Chapter 1

Introduction

Turmeric (*Curcuma longa L.*) belongs to the Zingiberaceae family along with the noteworthy members like ginger, cardamom and galangal. It belongs to the genus *Curcuma* that consists of hundreds of species of plants that possess rhizomes and underground root like stems. Turmeric is of special importance to humans with the discovery that its rhizome powder, when added to various food preparations, preserves their freshness and imparts a characteristic flavour. Turmeric, which belongs to a group of aromatic spices, had been originally used as a food additive in curries to improve the storage condition, palatability and preservation of food. Turmeric is grown in warm, rainy regions of the world (Jayaprakasha, et al., 2005).

In old Hindu texts it is ascribed for its aromatic, stimulant and carminative properties. Turmeric mixed with slaked lime is known as a household remedy for the treatment of sprains and swellings caused by injury. For this purpose it is applied locally over the affected area. Current traditional Indian medicine claims the use of turmeric against biliary disorders, rheumatism and sinusitis. The traditional medicine in China uses *Curcuma longa* in diseases which are associated with abdominal pains, icterus etc. Ethnologically, Curcuma longa still occupies an important position as every food should contain it in India. Religious ceremonies always make use of turmeric in any form (Hermann, et al., 1990).

The chemistry study of different samples of turmeric has yielded turmerin (a water-soluble peptide), essential oils (such as turmerones, atlantones and zingiberene) and curcuminoids including curcumin [1,7-bis-(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione]. Curcumin is a natural yellow-orange dye, a variety of pharmacological properties such as antitumour and anticancer activities were reported.

It has also been used as a photodynamic agent useful for the destruction of bacteria and tumor cells. Attempts to use it as an antioxidant additive for lubricants and motor oils, photoresists and sunscreen compounds have also been made. From the toxicological studies, however, curcumin is non-toxic even at high dosage.

Curcumin has molecular weight of 368.37 and a melting point of 183 °C. The compound is slightly soluble in water however, soluble in alkali or in glacial acetic acid. Its color is not constant in aqueous media or in an organic solvent due to its degradation or conversion to its dissociation form. It is exposed to hydrolytic degradative reaction in aqueous solution. Ferulic acid, feruloylmethane, vanilline and acetone have been identified as the main degradation products. T∅nnesen reported that below pH 7 the degradation rate is lower than that at higher pH (Bong, et al., 2000). Commercial grade curcumin contains the curcuminoids demethoxycurcumin (MW 338; typically 10–20%) and bisdemethoxycurcumin (MW 308; typically less than 5%) (Figure 1).

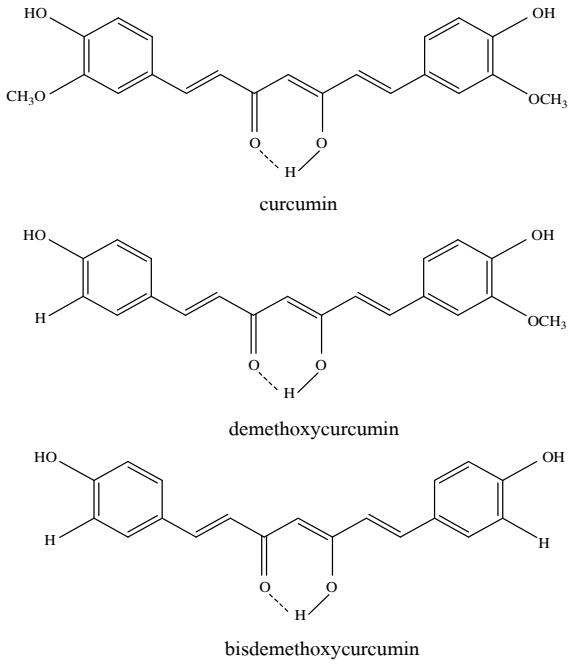


Figure 1 Structure of curcumin and curcuminoids

Curcumin is a bis-α,β-unsaturated β-diketone. As such, curcumin exists in equilibrium with its enol tautomer. The bis-keto form predominates in acidic and neutral aqueous solutions. At pH 3–7, curcumin acts as an extraordinarily potent H-atom donor. This is because, in the keto form of curcumin, the heptadienone linkage between the two methoxyphenol rings contains a highly activated carbon atom, and the C–H carbon bonds on this carbon are very weak due to delocalisation of the unpaired electron on the adjacent oxygens (Figure 2). In contrast, above pH 8, the enolate form of the heptadienone chain predominates, and curcumin act mainly as an electron donor, a mechanism more typical for the scavenging activity of phenolic antioxidant. (Khopde, et al., 1999 and Sharma, et al., 2005).

