



RESEARCH ARTICLE

SYNTHESIS AND CHARACTERIZATION OF Cu(II), Cd(II) AND Pb(II) COMPLEXES WITH TRIDENTATE S,N,O DONOR SCHIFF BASE: INTERACTION WITH HUMAN SERUM ALBUMIN (HSA) WITH Cu(II) COMPLEX

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ABSTRACT

Metal complexes of Schiff base derived from 2-amino thiophenol and 2-hydroxy naphthaldehyde (HL) have been synthesized and characterised by elemental analysis (C,H,N), infrared, electronic spectroscopic tools. The complexes are found to have the formula [ML(H₂O)] where M is Cu(II), Cd(II), Pb(II). The interaction of Cu(II) complex towards Human Serum Albumin (HSA) was examined with the help of electronic spectroscopic tools. The electron transfer mechanism of copper (II) complex examined by cyclic voltammetry and indicate copper (II) complex gives Cu(II)/Cu(I) couple. Antibacterial activities of the complexes were studied by agar disc diffusion method and exhibited significant activities against gram-positive and gram-negative bacteria.

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INTRODUCTION

Since 1864 Schiff base has been known when Hugo Schiff reported the condensation of primary amine with carbonyl compounds. Generally, Schiff bases of aliphatic aldehyde are unstable in nature and rapidly get polymerised whereas Schiff bases of aromatic aldehyde relatively more stable (Ali et al., 1992). Schiff bases have been widely used as ligands due to its high stability of co-ordination compound, of them and good solubility in common solvents like ethanol, methanol, Chloroform etc. Schiff bases contain S,N,O organic moiety which readily form stable complexes with most of the transition metals play an important role in the development of co-ordination chemistry (Asadi et al., 2012). The chemistry of Schiff base ligand species has been gaining considerable interest primarily because of their functional structural derivatives (Maity et al., 2010). The importance of Schiff base complexes for bio-inorganic chemistry, biomedical application, supramolecular chemistry, catalysis and material science, separation and encapsulation process, formation of compounds with unusual properties (Cordes et al., 1962) and structures has been well recognised and reviewed (Chakraborty et al., 2010). As well as used in analytical reagent, polymer

coating ink, pigment, fluorescence materials (Cimerman et al., 2000), and catalytic agents. Schiff bases are active against a wide range of organism for example candida Albicans, E.Coli, Staphylococcus aureus. They serve as models for biological important species. Human serum albumin is the most important soluble protein in the circulatory system and secreted from liver cells. It is composed of three structurally homologous domains (I, II and III), each subdomains containing A and B. Each domain contains 10 helices; 1-6 helices form the respective subdomains A, and helices 7-10 comprise subdomains B. It plays an important role in plasma as well as in interstitial fluids and has many physiological functions, such as maintaining the osmotic pressure, pH of blood and transportation of various number of endogenous and exogenous compounds including fatty acids, amino acids, steroids, drugs, and pharmaceuticals. Generally, Schiff bases have been prepared by refluxing mixture of amine and carbonyl compounds in organic solvents. In this respect, the Schiff base oh 2-amino thiophenol and 2-hydroxy-1-naphthaldehyde has been synthesised in methanol medium using acid catalyst and products were isolated simply by filtration. Here we report an account of the synthesis and characterization and protein binding study of synthesized ligand and their complex with Cu(II) using absorption spectroscopic tools in this paper.

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MATERIALS AND METHODS

Materials

All chemicals and reagents were obtained from commercial sources and used as received, unless otherwise stated. Solvents were distilled from an appropriate drying agent. The organic moieties were synthesized following the procedure. The elemental (C, H, N) analyses were performed on a PERKIN ELMER MODEL 2400 elemental analyzer. Electronic absorption spectra were recorded on a SHIMADZU UV-1800 spectrophotometer. IR spectra (KBr discs, 4000–400 cm^{-1}) were recorded using a PERKIN ELMER MODEL FTIR model RX1 spectrometer.

