



International Journal of Life Sciences Biotechnology and Pharma Research





Research Paper

MICROWAVE ASSISTED SYNTHESIS, SPECTRAL STUDIES AND BIOLOGICAL ACTIVITIES OF SOME TRANSITION METAL COMPLEXES WITH MIXED LIGANDS

Jeeva J^{1*}, Ramachandramoorthy T¹ and Paul Raj A²

*Corresponding Author: **Jeeva J**, ✉ jjeeva1972@gmail.com

Transition metal complexes of Ni(II), Zn(II) and Cd(II) were prepared with mixed ligands, 4-hydroxypyridine(4-HP) and thiocyanate (SCN)- using microwave irradiation. The prepared complexes were characterized by metal estimation, electrical conductance, CHNS analysis, IR, UV-visible and NMR spectral data and their formulae and probable geometries were determined. All these complexes were tested for antibacterial and antifungal activities.

Keywords: 4-hydroxypyridine, Thiocyanate, Antifungal, Antibacterial

INTRODUCTION

Coordination compounds of nickel, zinc and cadmium play a vital role in biological systems (Shriver and Atkins, 1999; Brij Bhushan Tewari, 2012; George and Dimitris, 2013; Joske *et al.*, 2013) and in chemical industry (Helm *et al.*, 2011) which have paved the way for many research work in synthesizing and studying the properties of these transition metal complexes. In all living organisms nickel is distributed in organelles of biological cells and zinc in cytoplasm (Brown and Chatel, 1978). Though cadmium is toxic to biological systems, its complexes are actively

used as fungicides and pesticides (Hartley and Kidd, 1983). These metals form complex compounds with many organic ligands (Shaker and Yang., 2009; Shaker *et al.*, 2009).

Nickel, zinc and cadmium complexes were prepared with 4-hydroxypyridine (4-HP) and thiocyanate ion (SCN)- ligands using microwave irradiation. These synthesized complexes were studied on the basis of metal estimation, electrical conductance, CHNS analysis, IR, UV-visible and NMR spectral data. Then their antibacterial and antifungal activities were screened.

¹ IPG & Research Department of Chemistry, Bishop Heber College (Autonomous), Tiruchirappalli - 620017, India.

² Department of Chemistry, St. Joseph's College (Autonomous), Tiruchirappalli - 620002, India.

MATERIALS AND METHODS

Metal Nitrates and the solvents, viz., DMSO, acetonitrile, DMF, methanol and ethanol used in the synthesis were of AnalaR grade and no further purification was needed. The ligand 4-hydroxypyridine was purchased from Alfa Aesar company and used as such.

INSTRUMENTAL ANALYSIS

Metal estimation for nickel was done colorimetrically and, for zinc and cadmium, volumetrically. For elemental analysis, Elementor Vario EL III was used. Using digital conductivity bridge (Equiptronics, EQ660) at 30°C in acetonitrile medium (10^{-3} M) the electrical conductivity measurements for the complexes were done. The IR spectra were taken using Perkin Elmer Spectrum RXI in 4000-400 cm^{-1} range based on KBr pellet technique. The UV visible spectra were taken by Varian Cary 5000 of range 175-800 nm by solid state diffused reflectance technique. The ^1H NMR and ^{13}C NMR spectra were taken using Bruker AV III of 500 MHz FT NMR Spectrometer with TMS as internal standard reference. The antibacterial and antifungal studies were done by agar well diffusion method.

SYNTHESIS OF THE COMPLEXES

In methanol medium the nitrate of nickel, zinc and cadmium 1 g each (3.40 mmol, 3.30 mmol and 3.22 mmol) were mixed with 4-hydroxypyridine of about 1.3 g, 0.63 g, 0.61 g (13.79 mmol, 6.63 mmol, 6.42 mmol), respectively and irradiated in a domestic micro wave oven for about 10 s. Then, potassium thiocyanate 0.7 g, 0.67 g, 0.65 g (7.0 mmol, 6.7 mmol, 6.46 mmol, respectively) was added to each mixture in ethanol medium and irradiated further for about 10 s. The precipitated complexes were filtered, washed with ethanol, dried and kept in air tight containers.

RESULTS AND DISCUSSION

The analytical data for the Ni(II), Zn(II) and Cd(II) complexes along with their electrical conductance values are given in Table 1. The low electrical conductivity values ascertain the formulae of the complexes with neutral nature (Geary, 1971).

