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SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL APPLICATION OF CURCUMIN BASED SCHIFF'S BASE LIGAND

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Abstract-Many drugs posses modified toxicological and pharmacological properties in the form of metal complex and probably Schiff's bases are versatile, C=N(Imine) containing compounds possessing broad spectrum of biological activity and incorporation of metals in the form of complexes show enhanced activity. In this paper, a Schiff's base ligand was prepared by the condensation of Arginine with curcumin and the Schiff's base ligand was complexed with Cu(II),Co(II),Ni(II) andMn(II) metals.The synthesized ligand and complexes were structurally characterized by spectral techniques like IR and UV.The ligand and their metal chelates have been screened for their antimicrobial activities using well diffusion method against the selected bacteria and fungi.
Key words:Schiff's base,curcumin,aminoacid, antimicrobial activity.

1.Introduction

Many microorganisms are naturally becoming resistant to already existing drugs due to morphological changes, cell divisions and mutations of their genome. Therefore, the improvement of antimicrobial drugs has to be a continuous process. The coordination behavior of Schiff's base ligand with transition metals plays a vital role in the development of drugs in recent days. Especially, transition metal complexes derived from amino acid Schiff bases have received much attention because of possible biological and pharmacological activities. In view of diversified roles of Schiff base transition metal complexes, in this paper the metal complexes of Cu(II), Co(II), Ni(II) and Mn(II) with Schiff's base derived from Arginine and curcumin have been synthesized, characterized using different spectal techniques and screened for their antimicrobial activities using well diffusion method against the selected bacteria and fungi.

2. Experimental

2.1 Reagents

All the chemicals used were of analytical grade and used without further purification. All reagents were purchased from Aldrich and sigma chemicals companies.

2.2 Synthesis of L-Arginine Curcumin

The Schiff's base ligand was synthesized as per the following literature procedure[2]. An ethonolic solution of L-Arginine (0.001M) was added while stirring into ethonolic solution of Curcumin (0.001M), three drops of glacial acetic acid were added and heated under reflux for 3-5 hrson a hot plate at 50^{o}C. The volume of the resulting solution was reduced to one-third. An air sensitive dark brownish yellow precipitate was filtered off washed with ethanol and dried over fused calcium chloride. The Schiff base recrystallized with ethanol and water mixture. The yield was found to be 50%.

NH
II

2.3 Synthesis of Metal Complexes

The Schiff based metal complexes were synthesized as per the following literature procedure [2].
Metal Chloride (0.001M) dissolved in ethanol and added to the ethanolic solution of the ligand (0.001M L-Arginine Curcumin) followed by fewdrops of sodium hydroxide and finally heated under reflex for 2-3 hrs, on a hot plate at 50^{o}C. The fine precipitate of the solid complexes formed was filtered off, washed with ethanol and stored in a vacuum desiccator over anhydrous calcium chloride.

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2.4 Antimicrobial Activities

The antimicrobial activity of synthesized Cu(II), Co(II), Ni(II) and Mn(II) complexes was evaluated by the agar well diffusion method. Muller Hinton agar medium (20ml) was poured into each Petri plate and plates were swabbed with 100µl inocula of the test microorganisms and kept for 15 min for absorption. Using sterile cork borer of 8mm diameter, wells were loaded with a 100µl solution of each complex in DMSO. All the plates were incubated at 37^{o}C for 24hrs. Antibacterial activity of each synthesized complexes were evaluated by measuring the zone of inhibition againstB. subtilis, B.thuringiensis, B. cereus, B.sphaericus, B. laterosporus, B. megaterium[3].

3. Results and Discussion

Some physical properties of the ligand and metal complexes are noted in table 1.

Table 1: Physical properties of the ligand and metal complexes.

