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Research Article

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Synthesis, characterization and antimicrobial activities of some pyridoxine based metal complexes

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ABSTRACT

A series of transition metal complexes of pyridoxine (PD) were prepared and their structures were elucidated on the basis of elemental analyses, conductance measurements, spectral (IR, NMR, UV-Visible and EPR) and thermal studies. On the basis of spectral studies, an octahedral geometry assigned for metal complexes of the type $[M(PD)_2(H_2O)_2]$ $(NO_3)_2$, where M = Mn(II) ***1*** *, Co(II)* ***2*** *, Ni(II)* ***3*** *, Cu(II)* ***4*** *, Zn(II)* ***5****. The complexes exhibit an octahedral geometry around the metal center. The bidentate behavior of the ligand was proposed on the basis of spectral studies. It was found that pyridoxine formed stable metal complexes with these metal ions. The thermal stability of the complexes has been studied by thermogravimetric analysis which support the presence of water in coordination sphere. Cyclic voltammetry studies showed the redox behavior of all complexes. These complexes were screened for their antibacterial and antifungal activities against Escherichia coli, Staphylococcus and Bacillus subtilis, Aspergillus niger and candida albicans species. The results of the antimicrobial studies showed that the metal complexes have higher inhibitory activity than the ligand pyridoxine against the tested bacteria and fungi species.*

Keywords: Pyridoxine complexes, Redox behavior, Thermal studies, Antimicrobial activity

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INTRODUCTION

Metal-based drugs have enormous impact in modern chemotherapy [1].Some metal drug complexes have been found to have antimicrobial, antiparastic and antiviral properties [2]. This has led to numerous investigations on metal drug interactions, and more studies on metal complexes with the aim of discovering more effective chemotherapeutic agents to fight diseases.

Many metal complexes have been used for the treatment of variety of ailments viz, anthiritis, diabetes, inflammatory, diaprostic agents as well as radio sensitivity. Some drugs act as potential ligands in complex formation reaction[3]. Metal complexes are one of the attractive compounds in the development of chemotherapeutic agents because of their chemical reactivity. The nature of ligands and the oxidation state of the metal regulate the biological activity of metal based drugs and also oxidation state of the metal ion dictate coordination geometry among metal ion [4-7]. Study of vitamin -metal complexes is important in drug design and antioxidant activity. Interesting biological properties have been focused in the some of metal-vitamin complexes [8-10].Also it has opened door for basic research in coordination chemistry.

Pyridoxine 2-methyl-3-hydroxy-4,5-bis(hydroxymethyl)pyridine has vitamin activity and essential for the metabolism of amino acids and the maintenance of body cells [11,12]. The investigation of metal complexes of pyridoxines gave promising results as well. Pyridoxine has several potent donor groups and exist in two tautomeric forms [13]. Chelation through the phenolate oxygen and adjacent oxymethyl is common for pyridoxinato(-I)[14],

(N)H-pyridoxinato(II) [15,16] and zwitterionic N-protonated, phenol-deprotonated pyridoxine(0)[17-20]. This present work reports spectral studies, thermal studies, redox behavior and antimicrobial activities of synthesized pyridoxine metal complexes.

EXPERIMENTAL SECTION

All chemicals and solvents employed were of analytical grade and used as received without prior purification unless otherwise stated. Pyridoxine was obtained from Sigma-Aldrich co and was recrystallized from water. Microanalyses were carried out with a Perkin-Elmer 2400 elemental analyzer and magnetic moment with a magnetometer at SAIF, Cochin University, Kerala, India. IR spectra were recorded on FT-IR JASCO 460 PLUS spectrophotometer with samples prepared as KBr pellets. JEOL-FA200 EPR spectrometer was employed to record electron paramagnetic resonance spectra. Shimadzu UV-3101PC spectrophotometer and cuvettes of 1 cm path length were used for recording electronic spectra. Conductivity measurements were carried out in non aqueous solutions of the complexes with an Elico conductivity bridge type CM 82 and a dip-type cell of cell constant, 1.0. Cyclic voltammetry measurements were made on Princeton EG and G-PARC model potentiostat. The thermal analyses were performed with a Perkin Elmer Diamond instrument at a heating rate of 5 °C/min under a dynamic air atmosphere (150 ml/min) in the temperature range of 20-800°C. The antimicrobial activity of all complexes and drug was measured by Disc diffusion method. The bacterial subcultures were auto claved for 20 min at 121^0C. The bacteria were then cultured for 24 h at 37^0C in an incubator. The test solution was added dropwise to a 10mm diameter Whatman No. 1 filter paper disc placed at the center of each agar plate. These discs were then kept at incubator maintained at 37^0C. After 4 days, the inhibition zone around the discs in each plate was measured.