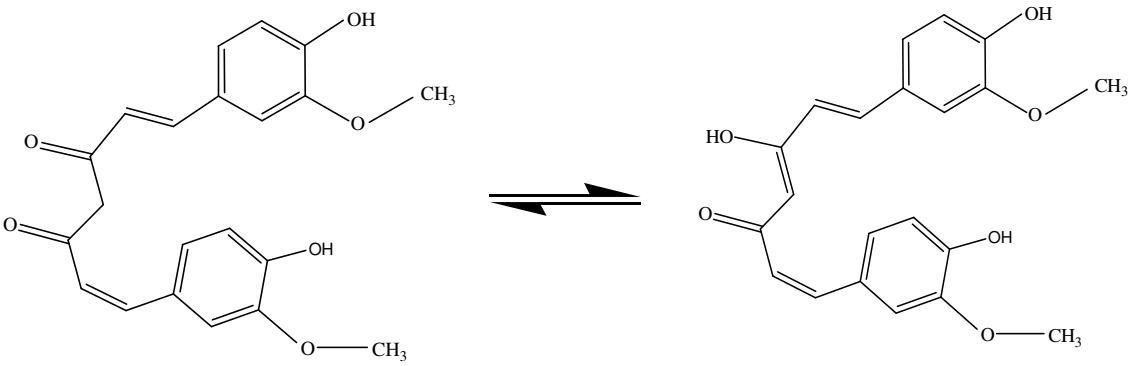


Figure 2 Keto–enol equilibrium of curcumin molecule

Structure-activity relationships studies suggest that hydroxyl group at *para* position is most critical for the expression of biological activity and these group are also essential for the inhibition of prostaglandins synthetase and leucotrienes synthesis. Claeson et al., suggested that the anti-inflammatory action is associated with the β-dicarbonylic system which has the conjugated double bond (dienes) (Jayaprakasha, et al., 2005). The strong chelating ability of diketones has been widely investigated towards a great number of metal ions; therefore, curcumin could be of great importance in the chelating treatment of metal intoxication and overload. Curcumin

has been known for its ability to form colored complexes with other molecules. Moreover, curcumin forms strong colored chelates with transition metals Cu^{2+}, Ni^{2+}, Zn^{2+}, Pd^{2+}, Fe^{3+} (Sundaryonoa, et al., 2003).

The toxicities produced by metals generally involve neurotoxicity, hepatotoxicities and nephrotoxicity. Specific differences in the toxicities of metal ions may be related to differences in solubilities, absorbability, transport, chemical reactivity and the complexes that are formed within the body. The toxicities of metal ions will be summarized.

Chromium is a chemical element symbolized by Cr with atomic number 24. The electronic configuration is $[Ar]3d^5 4s^1$. The highest oxidation state is that corresponding to the total number of 3d and 4s electrons. The oxidation states are 2+, 3+, 4+ and 6+. The most stable and important state is Cr^{3+}, d^3 (Cotton and Wilkinson, 1972). Chromium is a widely used industrial chemical finding uses in steel, alloy cast irons, chrome, paints, metal finishes, ceramics, photography and wood treatment. Chromium is widely known to cause allergic dermatitis as well as toxic and carcinogenic effects in human and animals (Sanat, 1973).

Manganese is a chemical element symbolized by Mn with atomic number 25. The electronic configuration is $[Ar]3d^5 4s^2$. The highest oxidation state is that corresponding to the total number of 3d and 4s electrons. The oxidation states are 2+, 3+, 4+, 6+ and 7+. The most stable and important state is Mn^{2+}, d^5 (Jantima, 1982). Manganese were used in steel alloys, dry-cell batteries, inks, glass and ceramics, paints and varnishes. Manganese compounds are essential to life. They are essential for the action of some enzymes. Excessive manganese intake can lead to chronic manganism. Symptoms include mental disturbances, progressive bradykinesia (abnormal slowness of movement), asthenia (weakness), paresis (incomplete paralysis), dystonia (disordered muscle tone) and disturbances of gait (Olmsted and Williams, 2002).

Cobalt is a chemical element symbolized by Co with atomic number 27. The electronic configuration is $[Ar]3d^7 4s^2$. The highest oxidation state is that corresponding to the total number of 3d and 4s electrons. The oxidation states are 2+ and 3+. The most stable and important state is Co^{2+}, d^7 (Jantima, 1982). Cobalt is used in magnet steels, stainless steels, electroplating and alloys used in jet turbines and gas turbine generators (Sanat, 1973). Cobalt salts in small amounts are essential to many life forms including humans. It is at the core of a vitamin-B_{12}. All cobalt compounds should be regarded as toxic although the most are probably not particularly toxic. Some cobalt compounds may be carcinogenic.

Nickel is a chemical element symbolized by Ni with atomic number 28. The electronic configuration is $[Ar]3d^8 4s^2$. The highest oxidation state is that corresponding to the total number of 3d and 4s electrons. The oxidation states are 2+ and 3+. The most stable and important state is Ni^{2+}, d^8. Nickel used extensively in coinage and in making nickel steel, catalyst, batteries and electroplating. Nickel is an essential trace element for many species. All nickel compounds should be regarded as toxic. Nickel compounds are very toxic for plants. Some are carcinogenic and teratogenic (Jantima, 1982).

Copper is a chemical element symbolized by Cu with atomic number 29. The electronic configuration is $[Ar]3d^{10} 4s^1$. The highest oxidation state is that corresponding to the total number of 3d and 4s electrons. The oxidation states are 1+, and 2+. The most stable and important state are Cu^{2+}, d^9 (Cotton and Wilkinson, 1972). Copper is used in alloys, electrical equipment, pipes and roofing, textile processes, pigmentation tanning, photography, electroplating, insecticides and fungicides. Copper is widely distributed in nature and is an essential element. Acute poisoning occurs most frequently from the ingestion of copper salts and hepatic is characteristic of copper poisoning (Stohs, et al., 1994).

Zinc is a chemical element symbolized by Zn with atomic number 30. The electronic configuration is $[Ar]3d^{10}4s^2$. The oxidation state is 2+, d^{10} (Cotton and Wilkinson, 1972). Zinc is widely used in galvanizing pipes, alloys, electrical purposes printing plates and pharmaceuticals. Zinc metal is a human skin irritant and a severe fire hazard but otherwise is non-toxic. Most common zinc compounds are not very toxic but a few zinc salts may be carcinogens. Use of some zinc compounds is permitted around food. Pollution from industrial smoke may cause lung disease.

