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Research Article

Synthesis, Characterization, Antibacterial, Antifungal and Cytotoxic Activity of Curcuminoid Analogues with Trisubstituted Phenyl and Anthracenyl ring and their Zinc (II), Copper (II) and Vanadyl (IV) Chelates

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Abstract

Two curcuminoid analogues 1,7-Bis(3,4,5-trimethoxy phenyl)-1,6-heptadiene-3,5-dione;1,7-di(9-anthracenyl)-1,6-heptadiene–3,5–dione, were synthesized and characterized by UV, IR, ^{1}H NMR, ^{13}C NMR and mass spectral techniques. The Zn (II), Cu (II), VO (IV) complexes of the two curcuminiod analogues were synthesized and characterized. Antibacterial, Antifungal and cytotoxic activity of the curcuminoid analogues and their transition metal chelates were studied. The metal chelates were found to be more active than curcuminoid analogues in antibacterial and antifungal activities. Curcuminod analogue-Metal complexes exhibited more cytotoxicity in cancer cell lines than the curcuminoid analogues. Among the metal chelates, the Cu (II) chelate of 1,7-di(9-anthracenyl)-1,6-heptadiene–3,5–dione compound was found to be very active against cancer causing cells. VO(IV)complex of 1,7-di(9-anthracenyl)-1,6-heptadiene–3,5–dione showed enhanced antifungal activity and Cu(II) complex of 1,7-di(9-anthracenyl)-1,6-heptadiene–3,5–dione was most effective against bacterial strains.

Keywords: Curcuminoid analogues; Transition metal chelates; UV; IR; NMR; Mass spectra; Cytotoxicity; Antibacterial

1. Introduction

Curcumin, a pigment from turmeric is one of the very few promising natural products that have been extensively investigated by researchers from both the biological and chemical point of view. Turmeric is known for its medicinal values in the Indian traditional system of medicine where it has been used as a home remedy for several ailments for ages. It exhibits antioxidant [1-5], anti-inflammatory [6-9], antibacterial [10-12], antirhuematic [13], anticarcinogenic [14-20] activities etc. Scientific research spanning over more than four decades has confirmed the diverse pharmacological effects of curcumin and established its ability to act as a chemopreventive agent [21] as well as a potential therapeutic agent against several chronic diseases.

Curcuminoids are chemically 1,7-diaryl-1,6- hepta diene- 3,5–diones. They are 1,3- diketones in which the diketo function is directly attached to olefinic groups. It has two aromatic ring systems connected by a seven carbon linker consisting of an α , β - unsaturated 1,3- diketo moiety[22]. Curcuminoid analogues are synthesized [23-25] with similar structures where the α, β - unsaturated 1,3- diketo moiety is retained and the aryl ring is modified. The present study reports the synthesis of two curcuminoid analogues, one with a trisubstituted aryl ring and another with a polynuclear ring.

Curcuminoids are expected to form metal complexes [26-28] similar to other 1,3- diketones . They are powerful natural chelating agents. Here Cu (II), Zn (II) and VO (IV) complexes of curcuminoid analogues were prepared. The synthesized compounds and metal chelates were studied for their antibacterial activity, antifungal nature and *in vitro* cytotoxicity using DLA cancer cells. The effect of these compounds on ascites tumour

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development in mice was also studied. The death patterns of the animals were noted and increase in life span was calculated.

2. Materials and Methods

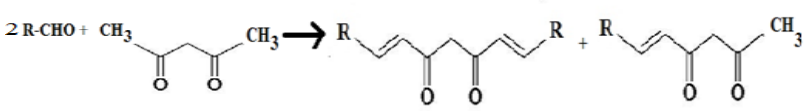
The chemicals required were obtained from Sigma and Aldrich chemical suppliers and are of analar grade. UV spectras were recorded in methanol solution using JASCO V- 530 UV/VIS spectrophotometer. IR spectra were recorded on Schimadzu 8110IA FTIR spectrophotometer. NMR spectra were taken on Jeol 400 NMR spectrophotometer and Mass spectra on a Jeol/ Sx-102(FAB) mass spectrometer.

Cells: Daltons Lymphoma Ascites (DLA) was obtained from the Cancer Research Institute, Mumbai, India. Bacterial strains namely *Escherichia coli*, *Klebsiella pneumoniae* and *Bacillus subtilis* and fungal cultures were obtained from the culture collection of Institute of Microbial Technology (IMTECH), Chandigarh, India.

