

Synthesis, Spectral Characterization and Antimicrobial Studies of Schiff base Transition Metal Complexes derived from Cuminaldehyde and 4-Aminoantipyrine

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Abstract: A new Schiff base derived from cuminaldehyde and 4-aminoantipyrine and its metal complexes with Co(II), Ni(II), Cu(II) and Zn(II) have been synthesized and characterized. Their structural features have been established on the basis of analytical, magnetic, conductance, IR, UV-visible, mass, ¹H NMR spectral studies. The low conductance values indicate that the complexes are non-electrolytes. On the basis of colour, magnetic moments and electronic spectral data, octahedral geometry was assigned to Co(II) and Ni(II) complexes, while Cu(II) complex showed distorted octahedral arrangement. The antimicrobial activity of the ligand and its complexes has been studied with *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella pneumonia*, *Proteus vulgaris*, *Candida albicans* and *Aspergillus niger*, employing agar-well diffusion method. Both the Schiff base as well as its complexes possess significant antimicrobial activity.

Keywords: Cuminaldehyde, Schiff base complexes, 3-d transition metals, Antimicrobial activity.

Introduction

Over the past few decades, Schiff bases and their transition metal complexes have made significant contribution in the development of coordination chemistry. Schiff base metal complexes have been studied extensively¹ because of their attractive chemical and physical properties and their wide range of applications such as catalysts, antimicrobials, corrosion inhibitors *etc.* The presence of the imino nitrogen atom of the azomethine group makes the Schiff bases more significant chemically and biologically. Antipyrine (2,3-dimethyl-1-phenyl-5-pyrazolone) and its derivatives exhibit a wide range of biological activities and applications²⁻⁵. Cuminaldehyde, or 4-isopropylbenzaldehyde is a constituent of the essential oils of eucalyptus, myrrh, cassia, cumin and others. In this present study, we report the synthesis, characterization and antimicrobial screening of the Schiff base complexes of 3d transition metal ions Co(II), Ni(II), Cu(II) and Zn(II) with 4-aminoantipyrine and cuminaldehyde.

Experimental

Cuminaldehyde and 4-aminoantipyrine were purchased from Sigma Aldrich and used as such. Co(II), Ni(II), Cu(II) and Zn(II) metal salts were of analytical grade from Merck. All other reagents and solvents were purchased from commercial sources and were of analytical grade and were purified by distillation. Melting points of the solid samples were determined using 'TECHNICO' melting point apparatus. The infrared spectra of the solid samples were recorded in JASCO/FT-IR 410 spectrometer in the range of 4000-400 cm^{-1} . Potassium bromide disc method was employed for sample preparation. Electronic spectra were recorded using Perkin Elmer Lambda-25 UV-Vis. spectrophotometer using methanol as solvent in the range of 200-1100 nm. The molar conductivity measurements of the metal complexes were carried out in $\sim 10^{-3}\text{M}$ methanol solutions using a Coronation digital conductivity meter. Magnetic susceptibility measurements were carried out by employing the Guoy's method at room temperature using copper sulphate as calibrant. The ^1H NMR was recorded on a JEOL GSX-400 spectrometer employing DMSO as solvent at ambient temperature. The mass spectral study was carried out using JEOL D-300 (EI) mass spectrometer. Wet chemical analyses for chloride ions were performed using standard methods. Antimicrobial screening of the ligand and the complexes were carried out using agar-well diffusion method.

Synthesis of Schiff base ligand

An equimolar methanolic solution of 4-aminoantipyrine (5 mmol) and cuminaldehyde (5 mmol) were mixed and gently heated for 2 hours with constant stirring. The characteristic pale yellow precipitate obtained was filtered out and recrystallized from methanol. Fine pale yellow crystals were obtained upon slow evaporation at room temperature. It was washed with alcohol, ether and dried in vacuum desiccator over anhydrous calcium chloride. The structure of the new Schiff base, cuminalidene-4-aminoantipyrine (Cumal-4-AAP), formed is given in Figure 1.