Infrared Spectra

Only the relevant frequencies in the infra red spectra are considered for discussion. The infrared spectrum of the ligand 4-HP shows bands in the region 3644-3200 cm^{-1} corresponding to phenolic -OH of pyridine ring (Nakamoto, 1978). Strong bands at 3060 cm^{-1} , 1521 cm^{-1} and 1631 cm^{-1} are assigned to C - H of aromatic ring, C = N and C = C groups respectively. The broad band at 2083 - 2097 λ

Table 1: Analytical Data of the Complexes

S. No.	Complex	Color	Yield%	C%	H%	N%	S%	Metal %	Conductance $\text{ohm}^{-1} \text{cm}^2 \text{mol}^{-1}$
1.	$[\text{Ni}(\text{4-HP})_4 (\text{SCN})_2]$	Pale green	41.3	47.56(47.58)	3.60(3.63)	15.11(15.13)	11.52(11.54)	11.19(11.21)	71.50
2.	$[\text{Zn}(\text{4-HP})_2 (\text{SCN})_2]$	Colourless	52.3	38.44(38.46)	2.66(2.68)	14.92(14.95)	17.09(17.11)	19.23(19.25)	75.10
3.	$[\text{Cd}(\text{4-HP})_2 (\text{SCN})_2]$	Colourless	59.6	34.39(34.41)	2.38(2.40)	13.34(13.37)	15.29(15.31)	29.05(29.07)	68.70

Theoretical values are given in paranthesis

shows that (SCN)⁻ group is in the complexes. The negative and positive shifts of (11 – 48) and (10 – 53) cm⁻¹ respectively for the spectral bands in the complexes show the involvement of 4- HP and SCN⁻ in the coordination sphere. Thus the entry of both the ligands in the coordination sphere is confirmed. Further support of this coordination is the (M–N) bands at 561, 549 and 534 cm⁻¹ in the respective complexes (George, 2004) as shown in Table 2 and Figures 1 and 2.

UV-Visible Spectra

Nickel complex shows I max values (366), (567) and (839) nm corresponding to the transitions, ³A_{2g}(F) → ³T_{1g}(P) obscured by charge transfer transition, ³A_{2g}(F) → ³T_{1g}(F) and ³A_{2g}(F) → ³T_{2g}(F) respectively (Lever, 1984). Many mixed ligand nickel(II) complexes with six coordination are reported to have distorted octahedral geometry, corresponding to the above transitions. The zinc(II) and cadmium(II) ions in the

Table 2: IR Spectral data of the ligands and its complexes (cm⁻¹)

S.No.	Compound	Phenolic–OH	C – H Aromatic Ring	C = N	C – N	C = C	M – N	SCN
1.	4 - HP	3644	3060	1521	1377	1637	-	-
2.	[Ni(4-HP) ₄ (SCN) ₂]	3419	2932	1548	1408	1652	561	2090
3.	[Zn(4-HP) ₂ (SCN) ₂]	3458	3060	1464	1381	1611	549	2070
4.	[Cd(4-HP) ₂ (SCN) ₂]	3374	2934	1468	1327	1617	534	2075

Figure 1: IR Spectrum of Zinc Complex

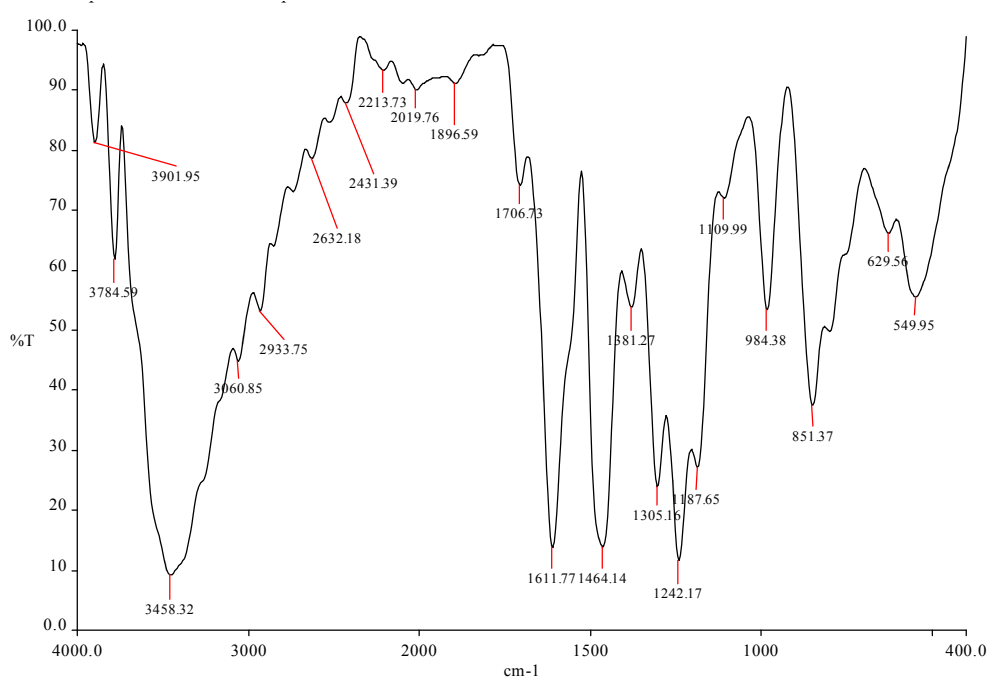
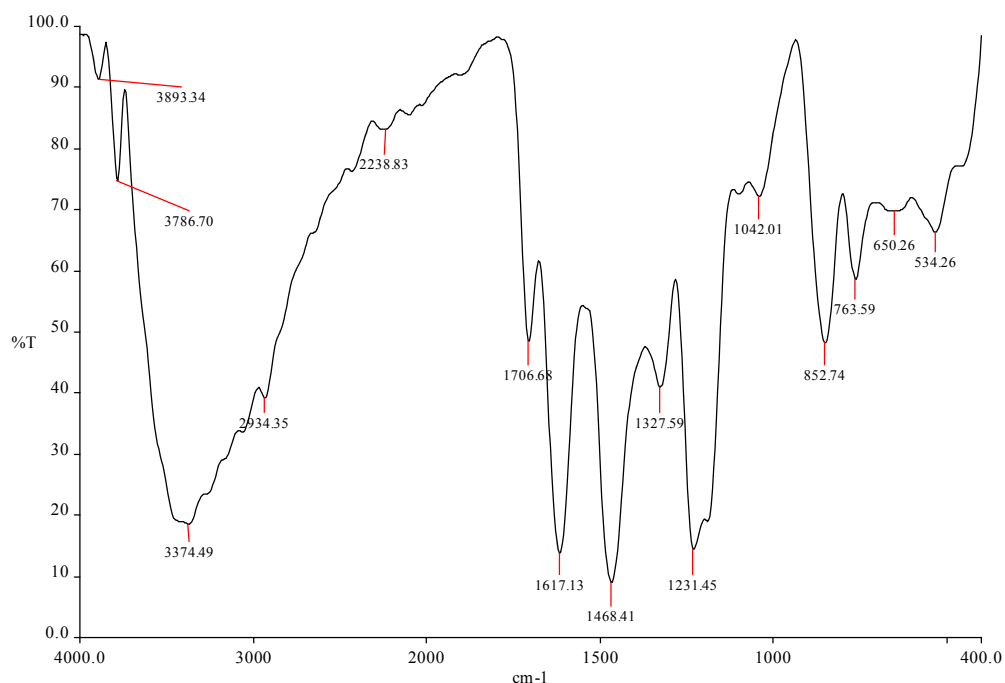


