

Research Article

Synthesis, Spectral and Antibacterial evaluation of Nickle (II) and Pt(II) metal complexes of chemotherapeutic importance

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Abstract

Metal complexes of Nickle II, Platinum II derived from 2[[[methyl 4 (2,2,2 trifluoroethoxy)2-pyridinyl]methyl]sulfonyl]-1H-benzimidazole] LAN have been characterized on the basis of elemental analysis, molecular weight determinations and spectral studies including IR, UV, magnetic susceptibility, ESR, X-ray studies, SEM, mass spectra and thermal studies. The spectroscopic results show the involvement of C=N and S=O groups in coordination to the central metal ion. The magnetic moment values of the Nickle II, complex is in the range 3.09-3.20 B.M. Suggesting a high spin state of Nickle, in this complex. Based on the spectral studies, octahedral geometry has been proposed for the Nickle II complex and Square planner for Platinum II complex. Antimicrobial effects of representative ligand and their complexes on different species of pathogenic fungi and bacteria have also been recorded. It was found that the complexes were more effective against all the bacteria and fungi.

Key Word: benzimidazole derivatives, complexes, SEM, ESR, antibacterial activity

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INTRODUCTION

The literature reveals that a large number of drugs have been used to synthesize the complex with many metals with a view to enhance their therapeutic action¹⁻². Some important examples of inorganic based drugs are metallocene anti-tumor complexes³, gold anti-arthritis compounds⁴, lithium antidepressants⁵. In all these cases, work is largely focused on elucidating the mechanism of action of these complexes. Lansoprazole (LAN) is a very common PPI⁶⁻⁷. PPIs have demonstrated gastric acid suppression superior to that of histamine H2 receptor blockers. Investigations are going on the formation of

metal complexes with benzimidazole ring containing ligands because benzimidazole and its derivatives play an important role in analysis and in several biological reactions⁸. Considering the importance of drugs and their complexes it has been desired to synthesize and study the metal complexes of Lansoprazole with metals. The present paper describes the synthesis and characterization of Ni (II) and Pt (II) complexes with Lansoprazole.

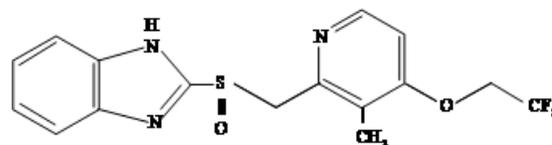


Figure 1: Structure of Lansoprazole Experimental

MATERIALS AND METHODS

All chemicals used were of Analytical Grade. Pure sample of Lansoprazole having molecular formula, C₁₆H₁₄F₃N₃O₂S, and molecular weight 369.363 gm/mol was obtained from Cipla Pharmaceutical Limited Mumbai. Metal salts were of Merck Chemicals. Melting

point of Lansoprazole is 166⁰C and the solvent used were acetone and distilled water. Metal-ligand ratio was calculated using Systronics digital conductivity meter. IR spectra were obtained from CDRI Lucknow. Magnetic susceptibility measurements were received from CAT Indore (Instrument used-Vibrating Sample Magnetometer). Nitrogen was determined by the Dumas method and sulphur was estimated by the Messenger's method. The elemental microanalyses of C, H, and N for ligand were carried out with Thomas and Coleman Analyzer Carlo Erba 7106.

Ligand -metal ratio

To confirm the Ligand-metal ratio, conductometric titration using mono-variation method was carried out at 21⁰ C. 0.01 M solution of Lansoprazole drug was prepared in 60:40 mixture of acetone and water. 20 ml of ligand was diluted to 200 ml with the same solvent. The ligand was titrated against 0.02 M metal solutions of metal salts NiCl₂ · 4H₂O, and PtCl₂ prepared in same solvent using mono-variation method and conductance was recorded after each addition of metal salt. From the equivalence point in the graph, it has been concluded that the complex formation takes place in the ratio of 2:1 (L: M). Further, stability constants and free energy changes

were also calculated using Job's method ⁹ of continuous variation modified by Turner and Anderson¹⁰.

