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BIOLOGICAL ACTIVITIES OF SCHIFF BASES AND THEIR COPPER (II) COMPLEXES

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ABSTRACT

Coordination Chemistry occupies a larger area of inorganic research. Generally coordination complexes are formed through chemical bond called coordination bond formed between a metal atom or ion and a molecule with one or more unshared electron pairs, called a ligand. Schiff base is one of the significant ligand in the field of coordination chemistry research. Schiff bases can be prepared by condensing carbonyl compounds and amines in different conditions and in different solvents with the elimination of water molecules. Schiff base ligands are able to coordinate many metal ions and stabilize them in various oxidation states. Among the various metal complexes, Schiff base copper metal complexes exhibits enormous biological properties like antibacterial, antifungal and larvicidal activity. This study deals the synthesis of two Schiff base metal complexes (**complex 1** and **complex 2**) with the general formula [Cu(II)L^1L^2] In **complex 1**(where L^1 = Schiff base derived from 2,6 diamino pyridine with o-hydroxy benzaldehyde, L^2 = L-cysteine) and in **complex 2** (where L^1= Schiff base derived from L-histidine with vanillin, L^2 = 2,6 diamino pyridine). Formation of imine moiety in **complex 1** and **complex 2** was confirmed by FTIR spectra. Antioxidant and larvicidal activity were carried out for the prepared Schiff base ligand and its metal complexes which confirms the scavenging and mortality activity.

KEYWORDS: Schiff base copper metal complexes, Antioxidant and Larvicidal activity.

INTRODUCTION

Coordination chemistry is one of the major pillars of Inorganic chemistry and it is generally attractive and experimentally challenging frontiers in recent chemical sciences. Today

coordination compounds are treated as most active area of research which brought about a synthetic revolution in inorganic chemistry which leads to new products of equally novel uses in broad areas such as bactericides, pharmaceuticals, fungicides, pigments, catalysis, paints, polymers and photoconductors.[1] Compounds containing an azomethine group (-CH=N-), known as Schiff bases are formed by the condensation of a primary amine with a carbonyl compound at different conditions with different solvent.[2] A large number of Schiff bases and their complexes have been studied because of their various chemical and biological properties. Schiff bases are considered as privileged ligands in the novel preparation of transition metal complexes due to their ability to stabilize the metal ions in various oxidation states and as the property of reversibly bind with oxygen.[3]

Several pharmaceutical agents have been used in treatment but many problems occurred such as side effect, hypoglycaemia and weight gain therefore new drug are needed. Metal based Schiff base complexes showed various applications in different fields.[9] In recent years, Schiff base metal complexes have attracted considerable interest due to their significant biological properties and many reports confirms that some drugs have greater activity when administered as metal complex as that as free organic compounds.[16,17] Schiff bases have greater affinity towards the chelation with transition metal ions, especially copper ions, utilized in synthesizing complexes. The chemistry of Schiff base copper complexes is of interest owing to their importance in biological and industrial processes.[4,5,6] The copper complexes derived from Schiff bases were found to be extremely efficient catalysts in both homogeneous[7] and heterogeneous[7] conditions. Current interest in Cu complexes is stemming from their potential use as antimicrobial, antiviral, anti-inflammatory, antitumor agents and enzyme inhibitors.[8,9]

Schiff base can also be prepared from amino acids and Schiff base complexes derived from amino acids exhibiting greater biological activity such as antimicrobial, antioxidant and larvicidal activity.[10] L-histidine and L-cysteine are essential and non-essential amino acids respectively. The characteristic functional group presents in these aminoacids exhibit numerous biological activities.[2]

Based on the above facts the prime aim of our present work is to synthesis Schiff base copper complexes derived from L-cysteine and L-histidine and to characterize the synthesized metal complexes using FTIR spectra. In vision of an increasing interest in developing complexes as

antimicrobial agent and as an insecticide, this study was undertaken to assess the antioxidant and larvicidal activity of the synthesized Schiff base transition metal complexes

MATERIALS AND METHODS

All common laboratory chemicals and reagents were of analytical grade and have been used without further purifications. The FTIR spectra of the synthesized compounds were recorded using SHIMADZU spectrometer in 4000 – 400 cm^{-1} using KBr pellets. Culex. quinquefasciatus larvae were procured from Zonal Entamological Unit, Velapadi, Vellore.

