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MIXED LIGAND COMPLEXES OF NICKEL(II), COPPER(II) AND ZINC(II) WITH NICOTINANILIDE AND THIOCYANATE

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ABSTRACT

Mixed ligand nickel(II), copper(II) and zinc(II) complexes of nicotinanilide and thiocyanate were prepared. Metal complexes were characterized by molar conductivity measurements, micro elemental analysis, FT-IR, UV-Visible spectroscopy, electrochemical and antimicrobial studies. The complexes are of 1: 2 (metal : ligand) stoichiometry and are non-electrolytes in solution. The structural analysis indicates a four-coordinated MN_2S_2 chromophore in a distorted tetrahedral geometry by two nicotinanilide and two thiocyanate ligands.

Keywords: Nicotinanilide, Potassium Thiocyanate, Nickel, Copper, Zinc, Spectral Studies, Biological activity.

INTRODUCTION

Transition metal ions are playing an important role in biological processes in the human body [1, 2]. For example, nickel (II), copper (II) and zinc (II) ions are the most abundant transition metals in humans. They are found either at the active sites or as structural components of a good number of enzymes [3, 4]. The study of the coordination chemistry of biologically important metal ions with mixed ligands has been one of the recent developments in the field of bioinorganic chemistry. Pyridine derivatives play significant role in many biological systems as the component of several vitamins, nucleic acids, enzymes and proteins [5]. But, studies on the antimicrobial activities of their metal complexes are rare in literature. Metal complexes containing nitrogen and sulphur donors have been proved to be potential antibacterial and fungial agents [6] as well as component of several vitamins and drugs [7, 8].The binding of metal ions to nicotinanilide groups has been a subject of increasing interest, because many of these reactions provide simple models for much more complex metal peptide systems and enzymes. We report here the synthesis, characterization and biological activities of some new nickel (II), copper (II) and zinc (II) mixed-ligand complexes containing nicotinanilide and thiocyanate as ligands. The synthesized complexes are characterized by elemental, IR and electronic spectroscopic analysis.

EXPERIMENTAL SECTION

General procedure

Nicotinanilide (NAL) and potassium thiocyanate were purchased from Sigma–Aldrich. Nickel nitrate,

copper nitrate and zinc nitrate used as received by S.D. Fine, Mumbai, (India). Commercial grade solvents were purified by standard procedure before use.

Methods and instrumentation

FT-IR spectra (4000–400 cm^{-1}) were collected on Thermo Nicolet Model 6700 FT-IR spectrometer with samples prepared as KBr pellets. UV–Vis spectra measurements were recorded on a Cary 5E model in the range of 200–800 nm. Elemental analyses were measured by Perkin-Elmer 2400 series. Metal analysis was obtained by Varian Spectra 200 atomic absorption spectrometer. The molar conductivity measurement of all the complexes at room temperature was determined using a digital conductivity bridge (Equiptronics, EQ 660) in acetonitrile medium (10^{-3} M). Cyclic voltammetry experiments were performed using a Cypress Electroanalytical System with a glassy carbon working electrode, silver wire reference electrode, platinum counter electrode and tetra (n-butyl) ammonium perchlorate as supporting electrolyte.

Antimicrobial assay

Agar diffusion assay was used to determine the anti-bacterial activity of Leaf extract. Nutrient agar was prepared and poured in the Petri dish. 24 hours growing culture (*K. pneumonia, V. cholera, M. luteus* and *S. aureus*) were swabbed on it. The different concentrations of the crude extract were loaded in the wells. The plates were then incubated at 37ºC for 24 hours. The inhibition diameter was measured. Potato Dextrose agar was prepared and poured in the Petri dish. 24 hours growing culture (*C. albicans, C. tropicalis* and *C. parapsilosis*) were swabbed on it. The different concentrations of the crude extract were loaded in the wells. The plates were then incubated at 37ºC for 24 hours. The inhibition diameter was measured.