Figure 2: IR Spectrum of Cadmium Complex



complexes(d^{10}) electronic configuration. Hence, they exhibit only charge transfer transition at 272 and 297 nm corresponding to square planar and pseudotetrahedral geometry, respectively as show in Table 3 and Figures 3 and 4.

¹H NMR Spectra

4-Hydroxypyridine(4-HP) and its complexes were recorded for ¹H NMR spectra in DMSO. For the ligand, 4-HP, δ 7.70 is for phenolic-OH, δ 6.22 –

6.24 for aromatic -H and δ 2.50 for H – C = N were recorded (Gottlieb *et al.*, 1997). When recorded for complexes, there is a little shift in the δ values. In the zinc complex, δ 7.70 for phenolic-OH, δ 6.18 for aromatic hydrogen and δ 2.50 for H – C = N, are indicated. In the cadmium complex, δ 7.86 for phenolic –OH, δ 6.47 for aromatic hydrogen and δ 2.50 for H – C = N showed little shift. This fact confirms the

Table 3: UV – Visible Spectral Data of the Complexes

S.No.	Compound	Absorption band (nm)	Assignment	Probable Geometry
1.	[Ni(4-HP) ₄ (SCN) ₂]	362, 366, 559, 563, 567, 569, 839, 844	${}^3A_{2g}(F) \rightarrow {}^3T_{1g}(P)$ ${}^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)$ ${}^3A_{2g}(F) \rightarrow {}^3T_{2g}(F)$	Distorted Octahedral
2.	[Zn(4-HP) ₂ (SCN) ₂]	272	Charge transfer	Square planar
3.	[Cd(4-HP) ₂ (SCN) ₂]	297	Charge transfer	Pseudo tetrahedral

