

Synthesis and Characterisation of Biologically Active Metal Complexes of N-Phenyl Anthranilic Acid

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1. Introduction

Interest in coordination chemistry is increasing continuously with the preparation of organic ligands containing a variety of donor groups^[1,2] and it is multiplied many fold when the ligand have biological importance^[3,4]. A large number of metal ion complexes of anthranilic acid and its derivatives of N-phenyl anthranilic acid have been reported in the literature^[5-8]. Some metal ion complexes of N-phenyl anthranilic acid have stimulated extensive research in biology, organic chemistry and medicine due to their antibiotic, antifungal and anti-inflammatory pharmacological properties^[9]. Transition metals have varying utility and are important due to their role in biological and chemical system in various ways. So that the transition metal complexes of N-phenyl anthranilic acid and its derivatives have been of considerable interest. Furthermore the coordination behaviour of the ligand also noted by the use of Infrared spectroscopic method.

Generally carbonyl group in N-phenyl anthranilic acid is a potential donor due to the large dipole moment (5.8 D) and strong basic character. In this investigation, an attempt is made to study the coordination behaviour of N-phenyl anthranilic acid. An extensive survey had been carried out in chemical literature to investigate the work done so far on the metal complexes of anthranilic acid but not much work has been done on the synthesis and characterization of derivatives of N-phenyl anthranilic acid as a ligand with transition metal ions. The most prominent metal ions which are biologically important in the 3d-series namely, Co(II), Ni(II) and Cu(II) were chosen for the present study^[10].

Sveta Zhiroslovna Ozkan *et al.* reported the Synthesis and analgesic activity of 2-Phenoxybenzoic acid and N-Phenyl anthranilic acid Hydrazides, Oxidative Polymerization of N-Phenyl anthranilic Acid in the Heterophase System^[11].

Elizabeth Yohannes *et al.* reported the Silver (I) complexes of anthranilic acid, N-phenyl anthranilic acid, 1-Nitroso-2-Naphthol and 2-Nitroso-1-Naphthol^[12].

Bharat Parashar *et al.* reported the synthesis of some novel N-arylhydrazone derivatives of N-phenyl anthranilic acid and also he reported the Microwave synthesis and antimicrobial activity of some N-aryl hydrazones^[13].

From the literature it is found only a few of the N-phenyl anthranilic acid metal complexes had been prepared, especially that of Silver, copper and Zinc and characterised by physicochemical methods. The present research reports the preparations and characterisation of some biologically active metal complexes of Co(II), Ni(II) and Cu(II) with N-phenyl anthranilic acid in non-aqueous medium which were characterised by physico-chemical methods and suitable structures were assigned on the basis of spectral measurements.

2. Experimental Techniques

2.1 Materials and Methods

All the chemicals used were of Analar grade. N-phenyl anthranilic acid were obtained from sigma Aldrich. Co (II), Ni (II) and Cu (II) were purchased from Merck. Solvents were purified and distilled before use.

2.2 Preparation of metal complexes of N-phenyl anthranilic acid

The ligand N-phenyl anthranilic acid (2 mmol) dissolved in ethanol, Co (II)/ Ni (II) / Cu (II) chloride (1 mmol) dissolved in ethanol was added drop wise. The above mixture was refluxed for 6 h. The complexes obtained were filtered, washed with ethanol and dried. (Yield: 65-70%).

2.3 Physical measurements

Melting points were determined by open capillary method and are uncorrected. Conductivity measurements were made on freshly prepared 10^{-3} M solutions in DMSO at room temperature. The room temperature magnetic moment measurements were carried out using Guoy method. The IR spectra were recorded on Perkin-Elmer RX I in the range $4000-400\text{ cm}^{-1}$ using KBr disc method. The electronic spectra were recorded on Perkin Elmer Lambda-35 UV/Visible spectrometer in the range 190-1100 nm.

2.4 Antimicrobial activity

The ligand and its complexes were tested against the bacterial species: *Shigella sonnei*, *Klebsiella pneumoniae*, *Proteus vulgaris*, *Salmonella typhi*, *Proteus mirabilis* and the fungal species *curvularia lunata*, *Aspergillus niger*, *Atternaria solani*, *Bipolaris sps*, *Aspergillus fumigates*. These studies were carried out using Kirby Bayer Disc diffusion method (Bayer *et al.*, 1966). Streptomycin and Nystatin were used as the standard for antibacterial and antifungal agents. The test organisms were grown on Nutrient Agar medium in petri plates for bacterial species and PDA broth medium for fungal species. The compound was dissolved in DMSO solution and soaked in filter paper disc of 5mm diameter and 1mm thickness. The discs were placed on the previously seeded plates and incubated at 37°C and the diameter of inhibition zone around each disc was measured after 24 h for bacterial species and 48 h for fungal species.