Synthesis of the complexes

$[Ni(NAL)_2(SCN)_2]$

The nicotinanilide (NAL) (1.86 g, 9.4 mmol) and Nickel nitrate trihydrate (1 g, 4.7 mmol) were dissolved in 40 mL of methanol, and the reaction mixture was allowed to react in microwave irradiation ~10 seconds. During the reaction, 20 mL methanolic solution of potassium thiocyanate (0.91 g, 9.4 mmol) was added to the reaction mixture [9]. The reaction mixture was kept undisturbed and irradiated at a stable medium power level (600W) in the Microwave oven. The pale green color precipitate was filtered and washed with cold methanol. The complexes $[Cu(NAL)_2(SCN)_2]$ and $[Zn(NAL)_2(SCN)_2]$ were synthesized by similar procedure, using corresponding metal nitrates. Yield: 44%. m.p:213 ^oC. Analytical data for $C_{26}H_{20}N_6NiO_2S_2$: Calc.(M.Wt: 571.3): C, 54.66; H, 3.53; N, 14.71, Ni, 10.27%. Found: C, 54.59; H, 3.40; N, 14.52, Ni, 10.46%. Selected IR data (KBr disc) (ν/cm^{-1}): 3294 ν (NH), 1669 ν (C=O), 1598 ν (C=N), 2083 ν (CN), 700 ν (CS), 583 ν (M-N), 454 ν (SCN). Conductance ($\Lambda_m/S\ cm^2\ mol^{-1}$) in CH_3CN: 67.6.

$[Cu(NAL)_2(SCN)_2]$

The nicotinanilide (NAL) (1.84 g, 9.2 mmol), Copper nitrate trihydrate (1g, 4.6 mmol) and Potassium thiocyanate (0.89g, 9.2 mmol). Blue color compound. Yield: 51%. m.p:186 ^oC. Analytical data for $C_{26}H_{20}N_6CuO_2S_2$: Calc.(M.Wt: 576.15): C, 54.20; H, 3.50; N, 14.59, Cu, 11.03%. Found: C, 54.28; H, 3.40; N, 14.49, Cu, 10.96%. Selected IR data (KBr disc) (ν/cm^{-1}): 3296 ν (NH), 1663 ν (C=O), 1601 ν (C=N), 2093 ν (CN), 696 ν (CS), 573 ν (M-N), 442 ν (SCN). Conductance ($\Lambda_m/S\ cm^2\ mol^{-1}$) in CH_3CN: 81.2.

$[Zn(NAL)_2(SCN)_2]$

The nicotinanilide (NAL) (1.82 g, 9.2 mmol), zinc nitrate trihydrate (1 g, 4.6 mmol) and Potassium thiocyanate (0.89 g, 9.2 mmol). Colorless compound. Yield: 53%. m.p:200 ^oC. Analytical data for $C_{26}H_{20}N_6ZnO_2S_2$: Calc.(M.Wt: 578): C, 54.03; H, 3.49; N, 14.54, Zn, 11.31%. Found: C, 54.14; H, 3.43; N, 14.45, Zn, 11.23%. Selected IR data (KBr disc) (ν/cm^{-1}): 3309 ν (NH), 1657 ν (C=O), 1602 ν (C=N), 2079 ν (CN), 695 ν (CS), 592 ν (M-N), 425 ν (SCN). Conductance ($\Lambda_m/S\ cm^2\ mol^{-1}$) in CH_3CN: 70.7.

RESULTS AND DISCUSSIONS

A new series of nicotinanilide based mononuclear nickel (II), copper (II) and zinc (II) complexes have been prepared by microwave irradiation method in the presence of corresponding metal nitrates. The complexes were stable in atmosphere and were

polycrystalline. The synthetic pathway of mononuclear complexes is shown in scheme I

FT – IR and Electronic spectra

The broad absorption band observed in all the complexes in the region 3293- 3309 cm^{-1} is due to the presence of -NH group. The peak around 1598 – 1602 cm^{-1} in the complexes, indicate the presence of C=N stretching frequency [10-11]. The presence of N-donor organic ligand nicotinanilide is evident from the strong absorption bands of the carbonyl (-C=O) vibration around 1657-1669 cm^{-1}. Coordination of sulphur is confirmed by the presence of new bands in the range 573–592 cm^{-1}, assignable to (M–N) for these complexes [12-13]. Another indication for S-bonded SCN is the weak bands appearing at 425-454 cm^{-1}[14]. The FT-IR spectrums of all complexes are shown in Fig.1a-1c. The electronic spectral data obtained are summarized in Table 1. All spectral studies were carried out in DMF solution. UV bands in the range of 260 – 275 nm were observed in the free ligand, due to intra-ligand charge transfer transition [15]. A moderately intense band observed in the range of 390–400 nm is assigned to ligand to metal charge transfer transition for all the complexes and a weak band observed in the visible range at 550–560 nm for copper (II) and nickel (II) complexes, are characteristic of the metal ions in a four coordination environment [16].