Compound	Colour	Yield
L	Dark Orange	50%
$[Cu(L)_2]$	Dark Green	60%
$[Co(L)_2]$	Green	65%
$[Ni(L)_2]$	Light Orange	55%
$[Mn(L)_2]$	Dark Brown	52%

3.1 IR Spectra

Information from the infrared spectrum revealed that the ligand shows broad bands in the region of 3200-3600 cm^{-1} assignable to –OH groups. The retention of this peak in LAC complex indicates that the presence of free –OH group. The strong band at 1600-1550 cm^{-1} in the spectra of the ligands are characteristic of the azomethine group. These bands were shifted to a lower wave number of (1583-1516 cm^{-1}) during coordination suggesting the involvement of the Nitrogen atom of the azomethine group in coordination to the metal ion. The carboxylate band (COO-) at 1342-1335 cm^{-1} and carbonyl band at 1646-1610 cm^{-1} were also shifted up by about 30-50cm^{-1} during coordination to the metal ion. Thus the ligand coordinated to the metal on through it azomethine Nitrogen and Oxygen atom of the carbonyl ion in a bidentate mode.The IR Spectra of Schiff base ligand and Cu(II) metal complex are shown in Fig. 1 & 2.

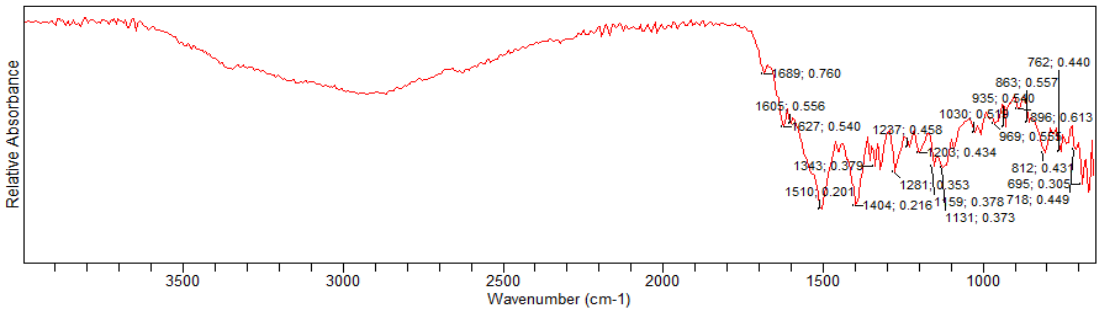

Figure 1: IR Spectrum of the Ligand

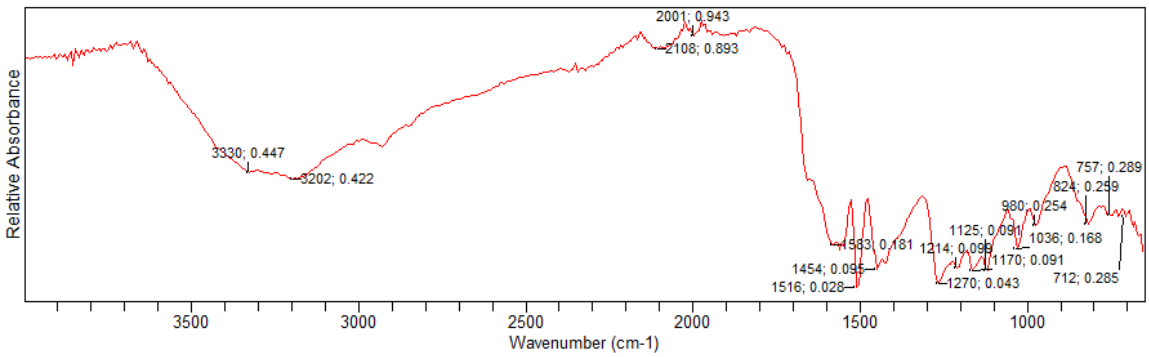

Figure2: IR Spectrum of Cu(II) Metal Complex

3.4 Electronic Absorption Spectra

The electronic spectra of the complexes were recorded from freshly prepared solution of ethanol at room temperature. The electronic spectrum of Schiff'sbases ligand there are two absorption bands assigned to π- π^* and n- π^* transition. These transitions are also found in the spectra of the complexes, but they are shifted towards longer wavelength to metals through the azomethine moiety. The Uv spectrum of Schiff base ligands and copper II metal complex are indicated in Fig. 3 & 4.