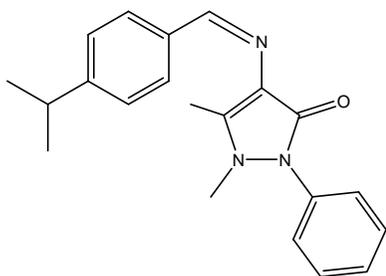


Figure 1. Proposed structure of the ligand

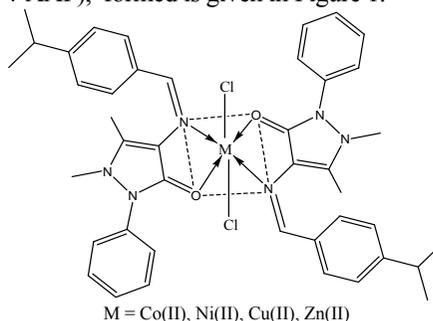


Figure 2. Proposed structure of metal complexes

Synthesis of Schiff base metal complexes

($M = \text{Co (II)}, \text{Ni (II)}, \text{Cu (II)}$ and Zn (II))

To the yellowish solution of 5 mmol of the ligand in 20 mL of methanol, a solution of metal(II) chloride (5 mmol) in 20 mL of aqueous methanol was added drop wise with constant stirring. The reaction mixture was refluxed for 2 h and the volume was reduced to half of the initial volume under reduced pressure. The precipitated metal complex was filtered, washed several times with cold ethanol, ether and then dried in vacuum over anhydrous CaCl_2 .

Antimicrobial activity

The antibacterial and antifungal activities of the synthesized Schiff base and its complexes with Co(II), Ni(II), Cu(II) and Zn(II) were studied by agar-well diffusion method using methanol as solvent. Amikacin, and Nystatin were used as standards. The antimicrobial studies were carried out against the bacterial strains *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella pneumonia*, *Proteus vulgaris* and fungal strains like *Candida albicans* and *Aspergillus niger*.

Results and Discussion

Structural characterization of the Schiff base (Cumal-4-AAP)

The structure of the ligand has been confirmed by the analytical and spectral data summarized in Table 1. The spectral data obtained for the ligand are furnished below.

Mass spectra

The mass spectrum of Cumal-4-AAP (Figure 3) shows a well-defined peak at $m/z = 333.18$, which coincides with formula weight of the Schiff base. The peak at $m/z = 667.39$ (100 %) can be attributed to dimeric structure of the Cumal-4-AAP. In addition, the spectrum of Cumal-4-AAP shows a series of peaks at $m/z = 115$ (3%) and 99(5 %) corresponding to its various fragments.

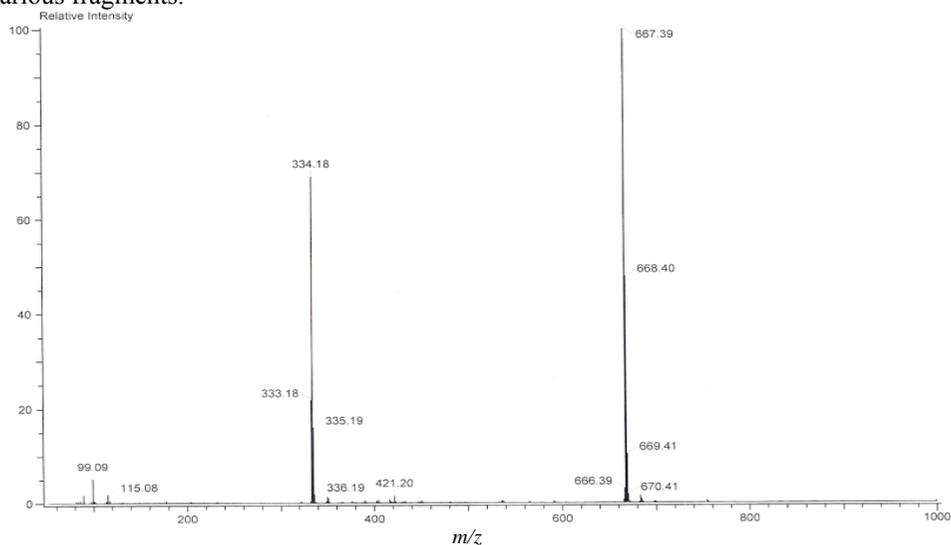


Figure 3. Mass spectrum of Cumal-4-AAP

¹H NMR spectra

The signal for azomethine proton (-CH=N-) in the ligand appears as a singlet at δ 9.556 ppm. The multiplet signals obtained in the range δ 7.0-8 ppm, is due to the aromatic protons of Schiff base ligand. The signal for the C-methyl proton (>C-CH₃) attached to pyrazolone ring appear as a singlet at 2.5 ppm, while the N-methyl protons (>N-CH₃) attached to pyrazolone ring appear as a singlet at δ 3.3 ppm. This down field shift is due to the methyl group attached to the more electronegative nitrogen atom and as a result the electron density around the methyl group is reduced. The isopropyl methyl protons appear as a doublet at 2.5 ppm. The ¹H NMR spectra of the ligand is given in Figure 4.