Synthesis of complexes

For the synthesis of complexes, Lansoprazole was dissolved in 100 ml of acetone–water (60:40) mixture and added slowly to the metal salt solutions. The mixtures were refluxed and the solutions were kept for few days. A green crystalline complex of nickel and Brown yellow granular complex of platinum was separated. Complexes were washed with 60:40 mixtures of acetone and water, filtered, dried, weighed and melting points were recorded. Carbon, hydrogen, nitrogen, metal and water were estimated micro analytically at CDRI, Lucknow

RESULTS AND DISCUSSION

The synthesized complexes are stable solids. They are soluble in DMF and DMSO and insoluble in all other organic solvents. Analytical data and conductometric studies suggest 2:1 [L: M] ratio. Measured conductance values of these complexes are too low to account for their electrolytic behavior. The magnetic studies indicate the Ni (II) complex to be paramagnetic with magnetic moment of 3.06 B.M. while Pt(II) complex to be diamagnetic.

Table 1: Stability Constant, Free Energy Change, Molar Conductance and Magnetic- Moment Data of Complexes

S.No.	Composition of Complex (m-wt.)	Stability constant logK (L/mole)	Free Energy change -ΔF (Kcal/mole)	Molar conductance (ohm ⁻¹ cm ² mol ⁻¹)	Magnetic Moment (B.M.)
1	(C ₁₆ H ₁₄ F ₃ N ₃ O ₂ S) ₂ Ni.2H ₂ O	12.0888	17.038	12.1	3.06
2	(C ₁₆ H ₁₄ F ₃ N ₃ O ₂ S) ₂ Pt	10.5231	15.5905	10.9	-

Infrared Spectra

The IR spectra of ligand and complexes have been recorded and the probable assignments are given in the Table 3. The IR spectra of the complexes indicate that the ligand behaves as a bidentate and co-ordinate to the metal via C=N and sulphonic acid group. In the ligand, band appearing at 3456 cm⁻¹ due to NH stretching remains unaffected in the complex. The band due to ν C= N in the ligand at 1590 cm⁻¹ is shifted to lower wave number at 1590-1576 cm⁻¹ in the complexes there by confirming the coordination through the azomethine nitrogen atom. The shifting of S=O stretching vibration to the lower wave number side as compared to the free ligand is indicative of participation of sulphonic acid group in coordination. In Ni(II) complex band appearing at region 3654-3640 cm⁻¹ is due to coordinated water molecules. The appearance of bands in the far IR region at 429-409 cm⁻¹ in the complex may be assignable to M-N frequency. Additional bands in the complex in the region 615-608cm⁻¹ compared with IR spectra of free ligand have tentatively been assigned to M-O frequency and new band appearing at 1380-1390 cm⁻¹ in the complexes might be due to chelate ring formation in the complexes¹¹⁻¹⁴.

Table 2: IR Absorption data of the complexes

Ligand and complex	ν(NH) cm ⁻¹	ν (C=N) cm ⁻¹	ν(S=O) cm ⁻¹	ν(M-N) cm ⁻¹	ν(M-O) cm ⁻¹	ν(H ₂ O) cm ⁻¹
C ₁₆ H ₁₄ N ₃ O ₃ S	3456	1590	1028	-	-	-
(C ₁₆ H ₁₄ N ₃ O ₃ S) ₂ Ni.2H ₂ O	3454	1585	1012	414	610	3644
(C ₁₆ H ₁₄ N ₃ O ₃ S) ₂ Pt	3452	1580	1020	410	615	-

Electronic Spectra and Magnetic Susceptibility Data

The electronic spectra of Ni(II) complex displays and three absorption bands at 8333 cm⁻¹, 13700 cm⁻¹ and

24640 cm⁻¹ which may be assigned to ³T_{2g}(F) ← ³A_{2g}(F) (v₁), ³T_{1g}(F) ← ³A_{2g}(F) (v₂) and ³T_{1g}(P) ← ³A_{2g}(F)(v₃) transitions indicating octahedral¹⁵ geometry of the

complex. The geometry of Ni (II) complex is further confirmed¹⁶⁻¹⁷ by the high μ_{eff} value in the range 3.09-3.20 B.M. Pt(II) complex is diamagnetic as expected for square planar d_8 systems. The electronic spectra of the complex under study display bands at 523 - 537 nm. These bands may be assigned to $^1A_{1g} \rightarrow ^1B_{1g} (v_2)$ transitions, respectively. The electronic spectra of that complex indicate the square planar geometry around the Pt (II) ion.