Figure 3: UV-Visible Spectrum of Nickel Complex

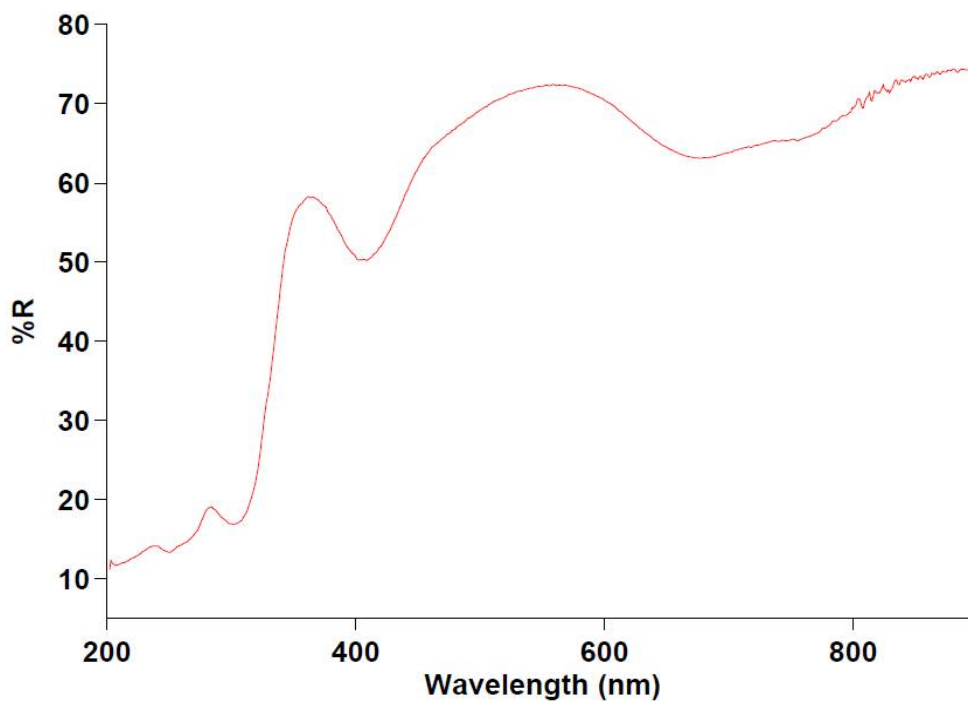


Figure 4: UV-Visible Spectrum of Cadmium Complex

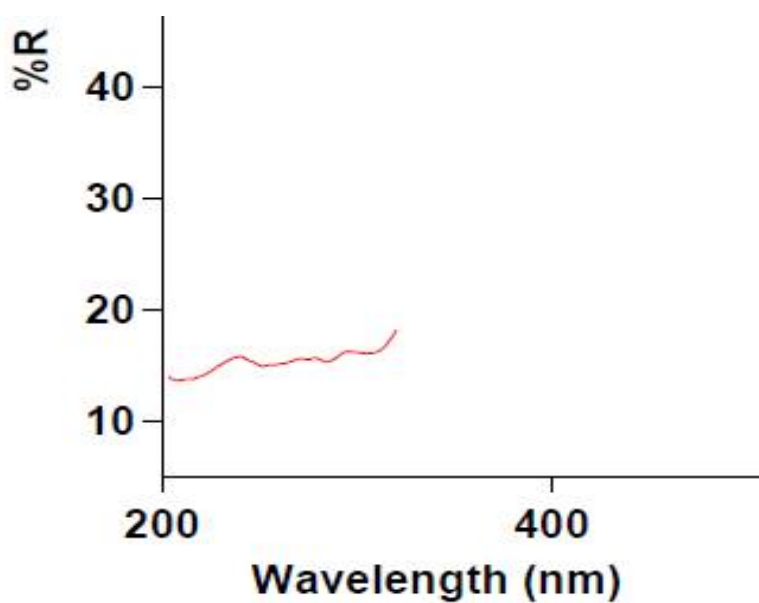
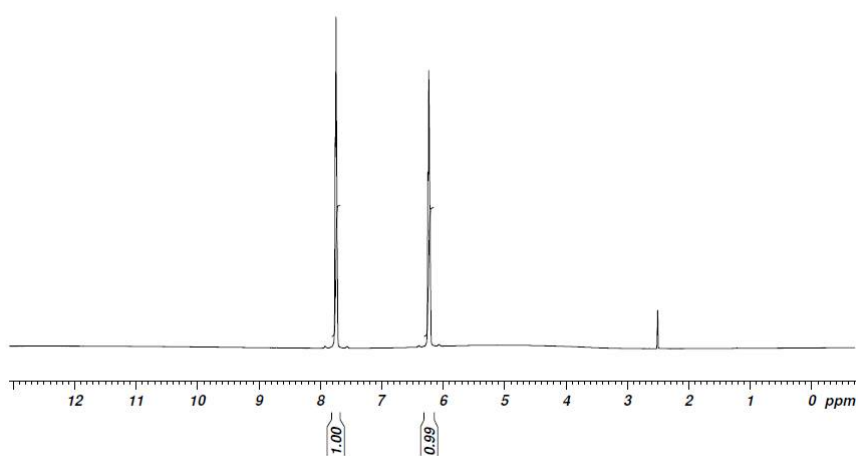
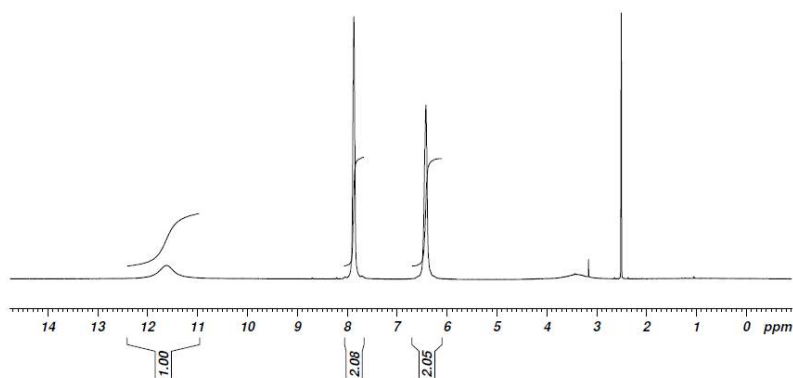