Cadmium is a chemical element symbolized by Cd with atomic number 48. The electronic configuration is $[Kr]4d^{10}5s^2$. The oxidation state is 2+, d^{10} (Cotton and Wilkinson, 1972). Cadmium is an abundant, nonessential element that is generating concern due to its accumulation in the environment as a results of industrial practices. It is widely used in electroplating and galvanizing, as a color pigment in paints, and in batteries. It is byproduct of zinc and lead mining and smelting. Soluble cadmium salts accumulate and result in toxicity to liver, kidneys, brain, lungs, heart, testes and the central nervous system (Stohs, et al., 1994).

Mercury is a chemical element symbolized by Hg with atomic number 80. The electronic configuration is $[Xe]4f^{14}5d^{10}6s^2$. The oxidation states are 1+, and 2+. Mercury is used in laboratories for making thermometers, barometers, diffusion pumps and many other instruments. It is used for mercury switches and other electrical apparatus. It is used as an electrode in some types of electrolysis and for making batteries (mercury cells) and also mercury is used for the basis of dental amalgams and preparations. The most significant hazards due to methyl mercury appear to be to fish-eating birds and mammals. The incidents of Minamata disease in Minamata and Nigata, Japan, are well documented. In its early stages the disease is characterized by relatively nonspecific symptoms due to impairment of the central nervous system. When the disease becomes well established, sensory defects of hearing and visual field

become evident. There is a loss of motor control and coordinatoin followed by paralysis, mental deterioration, loss of consciousness and death (Sanat, 1973).

Lead is a chemical element symbolized by Pb with atomic number 82. The electronic configuration is $[Xe]4f^{14}5d^{10}6s^{2}6p^{2}$. The oxidation states are 2+ and 4+. (Cotton and Wilkinson, 1972). Lead was used in pipes, water storage chambers, dyes and paints. Lead is a major environmental toxin that causes hematological, gastrointestinal and neurological dysfunction. Prolonged exposure to lead may also cause reproductive impairment, hypertension and nephropathy. Furthermore, lead slows nerve conduction, alters calcium homeostasis, inhibits enzymes and stimulates synthesis of binding proteins. Major sources of lead exposure are dust, water, paint, cosmetics, folk remedies and food supplements (Stohs, et al., 1994).

The harmful effect of heavy metals in humans can be minimized or prevented by chemically modifying the biochemically active forms of the metal ion. This can be accomplished by the administration of chemicals which form insoluble compounds with the metal, or chelating agents which form diffusible, readily excreated metal chelates. Nevertheless, the chelating agent may aggravate the toxic effects of the metal. Thus, the administration of a chelating agent may increase excretion of a toxic metal but, at the same time, accelerate the transfer of some of the mobilized metal into the organs. Therefore, it is important to seek for other alternative chelating agents that can be used for this purpose. Recently there have been many reports in the literature on the metal-chelating properties of curcumin, employing such techniques like potentiometry and absorption spectroscopy.

Literature review

Dyrssen, et al., (1972) studied on the stability of the reagent curcuma (H_3A) in the sulphuric acid-acetic acid medium both in the presence and absence of boric acid. Kinetic measurements showed that protonated curcumin decomposes according to a second order rate law. The decomposition was inhibited by the addition of boric acid which forms a complex with curcumin. This complex had a much slower decay rate. The complex was analyzed and found to be a 1:2 boric acid-curcumin compound. The acid dissociation constant of curcumin in water-ethanol solution was determined with $K_a = ([H^+][H_2A^-])/[H_3A] = 10^{-7.9}$.

Sharma, et al., (1986) synthesized and characterized curcumin gold complex by elemental analysis, magnetic moment, IR and electronic spectra. The curcumin gold complex was prepared by mixing curcumin with auric chloride in the ratio 2:1 in ethanol; the mixture was refluxed for eight hours. On cooling, brown crystals of curcumin-gold complex separated out; these were then dried over P_4O_{10}. Elemental analysis of the complex suggested that it had the composition $Au(CUR)_2Cl$. Conductivity of the complex could not be determined due to the poor solubility in all the common organic solvents. The electronic spectrum of the complex displayed two bands at 32000 and 26000 cm^{-1}. These bands could be due to charge transfer. IR spectroscopy provided direct information regarding the coordination of ligands. A comparative study of the ligand and the complex suggested that the ligand acted as neutral bidentate. A band at 1730 cm^{-1} in the ligand could be assigned to C=O. On complexation the position of this band was shifted towards lower wave number. This suggested that the ligand coordinate with the central metal ion through the C=O group. On the basis of IR and electronic spectra studies, the structure of the complex could be assigned as shown in Figure 3.

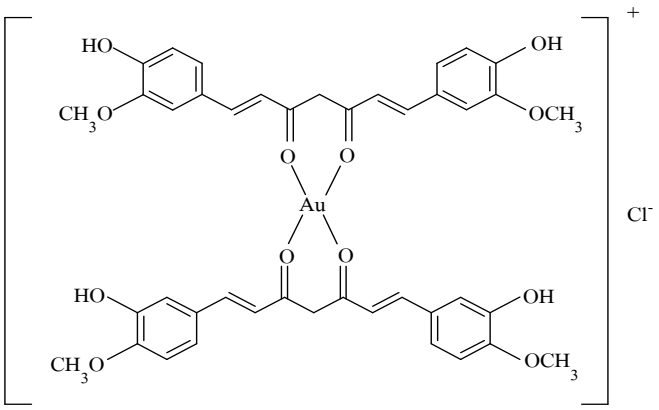


Figure 3 Structure of the curcumin gold complex

Rao, et al., (1988) studied the complex, formed by the reaction of curcumin with boron trifluoride etherate ($BF_3.OEt_2$). The stoichiometry of the complex as 1:1 was determined by Job's method. The NMR studies indicated that the two keto-oxygens in curcumin bonded to boron. This involved deprotonation of the enolic OH with concomitant delocalization of the double bonds leading to quinone form of one half of the curcumin molecule. The ^{11}B and ^{19}F NMR spectra of the complex indicated that a negative charge was on the boron atom and only two fluorine atoms were attached to boron atom in the complex, the third fluorine atom was probably removed as HF. On the basis of the NMR studies the structure of the complex was proposed for the complex as shown in Figure 4.