2.2 Synthesis of complexes [1-5]

To a solution of Pyridoxine, (0.338 g, 2 mmol) 20 ml of methanol was added a methanolic solution of manganese (II) nitrate (0.245 g, 1 mmol). The reaction mixture was stirred at room temperature for 5 hours in a magnetic stirrer, filtered and evaporated in vacuo to give the dark brown solid **(1)**. The solid was, then washed 3-4 times with hot methanol, then with diethyl ether (10 mL × 3 times) and finally dried in vacuo. The metal complexes **(2-5)** were obtained following a similar procedure as described for the manganese complex. The purity of the complexes was checked by C, H, N analysis and the results were found to be in good agreement with the calculated values given as follows: Complex **1** Found: C, 42.74%; H, 5.95%; N, 5.54%;Mn ,12.07%,O, 28.80% $C_{16}H_{26}MnN_4O_{14}$ calcd: C, 44.74% %; H, 6.05%;N, 6.52%; Mn, 12.81%; O, 29.83%; complex **2** Found: C, 43.99%; H, 5.99%; N, 6.10% ;Co, 12.9%; O,28.12%;$C_{16}H_{26}CoN_4O_{14}$ calcd: C, 44.34%; H,6.00%; N, 6.46%; Co.13.61%; O,29.57%; complex **3** Found: C, 44.01%; H, 6.99%; N, 5.96%;Ni,13.0%;O, 29.66% $C_{16}H_{26}NiN_4O_{14}$ calcd: C, 44.37%; H, 6.01%; N, 6.47%; Ni,13.56%;O,30.21%; complex **4** Found: C, 42.73%; H, 5.34%; N, 5.90%;Cu,13.00%;O,29.94%; $C_{16}H_{26}CuN_4O_{14}$ calcd: C, 43.88%; H, 5.94%; N, 6.47%;Cu,14.52%;O,29.25% complex **5** Found: C, 42.63%; H, 5.31%; N, 6.98%; Zn,13.9%;O,28.8%; $C_{16}H_{26}ZnN_4O_{14}$ calcd: C, 43.69%; H, 5.92%; N, 6.37%; Zn,14.88%;O,29.13%;

RESULTS AND DISCUSSION

3.1 Melting point and conductance

The powdered metal complexes are partially soluble in water and soluble in organic (DMSO and DMF) solvents. The analytical data (melting point and conductance) obtained and are presented in Table 1. The order of melting point of complexes are Mn(II) < Co(II) < Ni(II) < Cu(II) < Zn(II) which is also the order of increasing atomic number. It may be due to increasing ionic potential of the central metal ions that enhances the lattice energy as we move from **1** to **5.** The melting points of the synthesized metal complexes showed higher than their parent ligand Pyridoxine. This probably indicates the formation of complexes. The molar conductivity values showed that the complexes are weak electrolytes. The synthesized complexes obtained, showed a single spot on the thin layer chromatography. This indicates the coordination between the drug and metal ions; which also determines the purity of the complexes. The analytical data of these complexes showed that the solids are stable and can be stored for months without any significant change in their formulae.

3.2 Electronic absorption and EPR spectra

The electronic spectra of ligand and complexes were recorded in DMSO solution. Ligand exhibits a band around 289 nm which is due to the intra ligand π -π *transition. In cobalt complex, the band around 362 nm is assigned to LMCT, n- π *transition. The band at 552 nm is attributed to d-d transitions, which are represented as $^4T_{1g}$-$^4A_{2g}$ and $^4T_{1g}$ (F)-$^4T_{1g}$ (P) assigning the octahedral structure. In Ni(II) complex the lowest energy band observed at 910 nm was due to $^3A_{2g}$-$^3T_{2g}$(F) and bands at 590 and 420 nm were assigned to $^3A_{2g}$-$^3T_{1g}$ (F) and $^3A_{2g}$-$^3T_{2g}$(P) respectively, suggesting the octahedral geometry. The complex **4** showed a band at 960nm attributable to ^2E_g -$^2T_{2g}$ assuming the distorted octahedral geometry.The X band EPR spectrum of our copper (II) complex was recorded at X-band

frequencies at 300 K. The 300 K spectrum shows isotropic peak ($g_{isotropic}$ = 2.090) but does not reveal nitrogen coupling.