Table 4: ^1H NMR Spectral data for Ligand and Complexes (ppm)

S.No.	Compounds	Phenolic -OH	Aromatic hydrogen	H - C = N
1.	4 HP	7.70	6.22 – 6.24	2.50
2.	$[\text{Zn}(4\text{-HP})_2 (\text{SCN})_2]$	7.70	6.18	2.50
3.	$[\text{Cd}(4\text{-HP})_2 (\text{SCN})_2]$	7.86	6.42	2.50

Figure 5: ^1H NMR Spectrum for 4-HP**Figure 6: ^1H NMR Spectrum for Cadmium Complex**

coordination of ligand, 4-HP in the complexes. See Table 4 and Figures 5 and 6.

¹³C NMR Spectra

In the ¹³C NMR spectrum of the ligand, 4-HP the chemical shift at 116.00-140.00 ppm correspond to aromatic carbons, 116.68 ppm for C–OH and 39.39-40.39 ppm to C = N (Jacobsen, 2007). These values repeated with little shift in the complexes. See Table 5 and Figures 7 and 8.

Antibacterial and Antifungal Activity

The antimicrobial screening indicates that the ligand (4-HP) is as reactive as the standard ampicillin, against the bacteria *Escherichia coli* and *Bacillus subtilis*, The Ni(II) complex and Zn(II) complex are inactive to these two bacteria (Perez et al., 1990; Atlas and Parks, 1997). The reason may be as reported earlier that Ni(II) and Zn(II) metal ions participate in various metabolic activities of *Escherichia coli* and *Bacillus subtilis* whereas Cd(II)

Table 5: ¹³C NMR spectral data for ligand and complexes (ppm)

S.No.	Compound	Aromatic carbons	C – N	C – OH	SCN
1.	4-HP	116.00 – 140.00	39.39 – 40.39	116.68	-
2.	[Zn(4-HP) ₂ (SCN) ₂]	116.00 – 141.00	39.30 – 40.30	116.19	131.00
3.	[Cd(4-HP) ₂ (SCN) ₂]	116.00 – 142.00	39.40 – 40.40	116.03	133.27