3. Results and Discussion

The analytical data and physical properties of the ligand and its complexes are listed in (Table-1). The ligand N-phenyl anthranilic acid is soluble in acetone, ethanol, chloroform, DMF and DMSO and insoluble in ether and acetonitrile.

Table-1: Electrical conductance, Magnetic moments and Electronic Spectral Data of complexes

Complex	Λ_c ($\Omega^{-1}\text{cm}^2\text{mol}^{-1}$) in DMSO	μ_{eff} (BM)	Electronic spectra		Stereo Chemistry
			Energy max. cm^{-1}	Assignments	
[CoL ₂ Cl ₂]	22	4.86	19,377	${}^4\text{T}_{1g}(\text{F}) \rightarrow {}^4\text{T}_{1g}(\text{P})$	Octahedral
[NiL ₂ Cl ₂]	18	3.10	15,337 27,932	${}^3\text{A}_{2g} \rightarrow {}^3\text{T}_{1g}(\text{F})$ ${}^3\text{A}_{2g} \rightarrow {}^3\text{T}_{1g}(\text{P})$	Octahedral
[CuL ₂ Cl ₂]	21	1.91	15,221	${}^2\text{E}_g \rightarrow 2\text{T}_{2g}$	Distorted Octahedral

The solubility of the metal complexes was examined in common organic solvents. The complexes were found to be insoluble in ethanol, diethyl ether and acetone^[14]. However, the complexes were found to be soluble in DMSO.

The analytical data (Table- 1) indicates that the metal to ligand ratio is 1:2 for all the complexes. The molar conductance of all the complexes was measured in DMSO using 10^{-3} M solutions at room temperature. The low molar conductivity values of the metal complexes suggest the non-electrolyte nature. The magnetic moments, μ_{eff} of the complexes are given in (Table-1). The magnetic moments of Co (II), Ni (II) and Cu (II) suggest that octahedral geometry.

3.1 Infrared spectra of the complexes^[15-17]

IR spectrum of the complexes is very useful in determining the coordinating groups of the ligand. The shifts in the bands indicate the mode of linkage in the complexes. The IR spectral data of the ligand and its complexes were given in (Table-2).

Table-2: Infrared spectral data of ligand and its metal complexes (cm^{-1})

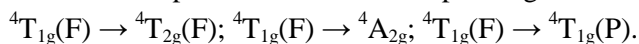
Compounds	$\nu_{\text{N-H}}$	$\nu_{\text{C=O}}$	ν_{OH}	$\nu_{\text{M-O}}$	$\nu_{\text{M-N}}$
L	3311	1682	1409	-	-
CoL ₂ Cl ₂	3334	1658	-	535	491
NiL ₂ Cl ₂	3335	1659	-	534	491
CuL ₂ Cl ₂	3334	1660	-	534	492

The band at 3311 cm^{-1} is assigned to the NH- stretching of the ligand and 3191 cm^{-1} assigned to the OH- stretching of COOH group. In the IR spectra of metal

complexes NH- stretching is shifted to 3335 cm^{-1} and the decrease in the stretching frequency is due to hydrogen coordination. The NH stretch found at 3300 cm^{-1} should decrease in coordination. However it depends upon the stretching of hydrogen bonding in the ligand and the M-N bond. Since the M-N bond is weaker than the hydrogen bonding we found increase NH stretching for nitrogen coordination. The spectrum of N-phenyl anthranilic acid shows a band at 1682 cm^{-1} which is the C=O stretch of the acid group is shifted to 1658 cm^{-1} in the complexes. In the IR Spectra of all the metal complexes, the carbonyl frequency of the acid group is shifted to lower frequency of about 20 cm^{-1} . Absence of asymmetric and symmetric stretch of carboxyl ate ion in the spectra of the complexes suggest that the acid group is not ionised and the C=O of oxygen is coordinated. Presence of anion in the complex and shift of CO stretching to lower level confirm the coordination furthermore. The band at 1156 cm^{-1} (due to C-N stretching of aromatic amine in the spectrum of the ligand) is slightly shifted to 1159 cm^{-1} in the spectrum of the complex. These further suggests that nitrogen of (-NH) group is involved in coordination. The appearance of new bands at 535 cm^{-1} and 492 cm^{-1} in the spectrum of the complexes are assigned to M-O and M-N stretching's respectively. Accordingly, one can deduce that the ligand binds the metal ion as a bidentate fashion through N of -NH group and neutral C=O of COOH group.

