CHAPTER-I

INTRODUCTION AND SCOPE OF THE PRESENT WORK.
1.1 Introduction

The everincreasing application of transitional metal complexes in various fields of science is the driving force for the research and development of coordination chemistry. The role of the central metal atom or ion and the ligands containing different donor atoms has received considerable attention not only in fundamental inorganic and organometallic chemistry but also in more applied areas such as environmental, bioinorganic, medicinal and bioorganic chemistry. Such studies have contributed significantly to the development of research in bioinorganic chemistry. Also, the rapid developments in this area over the past 10-20 years have benefited from the application of sophisticated spectroscopic techniques like IR, UV-Visible, EPR, NMR, X-ray diffraction studies etc. The research work in this area involves diverse type of studies such as

* Synthesis of metal complexes,
* Characterization,
* Theories of metal-ligand bonding,
* Structural relativity by employing spectroscopic techniques and
* Studies of the biological activity.

The selection of metal ions and design of potential ligand is very much important for the formation of complexes and study of application in all fields.

Due to the recent developments in the field of bioinorganic chemistry, the metal complexes also used as diagnostic and chemotherapeutic agents. These complexes are also possessing wide range of analytical, industrial, catalytic applications with diverse structures. Generally, the metal complexes containing different donor atoms such as nitrogen, oxygen or sulphur exhibit enhanced antifungal, antiviral, antitumour and anti HIV activities.
1.2 Ligand profile

Quinoline derivatives represent the major class of heterocycles, and a number of preparations have been known from the late 1980s. The quinoline ring system occurs in various natural products, especially in alkaloids. The quinoline skeleton is often used for the design of many synthetic compounds with diverse pharmacological properties. In 1820, quinine was isolated as the active ingredient from the bark of Cinchona trees and successively replaced the crude bark for the treatment of malaria. Despite its relatively low efficacy and tolerability, quinine still plays an important role in the treatment of multiresistant malaria\(^1\). This molecule has also played a historical role in organic chemistry as a target for structural determination and total synthesis\(^2\), and recently both stereoselective\(^3\) and enantioselective\(^4\) total synthesis.

Chimanine alkaloids, simple quinolines isolated from the bark of Galipea longiflora trees of Rutaceae family\(^5\-7\), are effective against the parasites Leishmania sp., which are the agents of leishmaniasis, a protozoan disease of the tropical areas in South America, particularly in the Amazonian forest. Cryptolepine is an indoloquinoline alkaloid found in the West African climbing shrub Cryptolepis sunguinoenta. A decoction of the roots of this species is used in traditional medicine for the treatment of malaria as well as for a number of other diseases\(^8\).

Dynemicin A and Streptonigrin, naturally occurring members of the class of antitumour antibiotics, whose syntheses are based on the utilization of preformed quinoline derivatives\(^9\-10\). The 8-(diethylaminohexylamino)-6-methoxy-4-methylquinoline is highly effective against the protozoan parasite Trypanosoma cruzi, which is the agent of Chagas' disease\(^11\) and the 2-(2-methylquinolin-4-ylamino)-N-phenylacetamide is more active than the standard antileishmanial drug sodium antimony gluconate\(^12\).
The centipede, *Scolopendra Subspines mutilans* L. which is found to contain 3,8-dihydroxyquinoline called *Jineol* has been used in the traditional Chinese medicine. WU Gong\textsuperscript{13} has prescribed this for tetanus and childhood convulsions. This drug has also been used for many other clinical purposes, such as the treatment of acute heart attack and as a toxicide in Korea\textsuperscript{14}.

A plant alkaloid neocryptolepine (5-methyl-5H-indolo[2,3-b]quinoline), which (together with cryptolepine) is present in *Cryptolepis sanguinolenta* extracts used in natural medicine in Africa. Cryptolepine (5-methyl-5H-indolo[3,2-b]quinoline)-major *Cryptolepis sanguinolenta* alkaloid-displays a plenty of pharmacological effects, such as antimuscarinic, noradrenergic receptor antagonistic, antihypertensive, vasodilative, antithrombotic, antipyretic and anti-inflammatory properties. Neocryptolepine and cryptolepine derivatives reveal antiplasmodial and antitrypanosomal and first of all, cytotoxic activities\textsuperscript{15-17}.

