



Synthesis, Characterization and Antioxidant studies of Cd(II), Hg(II) and Pb(II) Complexes of some Synthetic Curcuminoids

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Abstract

Cd (II), Hg (II) and Pb (II) complexes of two synthetic curcuminoid analogues derived from pentane-2,4-dione and aromatic aldehydes (furfural and naphthalene-2-carbaldehyde) have been synthesized and characterized by analytical and spectral data. In all the chelates, ligands behaved as monobasic bidentate where the hydrogen bonded enolic proton is substituted by the metal ion. Antioxidant studies of four synthetic curcuminoids (derived from benzaldehyde, cinnamaldehyde, furfural and naphthalene-2-carbaldehyde) revealed that all the ligands possess significant antioxidant activities. Maximum activity was observed with 2-naphthyl curcumin. Metal complexation enhanced the antioxidant activity of all the compounds and among these Hg(II) complexes showed highest activity.

Keywords: Synthetic curcuminoids, metal complexes, spectral data, antioxidant studies.

Introduction

An imbalance between free radicals and antioxidant systems in our body cause oxidative stress leading to chronic diseases¹. The formation of free radicals due to normal metabolic processes and other environmental factors harmfully affect the physiological activities of cells^{2,3}. Synthetic organic chemists have developed many effective antioxidants for rubber⁴, hydrocarbon fuels⁵, plastics⁶ and food stuffs⁷. Propyl gallate, BHA and BHT are antioxidants used as food additives⁸. Certain vitamins (vitamin E and C), minerals and natural phenolic compounds, flavanoids and carotenoids have the capacity to counteract free radicals by scavenging them⁹⁻¹¹. Recent literatures¹²⁻¹⁴ provides a number of evidences for the antioxidant characteristics of curcuminoids. Both turmeric and curcuminoids prevent the formation of free radicals like superoxide and hydroxyl radicals¹⁵. The antioxidant properties of curcumin in the prevention of lipid peroxide, another process that generates free radicals, is well recognized^{16,17}. As an extension of our research work on synthetic curcuminoids and their metal complexes¹⁸⁻²¹, we report herein the synthesis, characterization and antioxidant studies of the Cd(II), Hg(II) and Pb(II) chelates some novel curcuminoid analogues.

Material and Methods

Experimental: Carbon and hydrogen percentages were calculated by microanalyses (Heraeus Elemental Analyzer) and metal contents of the chelates by AAS (Perkin Elmer 2380). The UV spectra of the compounds were recorded in methanol (10^{-6} M) on a JASCO V-550 UV-Visible spectrophotometer, IR spectra (KBr disks) on a JASCO FT/IR 4100 instrument, ¹H NMR spectra (CDCl₃ or DMSO-d₆) on a JEOL 400 NMR spectrometer and mass spectra on a JEOL-JMS 600H FAB mass

spectrometer. The determination of molar conductance of the chelates was carried out in DMF ($\sim 10^{-3}$ mol/L) at 301 ± 1 K. Magnetic moments of the complexes were determined at room temperature (301 ± 1 K) on a SHERWOOD Scientific Magnetic susceptibility balance with Hg[Co(NCS)₄] as the standard. The reagents used were Merck and Aldrich or chemically pure grade.

Synthesis of curcuminoid analogues (HL): The curcuminoid analogues were synthesized using pentane-2,4-dione and aromatic aldehydes (benzaldehyde, cinnamaldehyde, furfural and naphthalene-2-carbaldehyde) as reported earlier²²⁻²⁴.

Synthesis of metal chelates: To a boiling solution of the compound in methanol (0.02 mol, 20 mL) a methanolic solution of the metal (II) acetate (0.01 mol, 15 mL) was poured and the reaction mixture was refluxed for ~ 2 h. The volume of the solution was reduced to half by concentration and then cooled to room temperature. The precipitated metal chelate was filtered and washed with water. All the chelates were recrystallized from hot methanol.

