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Structural and Antimicrobial Studies of Some Newly Synthesised Complexes of Cobalt(II) of Bioinorganic Relevance

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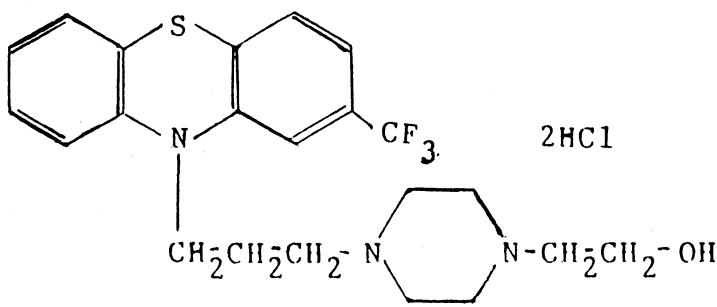
Five new complexes of cobalt(II) have been synthesised by the interaction of fluphenazine (FPH) with cobalt(II) chloride, bromide, perchlorate, acetate or sulphate. The complexes which have been found to possess a stoichiometric composition of $[Co(C_{22}H_{26}F_3N_3OS)(H_2O)_2X_2]$ have been characterised for their purity with the help of elemental studies, conductivity and magnetic measurements. An octahedral structure has been proposed based on thermal, electronic and IR spectral data. The new complexes have been tested *in vitro* for their antimicrobial activity against *Alternaria* alternata, Aspergillus flavus, *Escherichia coli* and *Staphylococcus* aureus. The antibacterial activity of the cobalt(II) complexes against *E. coli* and *S. aureus* increases in the order:
sulphate > chloride > perchlorate.

INTRODUCTION

Fluophenazine (FPH) is an important derivative of phenothiazine having the following structure.



FPH and its ester derivatives differ from other phenothiazines in several aspects and hence have become the most widely used drugs in practice of medicine to-day. Because of the importance of FPH and its more potent effect on a milligram basis than those of other phenothiazines considerable work has been done on it.[1–3] FPH exhibits a number of interesting analytical and coordinating properties due to its characteristic structure. The complexing ability of FPH with Cu(II), Pd(II) and Pt(II) chloride has been reported[4]. In this communication, the isolation and characterisation of five new complexes of FPH with Co(II) salts

have been studied. The biological activity of these complexes against some bacteria and fungi has also been investigated.

EXPERIMENTAL

Synthesis of the Cobalt(II) Complexes

Cobalt(II) complexes with chloride, bromide and perchlorate anions were prepared by warming hot ethanolic solution of an appropriate amount of the ligand (FPH) with a calculated amount of the Co(II) salt (in the molar ratio 1:1) dissolved in ethanol on a water bath (70–80°C). After 45 min, the contents were cooled until the solid was separated out. This was collected by filtration and washed with cold ethanol to remove excess ligand, then with ether. The final product was dried over fused calcium chloride.

The Co(II) complexes with acetate and sulphate anions were prepared by refluxing an aqueous solution of an appropriate amount of the fluphenazine with a calculated amount of the cobalt(II) salt (in the molar ratio 1:1). After an hour of refluxing, the contents were cooled until the solid was separated out. This was collected by filtration and washed with ethanol and then with ether. The final product was dried in air.

The biocidal activities of the investigated compounds (0.1, 0.2 and 0.3% per test) were screened against *Alternaria alternata* and *Aspergillus flavus*. Also, these compounds were screened against *Staphylococcus aureus* and *Escherichia coli* bacteria, following cup-diffusion technique[5]. All plates were run in triplicate, the inhibition zones were measured and the mean in millimetres was recorded.

RESULTS AND DISCUSSION

The analytical data, decomposition temperature and molar conductance values of the new complexes are presented in Table-1. It is evident from the elemental analysis that Co(II) forms 1:1 complex with the ligand fluphenazine. Molar conductance values of 10^{-4} M DMF solutions are in the range 14.2–22.1 mhos mol^{-1} cm^{-2} thus indicating non-electrolytic nature of the complexes.