Figure 7: ¹³C NMR Spectrum for 4-HP

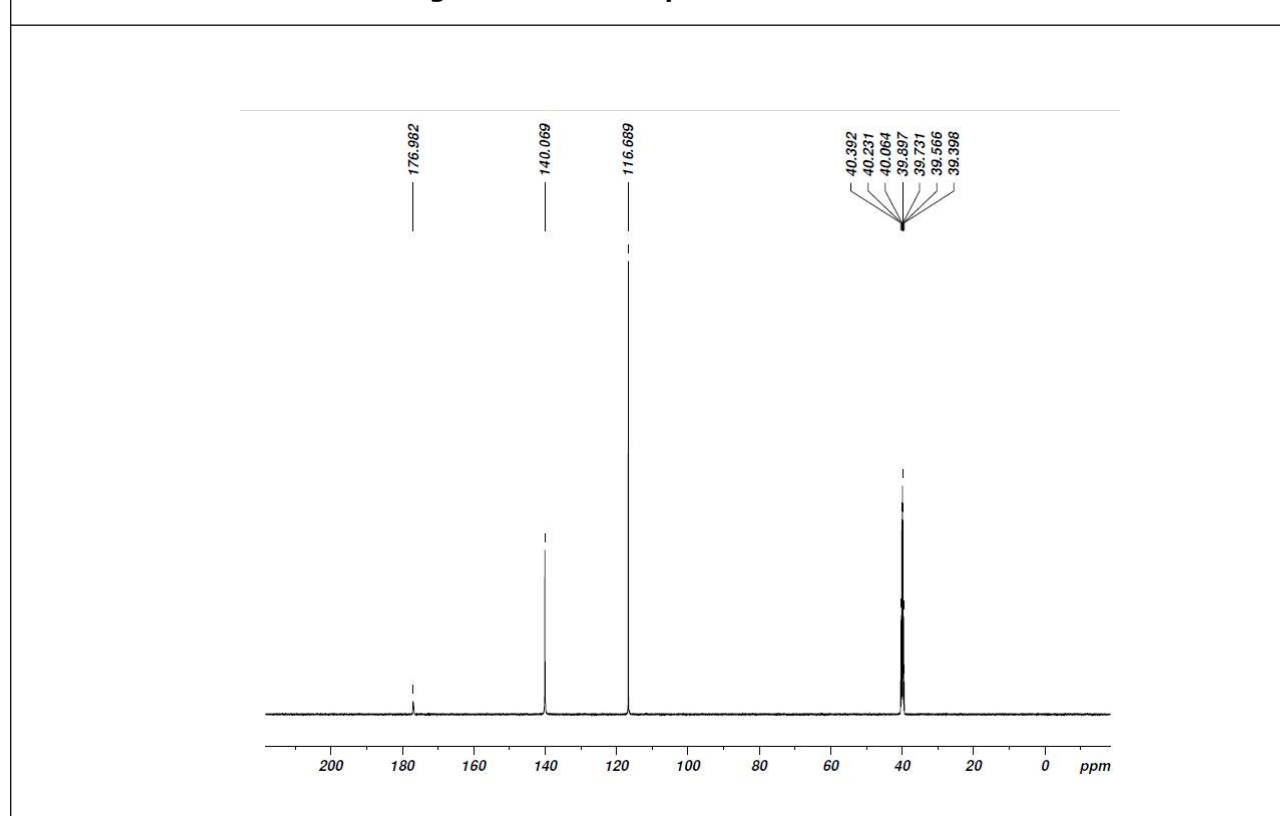
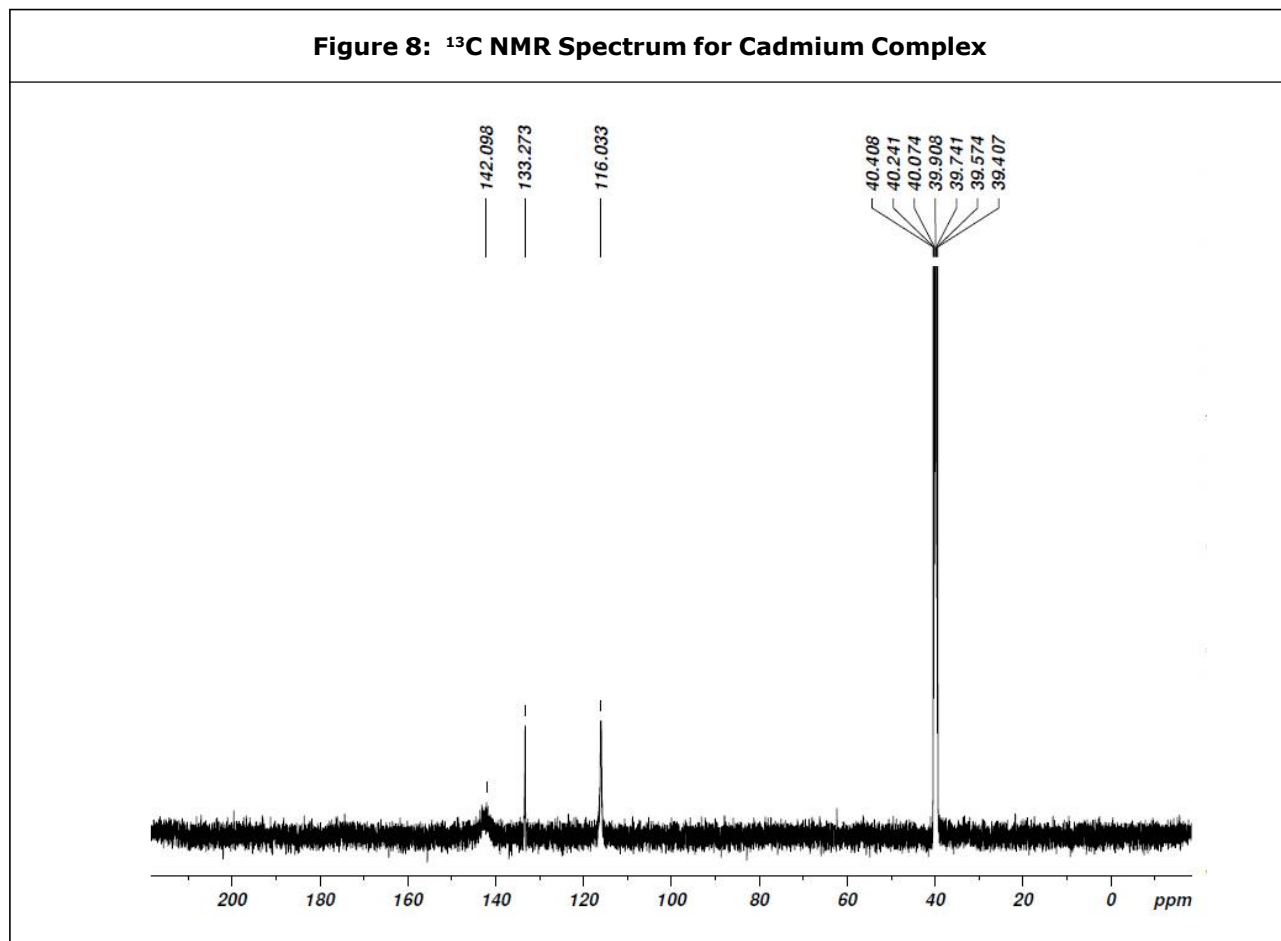


Figure 8: ^{13}C NMR Spectrum for Cadmium Complex

complex is in least participation. In the activity against fungus, the ligand (4-HP) is inactive to *Aspergillus Niger* and less active to *Aspergillus flavus*. When compared to the standard fluconazole, the complexes of Ni(II) and Zn(II) are inactive and cadmium complex is more active.

