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Copper Schiff Base Complex and its Antimicrobial and Anticancer Activities

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ABSTRACT

Schiff base ligands are synthesized from the condensation of an amino compound with aldehyde compounds and these coordinate to metal ions via azomethine nitrogen Schiff's base and their copper chelates possess remarkable properties as initiators in various biological systems, polymers, dyes, antimicrobial activities, antiviral activities, insecticides, cytotoxic activities, plant growth regulator, enzymatic activity and Pharmaceutical fields. A variety of Schiff's base and its chelates have been studied extensively. Several model systems, including those with bidentate, tridentate, tetra dentate, multidentate Schiff base ligands, and their coordination chemistry of copper and other metals attracts much attention due to its biological relevance and its interesting coordination chemistry such as geometry, flexible redox property, and oxidation state.

KEY WORDS: Schiff's bases, Copper, Antimicrobial and Cytotoxic activity,

1. INTRODUCTION

The copper metal is an important essential micro nutrient for feeding and a co-factor of several biocatalysts involved in oxidative metabolism like β-hydroxylases, quercetinase, ceruloplasmine, cytochrome oxidase, Mono amino oxidize, super oxy dismutase, ascorbic acid oxidize and tyrosinase (Berdanier, 1999). The analytical role of these enzymes is a two-step reaction, i.e. the reduction of Cu^{+2} to Cu^{+} and the fixation of molecular oxygen (Halfen, 1996). The rutine-Cu (II) chelate shows the very better activity as antioxidants and anti free radical agents than free rutine. The copper chelates of multi dentate Schiff base ligands have played a prominent role in the extension of inorganic chemistry. Di-nuclear copper (II) complexes have further attracted a much attention due to the spin-spin interaction among two metallic centers and the stereochemistry of the complexes. The di-nuclear copper (II) complexes which mimic the 'type 3' active site of copper proteins were studied extensively with magnetic interactions, ligand environment and oxygen uptake of these active sites.

2. MATERIALS AND METHODS

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 Agilant Triple Quard (LC-MS/MS) mass spectrometer. Proton NMR spectrum is recorded on Bruker-Ascend (400).

Synthesis of $[(Cu)_2(OH)(SAL)_2(OPD)_2(AA)_2(N_3)_2]$: A solution of Schiff's base (0.5mmol, 0.156gms) is dissolved in 10ml of hot methanol is mixed into a to a solution of copper per chlorate (0.5mmol, 0.185gms) in 10ml of water, immediately a royal crown colored solution is formed. Sodium azide (0.5mmol, 0.032gms) is dissolved in 10ml of water and added to the above solution. A brown colored precipitate is obtained after one hour on constant stirring at room temperature.

Anal. expt. $C_{40}H_{47}N_{10}Co_2O_7$ (M.Wt. 897.73) C, 53.52; H, 5.28; N, 15.60.Found: C, 53.33; H, 4.86; N, 13.56. Important IR absorptions (KBr disk, cm^{-1}): 3728, 3420, 2316, 2017, 1760, 1609, 1276, 1250, 1252, 905. Mass peaks (m/z): 72, 211, 125, 498, 631, 771, 927. M.P: 328^{0}C, Yield: 0.196g (53%).

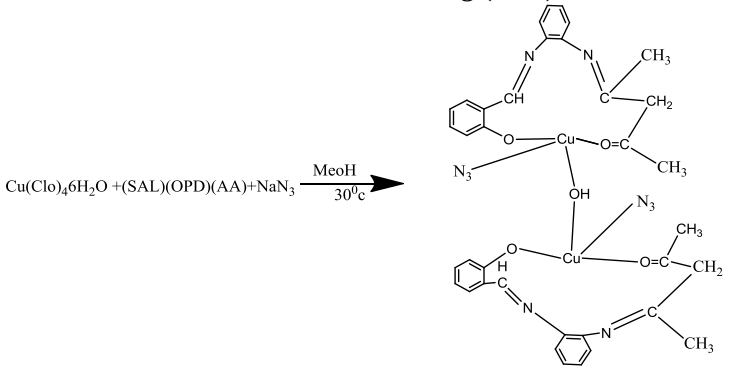

Figure.1. Proposed diagram of $[(Cu)_2(OH)(SAL)_2(OPD)_2(AA)_2(N_3)_2]$

UV-visible spectrum of $[(Cu)_2(OH)(SAL)_2(OPD)_2(AA)_2(N_3)_2]$: The electronic absorption spectrum of metal complex is recorded with DMF in the range from 200-800nm.The UV-visible spectrum of free Schiff base showed three bands around 240, 350 and 450 nm characteristic of π-π^* and n-π* transitions. In the metal complexes, this band is shifted to a longer wave length 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 assignable to intra ligand n-π^*or π-π* transition (Kalia, 2007). The chelates showed shoulder broad wavelengths in the range from 300 to 325 nm may be assigned to the d–d transition. Important absorption spectral lines are presented in table.1.