Antioxidant studies: A solution (2.53%) of linoleic acid in 99.5% DMSO and 0.05 M phosphate buffer of pH 7 were prepared. Solution (4 mL) of the test compound (2 mg in 99.5% DMSO) was added to a solution containing linoleic acid (4.1 mL), phosphate buffer (8 mL) and distilled water (3.9 mL) taken in a stoppered Erlenmeyer flask, and incubated at 40 °C in the dark for 7-8 days. At periodic intervals during the incubation, 100 μ L of the mixture was used for the antioxidant assay by the thiocyanate method²⁵ as described below.

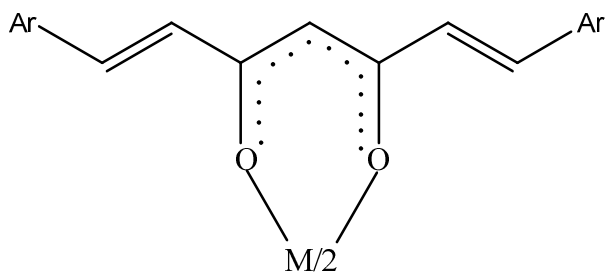
The incubated solution (100 μ L) was added to 75% DMSO (9.7

mL) and 30% ammonium thiocyanate solution (0.1 mL). Ferrous salt solution (0.1 mL, 2×10^{-2} M) in 3.5% HCl was added and precisely after 3 minutes the absorbance of the red colour products was determined at 500 nm. The antioxidant activity was judged from the decrease in the absorbance compared to the absorbance of a control maintained under identical condition.

Results and Discussion

Structural characterization of metal complexes: The synthesis and structural characterization of the Cd(II), Hg(II) and Pb(II) chelates of the synthetic curcuminoids produced from benzaldehyde and cinnamaldehyde have already been reported earlier²¹. Hence the curcuminoids derived from furfural and naphthalene-2-carbaldehyde is included in this section.

The observed elemental analytical data (table-1) of the metal complexes suggest $[ML_2]$ stoichiometry as in figure-1. All the chelates were found as non-electrolytes (specific conductance $<10 \Omega^{-1} \text{cm}^{-1}$; 10^{-3} M solution in DMF). The diamagnetic nature of all the chelates was proved from the magnetic measurements.



M = Cd(II), Hg(II) and Pb(II) Ar = 2-Furyl (HL³) and 2-Naphthyl (HL⁴)

Figure-1

Structure of the metal complexes of synthetic curcuminoids

In the IR spectra of the metal complexes, the band at $\sim 1620 \text{ cm}^{-1}$ of the ligand is absent and a strong band appeared at $\sim 1580 \text{ cm}^{-1}$ assignable to the stretching of the coordinated carbonyl moiety. The broad band in the $2800\text{-}3500 \text{ cm}^{-1}$ region of the ligands was vanished in the spectra of the chelates justifying the replacement of enolic hydrogen by the metal ion during complexation^{24,26}. The band at $\sim 975 \text{ cm}^{-1}$ is typical of a *trans* -CH=CH- group and found unchanged in the spectra of metal complexes^{24,26}. The participation of two keto groups in metal chelate formation as in figure 1 is further proved by the presence of two medium intensity bands at ~ 420 and $\sim 470 \text{ cm}^{-1}$ due to $\nu_{\text{M-O}}$ ^{26,27}. Important bands appeared in the IR spectra of the metal complexes are shown in table-1.

In the ¹H NMR spectra of the diamagnetic Cd(II) complexes, the signal due to the enolic hydrogen of the ligand was absent indicating its replacement by the metal ion during the formation of chelates²⁴. The deprotonation of the OH group caused the shifting of methine proton signal appreciably to low field. The integrated intensities of the signals appeared in the spectra were in accordance with the figure 1 of the chelates. The spectral data of the chelates are given in table-2.