Electrochemical properties of the complexes

Conductivity measurements of all the mononuclear complexes were carried out in DMF medium. The Λ_m values in range from 67 to 82 S cm^2 mol^{-1}, indicate that all the complexes are neutral [17]. The electrochemical properties of the complexes reported in the present work were studied by cyclic voltammetry in dimethylformamide containing 10^{-1} M tetra (n-butyl) ammonium perchlorate. The cyclic voltammograms for the nickel (II), copper (II) and zinc (II) complexes are shown in Fig.2a-d. The copper (II) and zinc (II) complexes undergo reduction at cathodic potentials. The nickel (II) complex undergoes both reduction and oxidation in cathodic and anodic potentials, respectively. The electrochemical data are summarized in Table 2.

Reduction process at negative potential

All the complexes showed reduction at the potential range of – 0.70 V to – 0.95 V (E_{pc}) and the reduction process is found to be irreversible in nature. The controlled potential electrolysis carried out at 100 mV is more positive than the anodic (oxidation) wave and conveys the consumption of one electron per molecule [17]. So, the one electron redox processes are assigned as follows,

$$M^{II} \longrightarrow M^{I}$$

Oxidation process at positive potential

The cyclic voltammetric behaviors of nickel (II) complexes were recorded at anodic potential in the range 0 to +2.00 V. The voltammogram displays an irreversible one electron reductive response at a positive potential in the range +1.15 V. The cyclic voltammogram for the nickel (II) complexes are shown in Fig. 4d. The electrochemical data are summarized in Table 2. The controlled potential electrolysis carried out at 100 mV, more positive than the anodic (oxidation) wave and conveys the consumption of one electron per molecule [17]. So, the oxidation processes are assigned as follows,

$$Ni^{II} \longrightarrow Ni^{III}$$

Screening of antimicrobial activities

All the prepared complexes were tested against selected four bacteria such as *Klebsiella pneumonia* (MTCC 109), *Vibrio cholera* (ATCC 14035), *Micrococcus luteus* (ATCC 14452), and *Staphylococcus aureus* (MTCC 96). The observed antifungal activity of all the complexes against *Candida albicans (*MTCC 183), *Candida tropicalis (*MTCC 184) and *Candida parapsilosis* (MTCC 2509). The observed antimicrobial activity values for all complexes are given in Table 3. Complexes containing nicotinanilide show apparently an

enhanced antimicrobial activity [18]. The results are quite promising. The bacterial screening results (Table 3) reveal that the complexes showed maximum activity against *Klebsiella pneumonia*. The antimicrobial data reveal that the complexes are more bioactive. The enhanced activity of the metal complexes may be ascribed to the increased lipophilic nature of the complexes arising due to chelation. It is probably due to faster diffusion of the chelates as a whole through the cell membrane or due to the chelation effect. Another interesting result observed here is that the complexes of $[Zn(NAL)_2(SCN)_2]$ and $[Cu(NAL)_2(SCN)_2]$ show higher activity than the complex$[Ni(NAL)_2(SCN)_2]$. These results suggest that the nature of the metal and the coordinated metal ion play significant roles in the inhibition activity.