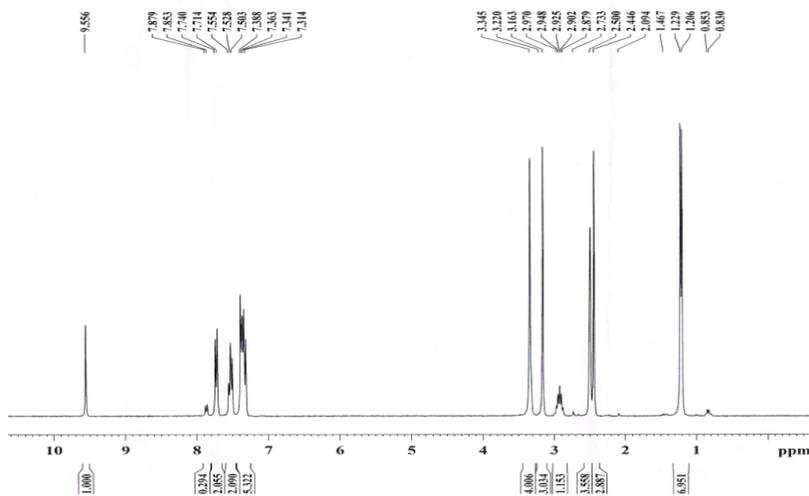


Figure 4. ^1H NMR spectrum of Cumal-4-AAP

FT-IR spectra

The infrared spectrum of the free cuminaldehyde (Figure 5) has a strong band at 1650 cm^{-1} , which corresponds to the $\nu(\text{CHO})$ and the infrared spectrum of 4-aminoantipyrine has strong bands at 3432 and 3328 cm^{-1} corresponding to the $-\text{NH}_2$ stretching frequency. On condensation these bands have disappeared and a new band appears at 1605 cm^{-1} , which is assigned to the $\nu(\text{C}=\text{N})$. This demonstrates the condensation between the aldehyde group in cuminaldehyde and amino group in 4-aminoantipyrine resulting in the formation of the Schiff base Cumal-4-AAP. Further, the spectrum of cumal-4-AAP shows the medium intensity band at 1223 cm^{-1} which can be assigned to $\nu(\text{C}-\text{N})$, and the strong band in the 1602 cm^{-1} region is assigned to aromatic ring $-\text{C}=\text{C}-$ stretching vibration. The other series of weak and strong bands between 3100 and 2800 cm^{-1} are related to $(-\text{C}-\text{H})$ modes of vibrations. The weak bands located between 2000 and 1750 cm^{-1} which can be assigned to overtones of the aromatic rings. In addition, several strong sharp bands at 2990 – 2940 cm^{-1} due to $\nu(\text{C}-\text{H})$ vibration of the isopropyl group have also been obtained. The mass, ^1H NMR and IR spectral data corresponds to the proposed structure of the ligand (*c.f.* Figure 1).

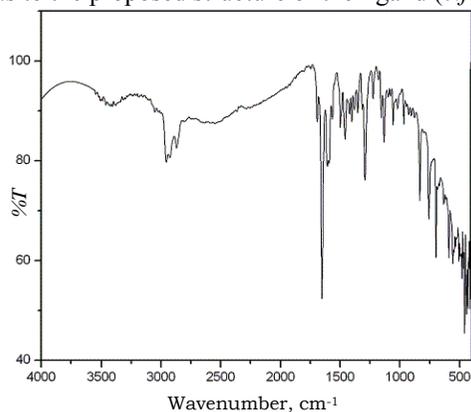


Figure 5. FT-IR spectrum of Cumal-4-AAP

Structural characterization of the metal complexes

The analytical and molar conductance data of Co(II), Ni(II), Cu(II) and Zn(II) complexes are provided in Tables 1 & 2. The conductance data⁶ indicate that all the metal complexes synthesized are non-electrolytes. The non-electrolytic nature of the metal complexes suggests that the anions of the salts have coordinated to the metal ions in the formation of metal complexes.

