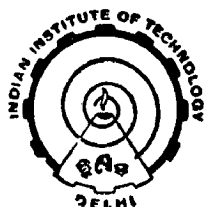


SYNTHESIS AND CHARACTERIZATION OF METAL COMPLEXES OF SOME PHARMACEUTICALS

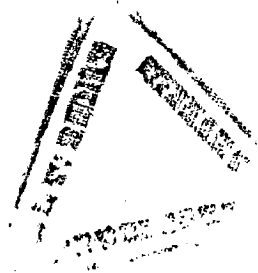
**BY
G. KANAGARAJ**

***THESIS SUBMITTED
IN FULFILMENT OF THE REQUIREMENTS
FOR THE AWARD OF THE DEGREE OF
DOCTOR OF PHILOSOPHY***



**Department of Chemistry
INDIAN INSTITUTE OF TECHNOLOGY, DELHI
JANUARY, 1991**

TO THOSE GOOD HEARTS
BEATING FOR ME



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CERTIFICATE

This is to certify that the thesis entitled, "Synthesis and Characterization of Metal Complexes of Some Pharmaceuticals" being submitted by G. Kanagaraj to the Indian Institute of Technology, Delhi for the award of the degree of "Doctor of Philosophy" is a record of bonafide research work carried out by him. Mr. G. Kanagaraj has worked under my guidance and supervision and has fulfilled the requirements for the submission of the thesis, which to my knowledge, has reached requisite standard.

The results contained in this thesis have not been submitted, in part or in full to any University or Institute for the award of any degree or diploma.



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10.01.1991
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ABSTRACT

Metal complexes of thiacetazone (an anti-tuberculosis drug), dapson (anti-leprosy drug) and urinary antiseptics like sulfamethoxazole, sulfisoxazole and nitrofurantoin have been synthesized. Bicine, a potential iron chelator was also included in the study of metal binding characteristics of the drugs mentioned above.

The metals studied include some first row transition elements, cadmium, mercury and lead. Elemental analysis, conductivity and magnetic susceptibility measurements, thermal analysis, electronic, infrared and proton magnetic resonance spectral analyses were employed to characterize the metal complexes.

Thiacetazone (p-acetamidobenzaldehydethiosemicarbazone) was shown to behave as a neutral, bidentate ligand with nitrogen and carbothioamide sulfur as donor atoms. Octahedral geometry is indicated for cobalt(II), nickel(II) and zinc(II) complexes while those of cadmium(II) and mercury(II) appear to be polymeric in structure.

Sulfamethoxazole and sulfisoxazole (both isoxazolyl derivatives of p-aminobenzenesulfonamide) were found to be deprotonated in their metal complexes. Sulfamethoxazole was found to act as a bidentate ligand binding the metal ion

through sulfonamide nitrogen and isoxazole ring nitrogen atoms in the case of copper(II) complex, and through sulfonyl oxygen and sulfonamide nitrogen atoms in the case of chromium(III), manganese(II), cobalt(II), nickel(II), cadmium(II) and mercury(II) complexes. However, in zinc(II), lead(II) and iron(III) complexes, sulfamethoxazole acts probably as a monodentate ligand binding the metal ion through deprotonated sulfonamide nitrogen.

Sulfisoxazole (SI) was found to act as a bidentate ligand binding the metal ion through sulfonamide nitrogen and sulfonyl oxygen in magnesium(II), copper(II), zinc(II) and mercury(II) complexes. In the nickel(II) complex $[\text{Ni}(\text{SI})_2(\text{H}_2\text{O})_4]2\text{H}_2\text{O}$, sulfisoxazole probably binds the metal ion only through sulfonyl oxygen.

Nitrofurantoin (NF), 1-[(5-nitro-2-furanyl)methylene]-amino]-2,4-imidazolidinedione was shown to behave as an anionic monodentate ligand binding the metal ion through enolic oxygen atom. Octahedral structure is proposed for manganese(II), cobalt(II), nickel(II), copper(II) and cadmium(II) complexes of the type $[\text{M}(\text{NF})_2(\text{H}_2\text{O})_4]x\text{H}_2\text{O}$. Four coordination is likely in zinc(II), mercury(II) and lead(II) complexes of the type $[\text{M}(\text{NF})_2(\text{H}_2\text{O})_2]x\text{H}_2\text{O}$.

Bicine, N-bis (2-hydroxyethyl)glycine appears to function as a multidentate ligand binding the metal ion

through nitrogen, carboxylic oxygen and alcoholic oxygen atoms in its complexes with magnesium(II), manganese(II), cobalt(II), copper(II), zinc(II) and cadmium(II).

Dapsone (4,4'-diaminodiphenylsulfone) was found to form adducts of the type $M(DDS)_2Cl_2$ with nickel(II), copper(II) and zinc(II) chlorides.

Mixed ligand copper(II) complexes containing some drugs like isoniazid, pyrazinamide, salicylamide, acetylsalicylic acid and theophylline were synthesized. Structural investigation revealed some interesting features in these complexes.

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