Scheme 1
M = Ni, Cu, Zn

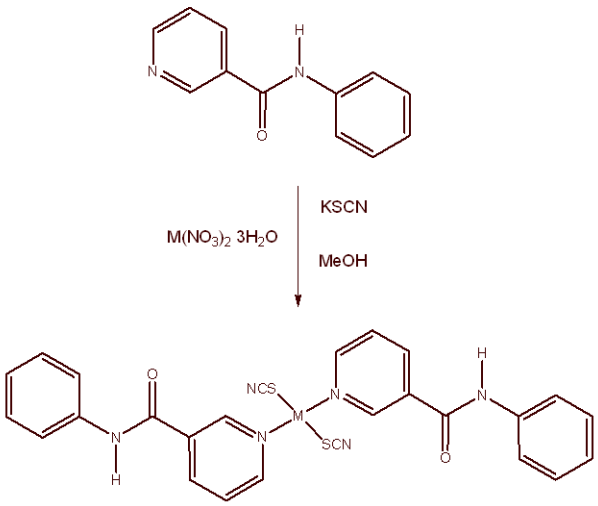

Figure 1a.
FT IR spectrum of the complex [NiL1]

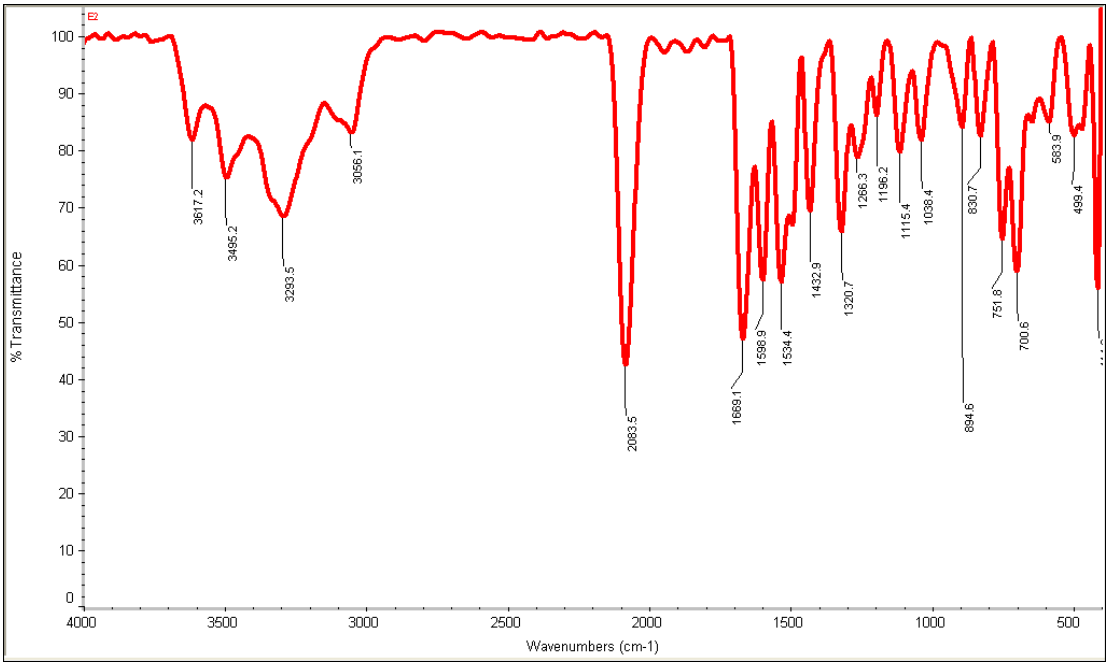

Figure 1b.
FT IR spectrum of the complex [CuL1]