The FAB mass spectra of the Cd(II) complexes displayed intense molecular ion peaks in accordance to their formulae. Peaks correspond to successive removal of aryl groups, $[\text{CdL}]^+$, L^+ and ligand fragments are also found in the spectra. Important fragments appeared in the spectra are given in table-2.

The UV spectra of the complexes showed close resemblance to that of the free ligands which indicate that no structural change of the ligand has taken place in the metal chelate formation. But the two spectral absorption maxima were shifted to higher wavelength in the spectra of the chelates confirming the participation of the metal cation¹⁹.

Table-1
Physical, analytical and IR spectral data of the metal complexes of synthetic curcuminoids

Compound/ molecular formula	Yield (%)	M.P. (°C)	Elemental analysis: found (calculated) %			IR stretching bands (cm ⁻¹)		
			C	H	M	C=O	CH=CH <i>trans</i>	M-O
$[\text{Cd}(\text{L}^3)_2]$ $\text{C}_{30}\text{H}_{22}\text{CdO}_8$	39	172	57.29 (57.84)	3.49 (3.53)	18.57 (18.06)	1582 s	974 m	472 m, 418 m
$[\text{Cd}(\text{L}^4)_2]$ $\text{C}_{54}\text{H}_{38}\text{CdO}_4$	42	164	75.00 (75.14)	4.41 (4.41)	13.00 (13.03)	1582 s	978 m	480 m, 424 m
$[\text{Hg}(\text{L}^3)_2]$ $\text{C}_{30}\text{H}_{22}\text{HgO}_8$	70	190	50.81 (50.66)	3.05 (3.10)	28.51 (28.23)	1578 s	976 m	476 m, 414 m
$[\text{Hg}(\text{L}^4)_2]$ $\text{C}_{54}\text{H}_{38}\text{HgO}_4$	78	136	67.88 (68.18)	4.01 (4.00)	21.61 (21.09)	1574 s	976 m	482 m, 420 m
$[\text{Pb}(\text{L}^3)_2]$ $\text{C}_{30}\text{H}_{22}\text{O}_8\text{Pb}$	51	142	50.60 (50.19)	3.04 (3.07)	28.80 (28.89)	1576 s	968 m	474 m, 420 m
$[\text{Pb}(\text{L}^4)_2]$ $\text{C}_{54}\text{H}_{38}\text{O}_4\text{Pb}$	56	192	67.69 (67.70)	3.79 (3.77)	21.83 (21.65)	1584 s	980 m	462 m, 418 m

Table-2

¹H NMR and mass spectral data of the Cd(II) complexes of synthetic curcuminoids

Compound	¹ H NMR (δ, ppm)			Mass spectral data (m/z)
	Methine	CH=CH	Aryl	
[Cd(L ³) ₂]	6.38	8.12, 8.28	7.18-7.90	622, 501, 417, 380, 205, 121, 93
[Cd(L ⁴) ₂]	6.40	8.25, 8.36	7.22-8.12	862, 681, 500, 487, 375, 181, 153

Antioxidant studies: The antioxidant activity of the phenyl, styryl, 2-furyl and 2-naphthyl curcumins are presented in figure-2. The results clearly indicated that all the ligands possess significant antioxidant activity. Maximum activity was observed in the case of 2-naphthyl curcumin. Metal complexation

enhanced the antioxidant activity of all the compounds. The antioxidant activity of the Cd(II), Pb(II) and Hg(II) complexes are shown in figures 3 to 6. In metal complexes the Hg(II) complexes showed highest activity.