3.3 FT-IR Spectra

Infrared spectra were recorded in the region of 4000-400 cm^{-1} and it provides some information regarding the mode of coordination in the transition metal complexes. Relevent IR frequencies with tentative assignments to various modes of vibration of complexes and ligand are presented in Table 2. The ligand pyridoxine behaves as an ionic bidentate ligand. The metal ion coordinated to ligand through the C(4)-CH_2OH and the deprotonated phenolic group. The IR spectra of all complexes show a strong band in the region 3420-3450 cm^{-1} , which can be attributed to ν O-H of H_2O and CH_2OH. This supports the presence of water molecule in the coordination sphere in all complexes. The very intense bands at 1325 cm^{-1} and 1155 cm^{-1}, which were assigned to phenolic C-O groups. The average intensity band at 1607 cm^{-1} was assigned to the C=N vibration frequency[21]. The IR spectra of metal complexes **1, 3 and 4** are given in Fig. 1, 2 and 3. There was sharp modification between the IR spectra of the metal complexes and drug (PD). The IR bands, $\nu_{(CH2OH)}$ 3410 cm^{-1}, $\nu_{(C-OH)}$ 3016 cm^{-1} observed for PD are shifted to 3338 cm^{-1} in the Cu (II)–PD complex (**4**). This shift can be explained on the basis of the fact that the oxygen atom of (CH_2OH group) of ligand donate a pair of electrons to the central Mn (II) metal, forming a coordinate covalent bond [22]. A band of medium intensity at 1500 cm^{-1} is characterization of coordinated phenolic C-O stretching vibration for pyridoxine – metal complexes. It is confirmed that the absorption band of phenolic group C-OH displaced with towards lower values, indicating the involvement of Oxygen in coordination [23]. The vibration frequencies $\nu_{C=N}$, $\nu_{C=C}$ of pyridine is not considerably shifted which was suggesting that N-atom of pyridine ring is not involved in complex formation. In all complexes **1-5** a very intense band appears in the region of appears in 1383 - 1389 cm^{-1} which is assigned to NO_3^- anion [24- 26]. Further, the presence of ionic nitrate is supported by the appearance of medium band in the region of 810 – 820 cm^{-1}.

3.4 ^{1}H-NMR Spectra

The H^1 NMR spectra of pyridoxine and its complexes were recorded in DMSO-d_6 solution using TMS as internal standards. The ^{1}H-NMR spectrum of PD shows a peak at 7.90 ppm assignable to pyridine ring (CH=N) which is not having any significant change in all complexes, indicating the non-involvement of pyridine in coordination. PD shows peaks at 2.50, 4.56, and 4.82 ppm, which are assignable to methyl and hydroxy methyl group, respectively. The signals at 2.50 and 4.56 are shifted to upfield indicating that the oxygen of hydroxymethyl at carbon four is involved in chelation process in metal complex **5** (Fig.4). The decreasing intensity of hydroxyl group (5.75 in PD) confirms that the hydroxyl group is participated in the coordination with the central metal atom in all metal complexes.

3.5 Thermal analysis

Thermal analysis is one of the intensity tools to confirm the composition and assessment of the role of the metal ions. The mass losses were accompanied by exothermic as well as endothermic effects [27]. The thermal studies of Pyridoxine and its complexes were carried out. The TG and DTG curves of pyridoxine heated in an air atmosphere at various heating rates indicate a sequential multistep decomposition. At 400^0C, approximately 5.2% of the initial sample remained as charred residue. From the result, there is no change up to 150^oC in PD which indicates water molecule is not present in pyridoxine. The TG curve of pyridoxine ligand shows a maximum mass loss at a range $390\text{-}650^0$C of DTG at 460^0C which is assigned to the exothermic release of C_7H_7NO fragment. In all metal complexes, the first mass loss occurs at temperature range $75\text{-}130^o$C suggesting coordinated water molecules are present in their complexes. Complexes within the temperature range 190^oC-600^oC with a mass loss 16% in complex **5**, 10% in complex **4**, 28 % in complex **2** and 9% in complex **1** corresponding to the removal of C_7H_7NO group with the formation of metal oxide as residue.

3.6 Cyclicvoltammetry

All the complexes show well-defined waves in cathodic and anodic regions. The redox property was studied in the potential range of +2 to -1.6V with the scan rate 0.1V/S. The cyclic voltammogram of Cu(II)–PD(Fig.5) shows two peaks, one in the positive region [Cu(I)/Cu(II)] and another in the negative potential region [Cu(II)/Cu(I)]. The corresponding two anodic peaks are observed at 0.9V [Cu(I)/Cu(II)] and -0.25V [Cu(II)/Cu(I)]. The difference between forward and backward peak potentials can provide a rough evaluation of the degree of the reversibility. The ratio of cathodic to anodic peak height was less than one. However, the peak current increases with the increase of the square root of the scan rates. As the scan rate increases, first cathodic peak is shifted to negative potential and its corresponding anodic peak is shifted to positive potential. The complex is electro active with respect to the metal center and exhibited redox processes.