Synthesis of Schiff base ligand-I

To an aqueous solution of 2,6 diaminopyridine (3 mmol) and KOH (6 mmol) an ethanolic solution of salicylaldehyde (3 mmol) was added in drops. The reaction mixture was stirred for about 1 h in a magnetic stirrer at 333 K. The solution turned yellow. The resultant product was filtered and dried.

Synthesis of Schiff base metal complex-I

To the synthesized Schiff base ligand-I (3 mmol), an ethanolic solution of an appropriate metal salt [copper (II) chloride (3 mmol)] was added and then reaction mixture was stirred for another 1 h. To this an ethanolic solution of L-cystiene (3mmol) was added in drops and the mixture was stirred for additional 2 h at the same temperature. The resultant product was filtered, washed with ethanol and dried.

Synthesis of Schiff base ligand-II

An ethanolic solution of L-histidine (3 mmol) and KOH (6 mmol) mixed with an ethanolic solution of vanillin (3 mmol). The reaction mixture was stirred for about 1 h in a magnetic stirrer at 333 K. The solution turned dark yellow, filtered and dried.

Synthesis of Schiff base metal complex-II

To the Schiff base ligand-II (3 mmol), an ethanolic solution of an appropriate metal salt [copper(II) chloride (3 mmol) was added and then reaction mixture was stirred for another 1 h. To this an aqueous solution of 2,6 diaminopyridine (3 mmol) was added in drops and the mixture was stirred for additional 2 h at the same temperature. The resultant product was filtered, washed with ethanol and dried.

Antioxidant Activity

Antioxidants are naturally occurring plant substances that protect the body from damage caused by harmful molecules called free radicals. Novel Schiff base metal complexes act as pharmaceutical drug and have been capable of acting as effective scavengers as antioxidants. An antioxidant is a molecule that inhibits the oxidation of other molecules. Free radicals are responsible for many diseases including cancer,[11] cardiovascular disease,[12] mild cognitive impairment,[13] Parkinson's disease and alcohol induced liver diseases.[14] Antioxidants help prevent oxidation and act as an essential role in the prevention of diseases. Hence the present work based on the study of the antioxidant property of the prepared Schiff base metal complexes.

Hydrogen Peroxide Scavenging Activity

Hydrogen peroxide scavenging activity is one of the best method to study antioxidant property.[15] A solution of hydrogen peroxide (40 mM) was prepared in phosphate buffer (50 mM, pH 7.4). The concentration of hydrogen peroxide is determined by adsorption at 230 nm using a spectrophotometer. Synthesized compounds with various concentrations (2 mg, 4 mg, 6 mg and 8 mg) are added to hydrogen peroxide and absorption at 230 nm is determined after 10 min against blank solution containing phosphate buffer without hydrogen peroxide. The percentage of hydrogen peroxide scavenging activity was calculated using following equation.

Scavenging activity = (Ac-As) / Ac x 100

Where, Ac - absorbance of control, As - absorbance of sample.

