
Research Article

Theme- New horizons in chemical sciences.

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A novel Schiff base of 3-formyl-6-methylchromone and 3-aminoquinoline and its Cu(II) and Co(II) complexes: Synthesis, characterization and Antimicrobial screening studies.

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ABSTRACT

A novel Schiff base 6-methyl-3-((quinolin-3-ylimino) methyl)-4H-chromen-4-one obtained by the condensation of 3-formyl-6-methylchromone and 3-aminoquinoline and synthesis of its Cu (II) and Co (II) complexes. Schiff base and its complexes have been characterized by analytical data, elemental analysis, molar conductance, magnetic moment and thermogravimetric analysis. The structural elucidation of prepared compounds carried out by UV-Visible, infrared ¹HNMR spectroscopic techniques. The elemental analysis revealed metal to ligand stoichiometry was 1:2. Spectroscopic studies and magnetic moment data interpret octahedral geometry of the complexes. The measured low molar conductance values in DMF indicate that complexes are non-electrolyte. The synthesized compounds were evaluated by in vitro antimicrobial analysis and results were compared with standard tetracycline. Schiff base and its metal complexes shown remarkable antibacterial and antifungal activity.

KEYWORDS

Schiff base, Antimicrobial activity, 3-aminoquinoline, 3-formyl-6-methylchromone.

1. INTRODUCTION

Development of coordination chemistry happens through the synthesis of newly emerged Schiff base and its transition metal complexes. Chromones are a group of naturally existing compounds that have immanent in nature especially in plants [1-3]. Molecules containing the chromone structure receive considerable attention of chemist due to their biological and physiological activities. Compounds contain chromone moiety show wide range of biological activities. Chromones derivatives exhibit biological and pharmaceutical importance such as anticancer, neuroprotective, HIV-inhibitory, antimicrobial, antifungal and antioxidant activity [4-12]. In the present work, we have synthesized novel ligand from 3-formyl-6-methylchromone and 3-aminoquinoline and its complexes with Cu(II) and Co(II) metal ion. Ligand and its complexes are characterized by IR, NMR, UV, elemental analysis. Thermogravimetric analysis. Emphasis has been put on biological evaluation of the complexes.

2. MATERIALS AND METHODS

2.1. Materials

3-aminoquinoline, 3-formyl-6-methylchromone, Copper chloride dihydrate, cobalt chloride hexahydrate and solvent used were AR grade.

2.2. Physical measurement

Molar conductance of the complexes was measured in DMF at 1×10^{-3} M using Elico CM-180 conductometer. Elemental analysis (CHN) was carried out using Thermo finnigan, Italy CHN analyzer. Thermal analysis carried out on a Perkin Elmer USAA TGA instrument at heating rate $10^{\circ}\text{C}/\text{min}$ and temperature range 30°C to 1150°C . The IR spectra ($4000\text{-}400\text{ cm}^{-1}$) in KBr disc were recorded on Bruker, Germany spectrophotometer. The NMR spectra were carried out by mercury plus 300 MHz NMR spectrometer, using TMS as internal standard. Electronic spectra were measured by using Shimadzu UV-160A spectrophotometer. The magnetic moment data obtained by Gouy-type magnetic balance at room temperature using $\text{Hg}[\text{Co}(\text{NCS})_4]$ as calibrant.

2.3. In vitro antimicrobial studies

The antibacterial and antifungal activity of Schiff base ligand and its Cu(II) and Co(II) complexes towards the bacteria *Klebsiella pneumoniae*, *Staphylococcus aureus* and *Proteus vulgaris* and fungi *Candida albicans* and *Aspergillus niger* was carried out at different concentration by using minimum inhibitory concentration (MIC) method and disc diffusion method. The assay was performed in flat bottom 96 well plate. 1st column was used as negative control while second column onward the test drug was added. Initially in second column $2 \times$ Muller Hinton broth (100 μl) was added while 3rd column onwards $1 \times$ Muller Hinton broth (100 μl) was added. Now 4000 ppm (100 μl) concentration of drug was added in second column the drug was mixed properly in order to achieve final concentration of 2000 ppm and now 100 μl of solution from second column was taken out and added into 3rd column in order to achieve the 2-fold dilution. Finally, 100 μl of culture was added to achieve 1.5×10^6 cell/ml in each well. Similarly, in the 1st row the culture along with diluent and $1 \times$ Muller Hinton broth was added. The plates were for incubation and after 24 hours, 5 μl resazurin (6.75 mg ml^{-1}) was added to all