IR spectra

The IR data are presented in Table-2. It was pointed out[6] that the heterocyclic nitrogen atom attached to the alkyl group (aromatic or aliphatic) gives a characteristic band in the region 2860–2850 cm^{-1}; the heterocyclic nitrogen atom attached to the alkyl group in the ligand FPH showed a band in the region 2920–2850 cm^{-1} This band disappeared in the IR spectra of cobalt(II) complexes, which indicates the heterocyclic nitrogen atom to be the site of coordination. It was reported in the literature[7] that $R_3\overset{+}{N}H$ combined with halogen in the molecules of many phenothiozines give rise to a broad band generally between 2500–2300 cm^{-1}. The broad band at 2350–2290 cm^{-1} observed in the IR spectra of FPH corresponds to alkyl nitrogen atom. The IR spectra of all five Co(II) complexes of FPH showed a flat absorption indicating one of the nitrogen atoms

TABLE-1
MICRO-CHEMICAL ANALYSIS: DATA, YIELD, DECOMPOSITION TEMPERATURE AND MOLAR CONDUCTANCE VALUES OF DIFFERENT Co(II) COMPLEXES

Complex	Yield %	Calculated (Found) %							m.p. (°C)	Molar Condutance mohs mol^{-1} cm^{-1}
		Co	C	H	N	Cl	Br	S		
$[Co(C_{22}H_{26}F_3N_3OS)(H_2O)_2Cl_2]$	83	9.77 (9.65)	43.79 (43.86)	5.01 (4.92)	6.96 (6.94)	11.75 (12.01)	— —	5.31 (5.25)	184–186	18.2
$[Co(C_{22}H_{26}F_3N_3OS)(H_2O)_2Br_2]$	68	8.51 (8.46)	38.17 (38.25)	4.37 (4.30)	6.07 (6.00)	— —	23.08 (22.95)	4.63 (4.54)	170–172	20.3
$[Co(C_{22}H_{26}F_3N_3OS)(H_2O)_2(ClO_4)_2]$	72	8.06 (7.92)	36.13 (36.50)	4.13 (3.96)	5.74 (5.74)	9.69 (10.0)	— —	4.38 (4.25)	194–195	22.1
$[Co(C_{22}H_{26}F_3N_3OS)(H_2O)_2(CH_3COO)_2]$	69	9.06 (8.85)	48.00 (47.98)	5.57 (5.54)	6.46 (6.50)	— —	— —	4.93 (5.0)	199–203	21.4
$[Co(C_{22}H_{26}F_3N_3OS)(H_2O)_2SO_4]$	58	8.92 (8.80)	40.00 (39.55)	4.58 (4.60)	6.30 (6.25)	— —	— —	9.71 (8.95)	220–224	14.2

of the side chain to be the site of interaction. In IR spectra of FPH the stretching frequency of C—S was observed in 730 cm^{-1}. This C—S stretching vibration frequency was unaffected on coordination with cobalt(II) ion. In case of $[Co(FPH)(H_2O)_2Br_2]$ and $[Co(FPH)(H_2O)_2(CH_3COO)_2]$ a slight displacement in C—S frequency band (about 5 cm^{-1}) was observed. This may be due to the effect of coordination of ligand molecules with the metal atom.

