and $^6A_{1g} \rightarrow {}^4E_{g(4D)}$ for octahedral geometry[23]. The Co(II) complex shows a band at 15152 cm^{-1} attributed to $^4A_{2(F)} \rightarrow {}^4T_{1(P)}$ transition of Co(II) in tetrahedral geometry[24].

Magnetic susceptibility for the prepared complexes were measured at room temperature and presented in Table-3. The magnetic susceptibility values for the complexes [Pd(PPTU)Cl$_2$], [Ni(PPTU)Cl$_2$] and [Pt(PPTU)Cl$_2$] are 0.1, 0.2 and 0.02 B.M., respectively suggest that these complexes are diamagnetic and have square planar geometries[25] . The magnetic susceptibility for the complex [Cu(PPTU)Cl$_2$] is 1.25 B.M. suggests a square

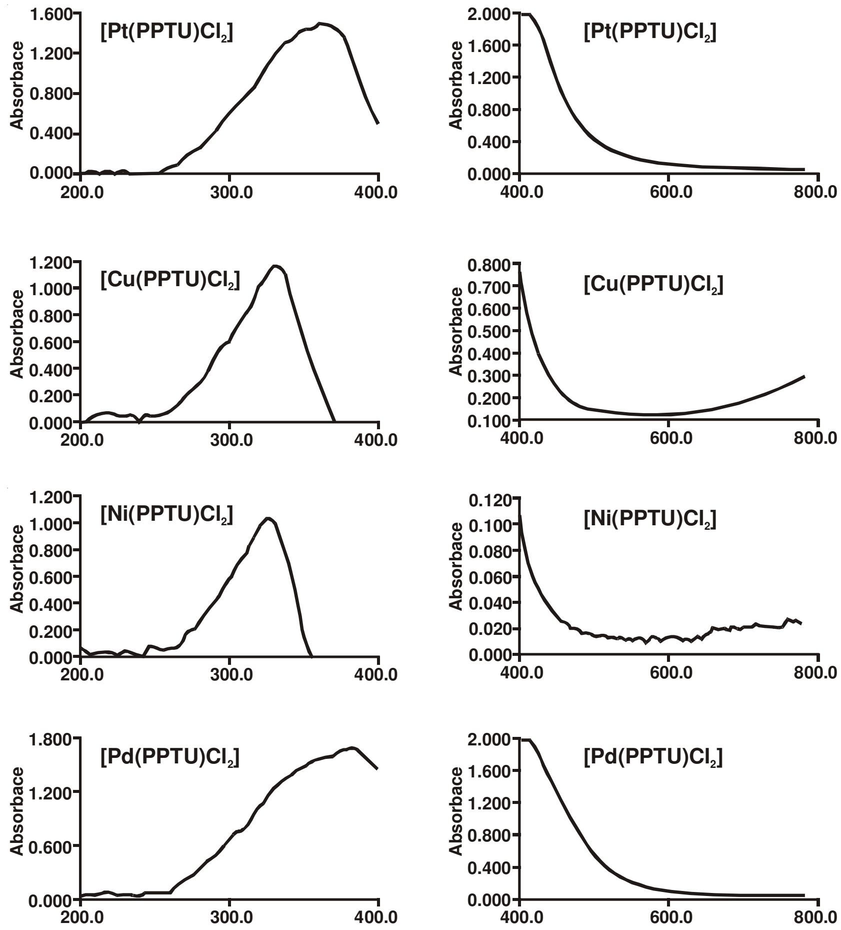


Fig. 1. Electronic spectra of the complexes: [Pt(PPTU)Cl$_2$], [Cu(PPTU)Cl$_2$], [Ni(PPTU)Cl$_2$] and [Pd(PPTU)Cl$_2$]

planar geometry[26]. The magnetic susceptibility value of [Co(PPTU)$_2$] is 4.84 B.M. confirms a tetrahedral geometry around Co(II) ion[27]. The magnetic susceptibility value of [Mn(PPTU)$_2$Cl$_2$] is 5.94 B.M. suggest an octahedral arrangement around the Mn(II) ion[21].

The biological activity of the prepared complexes were tested against *Staphylococcus aures*, *Escherichia coli* and *Pseudomonas aeruginosa* using a well assay method. Dunnett method was used to compare the biological activities of the complexes with the control (Table-4).

On the basis of spectral and magnetic susceptibility and micro-elemental analysis data, square planar geometry are proposed for Pd(II), Ni(II), Pt(II) and Cu(II) complexes (Fig. 2A), tetrahedral structures for Cd(II),Co(II) and Zn(II) complexes (Fig. 2B) and octahedral structure for Mn(II) complex (Fig. 2C).