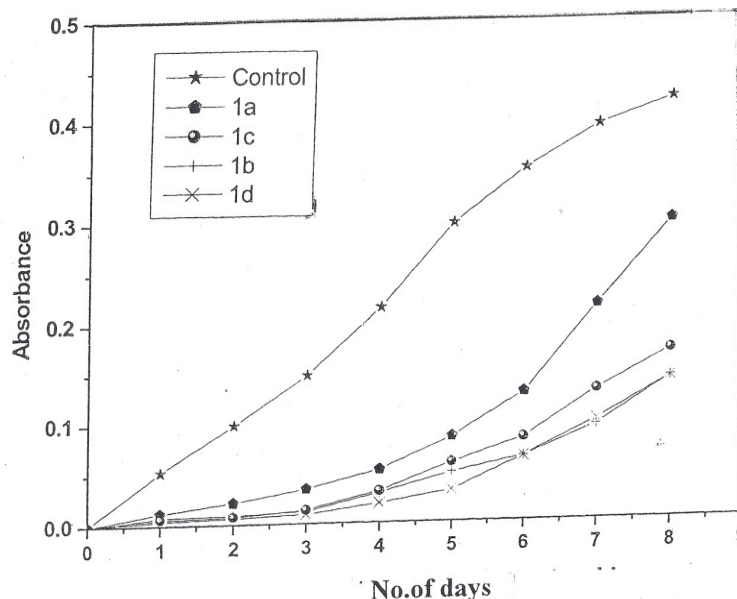


Figure-2

Antioxidant assay of synthetic curcuminoids

1a = Phenyl curcumin (HL¹); 1b = Styryl curcumin (HL²); 1c = 2-Furyl curcumin (HL³); 1d = 2-Naphthyl curcumin (HL⁴)