TABLE-2
IR DATA (cm^{-1}) OF Co(II) COMPLEXES OF FPH

Compound	ν(O—H)	ν(N—H)	ν(R_3^+N)	ν(Co—N)	ν(Co—X)	ν(C—S)
FPH	3270 S	2850–2920 br	2290–2350 br	—	—	730
$[Co(FPH)(H_2O)_2Cl_2]$	3250–3450 br	—	—	439 s	360 s	730
$[Co(FPH)(H_2O)_2Br_2]$	3260–3455 br	—	—	425 s	355 s	735
$[Co(FPH)(H_2O)_2ClO_4)_2]$	3300–3450 br	—	—	430 s	373 s	730
$[Co(FPH)(H_2O)_2(CH_3COO)_2]$	3280–3350 br	—	—	435 s	375 s	725
$[Co(FPH)(H_2O)_2SO_4]$	3200–3400 br	—	—	435 s	350 s	730

The sharp peak at 3270 cm^{-1} in the IR spectra of FPH was assigned for O—H stretching vibration which on complexation was broadened and shortened; this may be due to hydrogen bonding to R^1—H molecules. The decrease in frequency and broadening of the absorption band may be due to R^1—H stretching vibration [where $R^1 = (CH_2)_2O$—] the peaks in the region of 1380–1320 cm^{-1} in the IR spectra of FPH and its complexes with Co(II) ions are due to C—N stretching vibrations. Two sharp peaks in the region 1610–1560 cm^{-1} are characteristic of aromatic ring system, and the sharp peaks in the region 950–730 cm^{-1} are assignable to 2-substituted phenothiazines[8]. The new bands at 435–425 and 375–350 cm^{-1} are assigned to ν(Co—N) and ν(Co—X) respectively[9].

Magnetic Moments and Electronic Spectra

Cobalt(II) diaquo complexes have magnetic moment in the range 4.75–5.16 BM which suggest that the complexes have high spin octahedral geometry[10].

The electronic spectra of DMF solution of the Co(II) complexes are recorded in the wavelength range 200–900 nm (Fig. 1) and the values of the different absorption bands are recorded in Table-3. The bands at *ca.* 14350, *ca.* 14900 and *ca.* 16400 cm^{-1} are assigned to $^4T_{1g} \rightarrow {}^4T_{2g}$, $^4T_{1g} \rightarrow {}^4T_{2g}(F)$ and $^4T_{1g} \rightarrow {}^4T_{2g}(P)$ transitions, respectively in an octahedral field[10]. The more intense bands beyond *ca.* 31000 cm^{-1} are charge transfer bands. The crystal field splitting energies (10 Dq) calculated for cobalt(II) complexes (Table-3) are in agreement with the values obtained for known octahedral complexes[11].