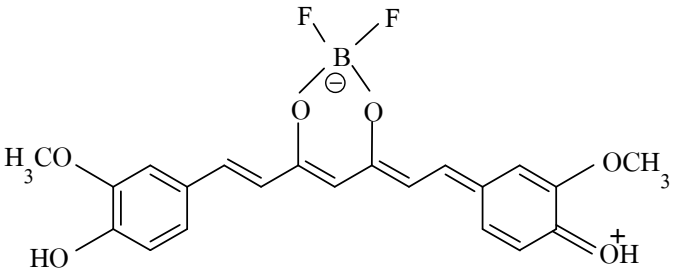


Figure 4 Structure of curcumin boron complex

Sui, et al., (1993) reported identification of curcumin and preliminary examination of possibility of using structures with orthogonal domains as inhibitor of HIV-1PR and HIV-2PR. Boron complexes of curcumin were prepared because the tetrahedral geometry about the boron atom forces two molecules, each of which provides two of the oxygen ligands, to assume an orthogonal orientation. Furthermore, boron complexes are readily formed with oxygen ligands and are relative stable. The simplest complex examined was the difluoroboron complex 1, in which two of the boron sites are occupied by fluorine atoms rather than by a second organic structure. The two fluorine atoms are replaced in mixed complexes by carboxyl oxygens of oxalic acid 2, a carboxyl and hydroxyl groups of citric acid 3, the two hydroxyl groups of dibenzyl tartramide 4, and a second molecule of curcumin 5. Compounds 4 and compound 5 are of particular interest because they consist of perpendicular domains, each of which is an extended organic structure with aromatic rings at the termini. In fact, all of the mixed boron complexes that contain at least one curcumin unit are more potent inhibitors of both HIV proteases than curcumin itself. The best of boron complex is 5, which gives IC_{50} values of 6 and 5.5 μM for HIV-1PR and HIV-2PR, respectively (Figure 5). Complexation with boron therefore does not account for higher inhibitory activity of 5. It is therefore possible that the higher affinity of 5 is due to simultaneous occupation of two binding site. One possible explanation for this is that the inhibitor domains are truly orthogonal, whereas they are not truly orthogonal in the enzyme active sites. The inflexibility of the orientation of the two curcumin groups about the boron atom therefore may not permit fit of the inhibitor in the substrate binding sites. On the other hand, binding to the boron activates the unsaturated carbonyl moiety of cucumin towards electrophilic additions and makes the curcumin complexes time-dependent inhibitors of two enzymes. Although the nature of the time-