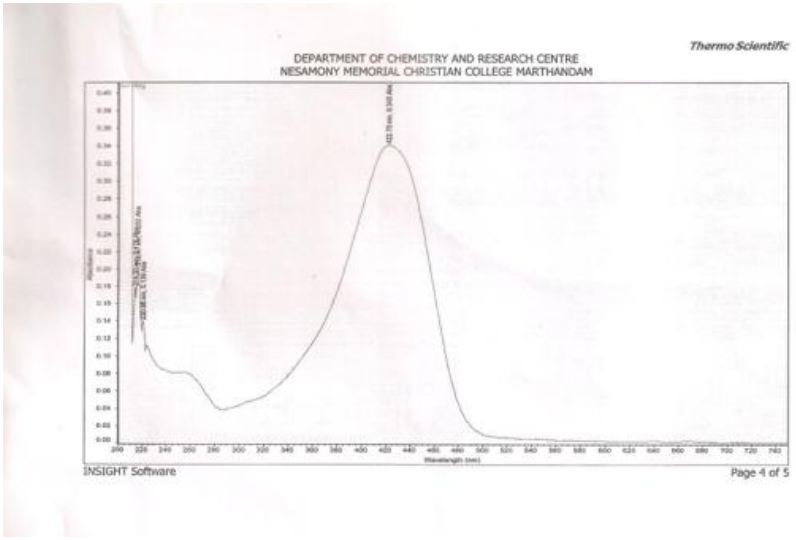

Figure 3: UV-Visible Spectrum of Ligand

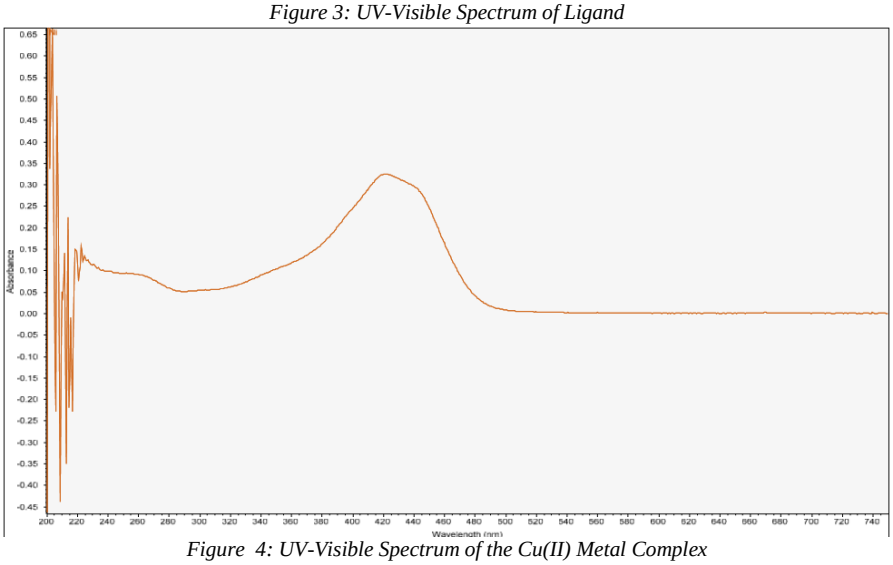

Figure 4: UV-Visible Spectrum of the Cu(II) Metal Complex

Compound	Geometry	Magnetic moment
L	-	-
$[Cu(L)_2]$	Square planar	1.83
$[Co(L)_2]$	Square planar	2.10
$[Ni(L)_2]$	Square planar	Diamagnetic
$[Mn(L)_2]$	Square planar	1.60

3.3 Cyclic Volammetry

The cyclic voltammogram of the $[Cu(L)_2]$ complex in ethanolic solution at 300k at scan rate $0.1vs^{-1}$ was recorded. It shows a well defined redox process corresponding to the formation of the quasi-reversible Cu(II)/Cu(I) couple. It has been shown in Fig. 5.