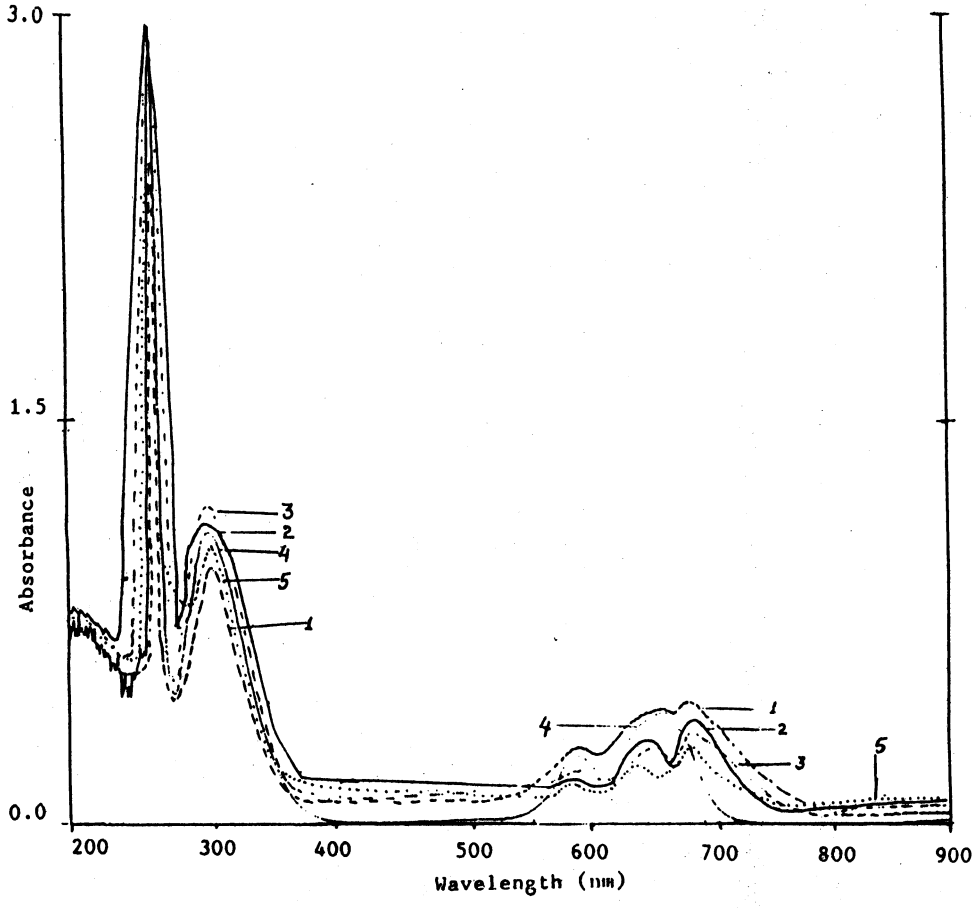


Fig. 1. Electronic Spectra of 1. $[Co(FPH)(H_2O)_2Cl_2]$ 2. $[Co(FPH)(H_2O)_2Br_2]$ 3. $[Co(FPH)(H_2O)_2ClO_4]$ 4. $[Co(FPH)(H_2O)_2(CH_3COO)_2]$ 5. $[Co(FPH)(H_2O)_2SO_4]$

TABLE-3
ELECTRONIC SPECTRAL AND MAGNETIC SUSCEPTIBILITIES DATA OF COBALT(II) COMPLEXES OF FPH

Complex	Electronic spectral data (cm^{-1})					10 Dq	μeff (BM)
$[Co(C_{22}H_{26}F_3N_3OS)(H_2O)_2Cl_2]$	14368	14885	16431	31949	37202	178.05	4.78
$[Co(C_{22}H_{26}F_3N_3OS)(H_2O)_2Br_2]$	14351	14890	16447	31928	37230	178.11	4.92
$[Co(C_{22}H_{26}F_3N_3OS)(H_2O)_2(ClO_4)_2]$	14367	14952	16453	319488	37258	178.85	5.06
$[Co(C_{22}H_{26}F_3N_3OS)(H_2O)_2(CH_3COO)_2]$	14351	14956	31908	37258	—	178.90	4.75
$[Co(C_{22}H_{26}F_3N_3OS)(H_2O)_2SO_4]$	14367	14903	16474	31928	37313	178.26	5.16

Thermogravimetric Analysis

The decomposition temperatures of the complexes obtained from their

thermograms are recorded in Fig. 2. The TG values (Table-4) of these Co(II)