IR Spectrum of $[(Cu)_2(OH)(SAL)_2(OPD)_2(AA)_2(N_3)_2]$: The weak bands in the range from 3746–3423 cm^{-1} due to hydrogen bonded OH group. These spectral lines represents that the Phenolic oxygen atoms. The strong m(C=N) band occurring in the between 1617- 1611cm^{-1} are shifted slightly toward lower frequency 1607cm^{-1} compared to the free Schiff bases, indicating the un co-ordinated azomethane nitrogen atom to the metal center. The s(CN) absorption at 2115 cm^{-1} declares the presence of N-coordinated terminal azide group. Major peaks are reported in table.2.

LC-MS Spectrum $[(Cu)_2(OH)(SAL)_2(OPD)_2(AA)_2(N_3)_2]$: The peak at 754(m/z) is complex bound to two salicylaldehyde, two ortho- phenylenediamine, two Acetyl acetone, two copper and one azide, $[(Cu)_2(sal)_2(opd)_2(AA)_2(N_3)]$. The peak at 650(m/z) refers to the one salicylaldehyde, two ortho-phenylenediamine, two acetyl acetone, two copper and one azide. $[(Cu)_2(SAL)(OPD)_2(AA)_2(N_3)]$. peak at 377(m/z) is complex bound to copper, one salicylaldehyde, one Ortho-phenylenediamine, one acetyl acetone and one water molecules represented as $[Cu(SAL)(OPD)(AA)(H_2O)]$. Moreover, peaks at 317(m/z), 137(m/z), represents complexes of $[(Cu)(SAL)(OPD)(N_3)]$,$[(SAL)(H_2O)]$ respectively.

^{1}H-NMR Spectrum OF $[(Cu)_2(OH)(SAL)_2(OPD)_2(AA)_2(N_3)_2]$: The ^{1}H-NMR spectra of the Schiff base ligand, the spectra of the complexes are examined in comparison with those of the parent Schiff bases Upon examination it was found that the N-CH signal that appeared in the spectrum of the ligand at 8.85-8.96ppm, is appeared in the spectrum of its copper complex, existence that the Presence of azomethane group in the complex. Signal at 5.45 indicating the active methylene group of acetyl acetone, moreover, signals observed at 2.5ppm indicating the free methyl groups of acetyl acetone. New signal was observed at 3-3.5 ppm assigned to presence of alcoholic group in the complex.

Antimicrobial Screening of $[(Cu)_2(OH)(SAL)_2(OPD)_2(AA)_2(N_3)_2]$: The metal chelate is screened *in vitro* for anti-microbial activity against *E.coli, B.subtilis* and *A.niger* by Agar-well diffusion method (Angela Kriza, 2010). These results are listed in table.4.

The minimum inhibitory concentrations (MIC) are calculated as the highest dilution showing complete inhibition of the tested strains and are reported in table.3. Complex showed good potency towards antibacterial activity. Low potency is observed with anti fungal activity.

Cytotoxic studies of $[(Cu)_2(OH)(SAL)_2(OPD)_2(AA)_2(N_3)_2]$: The synthesized complex is examined for their cytotoxicity (MCF-7, cell lines) from the given data, it is observed that the complex displayed their cytotoxic activities as IC_{50} (μg/mL) against breast cancer MCF-7. The IC_{50}values of the complex are listed in table.5.

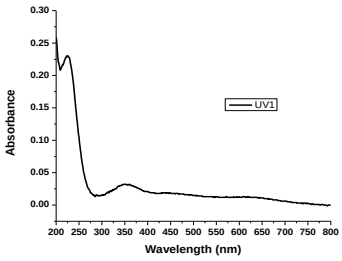

Figure.2. Electronic spectrum of $[(Cu)_2(SAL)_2(OPD)_2(AA)_2(N_3)(H_2O)_2(CH_3OH]$

