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Research Article

## SYNTHESIS AND CHARACTERIZATION OF COMPLEXES CU(II), NI(II) AND CO(II) WITH PROTON PUMP INHIBITOR

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## ABSTRACT

Benzimidazoles act as good ligand to transition metal ions and they exhibit several coordination modes. The synthesis of hetero-chelates of the type  $ML_2 \cdot 2H_2O$  has been reported here. The metal complex of Co(II), Ni(II) and Cu(II) Complexes have been synthesized with 6-(difluoromethoxy)-2-[(3,4-dimethoxypyridin-2-yl)methylsulfinyl]-1H-benzo[d]imidazole (Pantoprazole). Pantoprazole is a proton pump inhibitor (PPI) drug that inhibits gastric acid secretion. Proton pump inhibitors (or PPI) are a group of drugs whose main action is a pronounced and long-lasting reduction of gastric acid production. Conductometric titrations have suggested metal-ligand ratio of 1:2 for all Co(II), Ni(II) and Cu(II) complexes. The ligand behaves as a bidentate with N, O donor atoms. Complexes have been synthesized and characterized by elemental analysis, UV-visible and IR spectral studies.

**Keywords:** Complex, Pantoprazole, Co(II), Ni(II), IR, PPIs.

## INTRODUCTION

The coordination chemistry of nitrogen-oxygen donor ligands is an interesting area of research<sup>1</sup>. A great deal of attention in this area has been focused on the complexes formed by transition metal ions with benzimidazole derivatives<sup>2-7</sup>. The coordination chemistry and physiological activities of benzimidazole derivatives and their metal complexes are of recent interest<sup>8-13</sup>.

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 action<sup>14,15</sup>. PPI drugs are among the most widely selling drugs in the world and are generally considered safe and effective<sup>16,17</sup>. The vast majority of these drugs are benzimidazole derivatives. Benzimidazole derivatives constitute an important class of heterocyclic compounds for their versatile pharmacological activities<sup>18,19</sup>, such as antibacterial, antifungal, antihelminthic, antiallergic, antineoplastic, local analgesic, antihistaminic, antiulcer activities<sup>20,21</sup>. Pantoprazole, which contains benzimidazole and pyridine, is the best selling antiulcer drug now-a-days<sup>22</sup>. Compounds used as medicines are overwhelmingly organic compounds including small organic molecules and biopolymers. However, inorganic compounds and metal-containing compounds have been found to be useful as drugs. For example, the cis-platin series of platinum-containing complexes have found used as anti-cancer agents<sup>23</sup>.

Many drugs possess modified toxicological and pharmacological properties when they are in the form of metal complexes<sup>24</sup>. Complexation with Ni(II) resulted in improved antimicrobial profile of the drug while Mn(II) and Cu(II) metal complexes modulated oxidative burst response of phagocytes and unlike enoxacin could have potential to be anti-inflammatory, as they suppressed the production of reactive oxygen species<sup>25,26</sup>.

Here in this paper we are describing synthesis and characterization of Cobalt (II) complex with pantoprazole, (6-(difluoromethoxy)-2-[(3,4-dimethoxypyridin-2-yl)methylsulfinyl]-1H benzo[d]imidazole). Copper is an element that is very important for our good health. Actually, that may be understating the true importance of this element. Copper is critically important for dozens of body functions.

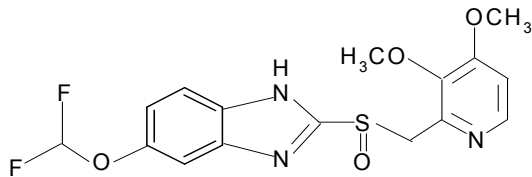
## MATERIALS AND METHODS

**(a) Reagents and Instruments:**

All chemicals and solvents used were of analytical grade. Pure sample of Pantoprazole, molecular formula  $C_{16}H_{15}F_2N_3O_4S$  and molecular weight 383.37, was obtained from Cornileus Pharmaceutics (P) Ltd. Metal salt  $CoCl_2 \cdot 6H_2O$ ,  $NiCl_2 \cdot 6H_2O$  and  $CuCl_2 \cdot 2H_2O$  used were of Merck chemicals.

Elemental analysis (C, H, N and S) were carried out using micro analytical technique on C,H,N,S,O Elemental analyzer at SAIF, IIT Bombay. IR and electronic spectra of the complex were obtained from DST-FIST Instrumentation

Laboratory of Sadhu Vaswani College, Bairagarh, Bhopal. Electronic spectra were recorded in the range 200-800nm on Perkin Elmer UV-visible spectrophotometer. Infrared spectra were recorded as KBr pellets in the range 4000-400  $\text{cm}^{-1}$  on Perkin Elmer FTIR spectrophotometer. Melting point were recorded using melting point apparatus and found to be 180°C



for Co(II), 200°C for Ni(II) and 220°C for Cu(II) complex.