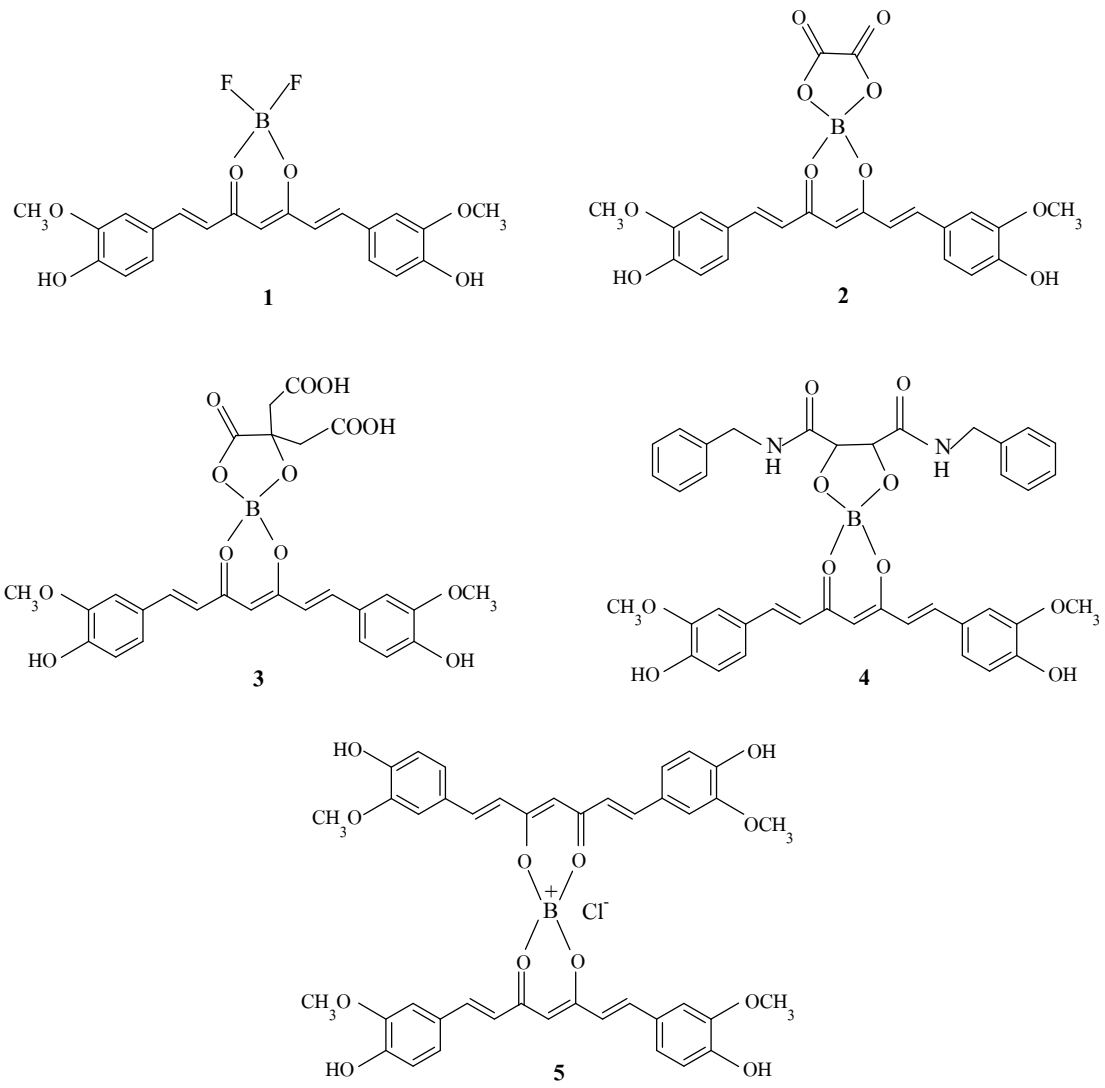


Figure 5 Structure of curcumin boron complexes

dependent inhibition has not been precisely defined, it is likely that it involves alkylation of one of the two active site aspartyls and/or one of the four cysteines of HIV-1PR, and one of the two active sites aspartyls in HIV-2PR, by the boron activated α,β-unsaturated carbonyl structure in the inhibitors.

Borsari, et al., (2002) focused their attention on curcumin and its derivative diacetylcurcumin as new potential chelating agents. In their study they have elucidated the active chelating site of these ligands and their complexing ability towards iron(III). The interaction of Fe^{3+} with curcumin and diacetylcurcumin, in water/methanol 1:1 solution, led to the formation of the complex species $[FeH_2CU(OH)_2]$ and $[FeDCU(OH)_2]$ (H_2CU and DCU=curcumin or diacetylcurcumin monoanion, respectively) close to pH 7. At more basic condition the prevailing species were $[FeH_2CU(OH)_3]^-$ and $[FeDCU(OH)_3]^-$, which prevented metal hydroxide precipitation. ^1H NMR data state that the dissociated β-diketo moiety of the ligands was involved in metal chelation. The pKa value of the deprotonation reaction is strongly anticipated by the metal ion as shown by UV spectral data. The stability constants, evaluated from potentiometric data, were close to that of desferrioxamine, which is, by now, the only iron chelating agent for clinical use.

Sundaryono, et al., (2003) studied complex of transition metals mainly Cu^{2+} curcumin, dimethylcurcumin, and new curcuminoids (Bis{2-hydroxy-3-methoxy-5-[7-(4-hydroxy-3-methoxyphenyl)-hepta-1E,6E-diene-3,5-dioxo]}methane (compound 3), and 7,20-Dimethoxy-5,22-di-[7-(4-hydroxy-3-methoxyphenyl)-hepta-1E,6E-diene3,5-dioxo]{[9,12,15,18-tetraoxatricyclo[17.4.0.03,8]tricosa-1(23),3(8),4, 6,19,21-hexaene} (compound 4), using molecular absorption spectroscopy combined with quantum molecular calculations. The stoichiometry of the complex was 2:1 for curcumin-Cu^{2+} and compound 3-Cu^{2+} complexes, and 1:1 for compound 4-Cu^{2+} complex.

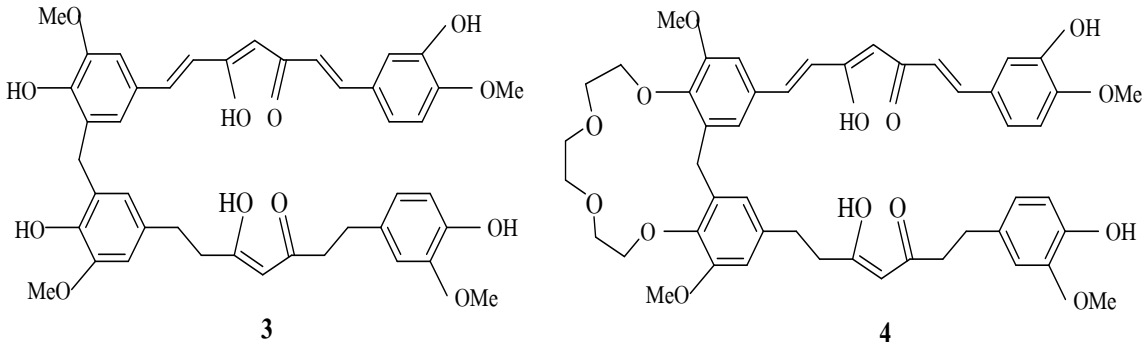
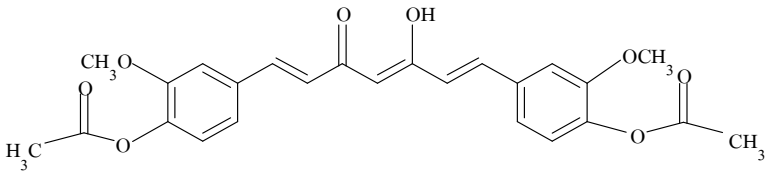
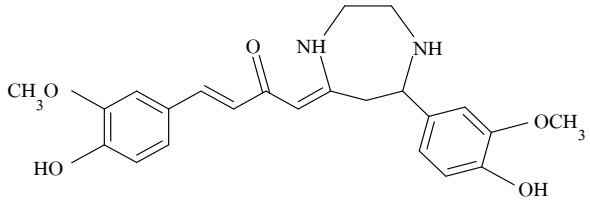