Preparation of Ligand (HL)

To synthesize the ligand (HL) about 0.5gm of 2-amino thiophenol (4mmol) and 0.688gm of 2-Hydroxy-1-naphthaldehyde (4 mmol) was added in a round bottom flask which contains 10ml of methanol. A small magnetic bar was added to the flask. The mixture was allowed to stir for two hours and then reflux upto 3 hours and kept over one night to get the precipitate of the yellow ligand (Scheme 1). The precipitate was filter by filter paper using vacuum pump and washed several times using ethanol, followed by crystallization in ethanol and dry the crystals as much as possible on the filter using vacuum, and then collect them and spread them on a piece of filter paper to air dry, Yields >70%.

Scheme 1. Synthetic procedure of the Ligand (HL)

Preparation of [Cu(L)(H₂O)](1)

To prepare this copper (II) complex (1) a common procedure was followed as described below, using copper acetate for complex (1) and the organic ligand (HL) in equimolar ratio(1:1). A methanolic solution of HL (0.093gm) was mixed with 0.0666gm of copper acetate with stirring condition and the mixture was refluxed for 3 hours. The product was collected by vacuum and washing with cold methanol and dried in vacuo.

Preparation of [Cd(L)(H₂O)](2)

For complex (2) 0.08884gm of Cadmium acetate in methanolic solution was added to methanolic solution of HL (0.093gm). The resulting solution was refluxed for 3 hr. The product was collected by vacuum and washing with cold methanol and dried in vacuo.

Preparation of [Pb(L)(H₂O)](3)

For complex (2) 0.126gm of Lead acetate in methanolic solution was added to methanolic solution of HL (0.093gm). The resulting solution was refluxed for 3 hr. The product was collected by vacuum and washing with cold methanol and dried in vacuo.

Antimicrobial Screening

The antibacterial activities of the ligand (HL) and its complexes have been studied by agar disc diffusion method. The antibacterial activities were done dissolved compounds in DMF solvent by using three pathogenic gram negative bacteria (*Vibrio cholerae*, *Bacillus subtilis*) and one gram positive

pathogenic bacteria (*Bacillus cereus*). The solution of ligand and its copper (II) complexes were added to the agar plates (Patil *et al.*, 2010). The DMF solvent was used as a negative control. Incubation of the plates was done at 37°C for 24 hours, inhibition of the organisms was measured and used to calculate mean of inhibition zones in millimetres (Mann *et al.*, 1998).

RESULTS AND DISCUSSION

Synthesis and Characterization

The organic ligand (HL = [(2-amino thiophenol-(2-dihydroxy-1-naphthaldehyde)]) was synthesized by the reaction of the respective of 2-amino thiophenol and of 2-hydroxy-1-naphthaldehyde in presence of Methanol. The complexes were obtained in good yield from the reaction of the Copper acetate (1), Cadmium acetate (2) and Lead acetate (3) with equimolar amount of respective organic moiety HL in methanol medium. In these complexes the organic molecule HL act as tridentate ligand through SNO- donor centres (Saadeh *et al.*, 2010), These complexes are air-stable, non-hygroscopic, coloured solids, partly soluble in ethanol and methanol, and soluble in DMF and are monomeric in nature (Keypour *et al.*, 2013). The elemental analysis data of the Schiff base and their complexes (given in Table 1) are consistent with the calculated results from the empirical formula of each compound. The probable structure of complexes is given in Fig.1.