3.2 Electronic Spectra and Bonding^[18]

The electronic spectra of cobalt (II) complex consist of three spin allowed transitions although it will not always be possible to observe all the three transitions. In the electronic spectra of high spin octahedral complexes of Co(II), one should expect three bands corresponding to the transitions,



The electronic spectra of Co(II) chloride complex shows the characteristic band of octahedral geometry having a band at $19,377\text{ cm}^{-1}$ due to ${}^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$ transition.

In the electronic spectra of octahedral Ni(II) complexes one should expect three bands corresponding to ${}^3A_{2g} \rightarrow {}^3T_{2g}(F)$; ${}^3A_{2g} \rightarrow {}^3T_{1g}(F)$; ${}^3A_{2g} \rightarrow {}^3T_{1g}(P)$ transitions at $10,000\text{ cm}^{-1}$, $14,000\text{--}18,000\text{ cm}^{-1}$, and $25,000\text{--}30,000\text{ cm}^{-1}$ respectively.

The electronic spectra of Ni(II) chloride complex shows the characteristic bands of octahedral geometry having a band at $15,337\text{ cm}^{-1}$ and $27,932\text{ cm}^{-1}$ due to ${}^3A_{2g} \rightarrow {}^3T_{1g}(F)$ and ${}^3A_{2g} \rightarrow {}^3T_{1g}(P)$ transitions respectively.

In the electronic spectra of Cu (II) complex one should expect three transitions ${}^2B_{1g} \rightarrow {}^2A_{1g}$; ${}^2B_{1g} \rightarrow {}^2B_{2g}$; ${}^2B_{1g} \rightarrow {}^2E_g$ for tetrahedral copper(II) complexes. The Cu (II) chloride complex displays a band at $15,221\text{ cm}^{-1}$ due to ${}^2E_g \rightarrow {}^2T_{2g}$ transition suggesting distorted octahedral geometry.

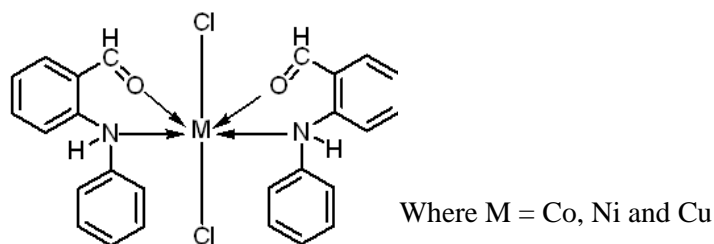
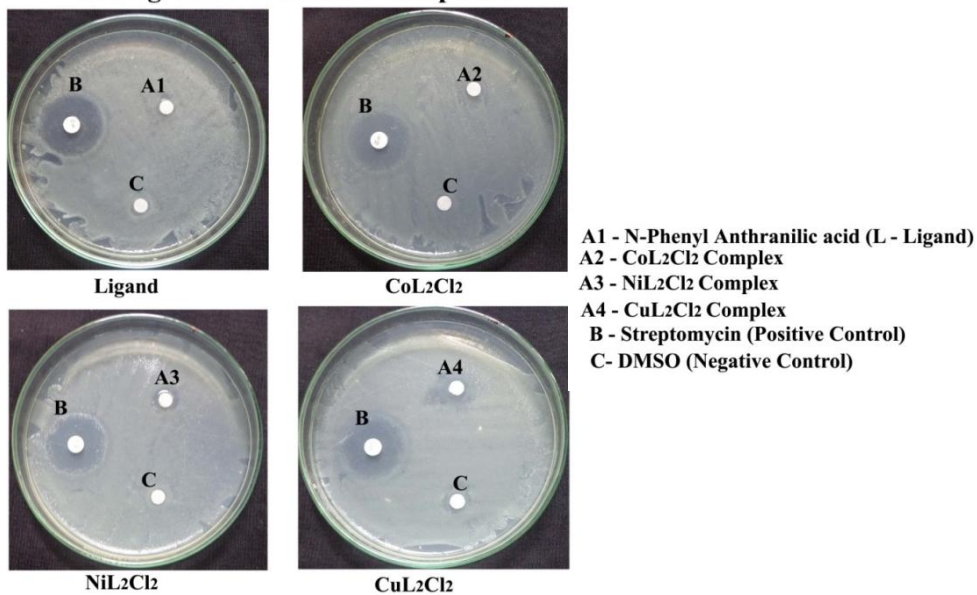