Figure 6 Structures of bis-curcuminoids 3 and 4

Vajragupta, et al., (2003) studied three manganese complexes of curcumin (Cp) and related compounds, diacetylcurcumin (AcylCp) and ethylenediamine derivative (CpED), by synthesizing and evaluating them in vitro for antilipid peroxidation and superoxide dismutase activity. The manganese complexes exhibited a great capacity to protect brain lipids against peroxidation. All manganese complexes showed much greater SOD activity than their corresponding antioxidant ligands. AcylCp and curcumin manganese complexes (AcylCpCpx and CpCpx) also gave the highest inhibitory activity to H_2O_2-induced cell damage, which were more potent than curcumin and related compounds. The manganese-base complexes, CpCpx, AcylCpCpx and CpEDCpx were prepared by the reaction of manganese acetate with the curcumin, diacetylcurcumin, or CpED, respectively, in ethanolic solution. The structures of compounds were identified by their melting points, FTIR, ^{1}H NMR, ^{13}C NMR and elemental analyses of C, H, N, and Mn. The metalloelement (Mn) in these complexes was determined after decomposing the complexes in acid using EPR technique. From this study, it was found that one manganese atom was coordinated with the keto-enol function of curcumin and diacetylcurcumin. For CpED, two manganese atoms were coordinated with the phenolic hydroxyl groups.



Diacetylcurcumin (AcylCp)



CpED

Figure 7 Structures of the ligands of manganese complexes

Bernabé-Pineda, et al., (2004) studied formation of complexes between curcumin, Fe^{3+} and Fe^{2+} in aqueous media within the 5–11 pH range by means of UV-Vis spectrophotometry and cyclic voltammetry. When the reaction between curcumin and the ions present in basic media took place, the resulting spectra of the systems curcumin–Fe^{3+} and curcumin–Fe^{2+} showed a similar behaviour. The cyclic voltammograms in basic media indicated that a chemical reaction has taken place between curcumin and Fe^{3+} before that of the formation of complexes. Data processing with SQUAD permitted calculation of the formation constants of the complexes curcumin–Fe^{3+}, corresponding to the species FeCur ($\log \beta_{110} = 22.25 \pm 0.03$) and $FeCur(OH)^-$ ($\log \beta_{11-1} = 12.14 \pm 0.03$), while for the complexes curcumin–Fe^{2+} the corresponding formation constants of the species $FeCur^-$ ($\log \beta_{110} = 9.20 \pm 0.04$), FeHCur ($\log \beta_{111} = 19.76 \pm 0.03$), FeH_2Cur^+ ($\log \beta_{112} = 28.11 \pm 0.02$).

Thompson, et al., (2004) synthesized vanadyl curcumin complex ($VO(cur)_2$) (Figure 9) and characterized its physicochemical properties in order to take advantage

of the pharmacological properties of both curcumin and vanadyl, with potential complementary efficacy. The vanadyl curcumin complex was prepared by the reaction of vanadyl acetylacetonate with the curcumin in dichloromethane solution. The structures of compounds were identified by FTIR, mass spectral, and elemental analysis. The elemental analysis indicated that essentially all of the product was in the bis(diferuloyl methane) form. A broad medium intensity IR band at ~3400 cm^{-1}(ν_{O-H}) strongly suggested that the phenolic OH group was not coordinated to the vanadyl ion. Curcumin alone absorbs at 964 and 1026 cm^{-1} ($\nu_{CH=CH,\ trans}$); these bands were obscured by a stronger one at 974 cm^{-1} ($\nu_{V=O}$) in the vanadyl complex. A band at 1628 cm^{-1}, present in the IR spectrum of curcumin, was shifted downfield (to ~1600 cm^{-1}) in the vanadyl complex spectrum, indicative of coordinated carbonyl moieties.

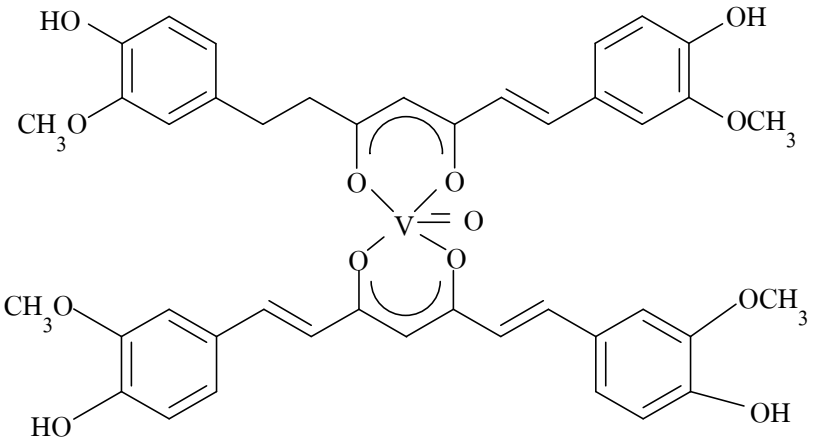


Figure 8 Structure of vanadyl curcumin, bis(1,7-bis[4-hydroxy-3-methyoxyphenyl]-1,6-heptadiene-3,5-dionato) oxovanadium(IV), $C_{42}H_{38}O_{13}V$

Danie, et al., (2004) examined the ability of this compound to protect against lead-induced damage to hippocampal cells of male Wistar rats, as well as lipid peroxidation induced by lead and cadmium in rat brain homogenate. Furthermore,

electrochemistry, UV-Vis spectrophotomety and infrared spectroscopy were used to gauge the interaction between curcumin and the metals lead and cadmium. In this study, it was shown that curcumin significantly protects against lipid peroxidation induced by heavy metals. In the electrochemical studies, the highly negative peak observed for curcumin and the metals were indicative of strong metal-ligand interactions as these reduction potentials were more negative than that of the metal alone. A high negative potential shift indicated that the species formed between the metal and the ligand was harder to reduce than the metal alone. UV-Vis analysis suggested interactions between curcumin and these metals in terms of a shift in the wavelength and an increase in absorbance of curcumin. IR analysis inferred that both the hydroxyl groups and the β-diketone moiety of curcumin were involved in metal-ligand complexation, either directly bonding to the metal, or in intermolecular hydrogen bonding.

