Abstract
Since many years ago, man has tried to overcome infections disease. Antibiotic drugs have been the most important source of chemotherapeutic treatment. As metal ions have been shown involved practically in every phase of biological activity, like most of the reactions occurring in the biological systems, the action of antibiotic drug also requires one or more metal ion apart from the reactant substrate and the presence of specific enzymes as catalyst. Complexes of drug molecules with metal ions is known to improve their biological activity with reduction of undesired side effects. The information on interaction and coordination behaviour of a drug with transition metal ion may, therefore, help in developing a suitable therapeutic agent with enhanced efficacy.

Nalidixic acid, Norfloxacin, Ciprofloxacin and Cloxacillin sodium are antibiotic drugs and well known for their medicinal values, but they have not received a thorough, adequate and conclusive investigation so far as their chemistry of coordination compound is concerned.

The present thesis deals with the ligational aspects of these drugs with Mn, Fe, Ni, Cu and Zn. The complexes of above drugs were prepared using adequate methods and characterised by molar conductance, magnetic moment, elemental analysis, electronic and infrared spectra. The results of author's investigation have been presented in the thesis entitled - "PHYSICO-CHEMICAL STUDIES ON SOME 3d - TRANSITION METAL COMPLEXES OF ANTIBIOTIC DRUGS."

The thesis consists of six chapters. The results have been used to project the aims of study as follows:

(1) To observe the stoichiometry and formation of complexes in solution and its crystallization.

(2) To observe the structure of complex compound and the structural change in the drug.

(3) To observe the respective change in the microbial (antibacterial and antifungal) activity of the drug as a result of complexation with metal ions:

CHAPTER - I

It deals with the brief introduction of coordination compounds in many type of chemical and biological processes. This also includes the importance of present work.

CHAPTER - II

In this chapter brief introduction of the drugs undertaken in the present work and survey of relevent literature on their metallic complexes has been described.

CHAPTER - III

This chapter comprises with the principles underlying the various physico-chemical methods employed in the present work i.e., molar conductance, magnetic moment, electronic and infrared spectroscopy. Elemental analysis of the complexes has also been carried out.

CHAPTER - IV

Various physico-chemical techniques used in the present investigation for the isolation of the complexes and the experimental data have been reported in this chapter. Water and organic solvents were used for preparing the complexes. Isolated complexes were purified and recrystallised employing
standard methods. All the complexes were highly stable, insoluble in water and most of the common organic solvents.

CHAPTER - V

This chapter comprises "Result and Discussion". First part of this chapter describes in general, the stereochemistry of the complexes, while the second part gives an account of the structural conclusions of individual drug complexes drawn on the basis of various physico-chemical data.

Nalidixic acid complexes were isolated at pH 4-5.5. On the basis of molar conductance, magnetic moment, elemental analysis, electronic and infra-red spectra it can be inferred that all the complexes are six coordinated with octahedral structure. Molecular formulae of the isolated complexes are:

(I) \[ \text{Mn} (\text{C}_{12}\text{H}_{11}\text{N}_2\text{O}_3)_2 (\text{H}_2\text{O})_2 \]

(II) \[ \text{Fe} (\text{C}_{12}\text{H}_{11}\text{N}_2\text{O}_3)_2 (\text{Cl}) (\text{H}_2\text{O}) \]

(III) \[ \text{Ni} (\text{C}_{12}\text{H}_{11}\text{N}_2\text{O}_3)_2 (\text{H}_2\text{O})_2 \]

(IV) \[ \text{Cu} (\text{C}_{12}\text{H}_{11}\text{N}_2\text{O}_3) (\text{OH}) (\text{H}_2\text{O})_3 \]

(V) \[ \text{Zn} (\text{C}_{12}\text{H}_{11}\text{N}_2\text{O}_3) (\text{OH}) (\text{H}_2\text{O})_3 \]

On the basis of various physico-chemical investigations it has been found that the drug nalidixic acid behaves as a monoprotic bidentate ligand coordinating through oxygen of \( >\text{C} = \text{O} \) and \( \text{COO}^- \) groups. The stoichiometry ratio of the metal ion and the ligand has been found to be 1 : 1 for Cu (II) and Zn
(II) and 1 : 2 for Mn (II), Fe (III) and Ni (II) complexes. One/two coordination position are occupied by water molecules. In case of Cu (II) and Zn (II) complexes three coordination positions are occupied by water molecules and another by OH⁻ group. Presence of coordinated water molecule, and OH⁻ groups has been confirmed by IR and elemental analysis. The presence of chloride ion in Fe (III) complex has been confirmed by elemental analysis.

Norfloxacin complexes were isolated at pH 5-6.5. Molecular formulae of the isolated complexes are:

(I)  \[ \text{Mn} \left( C_{16}H_{17}F \text{N}_3 \text{O}_3 \right) \text{(Cl)} \left( \text{H}_2\text{O} \right)_3 \]

(II)  \[ \text{Fe} \left( C_{16}H_{17}F \text{N}_3 \text{O}_3 \right) \text{(Cl)}_2 \left( \text{H}_2\text{O} \right)_2 \]

(III)  \[ \text{Ni} \left( C_{16}H_{17}F \text{N}_3 \text{O}_3 \right) \text{(CH}_3\text{COO)} \left( \text{H}_2\text{O} \right)_3 \]

(IV)  \[ \text{Cu} \left( C_{16}H_{17}F \text{N}_3 \text{O}_3 \right) \text{(CH}_3\text{COO)} \left( \text{H}_2\text{O} \right)_3 \]

(V)  \[ \text{Zn} \left( C_{16}H_{17}F \text{N}_3 \text{O}_3 \right) \text{(CH}_3\text{COO)} \left( \text{H}_2\text{O} \right)_3 \]

