

Synthesis Characterization and Antimicrobial Studies of Zn(II), Cu(II), Pb(II), Ni(II) and Co(II) Complexes of 3-(4'-Sulfamoyl iminophenyl) Isatin

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Carbonic anhydrase inhibitors are widely reported with antimicrobial action. The antibacterial actions of sulfanilamide and isatin are found to be enhanced on complexation with metals. Considering this Zn(II), Cu(II), Pb(II), Ni(II) and Co(II) complexes of 3-(4'-sulfamoyl iminophenyl) isatin were synthesized and evaluated against some urinary tract pathogens. The Cu(II) complex was found to be most potent against the pathogens.

Key Words: Synthesis, Characterization, Antimicrobial activity, Metal(II) complexes, Isatin.

INTRODUCTION

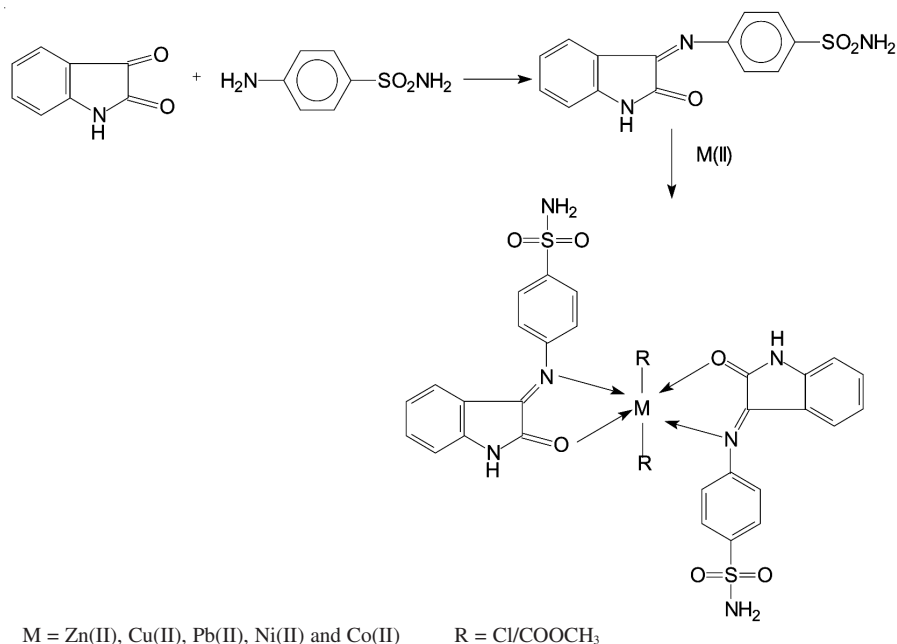
The development of carbonic anhydrase inhibitor based antimicrobials has shown promising results due to the presence of carbonic anhydrases in a multitude of bacteria and protozoa¹⁻³. Much attention has been directed to study the metal complexes of the Schiff base ligands derived from isatin and sulfanilamide^{4,5}, a prototype of carbonic anhydrase inhibitor⁶. The metal complexes are reported to enhance inhibitory activity of isatin derivatives against pathogens^{4,6}. In order to considering these features Zn(II), Cu(II), Pb(II), Ni(II) and Co(II) complexes of Schiff-base obtained from sulfanilamide and isatin are reported herein.

EXPERIMENTAL

Synthesis of 3-(4'-sulfamoyl iminophenyl) isatin and the corresponding metal complexes were made following the reported method⁷. To an ethanolic (20 mL) solution of 3-(4'-sulfamoyl iminophenyl) isatin (0.008 mol), an ethanolic solution of the corresponding metal (II) acetate (0.004 mol) was added. The mixture was refluxed for 2 h. The solution was left overnight at room temperature. The product was filtered, washed repeatedly with water dried and recrystallized from ethanol. The compound [CoL₂Cl₂] was prepared by adding a hot aqueous solution of CoCl₂·6H₂O (0.004 mol) to an ethanolic solution of the ligands (0.008 mol) and heating under reflux for 1 h. The compound [NiL₂Cl₂] was prepared similarly.

RESULTS AND DISCUSSION

The physico-chemical data of the synthesized compound are given in Table-1. The conductivity values (CM-180, Elico) for the complexes (in DMF, 10^{-3} mol, 25 °C), in the range of 6.7-11.2 $\Omega^{-1} \text{ cm}^2 \text{ mol}^{-1}$ indicate the non-electrolytic nature of the compounds. The three IR bands appearing at 3230, 1751 and 1654 cm^{-1} in the ligand spectra, were assigned to stretching vibration modes of NH, C=O and C=N, respectively. In the cases of the metal complex of compounds, the spectra reveal that the band at 1751 cm^{-1} in the free ligand is shifted to lower wave numbers indicating implication of carbonyl oxygen in the coordination at the metallic center. The band appearing at 1654 cm^{-1} in the free ligand, assignable to the C=N vibration mode, is shifted to lower wave numbers (1618 cm^{-1}) suggesting participation of azomethine nitrogen atom in coordination. The band due to the NH vibration mode in isatin, having the maximum at 3230 cm^{-1} in the free ligand, remains largely unaffected in the chelates. The most important conclusion drawn from this discussion is that the 3-(4'-sulfamoyl iminophenyl) isatin (ligand) is coordinated to the central metal ion as NO bidentate ligand. The formation of M-O and M-N bonds is further supported by the appearance of bands at 440-450 and 500-530 cm^{-1} , respectively in the spectra of chelates. The electronic spectra of the ligand in ethanol exhibit three bands at 254, 297 and 420 nm which shifts to lower values, proving the coordination of ligand at metallic center (**Scheme-I**). Further the quantitative estimation of Cu and Co by atomic absorption spectroscopy (AAnalyst-200) shows values, which are close to the values calculated for the proposed metal chelates.