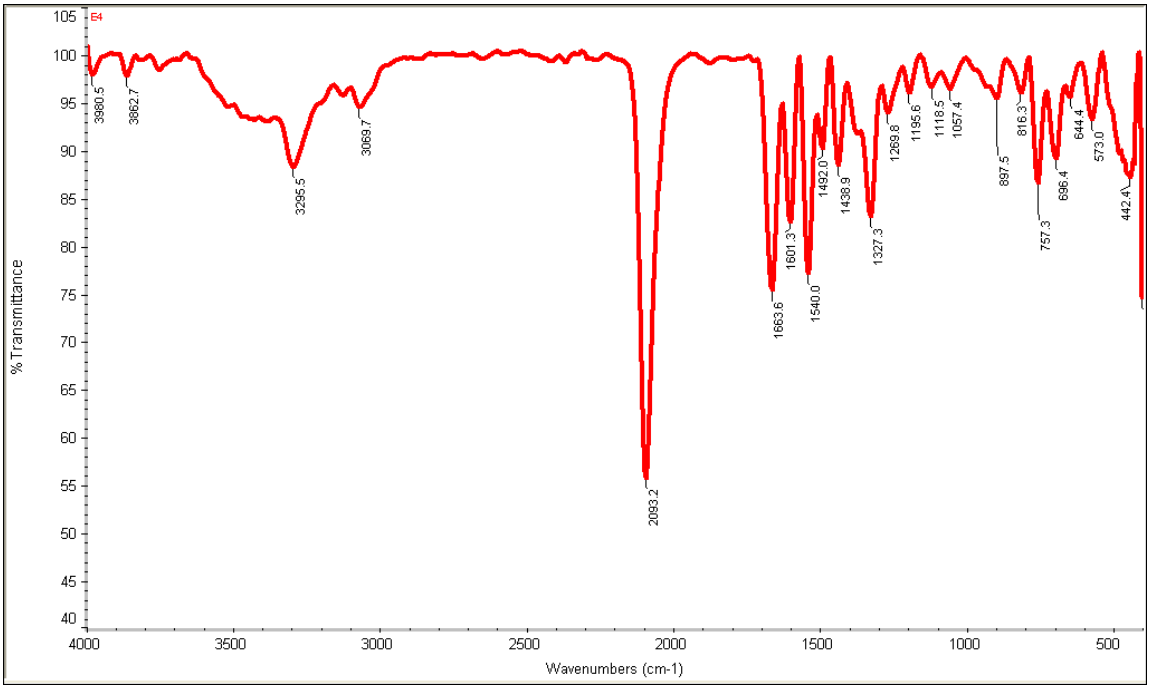

Figure 1c.
FT IR spectrum of the complex [ZnL1]

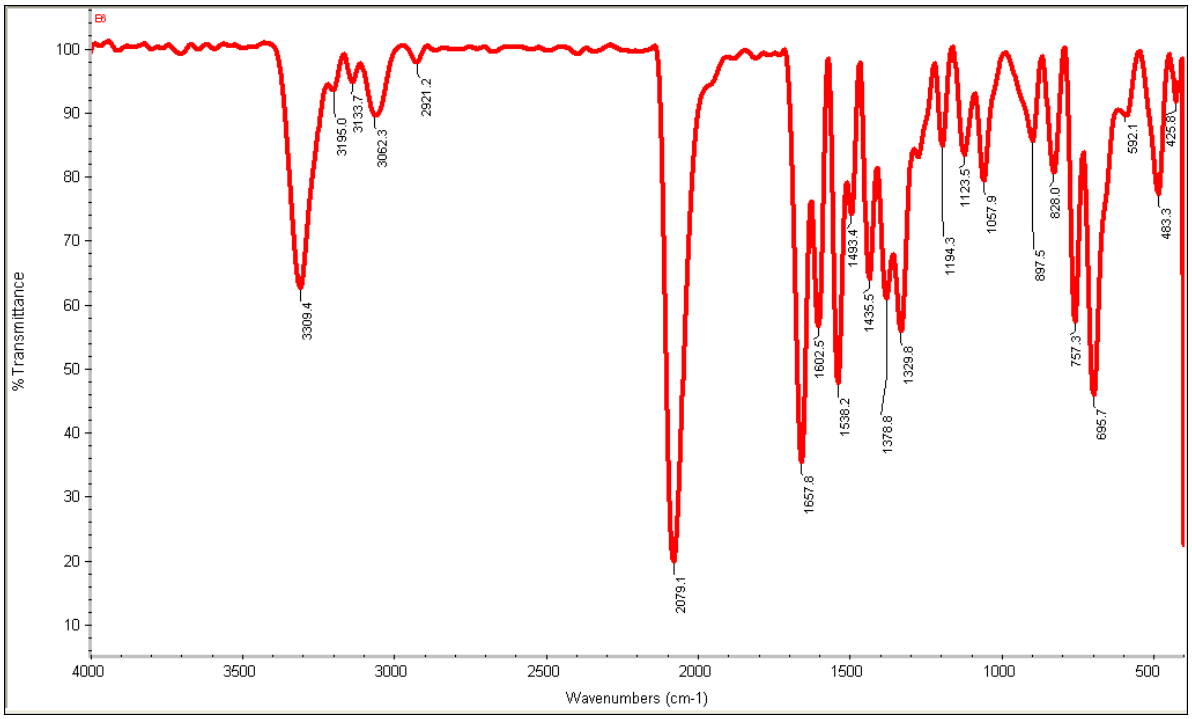

Figure 2a.
Cyclic voltammogram of the nickel(II) complex.(Reduction process)