Table 1. Analytical and physical data of the complexes

Compounds	Empirical formula	Colour	Melting point	Mol. wt	Calcd.,%				
					C	H	N	O	M
Co(II)- Cumal-4-AAP	C ₄₂ H ₄₆ Cl ₂ N ₆ O ₂ Co	Green	200	796	63.32	5.82	10.55	4.02	7.40
Ni(II)- Cumal-4-AAP	C ₄₂ H ₄₆ Cl ₂ N ₆ O ₂ Ni	ellow	230	796	63.34	5.82	10.55	4.02	7.37
Cu(II)- Cumal-4-AAP	C ₄₂ H ₄₆ Cl ₂ N ₆ O ₂ Cu	Brown	210	01	62.95	5.79	10.49	3.99	10.49
Zn(II)- Cumal-4-AAP	C ₄₂ H ₄₆ Cl ₂ N ₆ O ₂ Zn	Yellow	115	803	62.81	5.77	10.46	3.98	8.14

Table 2. Molar conductance data

Complexes	Molar conductance, Ohm ⁻¹ cm ² mol ⁻¹	Nature
Co(II)-Cumal-4-AAP	17.6	Non-electrolyte
Ni(II)-Cumal-4-AAP	16.50	Non-electrolyte
Cu(II)-Cumal-4-AAP	9.0	Non-electrolyte
Zn(II)-Cumal-4-AAP	7.4	Non-electrolyte

FT-IR spectra

In order to study the binding mode of the Schiff base to the metal in the complexes, the IR spectrum of the free ligand was compared with those of the complexes (Figures 6a, 6b, 6c, 6d). The band at 1605 cm⁻¹ for the azomethine group of the ligand has been shifted to lower frequencies in the IR spectra of Co(II), Ni(II) and Cu(II) complexes (1599 cm⁻¹, 1595 cm⁻¹, 1599 cm⁻¹)⁷ and higher frequency in the spectrum of Zn(II) complex (1613 cm⁻¹) indicating the coordination of the azomethine nitrogen atom to metal. The sharp band at 1650 cm⁻¹ for ν (C=O) group of the free ligand has been shifted in the spectra of Co(II), Ni(II), Cu(II) and Zn(II) complexes (1644 cm⁻¹, 1655 cm⁻¹, 1657 cm⁻¹, 1661 cm⁻¹) indicating the linkage between the metal ion and carbonyl oxygen atom^{8,9}. The IR spectra of metal complexes also show some new bands in the 502 cm⁻¹ and 454-463 cm⁻¹ region, which is due to the formation of M-O and M-N bands¹⁰. The characteristic IR absorption bands of the ligand and its complexes are given in Table 3.