Infrared spectra

Infrared spectral data of the Schiff base (Fig. 2) shows several bands at 3447; 826, 738; 1632 cm^{-1} due to phenolic O-H group, Thiophenol C-S and imine CH=N stretching vibrations in the solid state. These bands are shifted to lower frequency on complexation with, Cu(OAc)₂ given in (Table 2). New vibrations at 460- 462, 545-555 and 735-747 cm^{-1} which are not present in the free Schiff base are attributed to the existence of ν (M-O), ν (M-N) and ν M-S bond. The appearance of these vibrations confirmed the involvement of sulphur and oxygen atoms (Fig. 3) in chelation with metal ions (Cotton *et al.*, 1978). All the IR data suggest that the metal ions are bonded to the Schiff base through the phenolic oxygen, thiophenol sulphur and the imino-nitrogen (Dhar *et al.*, 2005).

Electrochemistry

The redox properties of the copper (II) complex (Fig. 4) was examined by cyclic voltammetry using a Pt-disk working electrode and a Pt-wire auxiliary electrode in dry dimethylformamide using [*n*-Bu₄N]ClO₄(0.1 M) as the supporting electrolyte. The cyclic voltammograms exhibit quasi-reversible transfer process with a reduction peak at $E_{pc} = -0.16\text{V}$ and with a corresponding oxidation peak at $E_{pa} = 0.6\text{V}$ for complex 1 at a scan rate interval 50–400 mV s^{-1} [37]. The ratio of cathodic to anodic peak height was close to one. From these data, it can be deduced that the redox couple is related to a quasi-reversible one-electron transfer process controlled by diffusion.

Electronic Absorption Spectral Study

The electronic spectra of all complexes were recorded in DMF at room temperature. The electronic spectral data (Fig.6) of the Schiff base and their complexes are shown in Fig. 5.