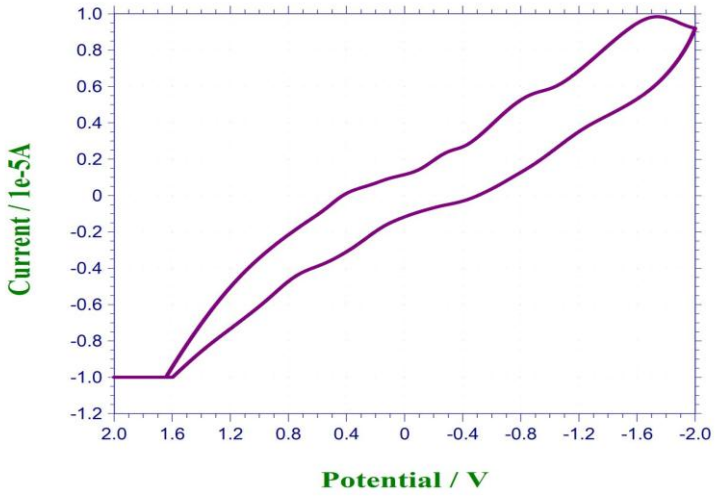

Figure 5: CV of Cu(II) Complex

3.4 Antimicrobial Activity

Antibacterial Activity

The inviro biological screening effects of the investigated compounds were tested against the bacterial speciesB. subtilis, B.thuringiensis, B. cereus, B.sphaericus, B. laterosporus, B. megateriumby the well diffusion method. The inhibition zone was measured in mm and results are shown in Table 2. A comparative study of the ligand and complexes indicate that complexes exhibit higher antibacterial activity than the free ligand.

The enhancement in activity may be explained on the basis of chelation theory. Chelation reduces the polarity of the metal ion, so a complex has lipophilic character and increase the interaction between the metal ion and the lipid is favored. This leads to the breakdown of the permeability barrier of the cell, resulting in interference with the normal cellular processes.

Table 2: Antibacterial Activity of the Schiff's base Ligand and its metal complexes.

	Zone of Inhibition (diameter in mm)					
	B. subtilis	*B.thuringiensis*	*B. cereus*	*B.sphaericus*	*B. laterosporus*	*B. megaterium*
Control	15	16	14	15	10	13
Ar	17	16	15	15	12	14
Mn	16	17	18	11	11	14
Cu	17	13	14	15	13	12
Ni	14	11	12	14	11	10
Co	15	18	17	16	12	18

Antifungal Activity

The Schiff base ligand and its metal complex were assessed for their invitro antifungal activity by well diffusion method against fungi such as Aspergillus clavatus, Aspergillus flavus, Aspergillus fumigatus. The results of antifungal activities of synthesized complexes are summarized in table 3.

The invitro antifungal activity of metal complexes showed very good inhibition than the schiff's base ligand against fungal strains under investigation.

The Schiff base ligands also exhibited antifungal activity to some extent because chelation tends to make the schiffs base act as more powerful and potent bacteriostatic agent, thus inhibiting the growth of bacteria and fungi more than the parent compounds. The mode of action Schiff base compounds may involve the formation of hydrogen bond through the azomethine group (>C=N-) with the active centers of cell constituents resulting in interfenences with the normal cell process. It is suspected that factor such as solubility, conductivity, dipole moment and cell permeability mechanism (influenced by the presence of metal ions) may be possible reasons for the increased activity in the case of metal complexes.

Table 3: Antifungal activity of the schiff's base ligand and its metal complexes

	Zone of Inhibition in mm		
	Aspergillus clavatus	*Aspergillus flavus*	*Aspergillus fumigatus.*
Control	17	18	17
Ar	19	18	18
Mn	23	21	21
Cu	25	22	22

Ni	25	23	22
Co	28	26	24

Conclusion

The present work reveals the synthesis of the Schiff base ligand and its Cu(II), Co(II), Ni(II) and Mn(II) Schiff'sbase complexes. The synthesized ligand and the complexes were structurally characterized by spectral techniques like IR and UV. The ligand and their metal chelates have been screened for their antimicrobial activities. The result shows that the metal complexes have enhanced inhibitory activity than the Schiff base ligand under identical conditions.
Where is the geometry of the ligand

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