TABLE-3

ELECTRONIC SPECTRAL DATA AND MAGNETIC SUSCEPTIBILITIES FOR THE PREPARED COMPLEXES AND THE LIGAND PPTU

Complexes	$\varepsilon \times 10^3$	Band absorption		Assignments	Magnetic susceptibilities (B.M.)
		cm^{-1}	nm		
PPTU	1.385	28169	355	$n \rightarrow \Pi^*$	–
$[Pd(PPTU)Cl_2]$	1.711	24974	385	$^1A_{1g} \rightarrow {}^1Eg$	0.10
	1.983	24390	410	$^1A_{1g} \rightarrow {}^1B_1g$	Pd(II) square planar
$[Ni(PPTU)Cl_2]$	1.029	30769	325	$^1A_{1g} \rightarrow {}^1Eg$	0.20
	0.027	13158	760	$^1A_{1g} \rightarrow {}^1A_2g$	Ni(II) square planar
$[Pt(PPTU)Cl_2]$	1.519	27778	360	$^1A_{1g} \rightarrow {}^1Eg$	0.02
	2.000	24390	410	$^1A_{1g} \rightarrow {}^1B_1g$	Pt(II) square planar
$[Cu(PPTU)Cl_2]$	0.018	16260	615	$^2B_{1g} \rightarrow {}^2Eg$	1.25
	0.947	30303	330	CT	Cu(II) square planar
$[Cd(PPTU)Cl_2]$	1.103	30303	330	CT	–
$[Mn(PPTU)Cl_2]$	1.174	30769	325	$^6A_{1g} \rightarrow {}^4T_{1g(D)}$	5.94
	0.156	13158	660	$^6A_{1g} \rightarrow {}^4E_{g({}^4D)}$	Mn(II) octahedral
$[Co(PPTU)_2]$	1.379	28571	350	$n \rightarrow \pi^*$	4.84
	0.019	15152	660	$^4A_{2g(F)} \rightarrow {}^4T_{1(P)}$	Co(II) teterahedral
$[Zn(PPTU)_2]$	1.349	28985	345	CT	–

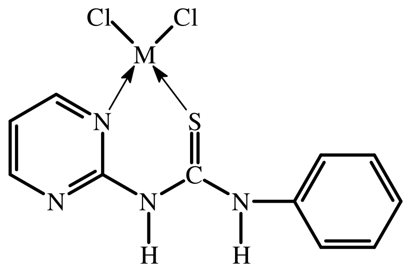
where ε = molar extinction coefficient, CT = charge transfer band.

TABLE-4

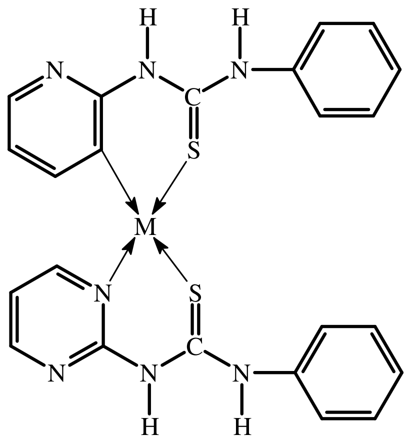
ANTIBACTERIAL ACTIVITIES OF THE PREPARED COMPLEXES

Complexes	Test organism		
	S. aureus G^+ activity	*E. coli* G^- activity	*P. aeruginoses* G^- activity
$[Pd(PPTU)Cl_2]$	SS	SS	SS
$[Ni(PPTU)Cl_2]$	NS	SS	NS
$[Pt(PPTU)Cl_2]$	NS	SS	NS
$[Cu(PPTU)Cl_2]$	SS	SS	NS
$[Cd(PPTU)Cl_2]$	SS	SS	SS
$[Mn(PPTU)_2Cl_2]$	NS	SS	SS
$[Co(PPTU)_2]$	NS	SS	SS
$[Zn(PPTU)_2]$	NS	SS	NS
Control	–	–	–

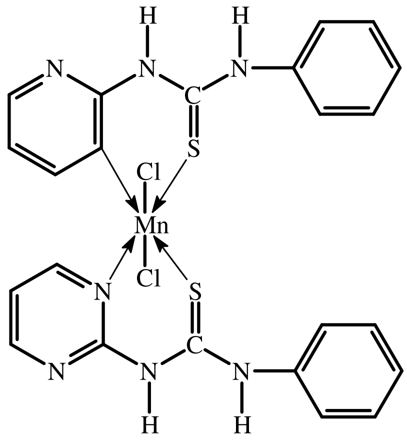
S = significant, SS = highly significant, NS = non-significant, R = resistant.



(A) M = Pd(II), Ni(II), Pt(II), Cu(II) or Cd(II)



(B) M = Co(II) or Zn(II)



(C)

Fig. 2. Proposed structures of the metal complexes

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