wells and incubated at 37°C for another 24 hours. Change of colour was observed and recorded. The lowest concentration prior to colour change was considered as Minimum Inhibitory Concentration (MIC). The culture equivalent to 10⁶ cells was added to molten agar and was poured in sterile petri dish and kept for solidification. Wells were made and samples were added in each well. DMSO and tetracycline was used as negative and positive control respectively. Plates were incubated at 37°C for 24 hours. The zone of clearance was considered for antibacterial activity and was measured in mm.

2. 4. Synthesis of ligand

The Synthesis of Schiff base (L) was carried out by refluxing hot ethanolic solution of 3-formyl-6-methylchromone (10 mmol, 1.88 gm) in 40 ml of alcohol and 3- aminoquinoline (10 mmol, 1.44 gm) in 15 ml of alcohol. The reaction mixture was refluxed for 5 hours. The progress of reaction was monitored by TLC. The resulting yellow coloured product precipitated, filtered off and washed with ether. The product thus obtained was recrystallized from ethanol [13].

2.5. Synthesis of the complexes

A hot ethanolic solution of ligand (10 mmol, 3.14 gm) was added to ethanolic solution CuCl₂·2H₂O (5 mmol, 0.85 gm) and CoCl₂·6H₂O (5 mmol 1.18 gm). The resulting reaction mixture was refluxed for 4-5 hours. After cooling, the coloured precipitate obtained was collected, filtered, washed with ether, recrystallized from ethanol and dried in vacuum.

3. RESULTS AND DISCUSSION

The colour of Schiff base ligand is yellow and it is soluble in chloroform. The solubility of Cu (II) and Co(II) complexes are in DMF and DMSO solvent. The complexes are stable in air and atmosphere. Interpretation of elemental analysis shown that metal to ligand ratio is 1:2 in both the complexes. The lower values of conductivity measurements indicate neutral nature of the complexes. The analytical, elemental, physical, molar conductance data and magnetic moment values are shown in table 1.

3.1. IR spectral data

IR spectral data of Schiff base and its complexes are given in table 2. In the IR spectrum of ligand, the band at 1598 cm⁻¹ shows azomethine formation. On complexation, this azomethine band was shifted to lower wave number by 16-39 cm⁻¹ [14]. The $\nu(\text{C}=\text{O})$ of chromone system of the ligand appear in the region of 1650-1620 cm⁻¹, while in their Cu(II) and Co(II) complexes the band is shifted to lower wave number by 6-40 cm⁻¹[14,15]. Furthermore, evidence for the presence of coordinated water shown by the broad band in the range of 3500-3400 cm⁻¹[16,17]. The spectral band observed in the spectral range of 600-400 cm⁻¹ corresponds to $\nu(\text{M}-\text{O})$ and $\nu(\text{M}-\text{N})$ vibrations respectively [18]. Thus the IR data suggest that Schiff base ligand (Fig. 1) in reported complexes is bidentate and metal ion (Cu(II) and Co(II)) coordinated by azomethine nitrogen and carbonyl oxygen of chromone moiety of ligand. The position in the coordination sphere would be completed by water molecule.

3.2. ¹HNMR spectra

The ¹HNMR spectrum of ligand recorded in chloroform-d₆ and its Ni(II) and Fe(III) metal complexes recorded in DMSO-d₆. The spectrum of ligand shows following signals: 8.07 ppm (H, S, -HC=N- azomethine proton); 2.35 ppm (3H, S, -CH₃ protons); 6.9-7.9 ppm (m, aromatic protons of chromone nucleus); 7.6-8.9 ppm (m, aromatic protons of quinolone nucleus). However, in metal complexes the NMR signal of azomethine proton shifted to downfield as compared to NMR signal of azomethine proton in Schiff base [19]. In Cu(II) and Co(II) complexes resonance signal for azomethine proton at 8.31 ppm and 8.27 ppm respectively. Thus there is confirming the metal complex formation.

