

Synthesis, Characterization, Antimicrobial and Cytotoxic Activities of Copper(II) Isocyanate Complex of Schiff Base

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In this paper, Schiff base ligand using acetyl acetone, *o*-phenylenediamine and salicylaldehyde and its copper complex have been synthesized using self-assembly method. The ligand and its copper(II) complex were characterized by spectroscopic techniques. The antimicrobial studies are carried out for ligand and its copper complex, which confirmed that copper complex does not show any activity against bacteria as well as fungal organisms. However, the cytotoxic studies showed that copper complex has good anticancer activity against MCF-7 (breast cancer) cell line.

Keywords: Copper complex, Acetyl acetone, *o*-Phenylenediamine, Salicylaldehyde, Antimicrobial activity, Cytotoxic activity.

INTRODUCTION

The copper metal is an essential micro nutrient for feeding and a co-factor of several enzymes involved in oxidative metabolism like β -hydroxylases, quercetinase, ceruloplasmine, cytochrom oxidase, Mono amine oxidize, super oxy dismutase, ascorbic acid oxidize and tyrosinase [1-3]. The analytical role of these enzymes is a two-step process, *i.e.* the reduction of Cu^{2+} ion to Cu^+ and the fixation of molecular oxygen [4]. The routine copper(II) complex shows better activity as antioxidants and anti free radical agents than free routine [5,6]. The copper(II) complexes of multidentate Schiff base ligands plays a key role in the development of coordination chemistry [7-9]. Di nuclear copper complexes have further fascinated a much attention as to correlate the spin-spin interaction between the two metal centers and the stereochemistry of the complexes [10,11]. The dinuclear copper complexes which imitate the 'type 3' active site of copper proteins were examined extensively with studies of magnetic interactions, ligand surroundings and oxygen acceptance of these active sites [12-17].

EXPERIMENTAL

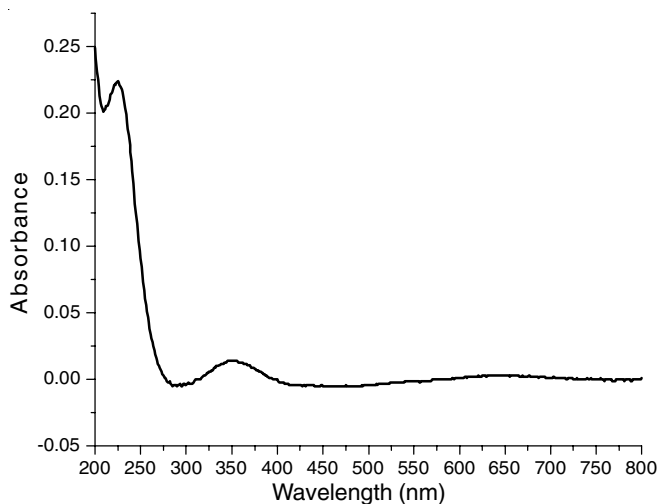
IR spectrum is obtained with a Bruker-alpha-T FT-IR spectrophotometer. UV spectrum is recorded on systronics 2700R UV spectrophotometer. LC-MS Spectrum is taken on Agilent Triple Quad (LC-MS/MS) mass spectrometer. Proton NMR spectrum is recorded on Bruker-Ascend (400).

Synthesis of $[(\text{Cu})_2(\text{OH})(\text{SAL})_2(\text{OPD})_2(\text{AA})_2(\text{NCO})_2]\cdot\text{ClO}_4$:
A solution of Schiff's base (0.5 mmol, 0.156 g) is dissolved in