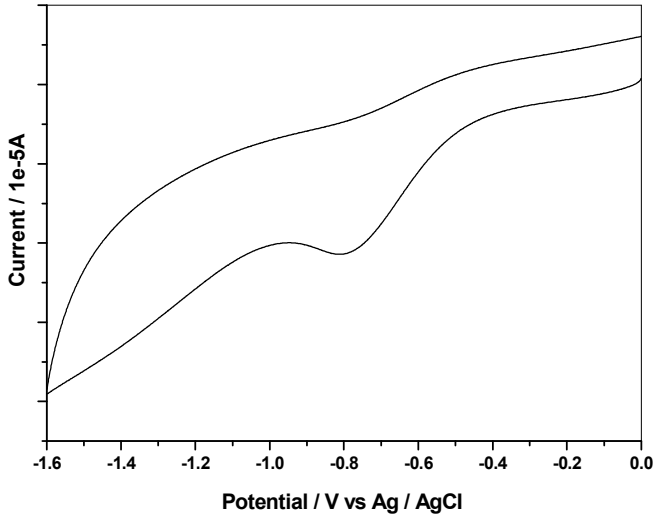

Figure 2b.
Cyclic voltammogram of the copper(II) complex. (Reduction process)

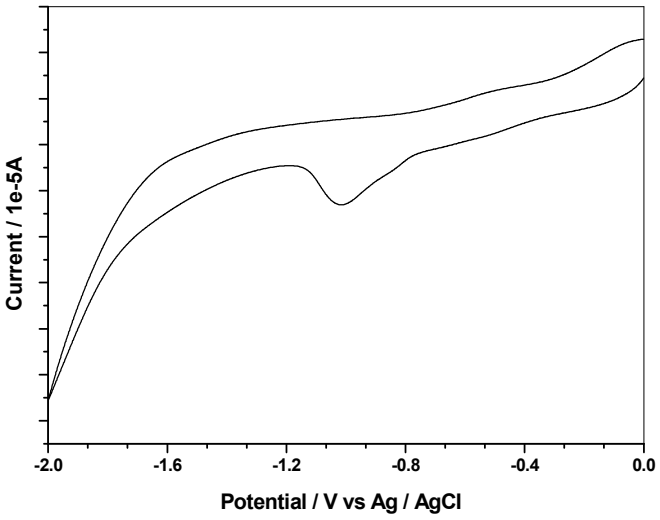

Figure 2c.
Cyclic voltammogram of the zinc(II) complex. (Reduction process)

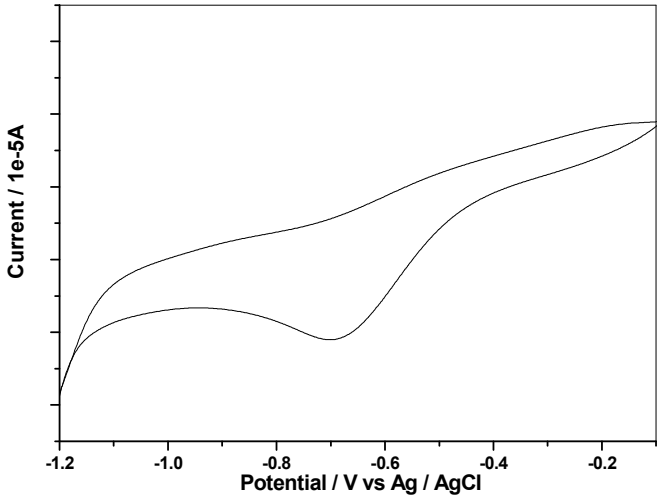

Figure 2d.
Cyclic voltammogram of the nickel(II) complex. (Oxidation process)