Animals: Swiss Albino Mice were purchased from Veterinary College, Thrissur, Kerala. All animal experiments in this study were carried out with the prior approval of the Institutional Animal Ethics Committee (IAEC) and were conducted strictly according to the guidelines of Committee for the Purpose of Control and Supervision of Experiments on Animals (No.149/1999/CPCSEA).

2.1 Synthesis of 1,7-Bis(3,4,5-trimethoxyphenyl)-1,6-heptadiene-3,5-dione,(L1);1,7-di(9-anthracenyl)-1,6-heptadiene–3,5–dione,(L2)

The curcuminoid analogues were prepared by the condensation of aldehydes(3,4,5-trimethoxy benzaldehyde,anthracene-9-carboxaldehyde) with acetyl acetone – boric oxide complex (which was formed by stirring acetyl acetone and B_2O_3 for 1 hour) in the presence of tri (Sec–butyl) borate and n-butyl amine as the condensing agent as in the reaction given below. (Scheme 1.1)



Scheme 1.1

R= 3,4,5-trimethoxyphenyl ring for (**L1**) and anthracenyl ring for (**L2**)

Here two moles of aldehyde condenses with one mole of diketone to form a bis condensation product. The product was separated from the monocondensation product and purified by column chromatography over silica gel (60-120 mesh) using 1: 5 acetone: chloroform mixture as the eluent and recrystallised twice from hot benzene to get pure crystalline material.

2.2 Preparation of metal complexes

Cu(II), Zn(II) and VO(IV) chelates of curcuminoid analogues were prepared by the following method. A methanolic solution of copper acetate (25ml, .001 mol), Zinc acetate (25ml, .001 mol), Vanadium(IV)oxide sulphate (25ml, .001 mol) was added with stirring to a solution of curcuminoid analogue (25ml, .002 mol) in methanol and refluxed gently for 2 hours to prepare Cu(II), Zn(II) and VO(IV) chelates respectively . After reducing the volume to half, the solution was cooled to room temperature. The precipitated complex was filtered, washed with 1:1 methanol- water mixture and recrystallised from hot methanol.

2.3 Characterisation of 1 ,7-Bis(3,4,5-trimethoxy phenyl)-1,6-heptadiene-3,5-dione,(L1);1,7-di(9-anthracenyl)-1,6-heptadiene–3,5–dione,(L2) and metal chelates

The ligands and their transition metal chelates were characterized by UV, IR, ^{1}HNMR, C^{13}NMR and mass spectral techniques. The structure of ligands is represented by **Figure 1** and **Figure 2**.The structure of the metal complex is represented by **Figure 3.**

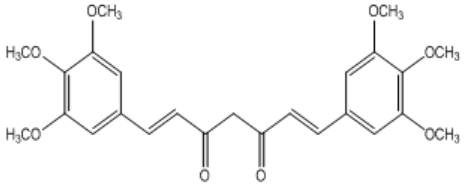


Figure 1: Structure of 1 ,7-Bis(3,4,5-trimethoxy phenyl)-1,6-heptadiene-3,5-dione

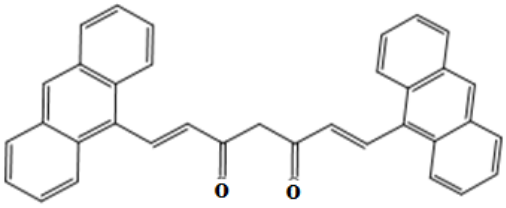


Figure 2: Structure of 1,7-di(9-anthracenyl)-1,6-heptadiene–3,5–dione

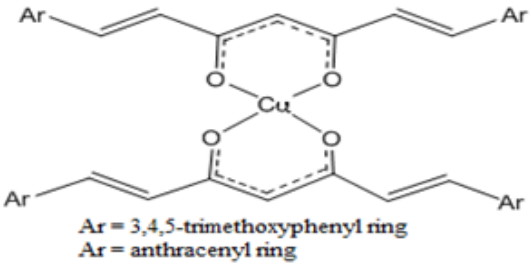


Figure 3: Structure of Cu (II) complex of ligands.