Valapatukutikadan, et al., (2005) reported the synthesis and characterization of some natural curcuminoid analogues (HL^1–HL^4), 1,7-diphenyl-1,6-heptadiene-3,5-dione (HL^1), 1,7-bis(4-methoxyphenyl)-1,6-heptadiene-3,5-dione (HL^2), 1,7-bis(3,4-dimethoxyphenyl)-1,6-heptadiene-3,5-dione (HL^3), 1,7-bis(3,4-dihydroxyphenyl)-1,6-heptadiene-3,5-dione (HL^4) and their copper(II) complexes. The observed UV, IR, ^{1}H NMR and mass spectral data of the compounds were in full agreement with the intramolecularly hydrogen bonded enol structure of the compounds (Figure 7). Their UV spectra in methanol showed two absorption maxima corresponding to $n \longrightarrow \pi^*$ (358–445 nm) and $\pi \longrightarrow \pi^*$ transitions (258–265 nm). The IR spectra showed a strong band at 1620 cm^{-1} (enolised conjugated 1,3-diketo group), and a broad band in the region 2800–3500 cm^{-1} due to intramolecularly hydrogen bonded enol form. The ^{1}H NMR spectra of all the compounds displayed singlets at ~16 and ~6 ppm,

assignable to an intramolecularly hydrogen bonded enolic proton and methine proton respectively.

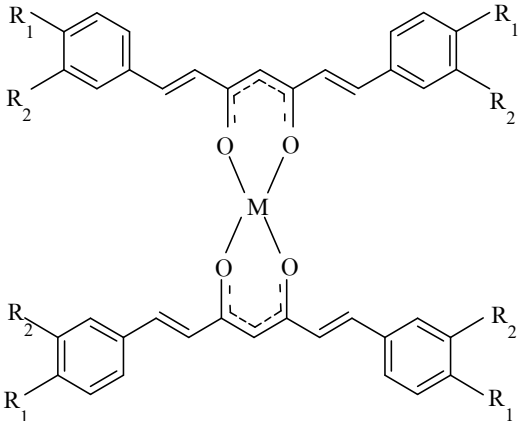


Figure 9 Structure of the metal complexes of 1,7 diarylheptanoids (HL^1–HL^4)

Barik, et al., (2005) studied a new mononuclear copper complex of curcumin and characterized by elemental analysis, IR, NMR, UV-VIS, EPR, mass spectroscopic methods and TG-DTA, from which it was found that the copper atom was coordinated through the keto-enol group of curcumin along with one acetate group and one water molecule. Cyclic voltammetric studies of the complex showed a reversible Cu^{2+}/Cu^{+} couple with a potential of 0.402 V vs NHE. The Cu^{2+}-curcumin complex was soluble in lipids and DMSO, and insoluble in water. From spectroscopic information, the structure of the complex was assigned as shown in Figure 10.

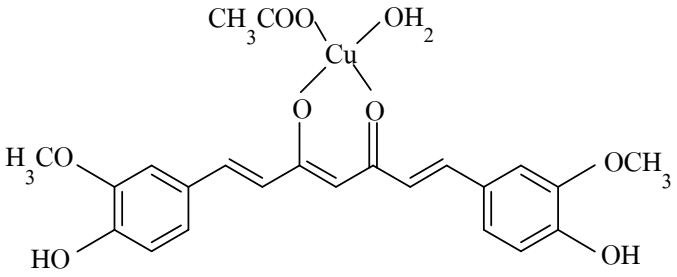
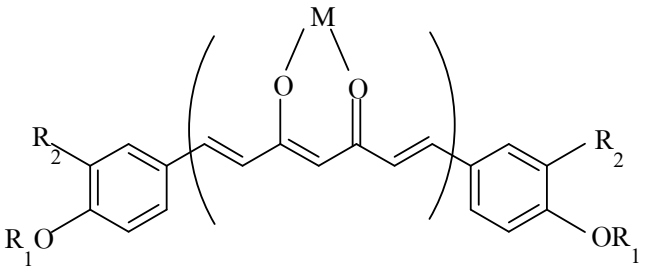


Figure 10 Structure of curcumin copper complex

Mohammadi, et al., (2005) studied curcumin complexes of the formula, ML_3, where M was Ga(III) or In(III), or of the formula, ML_2 where M was $[VO]^{2+}$ and characterized by mass spectrometry, infrared and absorption spectroscopies, and elemental analysis. Spectroscopic characterization of the ligands and their complexes confirmed the proposed structures as shown in Figure 11.