3.7 Antimicrobial activities

The metal complexes (**1–5)** were tested for their inhibitory effects on the growth of bacteria such as *P. aeruginosa, E. coli, S.cocci* species and fungi such as *Aspergillus niger, Candida albicans* by modified disc diffusion method. The minimum concentration (50 ppm) of standard drug and its complexes were tested for their antibacterial and antifungal activity at the same concentration. From the results (Fig.6a & 6b), it showed that the inhibition zone of metal complexes were higher than the parent ligand(PD). Complex **4** exibited higher anti bacterial and antifungal activities compared to other complexes.

Fig. 1. IR spectrum of $[Mn(PD)_2(H_2O)_2](NO_3)_2$

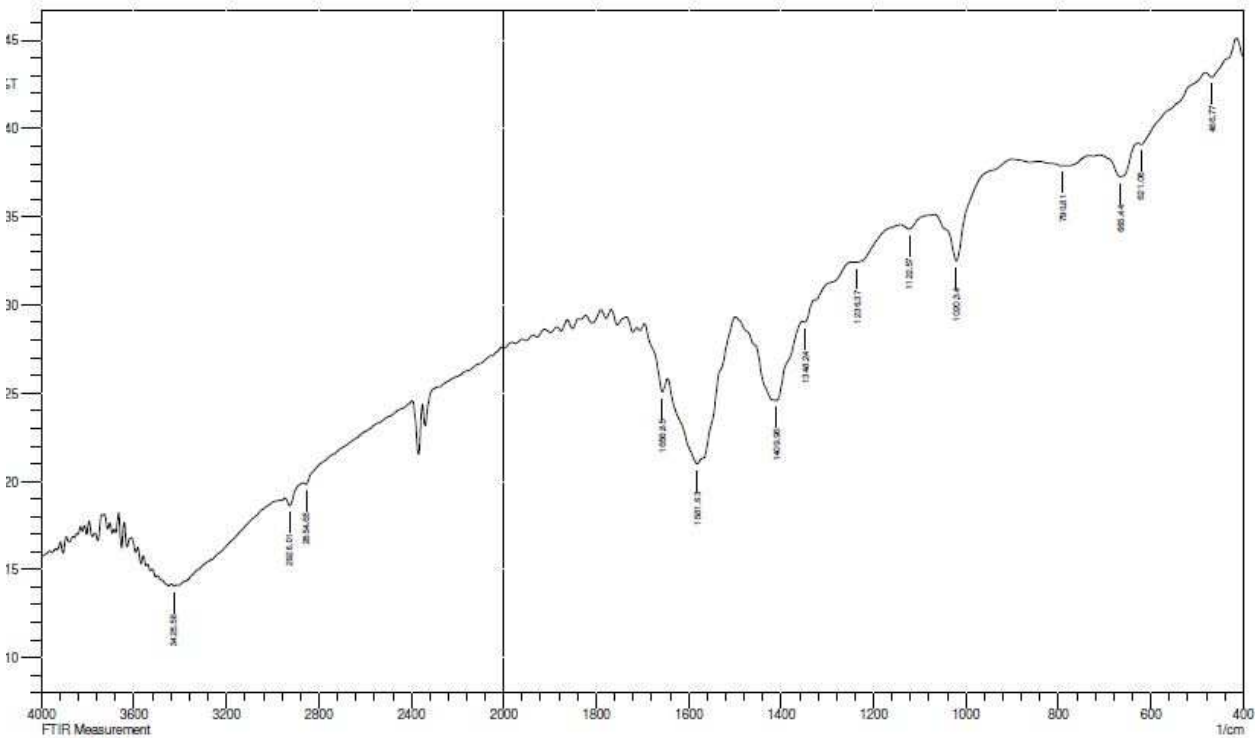

Fig. 2. IR spectrum of $[Ni(PD)_2(H_2O)_2]$ $(NO_3)_2$

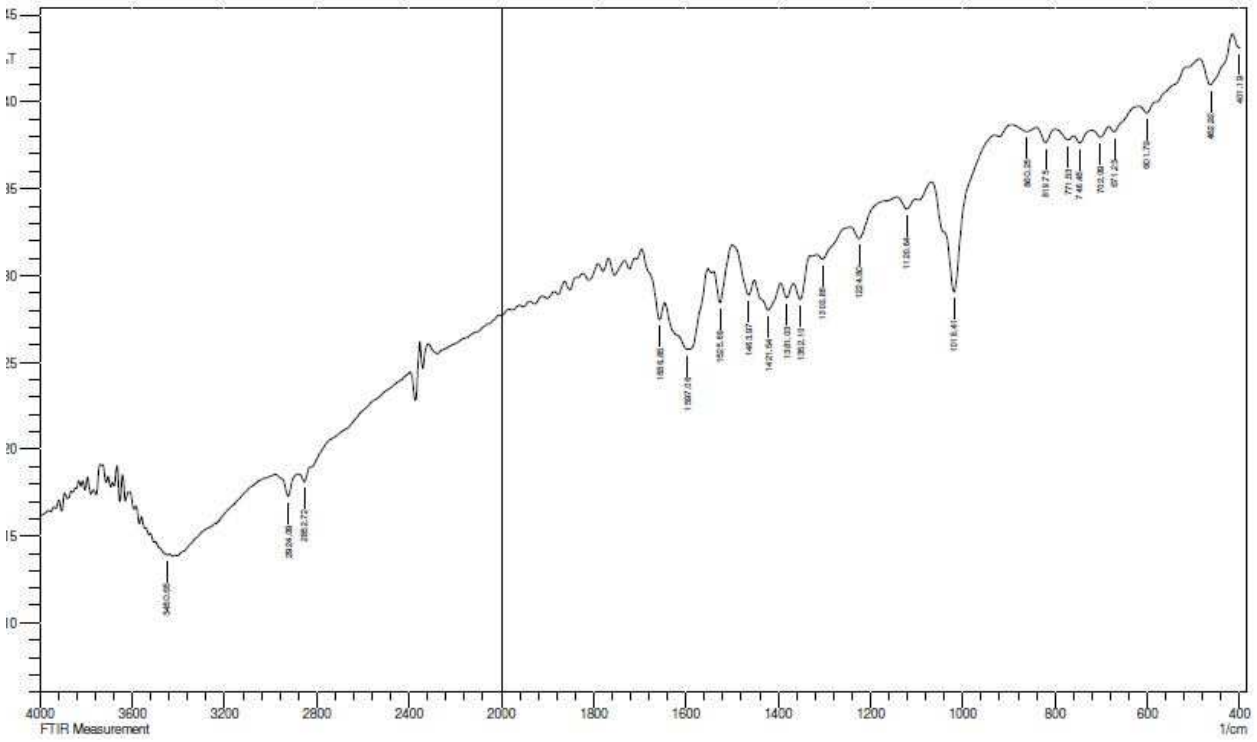

Fig. 3. IR spectrum of $[Cu(PD)_2(H_2O)_2]$ $(NO_3)_2$

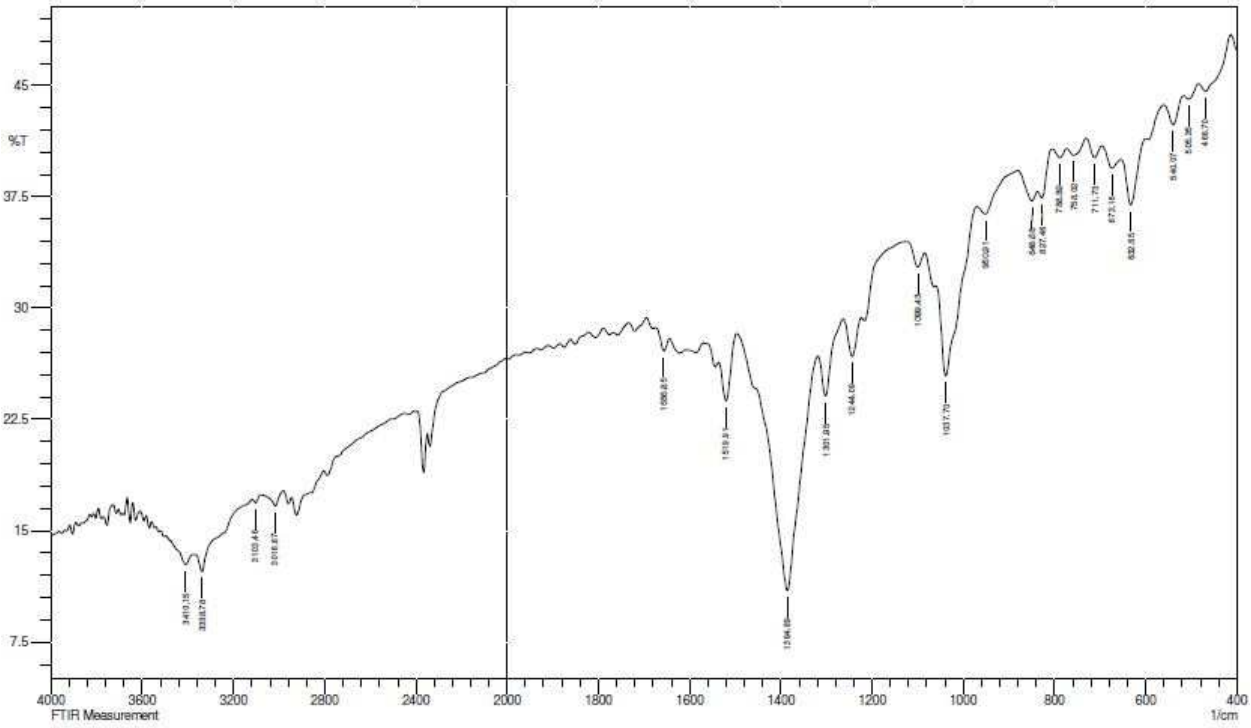

Fig. 4. ^{1}HNMR spectrum of $[Mn(PD)_2(H_2O)_2]$ $(NO_3)_2$

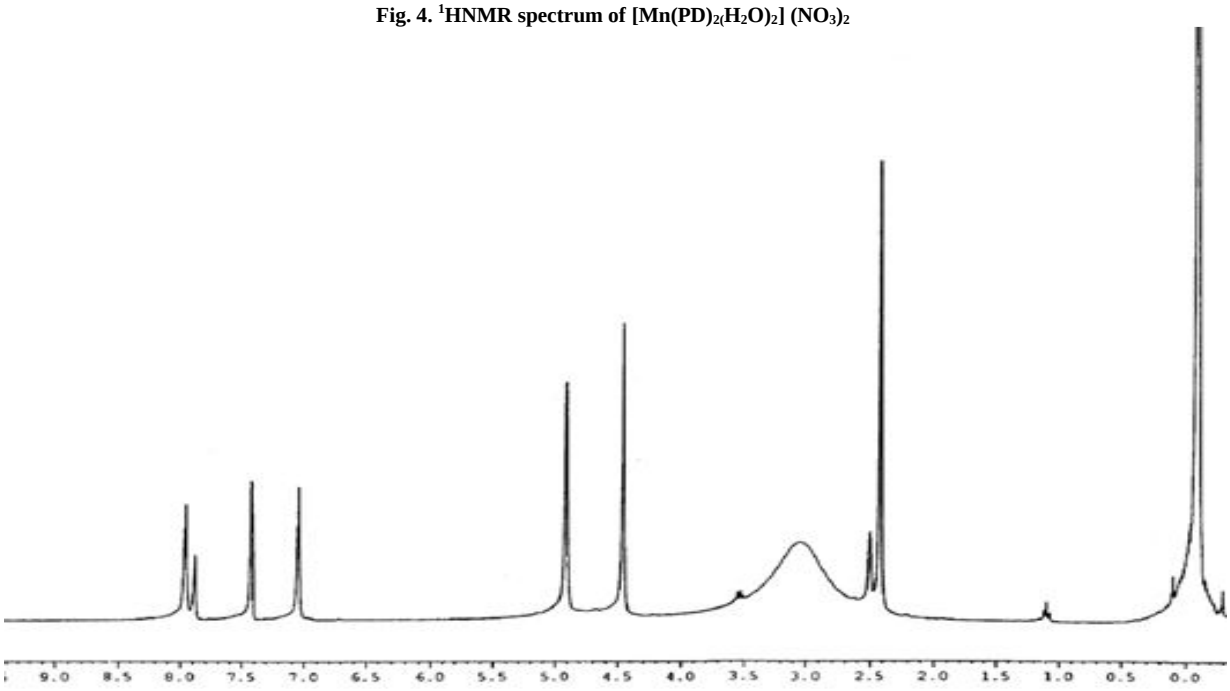

Fig. 5. Cyclic voltammogram of $[Cu(PD)_2(H_2O)_2]$ $(NO_3)_2$

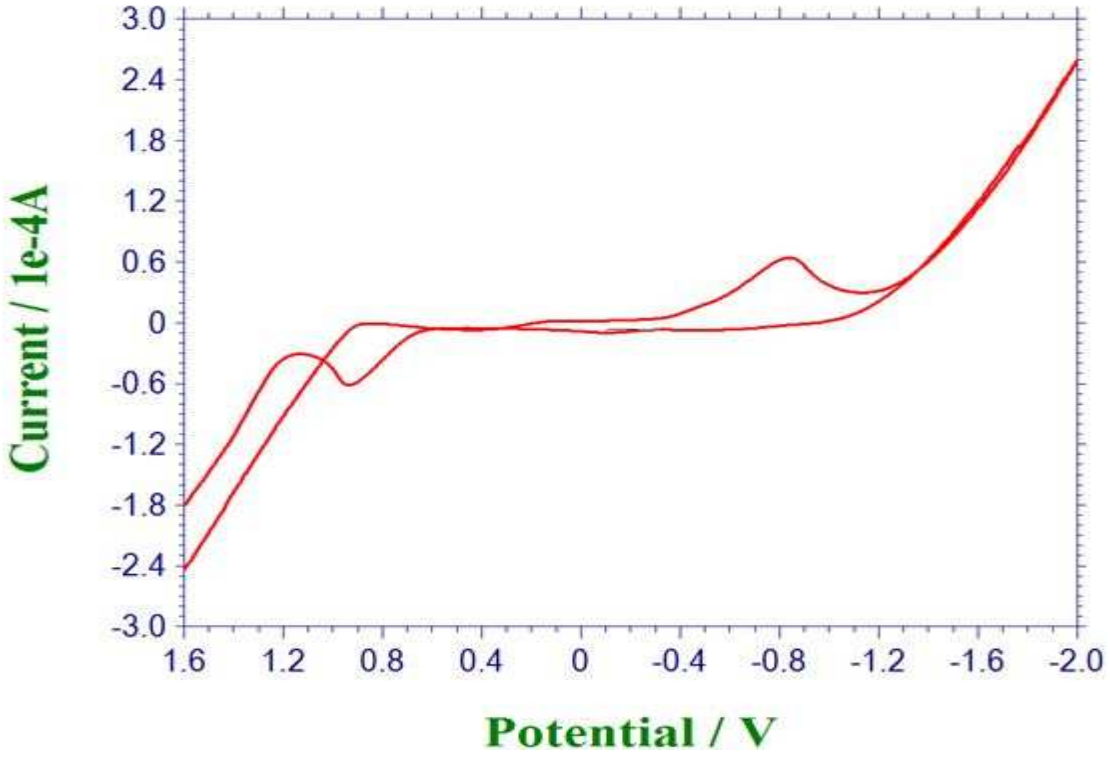

Fig. 6a Anti bacterial activities of Drug/Complexes

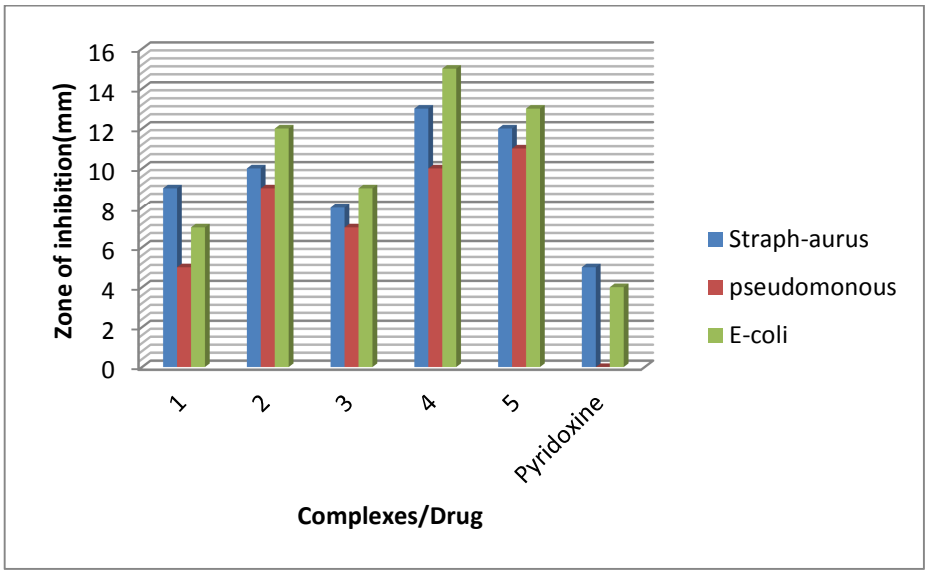

Fig. 6b Anti fungal activities of Drug/Complexes