Figure-1: Proposed structure of N-Phenyl Anthranilic acid metal complexes of Co (II), Ni (II) and Cu (II)

3.3 Antimicrobial activity^[19,20]

The *in vitro* antifungal and antibacterial investigation results are given in (Tables 3 and 4) respectively. DMSO is used as negative control and streptomycin is used as positive control for antibacterial and Nystatin for antifungal activities. These observations show that the majority of the metal complexes are more active than the free ligand. Among the above species all the metal complexes show better antifungal activity against *Curvularia lunata* and antibacterial activity against *Shigella sonnei*. The antifungal activity of *Curvularia lunata* against by the ligand and its metal complexes shown in Figure 2 and Antibacterial activity of *Shigella sonnei* against by the ligand and its metal complexes shown in Figure 3. The results are tabulated. The *In vitro* fungal activity results (Table-3) revealed that all the metal complexes are more active than the ligand. The Co (II) complex was found to be highly active towards *Curvularia lunata*. Similarly the *In vitro* antibacterial activity of *Shigella sonnei* the ligand and its metal complexes were given in (Table-4). In this case Cu (II) complex was found to be more active than the other metal complex. Figure 2 shows the Antifungal activity of *Curvularia lunata* against by the ligand and its metal complexes and Figure 3 Shows the Antibacterial activity of *Shigella sonnei* against by the ligand and its metal complexes

Antibacterial activity of *Shigella sonnei* against by the Ligand and its Metal Complexes



Antifungal activity of *Curvularia lunata* against by the Ligand its Metal Complexes

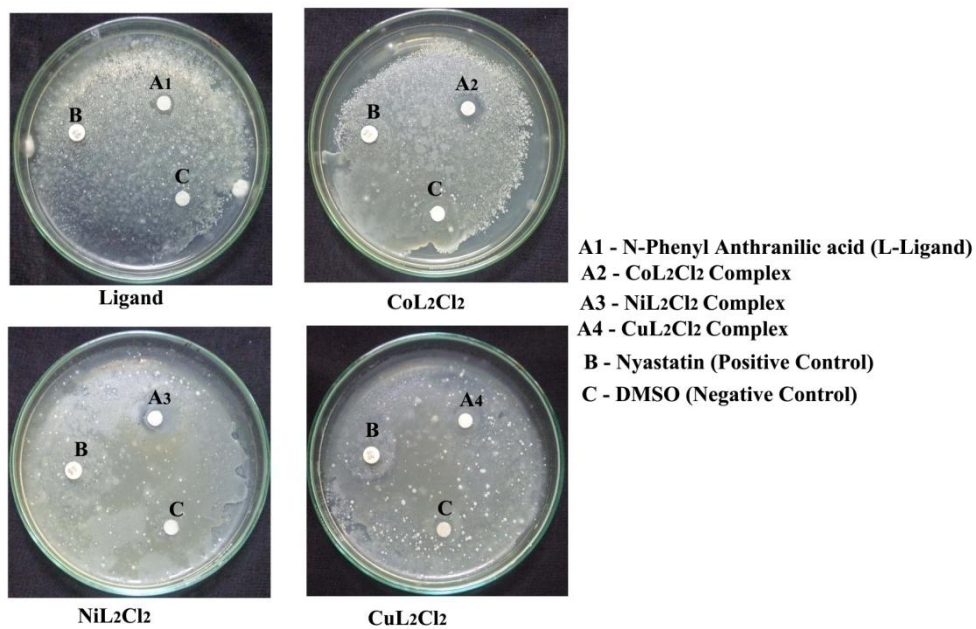


Table-3: Antifungal activity of *Curvularia lunata* against by the ligand and its metal complexes

Compound		Zone of inhibition (in mm)		
		M	B	C
A1	L	10	-	-
A2	CoL ₂ Cl ₂	13	-	-
A3	NiL ₂ Cl ₂	12	-	-
A4	CuL ₂ Cl ₂	12	11	10