2.4 *In vitro* cytotoxicity study using DLA cells (Dalton's Lymphoma Ascites cells)

The tumour cells aspirated from the peritoneal cavity of tumour bearing mice were washed thrice with PBS or normal saline. Cell viability was determined by trypan blue exclusion method. Viable cell suspension ($1x10^6$ cells in 0.1 ml) was added to tubes containing various concentrations of the test compounds and the volume was made up to 1 ml using phosphate buffered saline (PBS). Control tube contained only cell suspension. These assay mixture were incubated for 3 hours. Further cell suspension was mixed with 0.1 ml of 1% trypan blue and kept for 2-3 minutes and *loaded* on a haemocytometer. Dead cells take up the blue colour of trypan blue while live cells do not take up the dye. The number of stained and unstained cells was counted separately.

$$\% \text{ Cytotoxicity} = \frac{\text{No. of dead cells}}{\text{No. of live cell + No. of dead cells}} \times 100$$

2.5 Determination of the effect of compounds in reducing ascites tumour development.

Six groups of Swiss albino mice (6nos/ group)were injected intraperitoneally with DLA cells(10^6cells /animal).One group was kept as control, one group was injected with a standard drug cyclophosphamide and the other groups of mice, were simultaneously injected with the test compound in different concentrations namely 20,10,5µg/ml. and injection continued for 10 days . The animals were observed for survival for one month and their increase in life span (ILS) was calculated using the formula % ILS = 100(T-C)/C, T and C are the mean number of days survived by treated and control animals respectively .

2.6 Antibacterial activity

The antibacterial assay was performed using agar – well diffusion method with the test compounds. Agar plates were prepared using sterile agar medium. Selected bacterial strains of 24 hr culture were evenly spread on the surface of the agar plates using sterile swab sticks. Wells were cut in the plates with sterile gel puncture. The test compounds in the concentration 5 mg/ml were added in the wells. DMSO solvent served as negative control and streptomycin served as positive control. The plates were incubated at 37°C for 24 hrs and observed for zones of inhibition which was then measured and the activity was expressed in terms of the mean diameter of the zone of inhibition in millimeters.

2.7Antifungal activity by Kirby Bauer or Disc Diffusion Method

Antifungal test was carried out by disc diffusion method. The fungal cultures were maintained in Sabouraud's Dextrose broth. Each culture was uniformly distributed on SDA plates using sterile swabs. Sterile filter paper discs of 3mm diameter were placed on the surface of SD agar plates at a distance of 2cm using sterile forceps. 2 % DMSO was used to dissolve the drug, which was found to have no adverse effect on the bacterial cultures. Drugs of different concentrations [100,250,500µg/ml] were added on each disc with a micropipette. Disc with

DMSO but, without drug was used as control. Then the plates were incubated at room temperature for 2-3days. After incubation, zone diameter in mm was measured.

3. Results

3.1 Spectral data of 1,7-Bis(3,4,5-trimethoxy phenyl)-1,6-heptadiene-3,5-dione,(L1);1,7-di(9-anthracenyl)-1,6-heptadiene–3,5–dione,(L2)

The curcuminoid analogues (L1,L2) synthesized were crystalline in nature with sharp melting points. The curcuminoid analogues were soluble in acetone, ethyl acetate, methanol etc. They were characterized by different spectral techniques like UV,IR,^{1}H NMR,^{13}C NMR and Mass spectra. The spectral data obtained are given in **Table 1**.The ^{13}C NMR spectral data of the ligands are given in **Table 2** and Table **3** and the different carbon atoms are represented in **Figure 4 and Figure 5**.

Table 1: UV, IR, ^{1}H NMR and Mass spectral data of ligands

Compound	U V data λmax	IR data cm^{-1} ν C=O	^{1}HNMR spectral data (δ ppm)					Mass spectral data (m/z)
			Enol	Methine	Aryl	Alkenyl	Substituent	
L1	269, 445	1631	16.10	5.85	7.13-7.5	6.82-7.10	3.93 (methoxy)	456,288,263, 234,221, 207,180,168
L2	286, 420	1624	16.14	5.92	7.014-7.808	6.613-8.99		476,298,273, 245,232, 205,189,178

Table 2: ^{13} C NMR spectral data of 1,7-Bis(3,4,5-trimethoxy phenyl)-1,6-heptadiene-3,5-dione,(L1);