Table 1. Analytical data of ligand and metal complexes

Drug/Complexes	Melting Point(^{0}c)	Conductivity$\Omega^{-1}cm^2mol^{-1}$
Pyridoxine(PD)	164	4.98
$[Cu(PD)_2(H_2O)_2](NO_3)_2$**(4)**	196	5.78
$[Zn(PD)_2\ (H_2O)_2](NO_3)_2$**(5)**	210	4.32
$[Co(PD)_2(H_2O)_2]\ (NO_3)_2$**(2)**	179	5.56
$[Ni(PD)_2\ (H_2O)_2]\ (NO_3)_2$**(3)**	181	4.39
$[Mn(PD)_2\ (H_2O)_2]\ (NO_3)_2$**(1)**	174	4.56

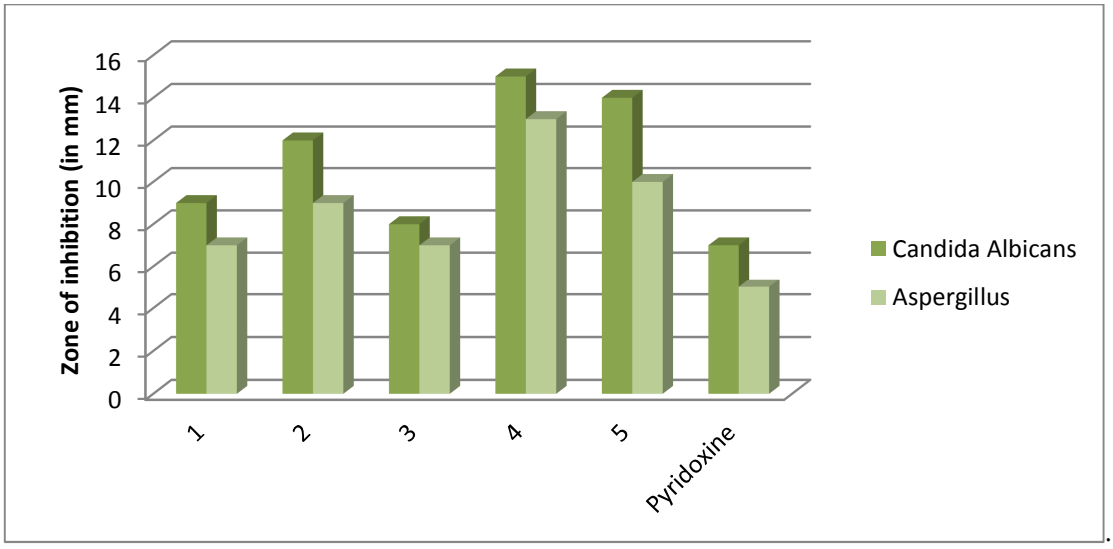

Table 2. Important infrared frequencies (cm^{-1}) of ligand and metal complexes

Assignment	Pyridoxine (cm^{-1})	Complex **1** (cm^{-1})	Complex **2** (cm^{-1})	Complex **3** (cm^{-1})	Complex **4** (cm^{-1})	Complex **5** (cm^{-1})