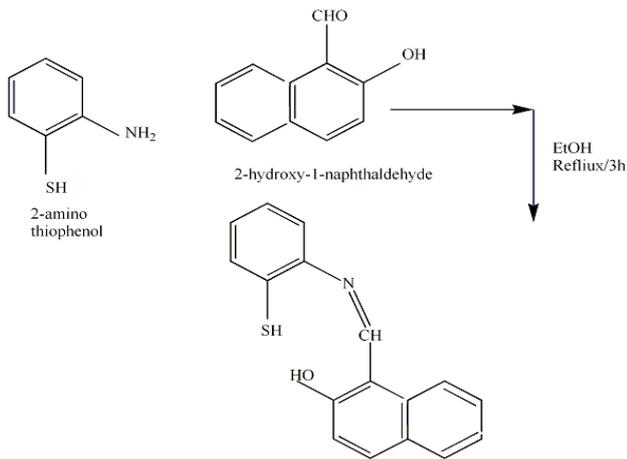


Fig.1. Probable structure of Cu (II), Cd(II) and Pb(II) complexes of 1, 2 and 3

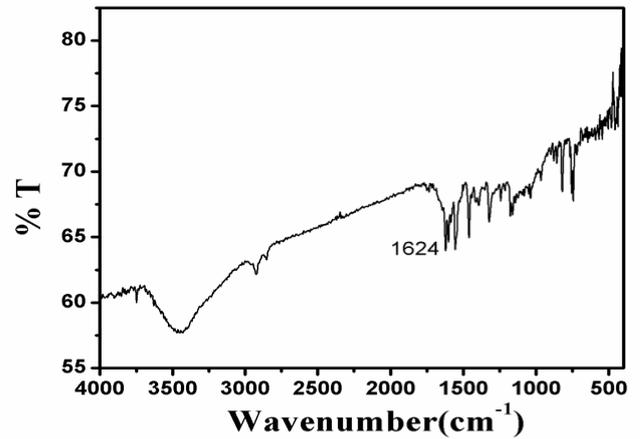


Fig.2. IR Spectrum of ligand HL

Table 1. Elemental analysis of ligand (HL) and its complexes

| Formula | Compound | Mol. weight | Colour | Found (Calculated) | | | | Melting point |
|---|----------|-------------|----------------|--------------------|-------------|-------------|---------------|---------------|
| | | | | C | H | N | M | |
| C ₁₇ H ₁₃ NOS | HL | 279 | Yellow | 73.12 (73.11) | 4.65 (4.68) | 5.02 (5.06) | - | 202 |
| C ₁₇ H ₁₅ NO ₂ SCu | 1 | 358.5 | Greenish Black | 56.90 (56.86) | 4.18 (4.16) | 3.90 (3.86) | 17.72 (17.68) | >225 |
| C ₁₇ H ₁₅ NO ₂ SCd | 2 | 407.4 | Green | 50.07 (50.02) | 3.68 (3.94) | 3.43 (3.46) | 27.59 (27.52) | >215 |
| C ₁₇ H ₁₅ NO ₂ SPb | 3 | 502.19 | Yellow | 44.08 (44.04) | 2.98 (2.96) | 2.79 (2.82) | 41.25 (41.12) | >225 |

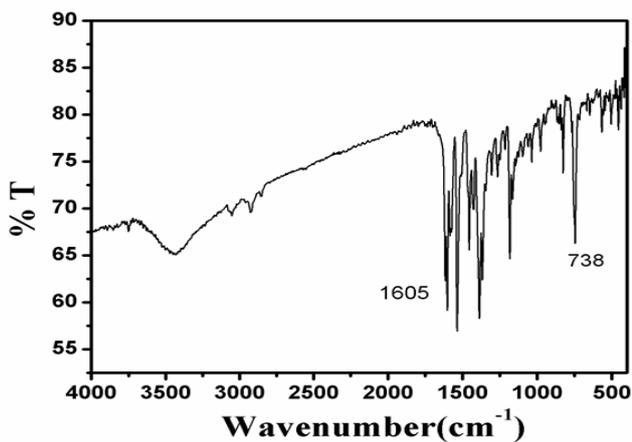
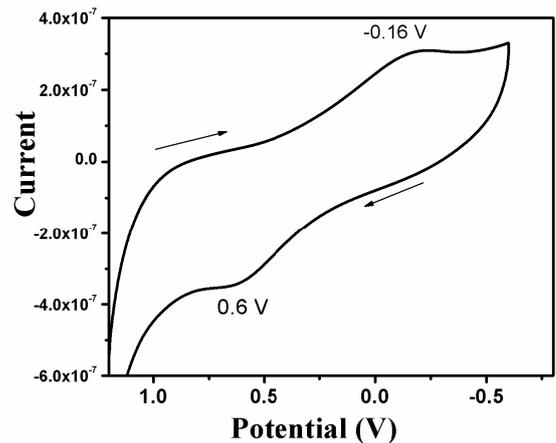
Fig.3. IR Spectrum of [Cu(L)(H₂O)] complex