Nickel in trace amount support for the growth of *Escherichia coli* (Iwig et al., 2006). In anaerobic growth nickel is needed (Wu et al., 1994). It has been found that low concentration of Ni leads *Escherichia coli* to form bio-film structures rather than growing as free floating cells (Claire et al., 2009). *Escherichia coli* RcnR is a 40.4 K Da tetrameric transcriptional repressor that responds to the binding of Ni(II) or Co(II) at micromolar

concentrations to allow the expression of the exporter RcnA (Khadine, 2012). About *Bacillus subtilis* there occurs biosorption of nickel (Abdel et al., 2010). The use of recombinant at spores of *Bacillus subtilis* as a potential bioremediation tool for adsorption of nickel ions has become common now (Hinc et al., 2010). Cells grown in Zn(II) deficient medium had a reduced growth rate and contained up to five times less cellular Zn(II) (Alison, 2009). There is sequential binding and sensing of Zn(II) by *Bacillus subtilis* (Zhen et al., 1992). Cadmium ions are bacteriocidal resulting in exponential killing when exposed (Ori and Eliora, 1993). These records show why Ni(II) and Zn(II) complexes are inactive and Cd(II) complex is active against these two bacterias. The

Table 6: Antibacterial and Antifungal activity of ligand and complexes (mm)

S.No.	Compounds	<i>Escherichia coli</i>	<i>Bacillus subtilis</i>	<i>Aspergillus Niger</i>	<i>Aspergillus Flavus</i>
1.	4-HP	25	10	-	10
2.	[Ni(4-HP) ₄ (SCN) ₂]	-	-	-	-
3.	[(Zn(4-HP) ₂ (SCN) ₂]	-	-	-	-
4.	[Cd(4-HP) ₂ (SCN) ₂]	5	15	28	30
5.	Ampicillin	25	15	-	-
6.	Fluconazole	-	-	25	20

previous records show that Ni(II) and Zn(II) complexes are inactive to *Aspergillus niger* and *Aspergillus Flavus*, whereas Cd(II) complex is active against these two fungi (See Table 6).

CONCLUSION

By proper experimental conditions, the complexes were prepared. From the results and discussion of the analytical data, it was confirmed that [Ni(4-HP)₄ (SCN)₂], [(Zn(4-HP)₂ (SCN)₂] and [Cd(4-HP)₂ (SCN)₂] were formed. The spectral data indicates the probable geometry of Ni(II) complex distorted octahedral, Zn(II) complex square planar and Cd(II) complex pseudotetrahedral. The antibacterial and antifungal studies were carried out for these complexes and screened for proper reason.

ACKNOWLEDGMENT

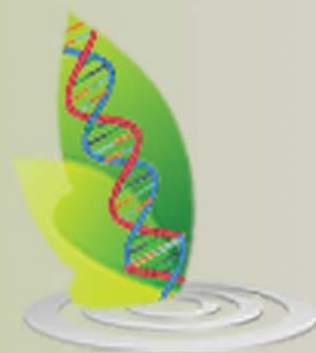
The authors are thankful to the Principals and Managements of Bishop Heber College (Autonomous) and St. Josephs College (Autonomous) Tiruchirappalli for encouragement and support. They also thank SAIF Chennai, STIC Cochin and Gowri Biotech for providing analytical data.

REFERENCES

1. Abdel – Monem M O, Al – Zubeiry A H and Al – Gheethi A A, (2010), "Biosorption Nickel By *Pseudomonas Cepacia* 120s and *Bacillus subtilis* 117s", *Water Sci Technol*, Vol 61 (12), pp. 2994- 3007.
2. Alison I, Graham, Stuart Hunt, Sarah L Stokes, Neil Bramall, Josephine Bunch, Alan G Cox, Cameron W Mcleod and Robert K Poole (2009), "Severe Zinc Depletion of *Escherichia coli* Roles for High Affinity Zinc Binding by Zin T, Zinc Transport and Zinc Independent Proteins", *The Journal of Biological Chem., Paper*, p. 284.
3. Atlas R M and Parks L C (1997), "Handbook of Microbiology Media", 2nd Ed., CRC Press, Boca Raton.
4. Brij Bhushan Tewari (2012), "Studies On Biologically Significant Mercury(II), Nickel(II) and Lead(II). Isoleucine Binary Complexes In Solution", *Nature and Science*, Vol. 10(1), pp. 45-52.
5. Brown D A, Chatel K W (1978), "Interactions Between Cadmium and Zinc In Cytoplasm of Duck Liver and Kidney", *Chem. Bid Interact*, Vol. 22 (2–3), pp. 271–9.