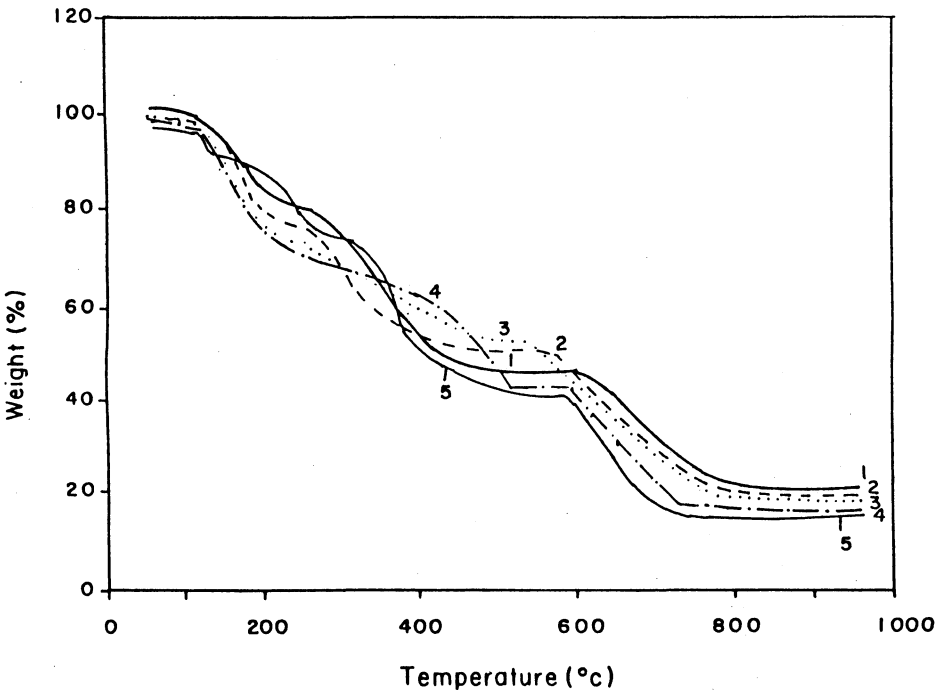


Fig. 2. TGA Curves6 of 1. $[Co(FPH)(H_2O)_2Cl_2]$ 2. $[Co(FPH)(H_2O)_2Br_2]$ 3. $[Co(FPH)(H_2O)_2ClO_4]$ 4. $[Co(FPH)(H_2O)_2(CH_3COO)_2]$ 5. $[Co(FPH)(H_2O)_2SO_4]$

complexes show weight loss in the temperature range 200–210°C corresponding to a water molecule. The expulsion of water from the complexes in the above temperature range indicates the presence of water molecules in the coordination sphere[12]. On the basis of percentage loss in weight, the thermal decomposition for the complexes can be formulated:

TABLE-4
THERMOGRAVIMETRIC ANALYSIS DATA OF COBALT(II) COMPLEXES

Compound	Weight taken (mg)	Temperature at decomposition °C	Temperature at weight loss attains constancy °C	Weight Loss (Mg)	
				Calculated	Found
$[Co(C_{22}H_{26}F_3N_3OS)(H_2O)_2Cl_2]$	86.4	195	800	75.51	76.2
$[Co(C_{22}H_{26}F_3N_3OS)(H_2O)_2Br_2]$	85.7	190	750	63.20	63.45
$[Co(C_{22}H_{26}F_3N_3OS)(H_2O)_2(ClO_4)_2]$	77.5	185	815	59.82	58.95
$[Co(C_{22}H_{26}F_3N_3OS)(H_2O)_2(CH_3COO)_2]$	78.6	183	810	67.26	66.50
$[Co(C_{22}H_{26}F_3N_3OS)(H_2O)_2SO_4]$	80.7	180	730	66.25	67.35

$$[Co(FPH)(H_2O)_2X_2] \xrightarrow{90\text{–}200^\circ C} [Co(FPH)X_2] \xrightarrow{220\text{–}450^\circ C}$$

$$[Co(FPH)]^{2+} \xrightarrow{530\text{–}840^\circ C} CoO$$

After 210°C the oxidation of organic substance begins. It has been found that concurrent with the decomposition and oxidation of organic moiety, some volatilization reaction also takes place. The final black product obtained in each case has been chemically identified as pure cobalt oxide. On the basis of the above results, it can be concluded that:

(i) Lattice water is removed within 75–95°C.

(ii) Coordinated water could be eliminated within the temperature 125–275°C.

(iii) Coordinated Cl, Br, ClO_4, CH_3COO and SO_4 could be removed within 275–445°C.

(iv) The decomposition of complexes leads to the metal oxide as a final product from which the metal content can be calculated.

(v) The thermal stability of the five Co(II) complexes is in the order: $[Co(FPH)(H_2O)_2Cl_2] > [Co(FPH)(H_2O)_2Br_2] > [Co(FPH)(H_2O)_2(ClO_4)_2] > [Co(FPH)(H_2O)_2(CH_3COO)_2] > [Co(FPH)(H_2O)_2SO_4]$.