Fig.4. Cyclic Voltammetry curve of Cu(II) complex

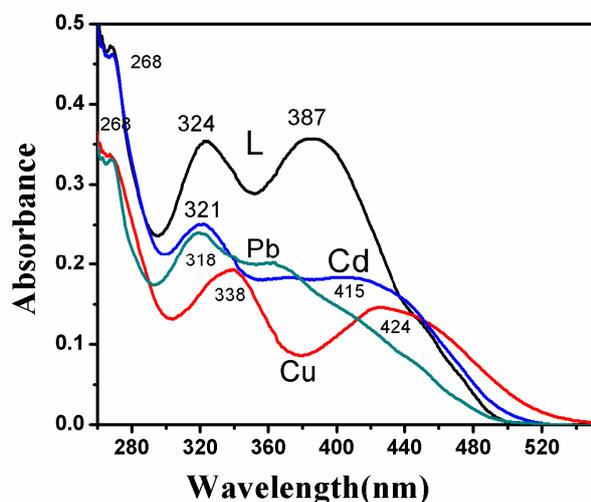


Fig.5. UV-Vis absorption spectrum of HL and its complexes

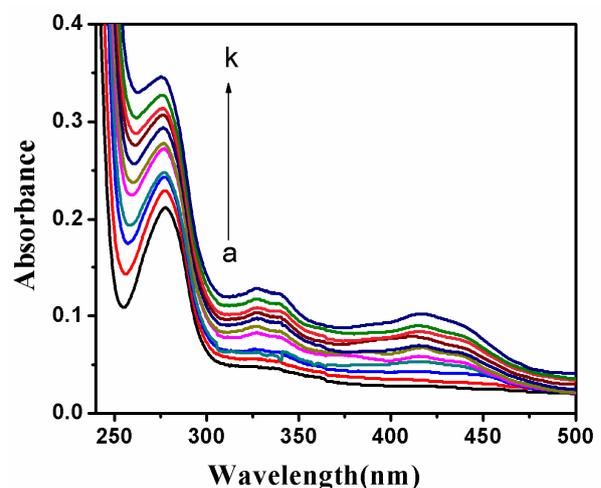


Fig.6. Electronic spectral titration of Cu complex with HSA at 277 nm in tris-HCl buffer Arrow indicates the direction of change upon the increase of HSA concentration

Table 2. IR Spectra of HL and its Complexes

| Compound | $\nu(\text{O-H})\text{cm}^{-1}$ | $\nu(\text{C-S})\text{cm}^{-1}$ | $\nu(\text{CH=N})\text{cm}^{-1}$ | $\nu(\text{M-S})\text{cm}^{-1}$ | $\nu(\text{M-N})\text{cm}^{-1}$ | $\nu(\text{M-O})\text{cm}^{-1}$ | $\nu(\text{M-O H}_2)\text{cm}^{-1}$ |
|----------|---------------------------------|---------------------------------|----------------------------------|---------------------------------|---------------------------------|---------------------------------|-------------------------------------|
| HL | 3447 | 826 | 1624 | | | | |
| 1 | - | 822 | 1605 | 738 | 554 | 461 | 3439 |
| 2 | - | 818 | 1603 | 734 | 550 | 466 | 3434 |
| 3 | - | 820 | 1608 | 741 | 557 | 464 | 3443 |

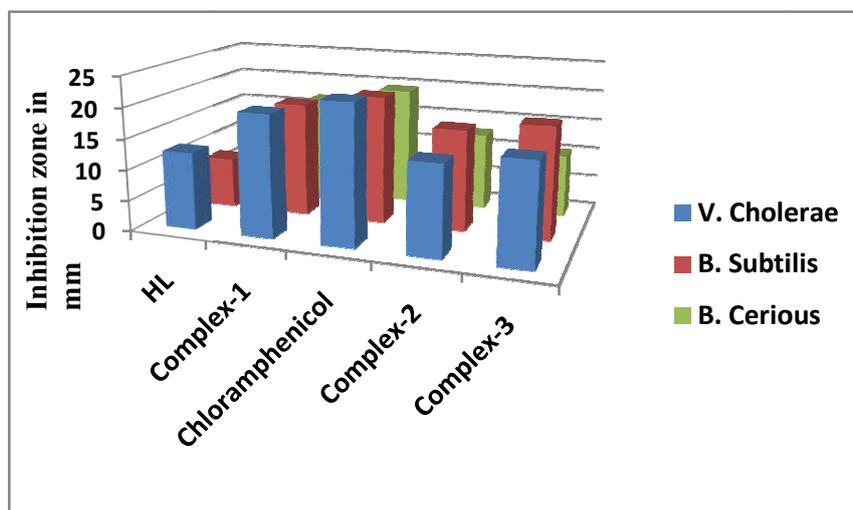


Fig. 7. Comparison the antimicrobial activity of Ligand (HL) and its complexes (1-3)