3.3. Electronic spectra and magnetic moment

The geometry of Cu(II) and Co(II) complexes was predicted from electronic spectra. The electronic spectra of ligand show two bands, one band at 23310 cm⁻¹ is attributed to the n→π* transition. Another band at 32258 cm⁻¹ is due to the π→π* transition [20]. The electronic spectra of Cu(II) complex exhibit bands at 11337 cm⁻¹, 14598 cm⁻¹ and 21598 cm⁻¹ are assigned to ²B_{1g} → ²B_{2g}, ²B_{1g} → ²E_g and LMCT transitions, respectively. These bands are characteristic for distorted octahedral geometry. Octahedral geometry of Cu (II) complex was also confirmed by magnetic moment value (1.78) [21-22]. The electronic spectra of Co(II) complex shown three bands at 8620 cm⁻¹, 15011 cm⁻¹ and 18621 cm⁻¹ are assignable to ⁴T_{1g} (F) → ⁴T_{2g} (F) (ν₁), ⁴T_{1g} (F) → ⁴A_{2g} (F) (ν₂), and ⁴T_{1g} (F) → ⁴T_{1g} (P) (ν₃) transitions, respectively, characteristic of octahedral geometry. Octahedral geometry of Co (II) complex was also confirmed by magnetic moment value (3.87) [21,22].

3.4. Antimicrobial activity

All synthesized compounds were screened for their antibacterial activities against two gram-negative i.e. *Klebsiella pneumoniae* and *Proteus vulgaris* and one gram-positive i.e. *Staphylococcus aureus*. Also screened for antifungal activities against fungi *Candida albicans* and *Aspergillus niger*. MIC (ppm) and zone of inhibition values for antimicrobial activity of the ligand and its Cu (II) and Co (II) complexes were shown in table 3. Schiff base and its complexes showed a varying degree of activity against respective organisms. Schiff base and its complexes found to be significantly active against all organisms at 1000 ppm and 2000 ppm. Schiff base showed good activity against *P. vulgaris*, *C. albicans* and *A. niger*. Cu (II) complex revealed significant activity against *K. pneumoniae*, *P. vulgaris* and *C. albicans*. Co (II) complex displayed significant activity against *K. pneumoniae*. Co (II) complex shown better activity than Cu (II) complex against *A. niger*. Cu (II) and Co (II) complexes demonstrated significant activity when compared with standard tetracycline at 2000 ppm against *A. niger*. There are also other factors which increase the activity are solubility, conductivity, and bond length between metal and ligand [23,24,25].

3.5. Thermogravimetric analysis

Thermogravimetric analysis carried out for [Cu(L)₂(H₂O)₂] and [Co(L)₂(H₂O)₂] complexes, the range of heating was 30⁰C to 1150⁰C and heating rate was 10⁰C/min. TG curves are shown in figure 2 and 3. Interpretation of thermal data is given in table no 4. Copper complexes,

[Cu(L)₂(H₂O)₂] decomposed in three step, in first step complex undergo decomposition with weight loss of 5.11 corresponds to two water molecules in the temperature range between 30⁰C and 130⁰C. In the second step, quinolone nucleus with azomethine group undergoes decomposition with weight loss 41.10 in the temperature range of 131⁰C and 730⁰C. In the third step complex decomposes gradually with remaining ligand moiety i.e. chromone nucleus and CuO with weight loss 53.78 in the temperature range greater than 731⁰C [26]. TGA studies of Co(II) complex shown three decomposition step. In the first step decomposition at 30⁰C to 120⁰C corresponds to the loss of two water molecules with weight loss 6.13. The second step of decomposition start from 121⁰C to 760⁰C corresponds to chromone nucleus with weight loss 41.98 and in third step temperature greater than 761⁰C shown decomposition of remaining ligand moiety and CoO residue with final weight loss 51.88 [26].