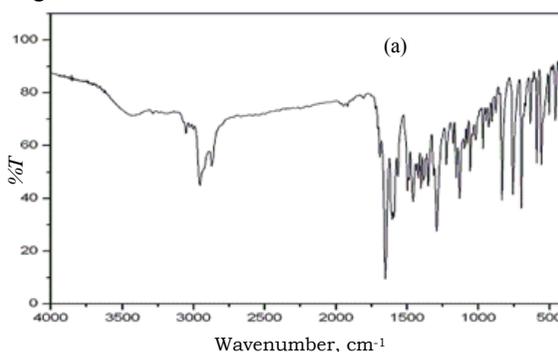


Figure 6a. FT-IR spectrum of Co(II)-Cumal-4-AAP complex

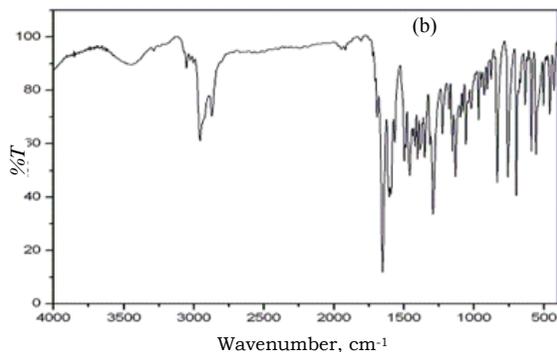


Figure 6b. FT-IR spectrum of Ni(II)-Cumal-4-AAP complex

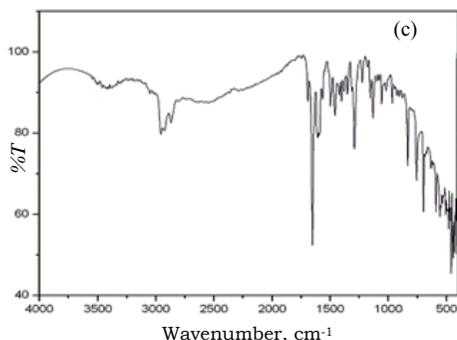


Figure 6c. FT-IR spectrum of Cu(II)-Cumal-4-AAP complexes

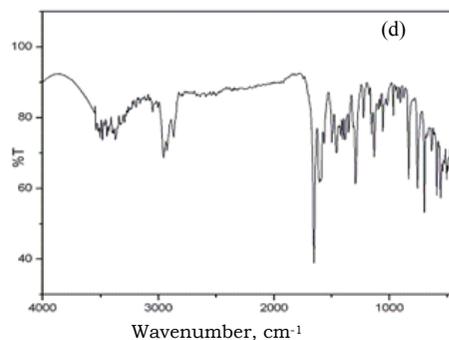


Figure 6d. FT-IR spectrum of Zn(II)-Cumal-4-AAP complexes

Table 3. FT-IR spectral data of Cumal-4-AAP and its complexes (cm^{-1})

Compounds	$\nu_{\text{azo.}}(\text{C}=\text{N})$	$\nu(\text{C}=\text{O})$	$\nu(\text{C}-\text{N})$	$\nu(\text{M}-\text{O})$	$\nu(\text{M}-\text{N})$
Cumal-4-AAP	1605	1650	1223	-	-
Co(II)-Cumal-4-AAP	1599	1644	1217	502	457
Ni(II)-Cumal-4-AAP	1595	1655	1230	502	463
Cu(II)-Cumal-4-AAP	1599	1657	1223	502	457
Zn(II)-Cumal-4-AAP	1613	1661	1231	502	454

Electronic spectra and magnetic moments

The colour, magnetic moments and electronic spectral data of the M (II)-Cumal-4-AAP complexes are summarized in Table 4. The spectrum of Co(II) complex (Figure 7a) exhibits transitions at 679 and 613 nm which may be assigned to ${}^4\text{T}_{1g}(\text{F}) \rightarrow {}^4\text{T}_{2g}(\text{F})$ and ${}^4\text{T}_{1g}(\text{F}) \rightarrow {}^4\text{A}_{2g}(\text{F})$ respectively, which indicate an octahedral geometry for the Co(II) complex which is also supported by the magnetic moment value (5.04BM) obtained for the complex. The Ni(II) complex (Figure 7b) shows three bands at ~ 1100 , 779 and 380 nm, respectively, due to the metal based transitions ${}^3\text{A}_{2g}(\text{F}) \rightarrow {}^3\text{T}_{2g}(\text{F})$, ${}^3\text{A}_{2g}(\text{F}) \rightarrow {}^3\text{T}_{1g}(\text{F})$ and ${}^3\text{A}_{2g}(\text{F}) \rightarrow {}^3\text{T}_{1g}(\text{P})$. This indicate octahedral orientation of donor centers around Ni(II) ion. The determined magnetic moment value (3.11 BM) also supports the same. The Cu(II) complex (Figure 7c) exhibits a broad absorption at 700 nm and a weak shoulder at 380 nm. This is due to d-d transitions, which corresponds to the ${}^2\text{E}_g \rightarrow {}^2\text{A}_{1g}$ and ${}^2\text{E}_g \rightarrow {}^2\text{B}_{1g}$ transitions. This predicts distorted octahedral geometry for the Cu(II) complex and it is further supported by the

observed magnetic moment value of 1.99 BM. Zn(II) complexes could not exhibit any d-d electronic transitions due to its completely filled d^{10} electronic configuration. The proposed structure of the metal complexes is given in Figure 2.

Table 4. Electronic spectral data of M(II)-Cumal-4-AAP complexes

Complexes	Absorption maxima, nm	Transition assignment	Magnetic moment B.M	Geometry
Co(II)-Cumal-4-AAP	679	${}^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$	5.04	Octahedral
	613	${}^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)$		
Ni(II)-Cumal-4-AAP	1100	${}^3A_{2g}(F) \rightarrow {}^3T_{2g}(F)$	3.11	Octahedral
	779	${}^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)$		
	380	${}^3A_{2g}(F) \rightarrow {}^3T_{1g}(P)$		
Cu(II)-Cumal-4-AAP	700	${}^2E_g \rightarrow {}^2A_{1g}$	1.99	Square planar