On the basis of various physico-chemical observations it has been found that the drug norfloxacin behaves as a monoprotonic bidentate ligand coordinating through oxygen of >C = O and COO⁻ groups. The complexes were octahedral with the metal ion and the ligand in the molar ratio 1 : 1 for Mn (II), Fe (III), Ni (II) and Zn (II) and 1:2 for Cu (II) complex. Two/three coordination positions are occupied by water molecules. Presence of coordinated water molecules and CH₃COO⁻ groups were confirmed by IR and elemental analysis. The presence of Cl⁻ ion in Fe (III) complex has been confirmed by elemental analysis.
Ciprofloxacin complexes were isolated at pH 5-6. Molecular formulae of the isolated complexes are:

(I)  \[ \text{Mn} \left( C_{17}H_{17}F N_3O_3 \right) (\text{Cl}) (H_2O)_3 \]

(II)  \[ \text{Fe} \left( C_{17}H_{17}F N_3O_3 \right)_2 (\text{OH}) (H_2O) \]

(III)  \[ \text{Ni} \left( C_{17}H_{17}F N_3O_3 \right) (\text{CH}_3\text{COO}) (H_2O)_2 \]

(IV)  \[ \text{Cu} \left( C_{17}H_{17}F N_3O_3 \right)_2 (H_2O)_2 \]

(V)  \[ \text{Zn} \left( C_{17}H_{17}F N_3O_3 \right) (\text{CH}_3\text{COO}) (H_2O)_2 \]

On the basis of various physico-chemical investigations it has been found that the drug ciprofloxacin behaves as a monoproptic bidentate ligand coordinating through oxygen of \( \text{C} = \text{O} \) and \( \text{COO}^- \) groups. The complexes were octahedral having metal to ligand stoichiometric ratio 1:1 for Mn (II), Ni (II) and Zn (II) and 1:2 for Fe (III) and Cu (II). Two/three coordination positions are occupied by water molecules but in the case of Fe (III) complex one coordination position is occupied by water molecule and another by \( \text{OH}^- \) group. Presence of coordinated water molecules, \( \text{OH}^- \) and \( \text{CH}_3\text{COO}^- \) groups has been confirmed by IR and elemental analysis. The presence of chloride ion in the Mn (II) complex has been confirmed by elemental analysis.

Cloxacillin complexes were isolated at pH 4.5-5.5. Molecular formulae of the isolated complexes are:

(I)  \[ \text{Mn} \left( C_{19}H_{19}Cl N_3O_6S \right) (\text{Cl}) (H_2O)_3 \]

(II)  \[ \text{Fe} \left( C_{19}H_{19}Cl N_3O_6S \right) (\text{SO}_4) (H_2O)_2 \]

(III)  \[ \text{Ni} \left( C_{19}H_{19}Cl N_3O_6S \right) (\text{OH}) (H_2O)_2 \]

(IV)  \[ \text{Cu} \left( C_{19}H_{19}Cl N_3O_6S \right) (\text{OH}) (H_2O)_2 \]
(V) \[\text{Zn} \left( \text{C}_{19}\text{H}_{19}\text{ClN}_{3}\text{O}_{6}\text{S} \right) \left( \text{OH} \right) \left( \text{H}_2\text{O} \right)_3\]

On the basis of various physico-chemical observation it has been found that the drug cloxacillin behaves as a monoproct Ligand. The complexes were octahedral having metal to ligand stoichiometric ratio 1 : 1 for all complexes. Two/three coordination position are occupied by water molecules. In case of Fe (III) complex the SO$^-_4$ ion present in the coordination sphere has been confirmed by IR bands and elemental analysis. In this complex Td symmetry of the SO$^-_4$ ion present in the drug was lowered to C$_2$V in the complex suggesting chelating bidentate coordination. Presence of coordinated water molecules and OH$^-_-$ group has been confirmed by IR and elemental analysis. The presence of chloride ion in the Mn (II) complex has been confirmed by elemental analysis.

**CHAPTER - VI**

This chapter deals with general description of the activity performed, techniques of the evaluation of antimicrobial [antibacterial and antifungal] activities.

The zone of inhibition of the complexes against a number of gram positive and gram negative pathogens bacteria like *Escherichia coli*, *Bacillus subtilis*, *Salmonella typhosa*, *Shigella flexneri*, *Bacillus pyocyaneus* and *Staphylococcus aureus* and *Aspergillus niger*, *Aspergillus flavus*, *Candida albicans*, *Trichoderma viride* and *Chrysosporium pannicale* fungi.

The nalidixic acid complexes show remarkable antibacterial activity against *Escherichia coli*, *Bacillus subtilis* at room temperature. The Fe (III) complex also shows good antibacterial activity against *Shigella flexenri* bacterium. These complexes also show remarkable antifungal activity against *Trichoderma viride*, *Chrysosporium pannicale* and *Candida albicans* species as compared to parent drug.
The norfloxacin and ciprofloxacin Mn (II), Fe (III), Ni (II), Cu (II) and Zn (II) complexes exhibit remarkable antibacterial activity against many organisms. These metal complexes show remarkable antifungal activity against *Trichoderma viride*, *Chrysosporium pannicale* and *Candida albicans* fungi.

It has been found that the complexes of Mn (II), Fe (III), Ni (II), Cu (II) and Zn (II) cloxacillin showed remarkable antibacterial activity against *Escherichia coli*, and *Bacillus subtilis* bacteria as compared to the parent drug. All the cloxacillin complexes also show antifungal activity against *Trochoderma viride*, *Chrysosporium pannicale* and *Candida albicans* fungi as compared to the parent drug.

All the 20 complexes prepared show nil activity against *Aspergillus niger* and *Aspergillus flavus* fungi.