4. CONCLUSION

The Schiff base complexes of Cu (II) and Co (II) obtained from 6-methyl-3-((quinolin-3-ylimino) methyl)-4H-chromen-4-one was synthesized and characterized on the basis of analytical and spectral data. IR spectra revealed coordination of Schiff base ligand with metal ion through azomethine nitrogen and carbonyl oxygen of chromone moiety. The structural elucidation studies by various spectral techniques (IR, UV-Visible, and NMR) suggested the nature of ligand is bidentate and octahedral geometry of the metal complexes. Thermogravimetric analysis studies demonstrate the stability of complexes as well as provided the number of coordinated water molecules. Antimicrobial activity was studied by minimum inhibitory concentration (MIC) method and disc diffusion technique. Antimicrobial studies suggest that Schiff base and its complexes play a vital role in developing a new class of antibiotics.

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6. REFERENCES

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Table 1. Physical, analytical, molar conductivity data and magnetic moment of Schiff base and Cu (II) and Co (II) complexes.

Compounds	Colour (%Yield)	M.P. (⁰ C)	% Found				Molar Cond. (ohm ⁻¹ cm ² mol ⁻¹)	μ _{eff} (BM)
			C	H	N	M		
L	Yellow (78)	215	76.91 (76.41)	4.06 (4.45)	7.47 (8.90)	—	7	—
[Cu(L) ₂ (H ₂ O) ₂]	Parrot	295	65.13	3.15	6.70	8.61	13	1.78

	Green (81)		(65.96)	(4.39)	(7.68)	(8.72)		
[Co(L) ₂ (H ₂ O) ₂]	Green (79)	226	66.93 (66.38)	3.66 (4.42)	6.32 (7.73)	8.47 (8.14)	10	3.87

Table 2. IR spectral data of ligand and its metal complexes.

Compound	$\nu(\text{C}=\text{N})$	$\nu(\text{C}=\text{O})$	$\nu(\text{M}-\text{O})$	$\nu(\text{M}-\text{N})$
L	1598 cm ⁻¹	1650 cm ⁻¹	-	-
[Cu(L) ₂ (H ₂ O) ₂]	1572 cm ⁻¹	1614 cm ⁻¹	470 cm ⁻¹	537 cm ⁻¹
[Co(L) ₂ (H ₂ O) ₂]	1550 cm ⁻¹	1615 cm ⁻¹	485 cm ⁻¹	535 cm ⁻¹

Table 3. MIC (ppm) and zone of inhibition values for antimicrobial activity of the ligand and its Cu(II) and Co(II) complexes.

Micro.	L diameter of zone of inhibition (mm)				[Cu(L) ₂ (H ₂ O) ₂] diameter of zone of inhibition (mm)				[Co(L) ₂ (H ₂ O) ₂] diameter of zone of inhibition (mm)				Std.
	250 pp m	500 ppm	1000 ppm	2000 ppm	250 ppm	500 ppm	1000 ppm	2000 ppm	250 ppm	500 ppm	1000 ppm	2000 ppm	
K. pneumoniae	9	12	13	15	6	9	13	17	6	10	14	18	18
S. aureus	8	10	12	16	7	9	13	17	3	6	10	13	16
P. vulgaris	12	14	16	18	6	8	12	16	5	9	13	16	19
C. albicans	10	16	18	20	7	10	13	15	4	7	11	14	14
A. niger	8	10	15	17	3	5	9	13	5	8	11	15	12

Table 4. Thermal data of complexes.