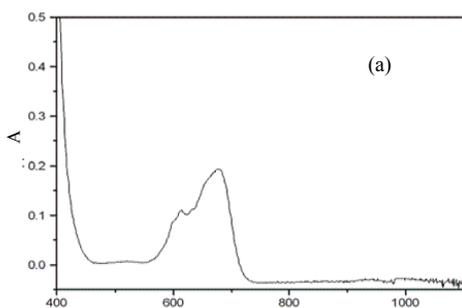


Figure 7a. Electronic spectrum of Co(II)-Cumal-4-AAP complex

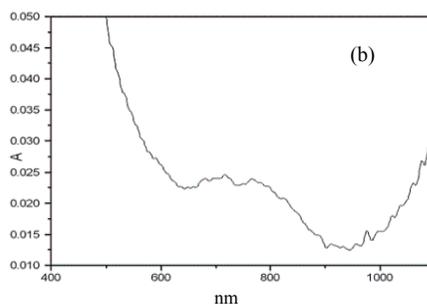


Figure 7b. Electronic spectrum of Ni(II)-Cumal-4-AAP complex

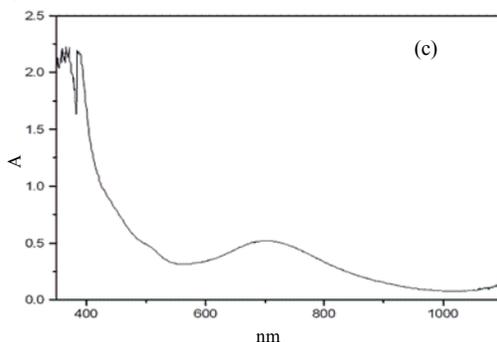


Figure 7c. Electronic spectrum of Cu(II)-Cumal-4-AAP complex

Antimicrobial activity

The antibacterial and antifungal activities of the Cumal-4-AAP and their complexes have been screened for their *in vitro* antibacterial activity against *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumonia*, *Proteus vulgaris*, *Candida albicans* and *Aspergillus niger*. The zones of inhibition produced by the test compounds are presented in Table 5. It is observed that the metal complexes possess higher growth inhibition potential compared to that of the ligand. It is suggested that the complexes having antibacterial and antifungal activities inhibit multiplication process of the microbe by blocking their active sites.

Table 5. Antimicrobial activity results of the Cumal-4-AAP and its complexes

Compound	Inhibition zone, $\mu\text{g/mL}$							
	Bacteria species				Fungi species			
	Control	<i>S.aures</i>	<i>E.coli</i>	<i>K.sps</i>	Control	<i>P.sps</i>	<i>C.sps</i>	<i>A.sps</i>
Cumal-4-AAP	10	10.2	-	12.0	12	-	-	-
Co(II)-Cumal-4-AAP	15	14.3	11.2	-	15	10.5	12.5	-
Ni(II)-Cumal-4-AAP	20	-	-	12.5	12	-	10.5	9.8
Cu(II)-Cumal-4-AAP	15	12.5	12.5	12.2	18	-	11.5	10.5
Zn(II)-Cumal-4-AAP	18	-	10.2	10.2	8	12.5	10.2	-

S.aures=*Staphylococcus aureus*; *E.coli*=*Escherichia coli*; *K.sps*= *Klebsiella pneumonia*; *P.sps* =*Proteus vulgaris*; *C.sps* =*Candida albicans*; *A.sps* =*Aspergillus nigers*

The mechanism of higher toxic activity of the complexes compared to those of the ligands can be ascribed to the increase in the lipophilic nature of the complexes arising from chelation¹¹. Chelation reduces the polarity of the metal atom mainly because of partial sharing of its positive charge with the donor groups and possible π electron delocalization within the whole chelate ring. The chelation also increases the lipophilic nature of the central metal atom, which subsequently favours the permeation through the lipid layer of cell membrane¹². The mode of action of complexes involves the formation of hydrogen bonds with the imino group by the active sites leading to interference with the cell wall synthesis. This hydrogen bond formation damages the cytoplasmic membrane and the cell permeability may also be altered leading to cell death.

Conclusion

Schiff base of 4-aminoantipyrene and Cuminaldehyde and its transition metal complexes with Co(II), Ni(II), Cu(II) and Zn(II) were synthesized. The ligand and its complexes were characterized by the analytical and spectral techniques. The antimicrobial activity of the ligand and its complexes were studied with bacterial strains like *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella pneumonia*, *Proteus vulgaris*, and fungal strains like *Candida albicans* and *Aspergillus niger*, employing agar-well diffusion method. Both the Schiff base as well as its complexes possess significant antimicrobial activity.

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