Based on chemical analysis and various physico-chemical studies, a six-coordinated octahedral structure is tentatively proposed for these new Co(II) complexes as shown in Fig. 3.

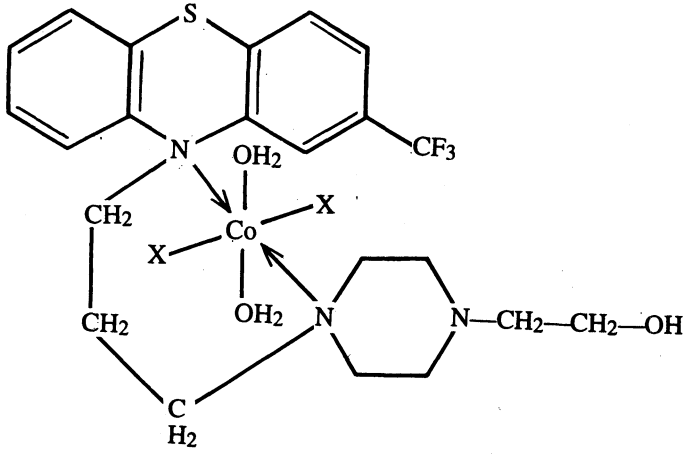


Fig. 3. [Co FPH $(H_2O)_2X_2$] where X = Cl^-, Br^-, ClO_4^-, CH_3COO^- or $\frac{1}{2}SO_4^{2-}$

Screening for antibacterial and antifungal activity

The data on antimicrobial activity of free ligand and its Co(II) complexes presented in Tables-5 and 6 clearly illustrate that the compounds have both antibacterial and antifungal potency against tested organisms. The antimicrobial

activity of the complexes is higher than for the ligand. The incorporation of chloride, perchlorate or sulphate increases the antifungal potency of the organic moiety towards the fungus tested. The antibacterial activity of the complexes against *E. soli* and *S. aureus* increases in the order:

sulphate > chloride > perchlorate.

TABLE-5
PERCENTAGE INHIBITION OF FUNGICIDAL GROWTH

Compound	*A. altenata*			*A. flavus*		
	0.1%	0.2%	0.3%	0.1%	0.2%	0.3%
$(C_{22}H_{26}F_3N_3OS)$	21.43	27.12	34.03	22.30	28.82	35.61
$[Co(C_{22}H_{26}F_3N_3OS)(H_2O)_2(ClO_4)_2]$	36.12	43.41	49.73	37.21	47.43	55.92
$[Co(C_{22}H_{26}F_3N_3OS)(H_2O)_2Cl_2]$	34.46	44.33	56.52	40.13	47.32	61.65
$[Co(C_{22}H_{26}F_3N_3OS)(H_2O)_2SO_4]$	44.23	60.14	65.25	46.64	63.81	70.23

TABLE-6
PERCENTAGE INHIBITION OF BACTERIAL GROWTH

Compound	*E. Coli*			*S. aureus*		
	0.1%	0.2%	0.3%	0.1%	0.2%	0.3%
$(C_{22}H_{26}F_3N_3OS)$	23.2	33.1	37.2	24.6	34.3	38.6
$[Co(C_{22}H_{26}F_3N_3OS)(H_2O)_2ClO_4)_2]$	40.3	51.2	58.4	41.3	53.5	61.7
$[Co(C_{22}H_{26}F_3N_3OS)(H_2O)_2Cl_2]$	42.4	53.5	60.3	44.0	57.6	62.8
$[Co(C_{22}H_{26}F_3N_3OS)(H_2O)_2SO_4]$	47.2	58.7	69.5	48.6	59.5	72.1

The complexation reduces the polarity of the metal ion due to its positive charge which is partially shared with donor atoms and T-electron delocalization over the whole molecule[13]. This increases the liphophilic character of the metal complexes which favours its permeation through lipoid layers of fungus membranes[13].

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