6. Claire Perrin, Romain Briandat, Gregoire Jubelin, Philippe Lejeune, Marie-Andree Mandrand-Berthelot, Agnes Rodrigue and Corine Dorel (2009), "Nickel Promotes Biofilm Formation By *Escherichia Coli* K-12 Strains That Produce Curlin", *Applied and Environmental Microbiology, American Society For Microbiology*.
7. Geary W J (1971), "The Use of Conductivity Measurements In Organic Solvents For Characterization of Coordination Compounds", *Coord. Chem. Rev.*, p. 7, 8.
8. George Psomas and Dimitris P Kessissoglou (2013), "Quinolones and Steroidal Anti - Inflammatory Drugs Interacting With Copper(II), Nickel(II), Cobalt(II) and Zinc(II): Structural Features Biological Evaluation and Perspectives", *Dalton Transactions*, Vol. (42), pp. 6252-6276.
9. George Socrates (2004), "Infrared and Raman Characteristic Group Frequencies Tables and Charts", John Wiley & Sons, pp. 18.
10. Gottlieb H E, Kotlyar V and Nudelman A (1997), "Nmr Chemical Shifts of Common Laboratory Solvents of Trace Impurities", *J. Org. Chem*, Vol. 62(1), pp. 7512-7515.
11. Hartley D and Kidd H (Eds) (1983), *The Agrochemicals Handbook*, Royal Society of Chemistry, 0851864006, Nottingham.
12. Hinc K, Ghandilis, Karbalace G, Shali A, Noqhabi K A, Ricca E and Ahmadian G (2010), "Efficient Binding of Nickel Ion To Recombinant *Bacillus Subtilis* Spores", *Res. Microbiol*, Vol. 161 (9), pp. 757-64.
13. Iwig J S, Rowe J L and Chivers P T (2006), "Nickel Homeostasis in *Escherichia Coli* - The RCNR - RCNA Efflux Pathway and Its Linkage To NIKR Function", *Mol. Microbiol*, Vol. 62(1), pp. 252 - 62.
14. Jacobsen N E (2007), "NMR Spectroscopy Explained: Simplified Theory, Applications and Examples For Organic Chemistry and Structural Biology", Wiley - Interscience Hoboken, N J, P. XV, p. 668.
15. Joske Ruytinx, Hoai Nguyen, May Van Hees, Michiel Op De Beeck, Jaco Vangronsvled., Robert Carleer, Jan V Colpaert and Kristin Adriaensen (2013), "Zinc Export Results In Adaptive Zinc Tolerance In The Ectomycorrhizal Basidiomycete *Suillus Bovinus*", *Metallomics*.
16. Kazoo Nakamoto (1978), *Infra Red and Raman Spectra of Inorganic and Coordination Compounds*, 3rd Edition., John Wiley and Sons, New York.
17. Khadine Athena Higgins (2012), "Metal Selectivity In The *E. Coli* N₁ (II) and Co (II) Responsive Transcriptional Regulator RCNR", Uni of Massachusetts, Electronic Doctoral Dissertations For Umass Amherst.
18. Lever A B P (1984), *Inorganic Electronic Spectroscopy*, 2nd Edn., Elsevier, New York.
19. Helm M L et al. (2011), "Enzyme inspired nickel complex races to produce hydrogen", *Science*, p. 333.
20. Ori Inbar and Eliora Z Ron, (1993) "Induction of Cadmium Tolerance In *Escherichia Coli*", *Fems Microbiology Letters*, Vol. 113, pp. 197-200.
21. Perez C, Pauli M and Bazerque P (1990),

- “An Antibiotic Assay By The Well Agar Method”, *Acta Biol. Med. Experim.*, Vol. 15, pp. 113-115.
22. Shaker Shayma A and Yang Farina (2009), “Preparing and Characterization of Some Mixed Ligand Complexes of 1, 3, 7-Dimethylxanthin, δ Picoline and Thiocyanate With Some Metal Ions”, *American Journal of Scientific Research*, Vol. 5, pp. 20-26.
23. Shaker Shayma A, Yang Farina, Sadia Mohmmod and Mohean Eskender (2009), “Co(ii), Ni(ii), Cu (II), Zn (II) and Cd (II) Mixed Ligand Complexes of Theophylline and Cyanate: Synthesis and Spectroscopy Characterizations”, *Modern Applied Science*, Vol. 3(12), pp. 88-94.
24. Shriver D F and Atkins P W (1999), “Bioinorganic Chemistry”, *Inorganic Chemistry*, 3rd Edn., Oxford University Press, Chapter 19.
25. Wu L F, Navarro C, De Pina K, Quenard M and Mandrand M A (1994), “Antagonistic Effect of Nickel On The Fermentative Growth of *Escherichia Coli* K – 12 and Comparison of Nickel and Cobalt Toxicity on The Aerobic and Anaerobic Growth”, *Environ Health Perspect*, Vol. 102, pp. 297- 300.
26. Zhen M A, Scott E Gabriel and John D Helman (1992), “Sequential Binding and Sensing of Zn(ii) By *Bacillus subtilis* Zur”, *Nucleic Acids Res.*, Vol. 39 (21), pp. 9130-9138.



International Journal of Life Sciences Biotechnology and Pharma Research

Hyderabad, INDIA. Ph: +91-09441351700, 09059645577

E-mail: editorijlbpr@gmail.com or editor@ijlbpr.com

Website: www.ijlbpr.com