Figure 1: Structure of Pantoprazole

#### (b) Ligand-Metal ratio:

Before the synthesis of complexes, we need to confirm metal-ligand ratio by conductometric titration method. 0.01 M solution of pantoprazole drug was prepared in 80:20 mixture of ethanol and distilled water. Similarly, solution of metal salts  $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$ ,  $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$  and  $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$  were prepared in the same solvent of 0.02 M concentration. 20 ml of ligand solution was diluted to 200 ml. The ligand was titrated against metal salt solutions and conductance was recorded after each addition of metal salt solution. From the graph between corrected conductance and volume of titrant added, it was concluded that the complex formation has taken place in the ratio of 1:2 (metal-ligand).

#### (c) Synthesis of complex:

After finding out the ligand-metal ratio, the solutions of ligand and metal salts were prepared in this ratio in 80:20 ethanol-water mixture. After mixing, the resulting mixture was refluxed for three hours after adjusting the pH and, there after, the solution was kept for a few days. A pink crystalline complex of cobalt, pistal green complex of nickel and brown colored complex of Copper were separated that were washed with ethanol, filtered, dried, weighed and melting point were recorded.

## RESULTS AND DISCUSSION

The synthesized complexes are stable solid towards air and moisture with high decomposition temperature. The metal complexes are insoluble in common organic solvents like benzene, chloroform, carbon tetrachloride, hexane, methanol, ethanol, acetone etc and soluble in DMF and DMSO. The analytical data (Table 1) of the metal complexes clearly shows the 1:2 metal to ligand stoichiometry.

**Infrared spectral studies:** The Infrared spectra<sup>27-31</sup> of the ligand PPZ and the complexes have been recorded and the probable assignments are given here. The IR spectra of the complexes indicates that the ligand behaves as a donor coordinating to the metal via C=N and sulphonic acid group. The shift of the  $\nu(\text{C}=\text{N})$  and  $\nu(\text{S}=\text{O})$  by 10-15  $\text{cm}^{-1}$  in the complexes indicates that these group are involved in the complexation. In the ligand, band appearing at 3500  $\text{cm}^{-1}$  due to NH stretching remains almost unchanged at 3510  $\text{cm}^{-1}$  in the complex and the band  $\nu(\text{C}=\text{N})$  in the ligand at 1589  $\text{cm}^{-1}$  is

shifted to 1573  $\text{cm}^{-1}$  in Co-complex, 1570  $\text{cm}^{-1}$  in Ni-complex and 1583  $\text{cm}^{-1}$  in Cu-complex. This confirms the coordination through the azomethine nitrogen atom. The IR band at 1039  $\text{cm}^{-1}$  in the ligand due to aromatic sulfoxide stretching is shifted to 1024  $\text{cm}^{-1}$  in the Co-complex, 1035  $\text{cm}^{-1}$  in the Ni-complex and 1029  $\text{cm}^{-1}$  in the Cu-complex indicating the involvement of oxygen of sulfoxide in complex formation. Band appearing in the region 3631  $\text{cm}^{-1}$  may be assigned to coordinated water molecules in Co-complex, 3610  $\text{cm}^{-1}$  in Ni-complex and 3668  $\text{cm}^{-1}$  in the Cu-complex. The appearance of band in far-IR region at 460  $\text{cm}^{-1}$  in the Co-complex, at 462  $\text{cm}^{-1}$  in the Ni-complex and at 465  $\text{cm}^{-1}$  in the Cu-complex may be assignable to M-N frequency. Additional band in the complex in the region 687  $\text{cm}^{-1}$  in Co-complex, at 622  $\text{cm}^{-1}$  in Ni-complex and 638.13  $\text{cm}^{-1}$  in Cu-complex compared with IR spectra of free ligand have tentatively been assigned to M-O frequency.