Larvicidal Activity

Mosquitoes are the major vector for the transmission of malaria, dengue fever, yellow fever, filariasis and Japanese encephalitis.[18] Hence, we made an new attempt to analyse Larvicidal activity of synthesized complex. The eggs and egg rafts of *C. quinquefasciatus* were dipped into a plastic bottle containing 500 mL of dechlorinated water for 30-40 min to hatch out larvae. They were maintained in the laboratory as per literature.[17] Mosquito larvae were fed with powdered nutrient broth once a day. After 4 days the hatched larvae turned into larvae in early fourth stage and were subjected for further experiment. The larvicidal activity was assessed by the procedure of WHO guide lines with some modification.[18] A total of 20 reared mosquito larvae of *C. quinquefasciatus* was placed in 200 mL of double distilled sterilized water containing various concentration (4 mg, 2 mg, 1 mg, 0.5 mg) of synthesized

compounds. The negative control was set up with sterile distilled water without compounds while the positive control was the commercial larvicide with test solution. Percentage of mortality was assessed after 24 h of incubation. A number of dead larvae in each batch were counted every 24 h exposure period. The treated larvae was mounted on a slide and examined under a microscope for image capture.

RESULTS AND DISCUSSION

All the synthesized compounds are found to be freely soluble in DMSO, DMF and ethanol. The analytical data of the synthesized compounds are shown in Table 1. The lower molar conductivity value of the complexes (10^{-3} M) in DMSO at 25 °C indicates their non-electrolytic nature.[19]

Table 1: Analytical data of the ligand and its complexes.

Compound	Molecular formula	Molecular weight	Colour	Decomposition point	Molar conducatance $Ohm^{-1}cm^{-2}mol^{-1}$
Ligand-I	$C_{19}H_{14}N_3O_2$	320	yellow	265˚C	-
Ligand-II	$C_{14}H_{16}N_3O_4$	298	Dark yellow	256˚C	-
Complex-I	$C_{21}H_{18}N_4O_4Cu$	462	Dark brown	>360˚C	3.3
Complex-II	$C_{19}H_{21}N_6O_4Cu$	469	Dark green	>360˚C	3.6

Infrared Spectra

Table 2. Vibrational spectral data of the ligand and its complexes (cm^{-1}).

Compound	ν(C=N)	ν(Cu=N)	ν(Cu=O)
Ligand-I	1595	-	-
Ligand-II	1565	-	-
Complex-I	1624	563	455
Complex-II	1604	547	486

The absence of absorption bands at 1680 cm^{-1} due to νC=O of aldehydic group and a band at 3240 cm^{-1} due to NH_2 along with appearance of new band at 1595 cm^{-1} and 1565 cm^{-1} (HC=N) in the IR spectrum of the **Ligand-I** and **Ligand-II** respectively confirmed that condensation had taken place between carbonyl compounds and amines. The synthesized **complex-I** and **complex-II** exhibited an intense band around 1624 cm^{-1} and 1604 cm^{-1} due to the coordinated imine group with the metal ions.[20] The absorption bands observed around 560 cm^{-1} and 450 cm^{-1} confirms the Cu-N and Cu-O linkages in the coordination complexes.[20]

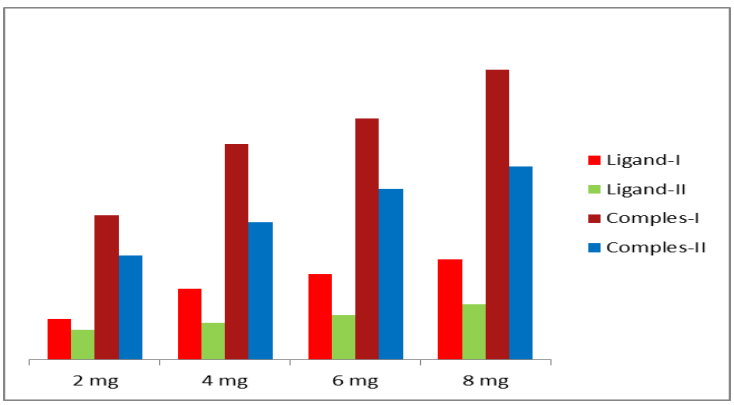
Antioxidant activity

Schiff base metal complexes exhibits moderate to high antioxidant activity.[15] Hence, to study the *in vitro* antioxidant activity of the prepared metal complexes, H_2O_2 method was adopted. Synthesized **Ligand-I**, **Ligand-II**, **Complex-I** and **Complex-II** subjected to study antioxidant activity. The results revealed that percentage of scavenging activity was minimum for **Ligand-I** and **Ligand-II**, but when it is coordinate to metal ions scavenging activity was gradually increased. When the concentration of test solution increases, percentage of antioxidant activity also increased. **Complex-I** showed highest scavenging potential whereas **complex-II** showed moderate to mild antioxidant activity ranging from 28-52%.