C1	C2,C2’	C3,C3’	C4,C4’	C5,C5’	C6,C6’	C7,C7’
105.631	191.99	140.35	106.023	131.47	140.35	143.60
C8,C8’	**C9,C9’**	**C10,C10’**	**C11,C11’**	**C12,C12’**	**C13,C13’**	
153.68	143.60	123.65	56.30	60.98	56.30	

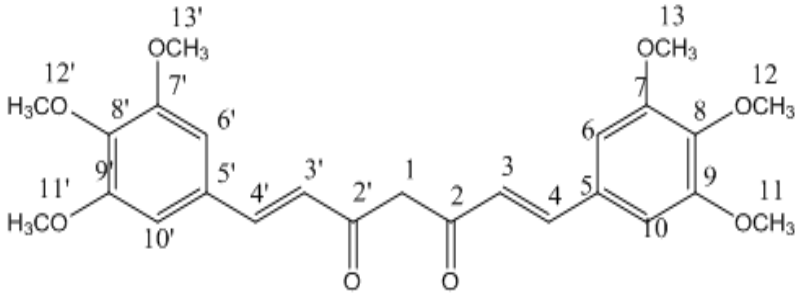


Figure 4.Structure representing distinct C atoms in L1.

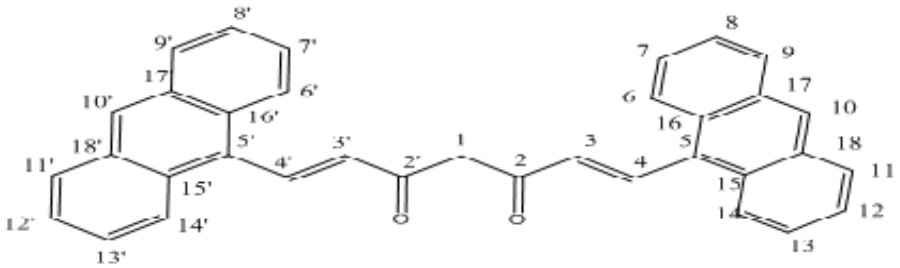


Figure 5: Structure representing distinct C atoms in L2.

Table 3: ^{13}C NMR spectral data of 1,7-di(9-anthracenyl)-1,6-heptadiene–3,5–dione,(L2)

C1	C2,C2'	C3,C3'	C4,C4'	C5,C5'	C6,C6'
104.68	191.45	139.65	123.83	135.63	127.56
C7,C7'	**C8,C8'**	**C9,C9'**	**C10,C10'**	**C11,C11'**	**C12,C12'**
126.47	126.92	128.34	129.56	128.34	126.92
C13,C13'	**C14,C14'**	**C15,C15'**	**C16,C16'**	**C17,C17'**	**C18,C18'**
126.47	127.56	123.65	122.58	121.55	121.35

3.2 Spectral details of metal complexes

These ligands formed stable complexes with Cu^{2+}, $Zn^{2+}$and VO^{2+}ions. The metal complexes were also crystalline in nature with sharp melting points .UV, IR and mass spectral data (**Table 4**) clearly suggests a ML2 stochiometry(1:2 metal-ligand stochiometry) for all complexes.

Table 4: Spectral data of Cu (II), Zn(II) and VO(IV) complexes of ligands

Complexes	U V data λmax	IR data cm-1		Mass spectral data(m/z)
		ν (C=O)	ν (M-O)	
$Cu(L1)_2$	271,446	1606	461,432	974,640,519,456,334,306,185,121
$Zn(L1)_2$	273,449	1604	468,429	976,642,521,456,334,308,187,121
$VO(L1)_2$	274,448	1601	478,417	977,643,523,456,334,309,188,121
$Cu(L2)_2$	288,421	1594	466,427	1014,660,539,476,354,306,185
$Zn(L2)_2$	287,422	1593	462,426	1016,662,541,476,354,308,187
$VO(L2)_2$	289,424	1596	475,425	1017,663,542,476,354,309,188

3.3 *In vitro* cytotoxicity towards DLA cells

In vitro cytotoxicity studies were carried out using the diketones(L1 andL2), and their Cu(II), Zn(II) and VO(IV)complexes towards DLA cells. These compounds (as drugs) were taken in different concentrations 200, 100, 50, 20 and10µg/ml in DMSO. The cytotoxicity is expressed as % cell death produced by the compounds. The results are given in **Table 5**.

