SYNOPSIS

Chemical investigations on metal complexes of naturally occurring ligand systems and their importance in biology and medicine constitute one of the most dynamic area of modern inorganic chemistry. Biochemical activity of many plant chemicals are known to be associated with their ability to form complexes with various inorganic species including metal ions. However, synthesis, characterisation and biological studies of metal complexes of synthetic analogues of many phytochemicals have not received as much attention as they deserve. The present investigation is an attempt in this direction on synthetic analogues of the active chemical components namely curcuminoids present in the herbacious Indian medicinal plant turmeric (*Curcuma longa* Linn.).

Structurally curcuminoids are a group of 1,3-diketones in which the keto groups are directly attached to olefinic linkages. In conformity with literature usage these compounds are represented as 1,7-diaryl-1,6-heptadiene-3,5-diones or simply 1,7-diarylheptanoids. Metal complexes of synthetic analogues of these naturally occurring 'unsaturated 1,3-diketones' have been studied from a structural context. Biological properties such as antioxidant activity, cytotoxicity and antitumour activities of these compounds have also been examined. A preliminary investigation on biodistribution of these compound on mice using radiolabelling technique was also carried out.

The break up of the Thesis is as follows:

CHAPTER 1 : GENERAL INTRODUCTION

Importance of 1,3-diketones and metal 1,3-diketonates have been brought out. Various chemical medicinal and biological aspects of the
naturally occurring unsaturated 1,3-diketones (curcuminoids) and related compounds have been discussed. Important studies appeared in the general literature on curcuminoids have also been included. Salient aspects of the present investigation have been interspersed at appropriate places.

CHAPTER 2 : SYNTHESIS AND CHARACTERISATION OF METAL COMPLEXES OF 1,7-DIARYLHEPTANOIDS

In this chapter synthesis and characterisation of a new curcuminoid analogue and its metal complexes and also some trivalent metal complexes of typical synthetic curcuminoids reported earlier are presented. For convenience this chapter is divided into three sections.

Section 1 : Synthesis and characterisation of some trivalent metal complexes of 1,7-diarylhepta-1,6-diene-3,5-diones

Synthesis and characterisation of aluminium(III), chromium(III) and iron(III) complexes of the 1,7-diarylheptanoids are considered in this section. Analytical and spectral data clearly indicated that the ligands function as monobasic bidentate in their [ML$_3$] complexes in which the dicarbonyl group is involved in the formation of C$_3$O$_2$M ring system.

Section 2 : Synthesis and characterisation of 1,7-dianthrylhepta-1,6-diene-3,5-dione and its metal complexes

In this section details on the synthesis and characterisation of a new curcuminoid analogue containing anthracene rings are given. Uv, ir, nmr and mass spectral data clearly indicated the existence of the compound entirely in the intramolecularly hydrogen bonded enol form. Based on analytical and spectral data the structure and nature of bonding in the [ML$_2$] complexes of Co(II), Ni(II) and Cu(II), and [ML$_3$] complexes of Al(III), Cr(III) and Fe(III) are also discussed.
Section 3 : Synthesis and characterisation of trivalent metal complexes of 1,7-bis(substitutedaryl)hepta-1,6-diene-3,5-diones

Details on the synthesis and characterisation of Al(III), Cr(III) and Fe(III) chelates of 1,7-diaryleptanoids having different aryl substituents are presented in this section. Analytical and spectral data clearly indicated that the aryl substituents having donor atoms are not involved in bonding with the metal ion in their [ML$_3$] complexes.

Chapter 3 : Biological studies of 1,7-diarylheptanoids and their metal complexes

The antioxidant and antitumour activity of two typical 1,7-diarylheptanoids and their metal complexes are presented in this chapter. The biodistribution assay of the synthetic analogue of the natural curcumin I have also been studied. These results are discussed separately in three sections.

Section 1 : Antioxidant activity

*In vitro* studies on inhibition of superoxide, hydroxyl and lipid peroxide showed that metal complexation increases the radical scavenging activity of curcuminoids.

Section 2 : Cytotoxicity and antitumour activity

Details of the studies on *in vitro* cytotoxicity and solid tumour reduction in Swiss albino mice were carried out using the curcuminoids and their metal complexes are given. The results indicated that metal complexation enhances both the cytotoxicity and solid tumour reduction.

Section 3 : Biodistribution assay

The biodistribution of the curcuminoids administered intraperitonially in mice were studied by $^{51}$Cr radioisotope labelled Cr(III) complex of the
curcuminoid. The labelling was carried out using Na$_2^{51}$CrO$_4$. Experimental details of the study are presented in this section. The results showed that after 1 h about 60% accumulation in liver ~ 13% in lung and ~ 15% in spleen.

References are given in serial order at the end of the Thesis.
SYNTHESIS, CHARACTERISATION AND BIOLOGICAL STUDIES ON METAL COMPLEXES OF 1,7-DIARYLHEPTA-1,6-DIENE-3,5-DIONES

Synopsis
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