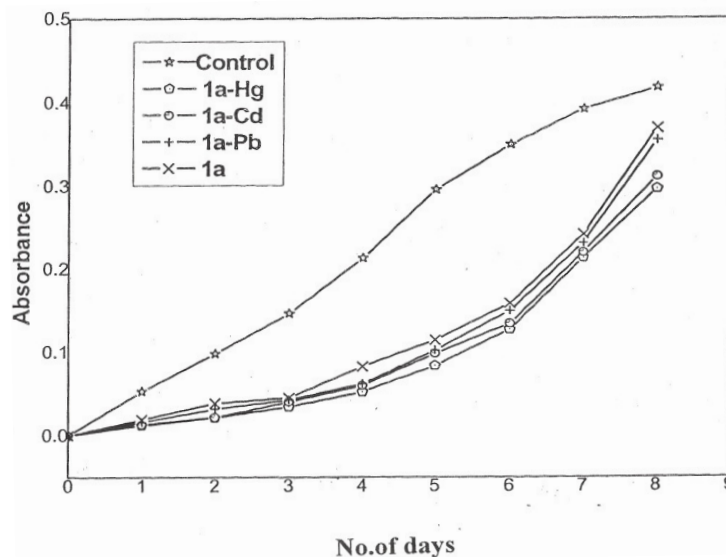


Figure-3

Antioxidant assay of the metal complexes of phenyl curcumin

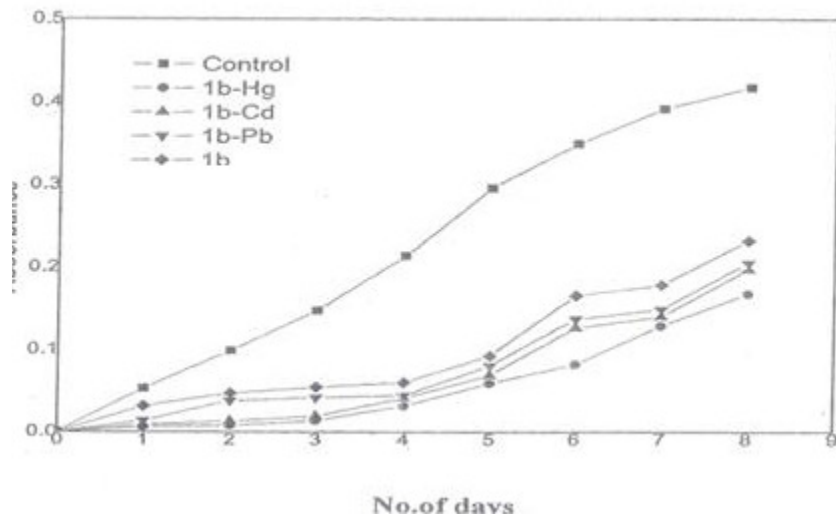


Figure-4
Antioxidant assay of the metal complexes of styryl curcumin

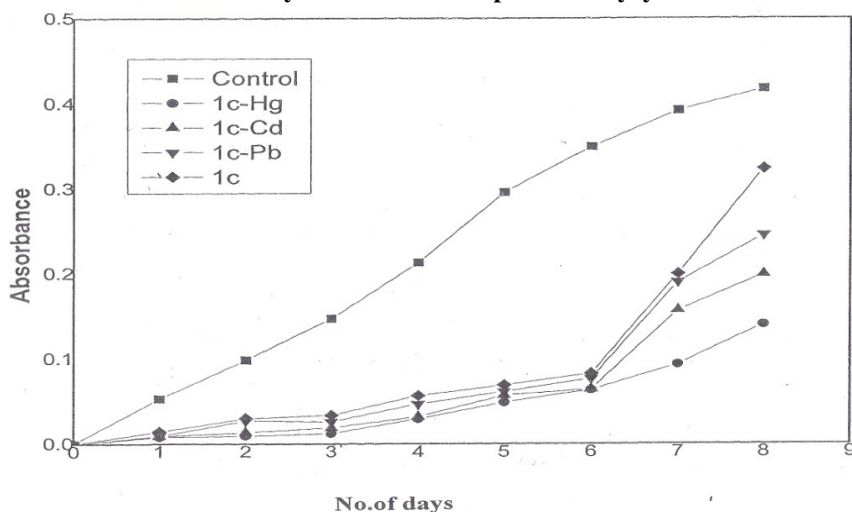


Figure-5
Antioxidant assay of the metal complexes of 2-furyl curcumin

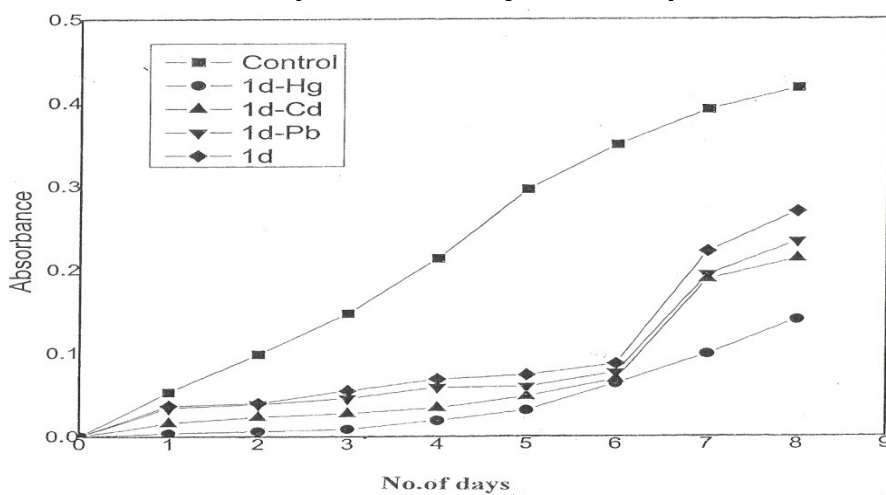


Figure-6
Antioxidant assay of the metal complexes of 2-naphthyl curcumin

Conclusion

Structural analogues of natural curcuminoids and their Cd(II), Hg(II) and Pb(II) complexes were synthesized and characterized using various physico-chemical and spectral techniques. These metal complexes of [ML₂] stoichiometry showed enhanced antioxidant activities compared to the free curcuminoids.

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