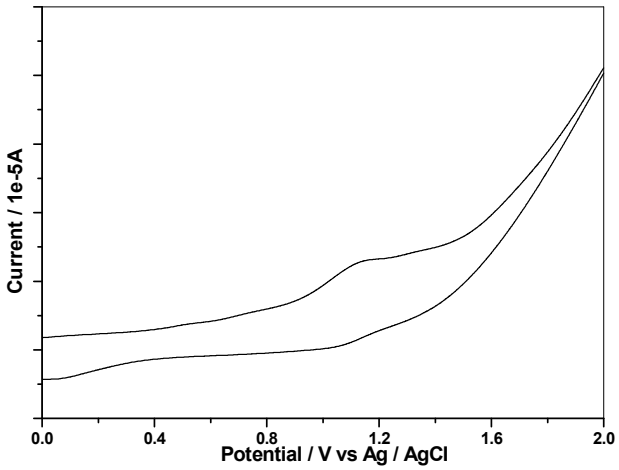

Table1
Electronic spectral data of mononuclear complexes.

No.	Complexes	[λ_{max} (nm) (ε, M^{-1} cm^{-1})]	
		d-d	Charge transfer
1	$[Ni(NAL)_2(SCN)_2]$	560 (150)	390 (11 500), 265 (17 500)
2	$[Cu(NAL)_2(SCN)_2]$	550 (140)	400 (10 635), 260 (17 700)
3	$[Zn(NAL)_2(SCN)_2]$	-	395 (11 110), 275 (17 900)

Table 2
Electrochemical data of mononuclear complexes

No.	Complexes	Reduction E^1_{pa}(V)	Oxidation E^1_{pc}(V)
1	$[Ni(NAL)_2(SCN)_2]$	-0.80	1.15
2	$[Cu(NAL)_2(SCN)_2]$	-0.95	-
3	$[Zn(NAL)_2(SCN)_2]$	-0.70	-

Measured by CV at 100 mV/s. E vs Ag/AgCl conditions: GC working and Ag/AgCl reference electrodes; supporting electrolyte TBAP; concentration of complex 1×10^{-3} M, concentration of TBAP 1×10^{-1} M.

Table 3
Antimicrobial properties of the complexes

No.	Test Bacteria	Zone of Inhibition (mm) µg/ml					
		$[Ni(NAL)_2(SCN)_2]$		$[Cu(NAL)_2(SCN)_2]$		$[Zn(NAL)_2(SCN)_2]$	
		50	100	50	100	50	100
1	*K. p*	18	26	23	29	38	46
2	*V. c*	20	25	25	30	28	32
3	*M. l*	13	15	16	22	29	36
4	*S. a*	15	18	14	20	20	28
	Test Fungal						
5	*C. a*	9	13	11	18	13	19
6	*C. t*	8	14	12	21	15	21
7	*C. p*	10	17	13	22	16	27

Notes: Klebsiella pneumonia (MTCC 109), Vibrio cholera (ATCC 14035), Micrococcus luteus ATCC (14452), Staphylococcus aureus (MTCC 96), Candida albicans (MTCC 183), Candida tropicalis (MTCC 184) and Candida parapsilosis (MTCC 2509).

CONCLUSION

The new nicotinanilide based mononuclear nickel(II), copper(II) and zinc(II) complexes were synthesized and characterized by elemental analyses, UV-vis, FT-IR, conductivity measurements, electrochemical and biological studies were carried out. The complexes are insoluble in most of organic solvents, but soluble in DMF and DMSO. The stoichiometry of the metal complexes is 1:2. Electronic spectra of all complexes indicate distorted tetrahedral geometry. Cyclicvoltammetry exhibit one electron irreversible process. General structures of all the complexes show distorted tetrahedral geometry around the central metal ions. All complexes show biological activity. Among these three complexes, $[Zn(NAL)_2(SCN)_2]$ show higher activity.