The spectra of the Schiff base HL exhibit main peaks: at 324 and 387 nm. The peaks were attributed to benzene $n \rightarrow \pi^*$ and imino $n \rightarrow \pi^*$ transitions, respectively. All the spectra of complexes shows lower bands than 400 nm are due to intramolecular $\pi \rightarrow \pi^*$ or $n \rightarrow \pi^*$ transitions for the aromatic ring. The spectra of the Copper(II) complex displays peak at 338 and 424 nm. An intense band at 338 nm is assigned to $\pi \rightarrow \pi^*$ intra-ligand transition.²¹ A broad band observed at 424 nm for complex 1 is well in agreement with the d-d transition for copper(II) in the distorted tetrahedral geometry (Konar *et al.*, 2011). For Pb(II) the peak at 318 and 415 nm assigned to the transition for benzene $n \rightarrow \pi^*$ and imino $n \rightarrow \pi^*$ along a broad peak at 415 nm arises due to charge transfer. Again for Cadmium (II) complex three peaks were found at 268, 321 and 415 nm. The peak at 268 and 321 nm found due to intraligand $\pi \rightarrow \pi^*$ transition. The Cd (II) complex displays again a peak at 415 nm is assigned to the charge transfer transition.

Protein (Human Serum Albumin) binding experiments by absorption characteristics of HSA-Cu (II) complex

The absorption spectra of HSA in the absence and presence of Cu (II) complex at different concentrations were studied (Fig. 6). From this study we observed that upon increasing the concentration of the complex the absorption of HSA increases regularly. It may be due to the adsorption of HSA on the surface of the complex. From these data the apparent association constant (K_{app}) of the complexes with HSA has been determined using the Benesi-Hilderbrand equation (Benesi *et al.*, 1994).

$$1/(A_{obs} - A_0) = 1/(A_c - A_0) + 1/K_{app}(A_c - A_0) [comp]$$

Where, A_{obs} is the observed absorbance of the solution containing different concentrations of the complex at 277 nm, A_0 and A_c are the absorbance of HSA and the complex at 280 nm, respectively, with a concentration of complex, and K_{app}

represents the apparent association constant. The enhancement of absorbance at 277 nm was due to adsorption of the surface complex, based on the linear relationship between $1/(A_{obs} - A_0)$ vs. reciprocal concentration of the complex with a slope equal to $1/K_{app}(A_c - A_0)$ and an intercept equal to $1/(A_c - A_0)$. The value of the apparent association constant (K_{app}) determined from this plot is $4.56 \times 10^{-4} \text{ M}^{-1}$ ($R = 0.99624$ for five points).

Antibacterial activity

Antibacterial activity of the ligand and its complexes are given in Fig.7. The biological activity of the synthesized ligand and its compounds compared with standard antibiotic Chloramphenicol. From the studies it is inferred that, all complexes have higher activity than ligand but lower than antibiotic. The metal chelates have higher activity than ligand; it can be explained by overtone concept and the Tweedy chelation theory³¹. It is observed that, in a complex, the metal positive charge is partially shared with the ligand; again it increases the delocalisation of pi-electrons over the whole chelate ring and increases the lipophilicity character of the metal complexes, which penetrate the lipid layer of the bacterial cell membranes and blocks the metal binding sites in enzymes of microorganisms. Due to higher lipophilicity, complexes exhibit higher antibacterial activity than free ligand.

Conclusion

The synthesis and characterization of mononuclear Cu (II), Cd (II) and Pb(II) complexes with a SNO- donor set have been performed. The ligand HL behaves as a SNO-donors organic moiety. On the basis of the physical and spectral data of the Schiff base and the complexes discussed above, one can assume that the metal ions are bonded to the Schiff base via thiophenol sulphur, phenolic oxygen and the imino nitrogen and the Cu(II), Cd(II) and Pb(II) complexes are distorted

tetrahedral geometry. The electrochemical study of copper (II) complexes demonstrated a quasi-reversible one-electron transfer process. The HSA binding of copper (II) complex is investigated by absorption spectra and giving Cu-complex strongly binds with HSA protein. Antibacterial studies confirmed that complexes are higher biologically active than ligand and less active than the standard antibiotic.

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