Table-4: Antibacterial activity of *Shigella sonnei* against by the ligand and its metal complexes

Compound		Zone of inhibition (in mm)		
		M	B	C
A1	L	10	23	11
A2	CoL ₂ Cl ₂	12	21	-
A3	NiL ₂ Cl ₂	14	16	10
A4	CuL ₂ Cl ₂	15	12	11

Conclusion

Metal complexes of N-Phenyl anthranilic acid were prepared and characterised using the conductance, magnetic, electronic and vibrational spectral analysis. IR spectral data demonstrates the ligand to act as a bidentate mode, coordinating through NH- group N atom and carbonyl group oxygen atom. Magnetic and electronic spectral studies reveal octahedral geometry for Co (II) and Ni (II) complexes while Cu (II) complex posses distorted octahedral geometry. The antimicrobial activities of the ligand and its complexes indicate that the complexes show higher activity than the ligand.

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References

1. Hyappa P.B., Young J.K. Moore and Suslic Dendrimer - Metalloprophyrine: *Synthesis and Catalysis, J. Am. Soc.*, 118, 5708 (1996)
2. Castillo-Blum S.E. and Barba-Behrens N., Coordination chemistry of some biologically active ligands, *Coord. Chem. Rev.*, (3), 196 (2000)
3. Mohan G., and Rajesh N., Synthesis and anti-inflammatory activity of N-phenyl anthranilic acid its metal complexes, *Indian J. Pharm*, 24, 207 (1992)

4. Kong D., Reibbenspies J., Mao J. and Clearfield A., Novel 30-membered octaazamacrocyclic ligand: synthesis, characterisation thermodynamic stabilities and DNA cleavage activity of homodinuclear copper and nickel complexes, *Inorg. Chem. Acta*, 342, 158 (2003)
5. Rioux, C.R.; Jordan, D.C.; Rattray, J.B.M. *Arch. Biochem. Biophys.* 1986, 248, 183; *Chem. Abstr.* 1986, 105, 39063j.
6. Hoppe, H.R.; Andra, K.Z. *Chem.* 1986, 26, 75; *Chem. Abstr.* 1986, 105, 34514x.
7. Banerjee, A. K.; Prasad, D; Roy, S.K. *J. Indian Chem. Soc.* 1987, 64, 9.
8. Fukumatto, H.; Tanaka, K.; Kawagishi, Y. *Jpn. Kokai Tokkyo Koho JP61, 141, 450 [86,141,450] (CLG03G9/08)*, 28 June 1986, *Appl.* 84/264, 756, 15 Dec 1984; *Chem. Abstr.* 1987, 106, 93605w.
9. Borges F., Roleira F., Milhazes N., Santana L and Uriarte E., Simple Coumarine & analogues in Medicinal Chem., 12, 88-916 (2005)
10. S. R. Bheeter "A Study of Metal Complexes of some Biologically Active Ligands". Dept of chemistry, St. Joseph's College, Trichy-02.
11. Open Journal of Polymer Chemistry, 2013, 3, 63-69 <http://dx.doi.org/10.4236/ojchem.2013.33012> Published Online August 2013 (<http://www.scirp.org/journal/ojchem>)
12. *Bull. Chem. Soc. Ethiop.* 1995 9(1), 1-8.
13. Scholars Research Library, *Der Pharma Chemica*, 2010, 2(2); 229-236
14. Vogel. A. I., 1978. "A Textbook of Quantitative Inorganic Analysis Including Elementary Instrumental Analysis", Fourth ed. Longman, London.
15. Kazuo Nakamoto, 1978. "Infrared and Raman Spectra of Inorganic and Coordination Compounds", third ed. John Wiley and Sons.
16. Silverstein. R. M.; Bassler. G.C.; Morrill. T. C., "Spectrometric Identification of Organic Compounds", fourth ed., John Wiley; New York; 1981.
17. Russel, S. Drago, "Physical Methods in Inorganic Chemistry", Hall of India Pvt. Ltd., New Delhi.
18. Cotton, F.A., & Wilkinson, G., "Advanced Inorganic Chemistry", fourth ed., Wiley Inter science, New York, 1980.
19. Lawrence, D.R & Bennett, P.N., "Clinical Pharmacology", fifth ed., The English Language Book Society & Churchill Livingstone.
20. Schild, H. O., "Applied Pharmacology", 12th ed., The English Language Book Society & Churchill Livingstone.

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