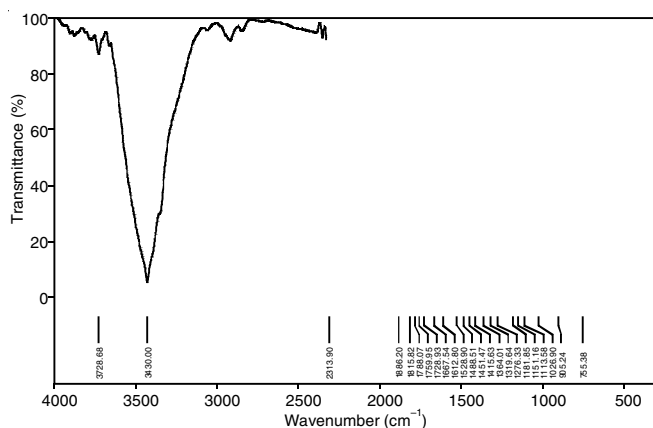
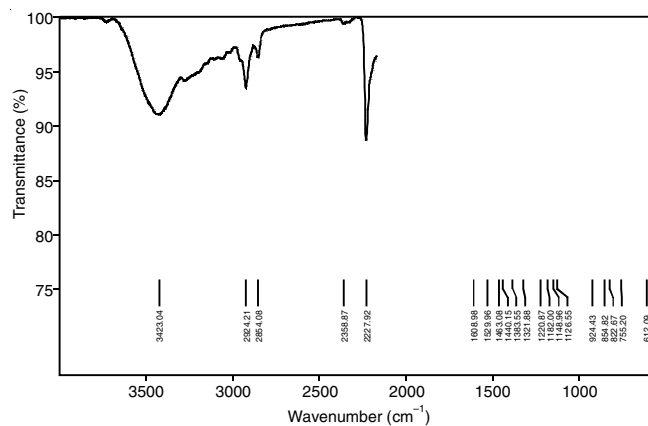
10 mL of hot methanol is added to a solution of copper perchlorate (0.5 mmol, 0.185 g) is dissolved in 10 mL of water, instantly a royal crown coloured solution is appears. To this, a solution of sodium isocyanate (0.5 mmol, 0.032 g) is dissolved in 10 mL of water is added, a dark green coloured precipitate is obtained after 1 h on constant stirring at room temperature. Anal. exptal. $\text{C}_{40}\text{H}_{36}\text{O}_5\text{N}_6\text{Cu}_2$ (m.w. 825.86) C, 58.17; H, 4.64; N, 10.18. Found: C, 57.92; H, 4.21; N, 8.92. IR (KBr disk, cm^{-1}): 3300, 3500, 2227, 1700, 1606, 1276, 1250, 1250, 924. Mass peaks (m/z): 377, 273, 211, 475, 317, 141, 652, 776, 890; m.p. 321 °C; Yield; 0.219 g (60 %).

RESULTS AND DISCUSSION

Electronic spectrum of $[(\text{Cu})_2(\text{OH})(\text{SAL})_2(\text{OPD})_2(\text{AA})_2(\text{NCO})_2]\cdot\text{ClO}_4$: The electronic absorption spectra of the copper(II) complex is recorded in DMF in the range 200-800 nm. The electronic spectrum of free Schiff base revealed three bands around 240, 350 and 450 nm characteristic of $\pi\text{-}\pi^*$ and $n\text{-}\pi^*$ transitions (Fig. 1). In the metal complex, this band is shifted to a longer wavelength with increasing intensity. This shift may be attributed to the donation of lone pair of electrons of oxygen of Schiff base to metal ion. The copper complexes exhibits bands around 255-300 nm, 350-355 nm and 477-498 nm. The broad intense and poorly resolved bands around 350-355 nm may be assigned to LMCT or MLCT. The high intensity band around 250 nm is of ligand cause assignable to intra ligand $n\text{-}\pi^*$ or $\pi\text{-}\pi^*$ transition [18]. The complexes exposed shoulder broad bands in the range of 300-325 nm may be assigned to the $d\text{-}d$ transition.

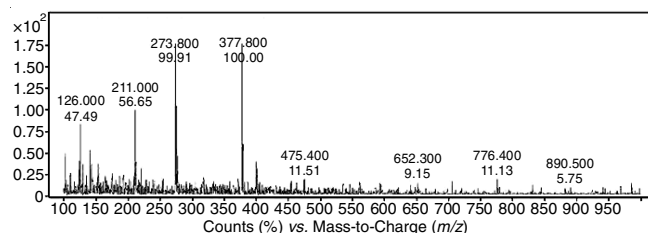
Fig. 1. Electronic spectrum of $[(\text{Cu})_2(\text{OH})(\text{SAL})_2(\text{OPD})_2(\text{AA})_2(\text{NCO})_2]\cdot\text{ClO}_4$

IR spectrum of $[(\text{Cu})_2(\text{OH})(\text{SAL})_2(\text{OPD})_2(\text{AA})_2(\text{NCO})_2]\cdot\text{ClO}_4$: The solid-state FT-IR spectrum of the complex is analyzed with its structural data as revealed from X-ray studies. In the IR spectrum of Schiff base (Fig. 2) a sharp band observed at 1612 cm^{-1} is dispersed to the $\nu(\text{C}=\text{N})$ mode of the azomethine group. A sharp band observed at 1612 cm^{-1} is assigned to the $\nu(\text{C}=\text{N})$ mode of the azomethine group. This shift is unaltered in the complex 1612 cm^{-1} suggesting the uncoordination of azomethine nitrogen to the metal centers [19]. The characteristic phenolic $\nu(\text{O}-\text{H})$ mode due to presence of a hydroxyl group at ortho position in the ligand was observed around $3500\text{--}3246\text{ cm}^{-1}$. The appearance of a new band around $543\text{--}440\text{ cm}^{-1}$ in the complexes due to $\nu(\text{Cu}-\text{O})$ bond formation [20] (Fig. 3). A strong sharp band observed at 1720 cm^{-1} is due to $\nu(\text{C}=\text{O})$ of acetyl acetone ligand. The intensity of this band has not only condensed but has shifted to lower wave numbers in the copper(II) complex confirming the contribution of the carbonyl group in complexation with Cu^{2+} ion [21]. The incidence of coordinated water in the copper complex is inveterate by the presence of bands around $928\text{--}875\text{ cm}^{-1}$ [22]. There is a single band at 3680 cm^{-1} , signifying the presence of hydroxide group [23]. The weak broad bands in the region $3746\text{--}3423\text{ cm}^{-1}$ due to hydrogen bonded OH group. This indicates that the phenolic oxygen atoms present in the Schiff bases are coordinated to the metal centers. The strong $\nu(\text{C}=\text{N})$ bands occurring in the range of $1617\text{--}1611\text{ cm}^{-1}$ are shifted slightly toward lower