REFERENCES

1. W. Kaim, B. Schwederski. Bioinorganic Chemistry: Inorganic Elements of Life, John Wiley and Sons: London. 1996:39-262pp.
2. C. Xiao-Ming, Y. Bao-Hui, C.H. Xiao, X.J. Zhi-Tao. Model complexes for the carboxylate– histidine–metal triad systems in metalloenzymes. Synthesis, crystal structures and spectroscopic properties of $[M(Him)_2(O_2CMe)_2]$(M = Zn^{II} or Co^{II}, Him = imidazole) Chem. Soc., Dalton Trans. 1996:3465-3468.
3. F.A. Cotton, G. Wilkinson. Advanced Inorganic Chemistry, 5th ed., John Wiley and Sons: New York. 1988:1358-1371pp.
4. N.N. Greenwood, A. Earnshaw. Chemistry of the Elements, Pergamon Press: Oxford. 1984:1392-1420pp.
5. S.C. Nayak, P.K. Doss and K. Sahoo. The thermal and spectral properties of trans-

[chloro-bis (dimethylglyoximato) Co(III)] complexes containing heterocyclic donor ligands. J.Anal.Appl.Pyrolysis. 2003; 70:699-709.
6. J. Crim and H. Petering. The Antitumor Activity of Cu(II)KTS, the Copper(II) Chelate of 3- Ethoxy-2-oxobutyraldehyde Bis(thiosemicarbazone). Cancer Res.1967; 27:1278-1285.
7. M. Kato and Y. Muto. Factors affecting the magnetic properties of dimeric copper(II) complexes. Coord. Chem. Rev. 1988; 92: 45-48.
8. R. Nagar. Syntheses, characterization, and microbial activity of some transition metal complexes involving potentially active O and N donor heterocyclic ligands. J. Inorg. Biochem. 1990; 40:349.
9. A. Maria Kulandai Raja Balan, M. Vasanthi, R. Prabu, A. Paulraj, T.Ramachandramoorthy. Complexes of Ni(II), Cu(II) and Zn(II) Benzoates with Nicotinanilide. International Journal of Modern Chemistry, 2013;4(2): 66-78.
10. B.A. Howell, B.B.S. Sastry. Comparison of the activation energies for the thermal decomposition of copper and nickel compounds obtained by various thermogravimetric methods. Thermochim. Acta. 1999; 341: 311-314.
11. F. Arjmand, B. Mohani & Shamima Parveen. New DihydroOO'Bis(salicylidene) 2.2' Aminobenzothiazolyl Borate Complexes: Kinetic and Voltammetric Studies of Dimethyltin Copper Complex with Guanine, Adenine and Calf Thymus DNA. Bioinorganic Chemistry and Applications. 2006: 32896.
12. E. Cramer Roger, M. Douglas Ho, William Van Doorn, A. James, Ibers, Ted Norton & K. Midori, Triphenylmethylphosphoniumtrichloro(caffeine)platinum(II). Inorg. Chem. 1981; 20: 2457- 2461.
13. E.B. Seena, R. Maliyeckal, Prathapachandra Kurup, Spectral and structural studies of mono- and binuclear copper(II) complexes of salicylaldehyde N(4)-substituted thiosemicarbazones. Polyhedron. 2007; 26: 829–836.
14. Michael Bron & Rudolf Holze, Cyanate and thiocyanate adsorption at copper and gold electrodes as probed by in situ infrared and surface-enhanced raman spectroscopy. Journal of Electronanalytical Chemistry. 1995; 385: 105-113.
15. J. Manonmani, M. Kandaswamy, V. Narayanan, R. Thirumurugan, S. Shanmuga Sundara Raj, G. Shanmugam, M.N. Ponnuswamy, H.K. Fun. Synthesis of copper(II) and nickel(II) complexes using compartmental ligands: X-ray, electrochemical and magnetic studies. Polyhedron, 2001; 20: 3039-3048.
16. A.B.P. Lever. Inorganic Electronic Spectroscopy, 2nd Edn, Elsevier, New York. 1984.
17. W.J. Geary. The use of conductivity measurements in organic solvents for the characterization of coordination compounds. Coord. Chem. Rev. 1971;7: 81-122.
18. R.N. Patel, N. Singh, K.K. Shukla, V.L.N. Gundla, U.K. Chauhan, Synthesis, characterization and biological activity of ternary copper(II) complexes containing polypyridyl ligands. Spectrochim. Acta. 2006;63: 21-26.