Complex	Temperature (°C)	Weight loss (calc. %)	found	Assignment
[Cu(L) ₂ (H ₂ O) ₂]	25-130	5.11(4.94)		2H ₂ O
	131-730	41.10(42.60)		C ₂₀ H ₁₄ N ₄
	>731	53.78(52.45)		C ₂₀ H ₁₄ O ₃ and CuO
[Co(L) ₂ (H ₂ O) ₂]	30-120	6.13(4.97)		2H ₂ O
	121-760	41.98(41.78)		C ₂₀ H ₁₄ O ₃
	>761	51.88(53.24)		C ₂₀ H ₁₄ N ₄ and CoO

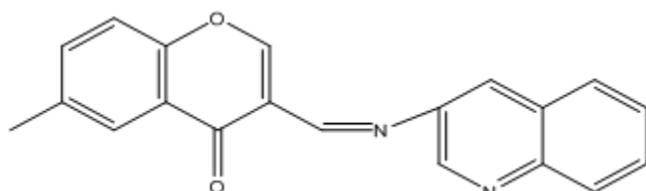


Fig. 1. Structure of ligand (L)

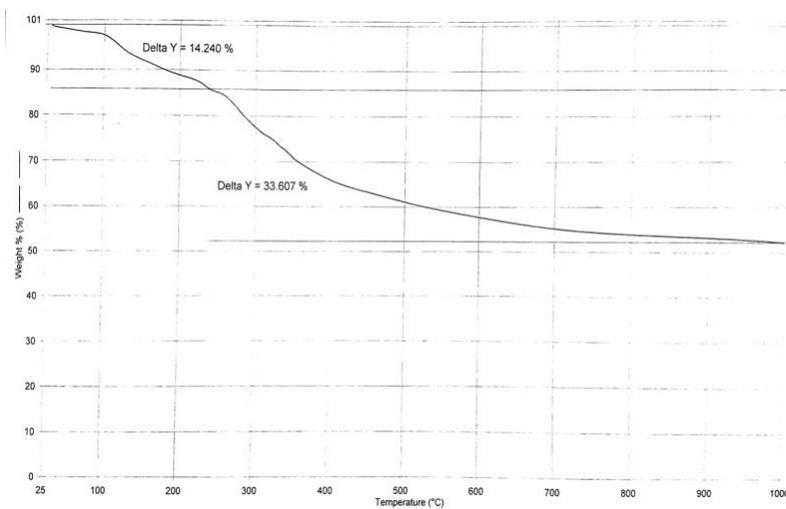


Fig. 2.TGA graph of Cu(II) complex.

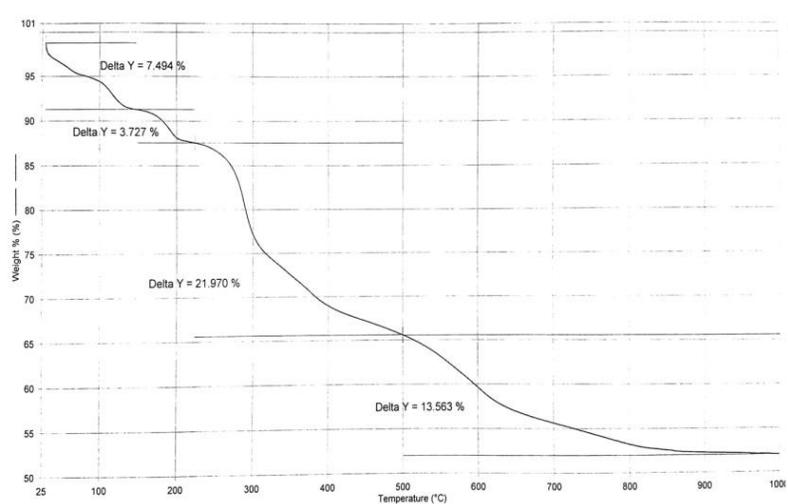
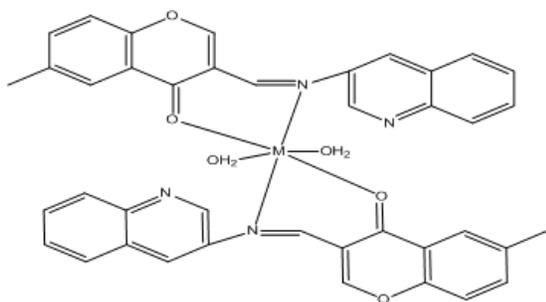


Fig. 3.TGA graph of Co(II) complex.



M = Ni(II) and Fe(III)

Fig. 4.Proposed structure of complexes.