Table 5: *In vitro* cytotoxicity of ligands and metal chelates

Drug concentration (µg/ml)	% cell death produced by the compounds							
	L1	$Cu(L1)_2$	$Zn(L1)_2$	$VO(L1)_2$	L2	$Cu(L2)_2$	$Zn(L2)_2$	$VO(L2)_2$
200	37	53	40	43	65	95	67	87
100	21	39	30	29	42	63	47	59
50	15	29	21	19	20	45	32	40
20	8	16	14	12	10	24	20	22
10	2	6	3	4	5	16	7	9

3.4 Effect of compounds on ascites tumour reduction(*in vivo)*

The ligands L1 andL2 and their metal complexes with Cu (II) ion were given as drug to study the effect of these compounds to increase the life span of tumour bearing mice. The values of no. of days survived are means of five determinations ±SD (std. deviation).The increase in life span (%ILS) corresponding to the test compounds are given in **Table 6** and **Table 7.**

Table 6: Effect of compounds on ascites tumour reduction(*in vivo*) of 1,7-Bis(3,4,5-trimethoxy phenyl)-1,6-heptadiene-3,5-dione,(L1) and Cu(II) chelate

Animal groups	Concentration (µg/ml)	No. of animals with tumour	No. of days survived	%ILS
1.Control			**17.3±1.1**	
2.Std.drug			**30.6±3.1**	**76.88**
3.L1	20	5/5	**25.2±2.1**	**45.73**
4.L1	10	5/5	**24.1±2.6**	**39.31**
5.L1	5	5/5	**18.0±2.60**	**8**
6.Cu(L1)2	20	5/5	**27.8±3.1**	**60.71**
7. Cu(L1)2	10	5/5	**26.7±2.4**	**54.34**
8. Cu(L1)2	5	5/5	**19.6±2.65**	**20.1**

Table 7: Effect of compounds on ascites tumour reduction(*in vivo*) of 1,7-di(9-anthracenyl)-1,6-heptadiene–3,5– dione,(L2) and Cu(II)complex

Animal groups	Concentration (µg/ml)	No. of animals with tumour	No. of days survived	%ILS
1.Control			**17.3±1.1**	
2.Std.drug			**30.6±3.1**	**76.88**
3.L2	20	5/5	**28.8±2.7**	**66.47**
4.L2	10	5/5	**27.8±3.1**	**60.71**
5.L2	5	5/5	**24.9±2.10**	**43.93**
6.Cu(L2)2	20	5/5	**30.9±2.2**	**78.62**
7. Cu(L2)2	10	5/5	**29.0±3.0**	**71.70**
8. Cu(L2)2	5	5/5	**27.6±2.8**	**56.59**

3.5Antibacterial activity

The results of antibacterial activity of curcuminoid analogues and their metal complexes are represented in **Table 8**. All the compounds were taken in the concentration 5mg/ml in DMSO. Results are compared with a std. drug. The activity is expressed as diameter of zone of inhibition in mm.

Table 8: Antibacterial activity of 1,7-Bis(3,4,5-trimethoxy phenyl)-1,6-heptadiene-3,5-dione and 1,7-di(9-anthracenyl)-1,6-heptadiene–3,5–dione and metal chelates

Bacterial strains	L1	Cu(L1)2	Zn(L1)2	VO(L1)2	L2	Cu(L2)2	Zn(L2)2	VO(L2)2
E Coli	13.5	18.5	12	17	15	19.5	16	18
Klebsiella Pnuemoniae	13	16.5	13	16	14.5	17.5	15.5	17
Bacillus Subtilis	11	14	11.5	13	13	16.5	14.5	16
Standard drug	20	20	20	20	20	20	20	20

3.6 Antifungal activity

The results of antifungal activity of ligands L1 andL2 and their VO (IV) celates are given in **Table 9.** The test compounds were taken in different concentrations, 100µg, 250µg, 500µg. The antifungal activity is expressed in terms of diameter of zone of inhibition in mm. The results are compared with a std. drug flucanazole.