$\nu_{O-H(CH2O-H)}$	3620	3425	3423	3450	3423	3426
$\nu_{C=NH+}$	2445	2443	2447	2449	2439	2451
$\nu_{(C=C)}$	1646	1655	1654	1656	1653	1654
$\nu_{(C-O);C(5)-(CH2O-H)}$	1017	1003	1026	1011	1037	1026
$\nu_{asym(NO3^-)}$	------	1403	1390	1383	1384	1391
Heterocyclic ring structure	1230	1234	1238	1236	1244	1242
$\nu_{(M-O)}$	-----	466	533	463	506	513
$\nu_{(phenolicO-H)def}$	3099	2926	2924	2919	3016	3039
$\nu_{(C=N)}$	1520	1518	1523	1525	1519	1522
$\nu_{O-H(H2O)}$	-------	890	975	916	960	935

CONCLUSION

The present work focuses on the synthesis and characterization and studies on biological properties of synthesized transition metal complexes (**1-5**) containing Pyridoxine drug as ligand.

The results obtained suggest that PD is a bidentate ligand, coordinated to metal through deprotonated phenolic oxygen and the oxygen of hydroxymethyl at carbon four. Spectral characterization reveals octahedral geometry is assigned for complexes. High thermal stability of the complexes indicates a strong metal–ligand bond in all metal complexes. Cyclic voltammetry studies of the metal complexes revealed the semi reversible in nature. The in vitro antimicrobial studies indicate that the complexes show higher anti microbial activity than the ligand (PD).

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