Fig. 2. IR spectrum of free Schiff's base $[(\text{SAL})(\text{OPD})(\text{AA})]$ Fig. 3. IR spectrum of complex $[(\text{Cu})_2(\text{OH})(\text{SAL})_2(\text{OPD})_2(\text{AA})_2(\text{NCO})_2]\cdot\text{ClO}_4$

frequency 1607 cm^{-1} compared to the free Schiff base indicating the un coordinated azomethine nitrogen atom to the metal center. The (CN) absorption at 2115 cm^{-1} as a single peak suggests the presence of N-coordinated terminal isocyanate group. (NCO) appears at 2227 cm^{-1} as a single peak indicating the presence of terminal cyanate ion coordination to the metal center.

LC-MS spectrum of $[(\text{Cu})_2(\text{OH})(\text{SAL})_2(\text{OPD})_2(\text{AA})_2(\text{NCO})_2]\cdot\text{ClO}_4$: The peak at 776 (m/z) in complex bound to two copper, two salicylaldehyde, two opd, two acetyl acetone, one isocyanate, two water molecules and one perchlorate $[(\text{Cu})_2(\text{SAL})_2(\text{OPD})_2(\text{AA})_2(\text{NCO})(\text{H}_2\text{O})(\text{ClO}_4)]$ complex. The peak at 652 (m/z) suggested two copper, one salicylaldehyde, two opd two acetyl acetone and one isocyanate $[(\text{Cu})_2(\text{SAL})(\text{OPD})_2(\text{AA})_2(\text{NCO})]$. The base peak at 377 (m/z) is complex, assured to one copper one salicylaldehyde and one opd, one acetyl acetone and one water molecules $[\text{Cu}(\text{SAL})(\text{OPD})(\text{AA})(\text{H}_2\text{O})]$. The peak at 273 (m/z) is suggested that one salicylaldehyde, one opd and one copper $[\text{Cu}(\text{SAL})(\text{OPD})]$ peaks at 211 (m/z) , 126 (m/z) , refers to the $[(\text{SAL})(\text{OPD})]$, $[(\text{SAL})(\text{H}_2\text{O})]$, respectively (Fig. 4).

Fig. 4. LC-MS spectrum of complex $[(\text{Cu})_2(\text{OH})(\text{SAL})_2(\text{OPD})_2(\text{AA})_2(\text{NCO})_2]\cdot\text{ClO}_4$

^1H NMR spectrum of $[(\text{Cu})_2(\text{OH})(\text{SAL})_2(\text{OPD})_2(\text{AA})_2(\text{NCO})_2]\cdot\text{ClO}_4$: The NMR spectra of the Schiff base are examined. It was found that the N-CH signal appeared in the spectrum of the ligand at $8.85\text{--}8.96\text{ ppm}$, is appeared in the spectrum of its $\text{Cu}(\text{II})$ complex, indicating that the presence of azomethine group in the complex. Signal at 5.45 ppm indicating the active methylene groups of acetyl acetone, moreover, signal observed at 2.5 ppm indicating the free methyl groups of acetyl acetone.

Antimicrobial screening of $[(\text{Cu})_2(\text{OH})(\text{SAL})_2(\text{OPD})_2(\text{AA})_2(\text{NCO})_2]\cdot\text{ClO}_4$: The complex is screened *in vitro* for antibacterial activity against *E. coli*, *B. subtilis* and antifungal activity against *A. niger* by Agar-well diffusion method [23–26].

The results showed that Schiff's base copper complex didn't show any antimicrobial activity.

Cytotoxic studies of [(Cu)₂(OH)(SAL)₂(OPD)₂(AA)₂(NCO)₂·ClO₄· The synthesized complex is screened for its cytotoxicity (MCF-7, cell lines). It is observed that the complex displayed the cytotoxic activities (Table-1) as IC₅₀ (µg/mL) against breast cancer MCF-7.

TABLE-1
IC₅₀ VALUES OF SCHIFF BASE COMPLEX

Conc. (µg/mL)	Cell survival (%)	Cell inhibition (%)
0.1	91.56288	8.437123
1	90.71916	9.280836
10	74.96987	25.03013
100	9.963841	90.03616

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