Scheme-I

TABLE-1
PHYSICOCHEMICAL DATA OF COMPOUNDS

Compound	m.f.	mol (wt.)	m.p. (°C)	IR (KBr, ν_{\max} , cm^{-1})	Color	Solubility
L (ligand)	C ₁₄ H ₁₂ N ₃ O ₃ S	302.00	185	3240, 1751, 1654	Yellowish	Ethanol
[Cu(L) ₂ (AcO) ₂]	C ₃₂ H ₂₆ N ₆ O ₁₀ S ₂ Cu	781.55	256	3246, 1734, 1616.40	Brown/black	DMF
[Zn(L) ₂ (AcO) ₂]	C ₃₂ H ₂₆ N ₆ O ₁₀ S ₂ Zn	783.39	251	3242, 1730, 1618.33	Violet	Ethanol
[Pb(L) ₂ (AcO) ₂]	C ₃₂ H ₂₆ N ₆ O ₁₀ S ₂ Pb	925.20	238	2342, 1734, 1616.40	Brown/grey	DMF
[Ni(L) ₂ Cl ₂]	C ₂₈ H ₂₂ N ₆ O ₆ S ₂ Cl ₂ Ni	631.70	163	3244, 1734, 1616.40	Brownish	DMF
[Co(L) ₂ Cl ₂]	C ₂₈ H ₂₂ N ₆ O ₆ S ₂ Cl ₂ Co	631.90	169	3240, 1730, 1617.35	Dark violet	DMF

The *in vitro* antibacterial activity evaluation of the metal complexes by disc diffusion method⁸ showed better zones of inhibition than nitrofurantoin. The activities of copper, zinc and cobalt complexes were equivalent to that of ciprofloxacin. The copper complex was most active against *Escherichia coli*, *Pseudomonas aeruginosa* and *Enterococcus faecalis*. The cobalt, zinc and copper complexes were equally active against *Staphylococcus aureus*. The lead and nickel complexes were more potent than nitrofurantoin but the zones of inhibition was less compared to that of other metal complexes (Table-2). This study reveals the capacity of the metallic complexes to inhibit some specific urinary tract pathogens *in vitro*. Further study to elucidate the pharmacokinetic behaviour of these complexes and their *in vivo* action are to be made to prove their therapeutic utility.

TABLE-2
In vitro ANTIBACTERIAL ACTIVITY OF COMPOUNDS AGAINST SELECTED URINARY TRACT PATHOGENS BY DISC DIFFUSION METHOD

Compound	Concen. ($\mu\text{g}/\text{disc}$)	<i>E. coli</i>	<i>P. aeruginosa</i>	<i>E. faecalis</i>	<i>S. aureus</i>
L (ligand)	300	14.5 \pm 1.30	15.0 \pm 0.84	10.5 \pm 1.40	13.7 \pm 0.68
[Cu(L) ₂ (AcO) ₂]	300	25.0 \pm 0.72	23.35 \pm 1.40	23.4 \pm 2.16	22.0 \pm 3.14
[Zn(L) ₂ (AcO) ₂]	300	21.0 \pm 0.74	20.8 \pm 0.14	19.0 \pm 1.45	22.5 \pm 2.70
[Pb(L) ₂ (AcO) ₂]	300	18.6 \pm 0.53	18.5 \pm 0.54	17.0 \pm 0.47	19.9 \pm 1.24
[Ni(L) ₂ Cl ₂]	300	17.5 \pm 2.40	19.6 \pm 2.10	16.3 \pm 1.21	17.8 \pm 0.74
[Co(L) ₂ Cl ₂]	300	23.2 \pm 0.82	22.4 \pm 1.43	19.7 \pm 0.87	22.6 \pm 0.66
Control	–	–	–	–	–
Ciprofloxacin	25	28.0 \pm 0.15	26.4 \pm 0.45	26.4 \pm 0.45	25.3 \pm 0.15
Nitrofurantoin	300	18.4 \pm 0.45	12.6 \pm 0.65	15.3 \pm 0.37	11.8 \pm 0.75

“–” Indicates no zone of inhibition. All the values are mean \pm standard deviation of three determinations. Values showed significant difference from solvent control at $p < 0.001$.

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