Table 9: Antifungal activity of 1,7-Bis(3,4,5-trimethoxy phenyl)-1,6-heptadiene-3,5-dione and 1,7-di(9-anthracenyl)-1,6-heptadiene–3,5–dione and VO(IV) chelates

Fungal cultures	Concentration											
	L1			VO(L1)2			L2			VO(L2)2		
	100 µg	250 µg	500 µg	100 µg	250 µg	500 µg	100 µg	250 µg	500 µg	100 µg	250 µg	500 µg
Aspergillus	14	17	19	15	18.5	20	13	16	18	15	19	21.5
Penicillium	13	16	18	15	17	19	12	15.5	19	14	17.5	20
Alternaria	13.5	17	19	14	18	20	12.5	16.5	19	13	18	21
Std. drug			25			25			25			25

4. Discussion

4.1 Structural characterization of ligands and metal complexes

UV Spectra

The UV Spectra of the compounds (L1,L2) in methanol shows two absorption maxima, the low energy band corresponds to the n - π* transition (330-400nm) and the high energy band corresponds to the π - π* transitions (230-280nm). The characteristic UV absorption maxima of the diketones due to π - π* and n- π* transition shows only slight bathochromic shifts in the spectra of the metal complexes.

Infrared Spectra

The IR Spectra of curcuminoid analogues are characterized by the presence of a strong band in the range 1605-1640cm^{-1} due to the enolised conjugated 1,3- diketo group. No other band is observed in the region 1600 – 1800cm^{-1} due to free carbonyl group indicating that the compound exist in the intramolecularly hydrogen bonded enolic form. The spectra of the compounds are also characterized by trans – CH=CH- absorption which occurs at ~ 970 cm^{-1}. The intramolecular hydrogen bonded enolic group gives a broad band in the region 2600 – 3800. In the

spectra of the metal complexes , the band due to hydrogen bonded dicarbonyl function of the free ligands, disappeared but instead a strong band assignable to the stretching of metal coordinated dicarbonyl group of the β-diketone moiety appeared at ~ 1595 cm^{-1}. Spectra of all complexes showed additional bands at ~465cm^{-1} and ~418 cm^{-1} assignable to ν(M-O) vibrations.

H^1 NMR Spectra

The H^1 NMR Spectra of the curcuminoid analogues displayed a one proton singlet at ~16 ppm and another singlet at ~5.9ppm assignable respectively to the strong intramolecularly hydrogen bonded enolic proton and to the methine proton. The observed downfield shift of the enolic proton of L2 is due to extended conjugation. The trans oriented alkenyl protons can be identified from the position of their signals δ~6.5-7.9 ppm. The phenyl protons as well as the methoxy protons in L1 can be identified from their signals in the H^1 NMR Spectra. In the NMR spectra of complexes, the low field enolic proton singlet of the free ligand is absent indicating that the chelate formation has occurred through the 1,3-diketo moiety of the ligand. Methine proton singlet and aromatic proton signals are shifted slightly to down field in complexes.

Mass Spectra

The FAB mass spectra of the curcuminoid analogues as well as the metal complexes show intense molecular ion peaks P+/(P+1)+. Important peaks appeared in the spectra corresponds to fragment ions which can be explained with the help of fragmentation patterns. Elimination of groups like CO, C_2H_2, C_2H_2O, CH_2, CH=C=O are clearly evident from the observed spectra of the ligands .The molecular ion peak in the mass spectra of complex corresponds to ML2 stochiometry. The peaks due to the stepwise elimination of one ligand, the aryl groups, the anthracenyl groups etc are clear in the spectra.

4.2 *In vitro* Cytotoxicity

The results of the *in vitro* cytotoxicity study of the curcuminoid analogues and their metal complexes towards DLA cells shows that both the curcuminoid analogues and their metal complexes are quite cytotoxic towards the cancerous cells. Comparing the cytotoxic nature of ligands, the one with polynuclear ring was very effective against DLA cells than the one with aryl ring. The ligands L1 andL2 showed 37% and 65% cell death respectively at a concentration of 200µg/ml. The ligand with a polynuclear ring showed activity nearly twice that of ligand with aryl ring. It is also observed that as concentration of the test compound increases the %cell death increases. For both ligands Cu(II)complexes were quite effective in producing cell death. The Cu (II) complex of L2 produced 95% cell death towards DLA cells. Among the complexes VO(II) and Zn(II) complexes showed almost comparable activities. The results of the study indicate that the metal complexes especially the Cu (II)complexes were found to be more effective than the corresponding curcuminoids . This indicates that metal chelation enhance the cytotoxicity of compounds considerably. The Cu (II) complex of L2 was found to be the most active compound.