With this, recently reported applications of quinoline derivatives are briefly discussed in the following paragraphs.

Quinoline containing drugs particularly 4-aminoquinolines, have a long and successful history as antimalarials\textsuperscript{18-19}. One of these, chloroquine, has been in worldwide use since the Second World War. However, resistance to chloroquine has become clinically significant in several areas of the world\textsuperscript{20-21}. Peter Madrid et.al.\textsuperscript{22} synthesized a new series of chloroquine analogues with a shortened side chain and diverse functionalities on the alkylamine side chain to develop a structure-activity relationship for these modifications.

Edmunds Lukevics et.al\textsuperscript{23} reported the neurotropic activity of hydroxyalkyl and carboxyalkyl derivatives of silatetrahydroisoquinoline, tetrahydroisoquinoline and tetrahydroquinoline. Depending on the nature of the heterocycle, N-substituent and
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presence of a silicon atom in the molecule, the compounds exhibited a predominant psychotropic activity; the tetrahydroisoquinoline shows a sedative activity; the silatetrahydroisoquinoline derivatives—an antihyptonic action; tetrahydroquinolines—anticonvulsant effects.

Kozlovski et.al\textsuperscript{24} tested antiarrhythmic and endothelial action of novel decahydroquinoline derivatives. Among the fifteen novel decahydroquinoline derivatives, four displayed antiarrhythmic activity. Among the four, two have keto-group at 4-position; whereas at 2-position they have 2,3-dimethoxyphenyl- and 2,4-dimethoxyphenyl- groups, respectively. Other two have 3-phenylpropyl- group at 1-position, methyl- group at 2-position and benzoxy- group at 4-position.

Noda et.al\textsuperscript{25} synthesized a series of novel substituted 2-cyanoquinolines and the structure activity relationships were evaluated with respect to their ability to inhibit the formation of leukotrienes via the 5-lipoxygenase enzyme. Further they found that the \[1S,5R\]-2-cyano-4(3-furyl)-7-{fluoro-5-[3-(3I-hydroxy-6,8-dioxiabicyclo[3,2,1]-octanylphenoxy)methyl}quinoline represents a distinct class of inhibitors and posses \textit{in vitro} and \textit{in vivo} potency comparable or superior to naphthalenic analog.

1.3 Scope of the present work

In the last decade, much attention has been given to the organic ligands and transition metal complexes because of their biological relevance, interesting spectral and magnetic properties. The fused aromatic heterocyclic ligands and their metal complexes are being used extensively as pharmaceutical and chemotherapeutic agents. These are used in the forefront of these applications, as they are stable, inert and soluble in water, containing spectroscopically active metal centers, which are extremely valuable as probes of biological system. Thus the search of the complexes
that can work as chemotherapeutic agents has been the subject of current research interest in coordination chemistry.

On the other hand, quinolines and their derivatives form an interesting class of compounds which display attractive applications as pharmaceuticals and are general synthetic building blocks, due to their chemical and biological relevance. Therefore, it was thought worthwhile to isolate and characterize some metal complexes of quinoline derivatives containing different donor atoms.

In the present study, the author reports on:

1. Synthesis and characterization of quinoline derivatives containing N S, N N and N O donor atoms and their metal complexes of cobalt(II), nickel(II), cadmium(II), zinc(II), palladium(II), rhodium(III) and ruthenium(III) by employing physicochemical techniques like electronic spectra, conductivity measurements, magnetic susceptibility measurements and modern spectroscopic techniques such as IR, NMR and X-ray diffraction studies.

2. Thermal studies for the evaluation of kinetic and thermodynamic parameters such as activation energy, entropy, enthalpy and free energy of metal complexes.

3. The antibacterial and antifungal studies on some of the metal complexes with *P. aerugenosa* (gram negative), *S. aureus* (gram positive) bacteria, and *C. albicans, A. flavus* and *A. niger* fungi.
Reference