**Electronic spectra:** The electronic spectra of the Co(II) and Ni(II) complex displays bands at 17762  $\text{cm}^{-1}$  ( $\nu_1$ ), 15385  $\text{cm}^{-1}$  ( $\nu_2$ ) for Co(II) and at 9134  $\text{cm}^{-1}$  ( $\nu_1$ ), 20000  $\text{cm}^{-1}$  ( $\nu_1$ ) 25773  $\text{cm}^{-1}$  ( $\nu_1$ ) for Ni(II) which can be assigned to  ${}^4\text{T}_{2g}(\text{G}) \leftarrow {}^6\text{A}_{1g}$ ,  ${}^4\text{T}_{1g}(\text{G}) \leftarrow {}^6\text{A}_{1g}$  transitions for Co(II), and  ${}^3\text{T}_{2g}(\text{F}) \leftarrow {}^3\text{A}_{2g}(\text{F})$ ,  ${}^3\text{T}_{1g}(\text{F}) \leftarrow {}^3\text{A}_{2g}(\text{F})$  and  ${}^3\text{T}_{1g}(\text{F}) \leftarrow {}^3\text{A}_{2g}(\text{F})$  transitions, for Ni(II) and two bands appear in Cu(II) complex at 886.04  $\text{cm}^{-1}$  ( $\nu_1$ ), 986.94  $\text{cm}^{-1}$  ( $\nu_2$ ) which can be assigned to  ${}^3\text{T}_{2g}(\text{F}) \leftarrow {}^3\text{A}_{2g}(\text{F})$  and  ${}^3\text{T}_{1g}(\text{F}) \leftarrow {}^3\text{A}_{2g}(\text{F})$  transitions, respectively suggesting an octahedral environment around the Copper, Cobalt and Nickel ions.

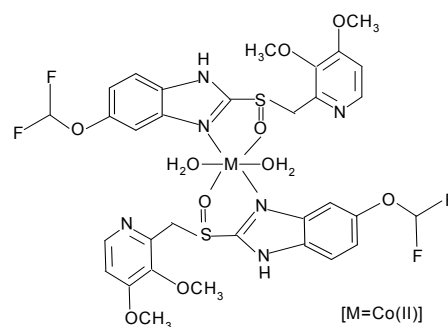


Figure 2: Structure of Pantoprazole -Co complex

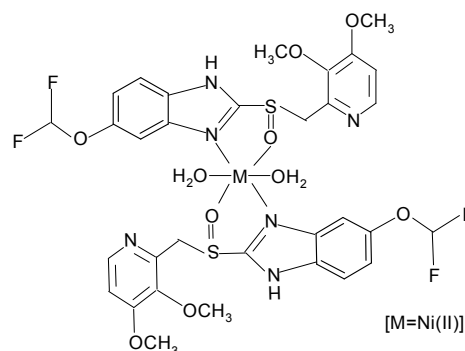


Figure 3: Structure of Pantoprazole -Ni complex

## CONCLUSION

From the analytical and spectral data, it can be concluded that the synthesized complexes of Co(II), Ni(II) and Cu(II) are stable with probably octahedral environment around it.

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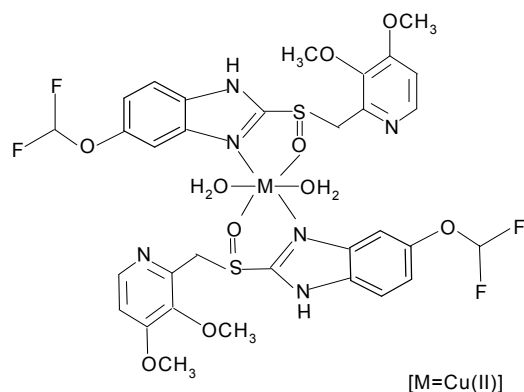


Figure 4: structure of Pantoprazole Cu complex

Table 1: Analytical data of the ligand and complex

Composition of complex (Mol.Wt.)	Color	Yield (%)	M.P. (°C)	Elemental analyses(%):found (calcd)			
				C	H	N	M
C <sub>16</sub> H <sub>15</sub> F <sub>2</sub> N <sub>3</sub> O <sub>4</sub> S (383.34)	white	-	140	(50.12)	(3.94)	(10.96)	-
(C <sub>16</sub> H <sub>15</sub> F <sub>2</sub> N <sub>3</sub> O <sub>4</sub> S) <sub>2</sub> Co.2H <sub>2</sub> O	pink	38	180	50.71	3.73	10.48	7.58
				(50.12)	(3.94)	(10.96)	(7.68)
(C <sub>16</sub> H <sub>15</sub> F <sub>2</sub> N <sub>3</sub> O <sub>4</sub> S) <sub>2</sub> Ni.2H <sub>2</sub> O	Pista Green	35	200	44.83	3.78	8.72	6.70
				(44.65)	(3.57)	(9.76)	(6.81)
(C <sub>16</sub> H <sub>15</sub> F <sub>2</sub> N <sub>3</sub> O <sub>4</sub> S) <sub>2</sub> Cu.2H <sub>2</sub> O	brown	49	220	44.83	3.78	8.72	6.70
				(44.65)	(3.57)	(9.76)	(6.81)

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