4.3 Effect of compounds on ascites tumour reduction.

The compounds L1and L2 and their Cu (II) complexes which were found to be quite cytotoxic towards DLA cells in *in vitro* studies conducted earlier were selected for this study. All the compounds when administered intraperitoneally could produce significant increase in the life span of mice bearing ascites tumour. The animals of the control group survived for a period of 17.3±1.1 days and those treated with std. drug cyclophosphamide for a period of 30.6±3.1days. Cu(II) complex of the compound produced an increase in life span of tumour bearing mice compared with that of the ligand . The percentage increase in life span(%ILS) of tumour bearing mice were 45.73, 39.31 and 8% for L1 and 60.71,54.34,20.1% for L2 at different concentrations namely 20,10,5µg/ml respectively. For the Cu (II) complexes of L1and L2 the % increase were 66.47 and 78.62% respectively at a concentration of 20µg/ml. The maximum value for the no. of days of survival was observed with Cu (II) complex of 1,7-di(9-anthracenyl)-1,6-heptadiene–3,5–dione i.e. 30.9 days, this is comparable to 30.6 days of the standard drug. So the studies reveal that Cu(II) complex is very effective in reducing tumour development in mice and increasing the life span of the animal.

4.4 Antibacterial activity

The results of the antibacterial activity of curcuminoid analogues and their complexes revealed that the ligands and their complexes possess comparable antibacterial activity to that of standard drug streptomycin. In all the cases metal complexes possess better antibacterial activity than that of ligands, which means that metal complexation enhance activity. Comparing the ligands, L2 with polynuclear ring showed greater zone of inhibition

towards all bacterial strains. The activity of the compounds towards the bacteria *Escherichia Coli* was maximum. Comparatively lesser activity was found towards the other two bacteria. Out of the three metal complexes, Cu (II) complexes of both ligands show maximum antibacterial activity. VO (IV) complexes showed comparable activity with Cu (II) complexes. Minimum antibacterial activity was given by Zn(II) complexes. The Cu(II) complex of L2 gave a zone of inhibition of 19.5mm which is comparable with 20mm,the zone of inhibition produced by the std. drug.

4.5 Antifungal activity

The antifungal activity of both the ligands and their VO (IV) chelates towards three fungal cultures namely Aspergillus, Penicillium, Alternaria were studied. The test compounds were taken in different concentrations of 100,250,500µg/ml. The results show that the ligands and their VO (IV) complexes possess comparable antifungal activity to that of std. drug flucanazole. The ligand with anthracenyl ring produced greater zone of inhibition for all the fungal cultures. The maximum activity of the compound was expressed at a higher concentration of 500µg/ml. It was observed from the study that the VO (IV) complex of L2 showed a maximum zone of inhibition of 21.5mm and the corresponding complex of L1 gave a zone of inhibition of 20mm.These are comparable with the zone of inhibition produced by the standard drug.

5. Conclusion

The ongoing discussion reveals that curcuminoid analogues namely1,7-Bis(3,4,5-trimethoxy phenyl)-1,6-heptadiene-3,5-dione,(L1);1,7-di(9-anthracenyl)-1,6-heptadiene–3,5–dione,(L2) and their metal complexes possess enhanced antitumour(both *in vivo* and *in vitro*)activity. The metal chelation considerably enhances the cytotoxicity of these compounds. Also it is found that Cu(II) complex of 1,7-di(9-anthracenyl)-1,6-heptadiene–3,5–dione which has a polynuclear ring, is the most active compound in *in-vitro* cytotoxicity studies with DLA. The antibacterial studies of both ligands and metal complexes show enhanced activity. The Cu(II)complex of 1,7-di(9-anthracenyl)-1,6-heptadiene–3,5–dione possessed better antibacterial activity than Zn(II) and VO(IV) complexes and ligands. The VO (IV) complex of 1,7-di(9-anthracenyl)-1,6-heptadiene–3,5–dione showed maximum antifungal activity compared with ligands. The structure of curcuminoids is suggested to be responsible for their biological activities and metal chelation modifies its biochemical activities [16].

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