NMR Spectra

The ^1H NMR spectra of the ligand have the expected characteristic signals. The CH_3 proton shows singlet at δ 2.2 and $\text{O-CH}_2\text{CH}_3$ proton at δ 3.5. The doublet peak observed at δ 4.36 and 4.66 ppm is attributed to CH_2 protons. In addition a multiplet peak at δ 6.9-8.3 may be

due to aromatic protons and peak at δ 13.2 may be due to NH proton of benzimidazole ring. Signals observed in the complexes at region of δ 8.18-8.23 due to the azomethine proton are either remained unaffected or shifted slightly downfield with reference to those of the parent ligand and the position of signal due to NH proton remains unaffected in the complexes. The aromatic protons show downfield shifts in the complexes. These observations support the assigned structure to the complex.

Scanning Electron Micrographs S.E.M

S.E.M. of metal complexes indicates the presence of well defined crystals free from any shadow of the metal ion on their external surface. The representative micrographs of a) Ligand; b) PtL_2 ; c) $[\text{NiL}_2(\text{H}_2\text{O})_2]$ are shown in Fig.2

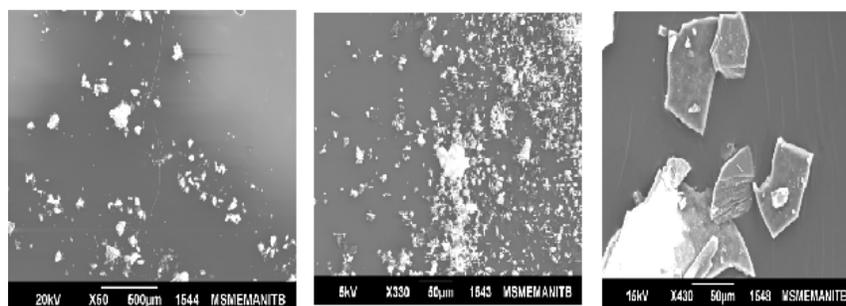


Figure 2: Scanning electron micrograph of Ligand and its Complexes Antimicrobial Activity

The antimicrobial activity of the ligand and the complexes were determined by the disc diffusion technique^{18,19}. The compounds were screened in vitro against *Pseudomonas*, *Staphylococcus aureus* and two strain of fungi, *Aspergillus niger* and *A.flavous*. A 1mg/ml solution in DMF was used. The standard used was gentamycin sulphate. The bacterium was maintained on nutrient agar and the agar media were incubated for different microorganism culture tests. After 24h of incubation at 37^oC for bacteria and 72h of incubation at 25^oC for fungi, the diameter of zone of inhibition (mm) thus formed around each disc containing the test compound were measured accurately. The Ni II complex show moderate activity against bacteria *Pseudomonas* and *Staphylococcus aureus* and fungi *Aspergillus niger* and *A. flavous* compared to the ligand and the Pt II complex shows significant activity against bacteria *Pseudomonas* and *Staphylococcus aureus* and fungi *Aspergillus niger* and *A. flavous* as compared to ligand.

Table 3: Antibacterial activity- zone of inhibition in mm.

S. No.	Compound	P. Aeruginosa	S. Aureus	A. niger	A. flavous
1.	Lansoprazole	13.1	11.2	14.22	12.11
2.	PtL_2	15.7	13.3	16.80	16.00
3.	$\text{Ni L}_2 \cdot 2\text{H}_2\text{O}$	12.11	12.11	14.82	12.11

CONCLUSION

The ligand molecule acts as a bidentate ligand. The spectroscopic results show the involvement of C=N and S=O groups in coordination to the central metal ion. Spectral studies suggests that Ni II complex possess octahedral geometry and Pt II complex possess square planar geometry. It is observed that the formed complexes are better anti-bacterial agents in comparison to ligand. In view of the foregoing discussions, the high melting points and insolubility in common organic solvents, we have assigned following probable structure of the complexes of Lansoprazole.

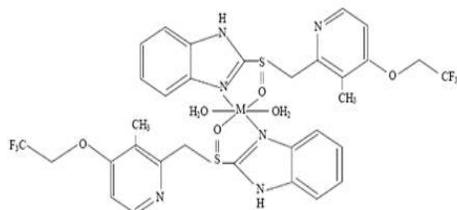


Figure 3: Structure of Lansoprazole complex with Ni(II) metal

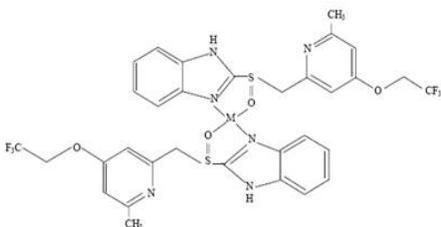


Figure 4: Structure of Lansoprazole complex with Pt (II) metal

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