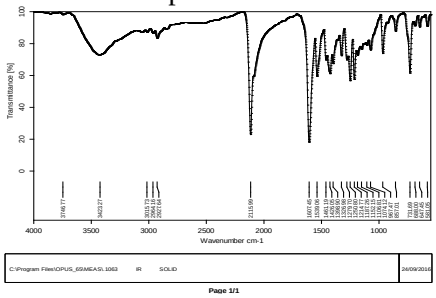

Figure.3. IR Spectrum of $[(Cu)_2(SAL)_2(OPD)_2(AA)_2(N_3)(H_2O)_2(CH_3OH]$

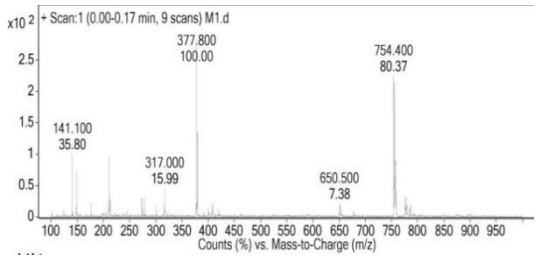

Figure.4. LC-MS Spectrum $[(Cu)_2(SAL)_2(OPD)_2(AA)_2(N_3)(H_2O)_2(CH_3OH]$ complex

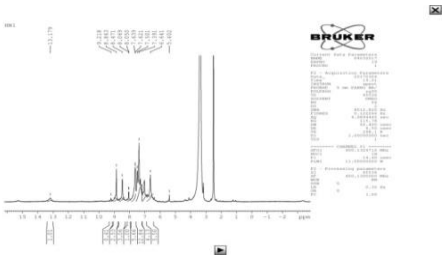

Figure.5. 1H-NMR Spectrum of $[(Cu)_2(SAL)_2(OPD)_2(AA)_2(N_3)(H_2O)_2(CH_3OH]$ complex

Antimicrobial Screening of $[(Cu)_2(SAL)_2(OPD)_2\,(AA)_2(N_3)(H_2O)_2(CH_3OH]$:

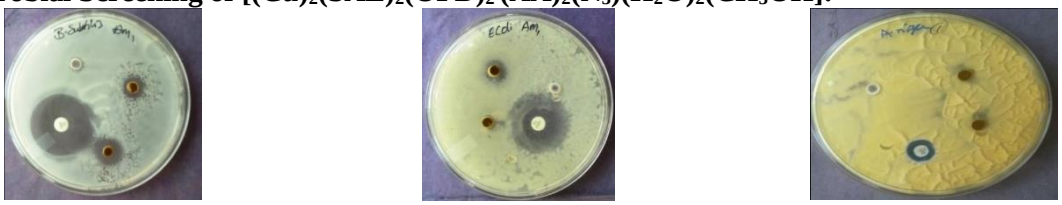

Figure.6. Inhibition zones for complex against *B.subtilis, E.coli, A.niger*

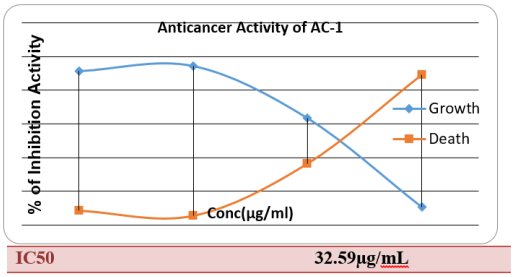

Figure.7. Anti-cancer activity of Schiff's base complex

3. RESULTS AND DISCUSSIONS

Table.1. Electronic spectral data of Schiff's base complex

Schiff's base complex	Absorbance	µ/cm^{-1}	Assignment
	350-450	355	MLCT
	240	250	n-π^*
	300-325	325	d-d

Table.2. IR Spectral data of Schiff's base complex

	µC=O	µC=N	µOH
Schiff's base complex	1700.31	1641.47	3228.95

Table.3. Determination of MIC values for Anti-microbial Activity of Schiff's base

Micro organisim	Concentration	
Bacteria	**5mg**	**10mg**
E.coli	-	+
B.subtilis	-	+
Fungi		
A.Niger	-	+

Table.4. Zone of inhibition of schiff's base complex

Micro organism	MIC values
Bacteria	**Inhibition zone (mm)**
E. coli	13
B. subtilis	17
Fungi	**Inhibition zone (mm)**
A. Niger	Nil

Table-5 IC_{50} values of Schiff's base complex

Conc.(µg/ml)	% cell survival	% cell inhibition
0.1	91.40216955	8.597830454
1	94.45560466	5.544395339
10	63.47930896	36.52069104
100	10.6870229	89.3129771

4. CONCLUSION

In this paper we have reported the synthesis of Schiff base ligand synthasized from acetyl acetone with o-phenylenediamine as well as salicylaldehyde and their Copper complex has been synthesized using the self-assembly method. The ligand and complex is characterized by spectroscopic studies. The antimicrobial studies are carried out with the complex confirm that they are good anti-microbial agents with their MIC values being 13 and 17 for bacterial organisms and no activity for fungal organisms. The cytotoxic studies are carried out with the complex confirm that they are good anti-cancer activity against MCF-7 (Breast cancer).

5. ACKNOWLEDGMENTS

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