This confirms that presence of thiol group of L-cysteine in **complex-I** are active towards scavenging activity.[2] The H_2O_2 radical scavenging activity of standard antioxidant α-tocopherol was also assayed for comparison.[2] 68.72% scavenging activity was obtained for 6 mg of α-tocopherol. Hence, synthesized **complex-I** and **complex-II** exhibits good scavenging activity compared with the standard.

Table 3: Antioxidant scavenging activity of synthesized compounds.

Concentrations	% of antioxidant scavenging activity			
	Ligand-I	Ligand-II	Complex-I	Complex-II
2 mg	11 %	08 %	39 %	28 %
4 mg	19 %	10 %	58 %	37 %
6 mg	23 %	12 %	65 %	46 %
8 mg	27 %	15 %	78 %	52 %



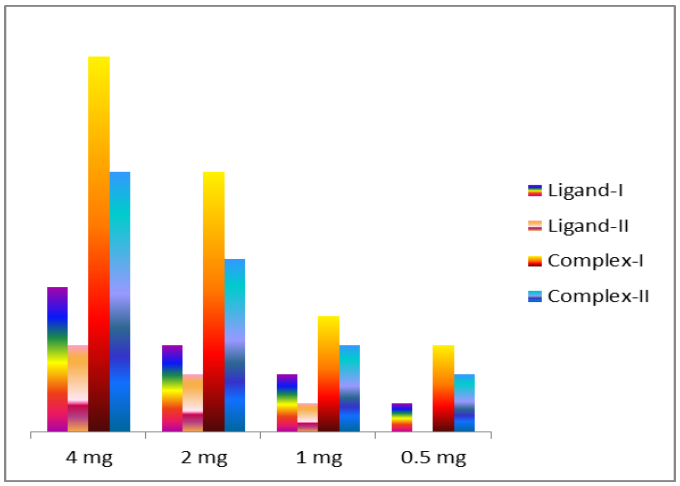
"Fig. 1" Graphical representation of antioxidant activity.

Larvicidal activity

The larvicidal activity of synthesized compounds **Ligand-I, Ligand-II**, **Complex-I** and **Complex-II** was studied against *C. quinquefasciatus* and the values are depicted in Table 4. The synthesized **Ligand-I and Ligand-II** showed moderate larvicidal activity this is due to active functional group present in it. The synthesized Schiff base **complex-I** and **complex-II** exhibits strong larvicidal activity. The highest mortality was obtained for **Complex-I** than **Complex-II** after 24 h contact period. When the exposure period is extended to 48 h, all the 20 larvae were dead present in **complex-I** and shows 100% mortality.

Table 4: Larvicidal activity of synthesized compounds.

Concentrations	Mortality(out of 20 larvae)			
	Ligand-I	Ligand-II	Complex-I	Complex-II
4 mg	5	3	13	9
2 mg	3	2	9	6
1 mg	2	1	4	3
0.5 mg	1	0	3	2



"Fig. 2" Graphical representation of scavenging activity.

CONCLUSION

In the present study, ternary Schiff base transition metal complexes has been synthesized and characterized by various physico-chemical and FTIR spectral analysis. The molar conductance of all the complexes suggested their nonelectrolytic nature. The presence of imine moiety, coordinating mode of Cu-N and Cu-O was confirmed by FTIR spectra. Larvicidal and *in vitro* antioxidant studies were carried out. The results revealed that all the complexes were found to exhibit very good antioxidant and larvicidal activity.

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