Preface

Studies on naturally occurring ligand systems and their synthetic analogues constitute an important area of modern coordination chemistry. Biological importance of many plant chemicals are known to be associated with their ability to form complexes with various inorganic species including metal ions. Active chemical constituents of several medicinal plants are good coordinating ligands, since they contain functional groups such as –OH, –COOH, –C=O, –SH, –OCH₃, –O– etc. However, structural and biological aspects of these types of complexes have not received as much attention as they deserve. The present investigation is an attempt in this direction.

Among the traditional Indian medicinal plants, turmeric (Curcuma longa) occupies a pride of place. The rhizomes of turmeric is an unavoidable constituent in numerous medicinal formulations, in Ayurveda, Unani, Siddha, etc. of the Indian subcontinent, from time immemorial. The medicinal properties of turmeric have been attributed mainly due to curcuminoids, the yellow constituent of the rhizomes. Structurally curcuminoids are 1,3-diketones in which the diketo function is attached directly to olefinic linkages. Numerous reports on the medicinal properties such as antitumour, antioxidant, antiinflammatory, antibacterial, etc. of turmeric and curcuminoids have been appeared recently. Several synthetic curcuminoid analogues and their metal complexes have been reported to exhibit enhanced biological properties compared to natural curcuminoids. Therefore studies on new synthetic analogues of curcuminoids have considerable importance. This is particularly true when such compounds containing biologically important heterocyclic ring systems. The present investigation is mainly on the
chemical and biochemical aspects of curcuminoid analogues containing indolyl ring, an important heterocycle in many biomolecules, and their typical metal complexes.

The thesis is divided into five chapters.

Chapter 1 is a general introduction highlighting the importance of various aspects of coordination chemistry in biological processes particularly in medicinal inorganic chemistry and chemotherapeutic application of food phytochemicals, with special emphasis on some heterocyclic analogues. Since compounds included in this study are typical 1,3-diketones, some of the salient structural features of 1,3-diketones and metal 1,3-diketonates are also discussed in this chapter. A brief account on the photochemical behaviour curcuminoids is also included. Importance of the present investigation has been interspersed at appropriate places.

Chapter 2 is a general description on various chemicals and methods employed, instruments used and techniques adopted for the study.

The present investigation focused on the study of various aspects of three different curcuminoids. They are 1,7-diindolyl-1,6-heptadiene-3,5-dione, 1-phenyl-5-indolyl-4-pentene-1,3-dione and 6-indolyl-5-hexene-2,4-dione. For convenience the results of the studies of these compounds are presented separately in three chapters.

Chapter 3 section 1 deals with the synthesis and characterisation of a new curcuminoid analogue, 1,7-diindolylheptanoid and its metal complexes. Spectral data clearly indicate the existence of the compound predominantly in the intramolecularly hydrogen bonded cis enol form. The behaviour of the compound as monobasic bidentate ligand in its
complexes are clearly indicated. The use of uv, ir, nmr, mass, esr and TG data in elucidating the structure of the compound and its metal complexes are well illuminated in this section. The spectral data unequivocally showed that only the diketo function is involved in bonding with metal ion. In section 2 fluorescence characteristics of the 1,7-diindolylheptanoid are discussed. The effect of solvents, water, pH of the medium and metal ions on the fluorescence intensity of the compound are discussed. The quantum yield of fluorescence of the compound is higher than that reported for natural curcuminoids. Details of the biological studies of the compound and its metal chelates are given in section 3. Results obtained on superoxide scavenging activity, hydroxyl radical scavenging activity and inhibition of lipid peroxidation showed that the diindolylheptanoid and their metal complexes are effective antioxidants. The cytotoxic and antitumour behaviour of the compound and its metal complexes are discussed separately. Result obtained on short in vitro cytotoxicity studies towards DLA cells are given. The effect of the compounds in reducing ascites tumours and tumour volume in mice are also discussed.

In chapter 4, section 1 details on the synthesis and spectral characterisation of 1-phenyl-5-indolyl-4-pentene-1,3-dione and its metal chelates are discussed. The single crystal XRD structure of 1-phenyl-5-indolyl pentanoid is also included in this section. In section 2 the experimental procedure employed for the study of the fluorescence behaviour of 1-phenyl-5-indolyl-1,3-dione are discussed. Effect of solvents, pH and metal ions on the fluorescence intensity of the compound are discussed. The fluorescence quantum yield is also given. In section 3 cytotoxicity towards DLA cells and antioxidant activity towards superoxide radical, hydroxyl radical and inhibition lipid
peroxidation are discussed. The results showed that the compounds are less active than 1,7-diindolylheptanoid and its metal complexes.

**Chapter 5** is on synthesis and characterisation of 6-indolyl-5-hexene-2,4-dione and its metal chelates. The results obtained in the various spectral and analytical techniques showed that the compound exists entirely in the intramolecularly hydrogen bonded *cis* enol form and the diketo function is involved in metal coordination.

**References** are given in serial order.

The work described in the thesis has partially been published/accepted/communicated for publication.


6. Synthesis and characterisation of 6-indolyl-5-hexene-2,4-dione and its metal complexes (to be communicated).

7. Fluorescence behaviour of 1,7-diiindolyl-1,6-heptadiene-3,5-dione (to be communicated).

8. Fluorescence behaviour of 1-phenyl-5-indolyl-4-pentene-1,3-dione (to be communicated).