$[VO(cur)_2]$, $VO(DAC)_2]$	n = 2; M=VO, R_1 = H, Ac; R_2 = OCH_3
$[VO(BDC)_2]$, $VO(DABC)_2]$	n = 2; M=VO, R_1 = H, Ac; R_2 = H
$Ga(cur)_3]$, $[Ga(DAC)_3]$	n = 3; M = Ga, R_1 = H, Ac; R_2 = OCH_3
$[In(cur)_3]$, $[In(DAC)_3]$	n = 3; M = In, R_1 = H, Ac; R_2 = OCH_3

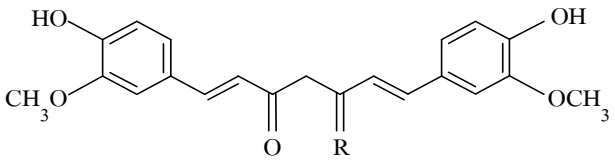
Figure 11 The structures of the metal complexes prepared by Mohammadi, et al. (2005)

IR spectra of all ligands showed $\nu_{C=O}$ in the typical 1600-1630 cm^{-1} range which shifted to lower energy in the vanadyl complexes of the same ligands. Vanadyl complexes also had no broad band in the 2600–3400 cm^{-1} range, related to the stretching of intramolecular H in the enol function, as noted for a previously synthesized vanadyl 1,7-diaryl-1,6-heptadiene-3,5-dione, with a different pattern of hydroxylation on the aromatic rings. Vanadyl complexes did show a $\nu_{V=O}$ medium intensity band at 975–995 cm^{-1}. A prominent band at 960–975 cm^{-1}, due to the trans –CH=CH– group, also remained unchanged in the vanadyl complexes. The curcumin ligands showed two absorption bands in the UV-Vis region; a π - π^* transition at 360–430 nm and a

π - π^* transition at 240–290 nm, which shifted to slightly higher energy in the vanadyl complexes, indicative of involvement of the carbonyl group in metal complexation. Further evidence of complexation came from the mass spectra of all complexes, which showed intense peaks for $[VOL_2]^+$, $[VOL2^+H]^+$ and $[VOL_2^+ Na]^+$, and confirm a stoichiometry of 2:1 curcuminoid to oxovanadium(IV).

Barik, et al., (2007) synthesized 1:1 and 1:2 complexes between copper(II) ion and curcumin in an extension from their earlier papers and described briefly here. The 1:1 Cu^{2+}-curcumin complex was synthesized by mixing equimolar ratio of copper acetate and curcumin. The 1:2 Cu^{2+}-curcumin complex was synthesized by mixing methanolic solution of curcumin and aqueous solution of $CuCl_2.H_2O$. Both the complexes were soluble in lipids and DMSO. The formation constants of the complexes were determined by voltammetry. The formation constant of 1:1 and 1:2 complex was determined to be 3.74×10^{14} and 3.9×10^{15}, respectively. EPR spectra of the complexes in DMSO at 77 K showed that the 1:2 Cu^{2+}-curcumin complex was square planar and the 1:1 Cu^{2+}-curcumin complex was distorted orthorhombic.

Dutty, et al., (2007) studied antioxidant properties of curcumin and three curcumin derivatives (Figure 12) in which the 1,3-diketone system is appended with nitrogen and sulfur donors and their copper conjugates are examined. Metal conjugation seems to offer distinct advantages in radical scavenging activities of curcumin compounds. The interaction of $CuCl_2$ with L1 and L2 yields compounds having composition CuL_2 while in case of L3 and L4 the stoichiometry of the resulting complexes is found to be [Cu(L)Cl] respectively. All complexes are found to be diamagnetic at 298 K indicating essentially a planar geometry for these compounds as shown in Figure l3 and l4.



R = O, curcumin (L1)

NOH, curcuminoxime (L2)

$NNHCONH_2$, curcuminsemicarbazone (L3)

$NNHCSNH_2$, curcuminthiosemicarbazone (L4)

Figure 12 Structure of curcumin and curcumin derivatives

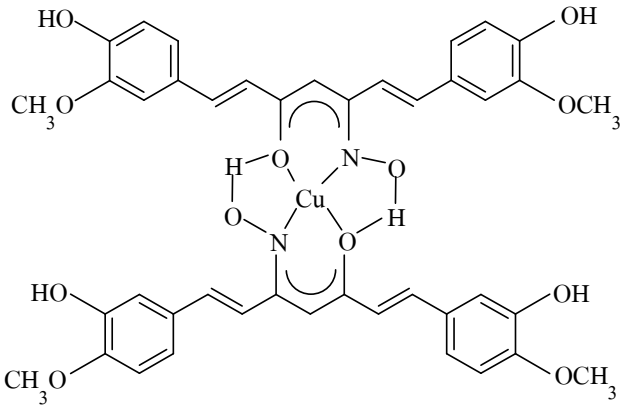


Figure 13 Proposed structure of the complex $[Cu(L1)_2]$

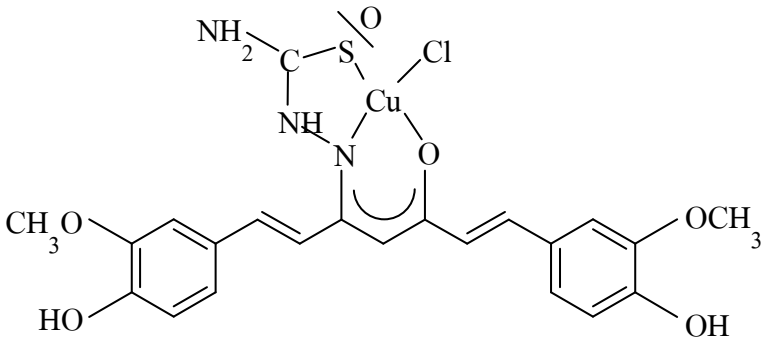


Figure 14 Proposed structure of the complex [Cu(L2)Cl] & [Cu(L3)Cl]

Objectives

1. To investigate the complex formation between curcumin and some metal ions.
2. For the metal ions that show good sign of complex forming, further studied to measure the complex formation constant will be attempted.