Antimicrobial and Fungus Activities of Cu(II)/Zn(II)/Cd(II) Metal complexes with 1,3-Diimine Spacer Group Ligand

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Received: May 20, 2018 Accepted: June 21, 2018

ABSTRACT *Self assemblies of compartmental N_2O_2 type Schiff base ligand 2,2'-(1E,1'E)-1,1'-(propane-1,3-diylbis(azan-1-yl-1-ylidene))bis(ethan-1-yl-1-ylidene)bis(4-chlorophenol) (H_2L) with Zinc acetate dihydrate, Cadmium acetate tetrahydrate and hydrated copper nitrate metal salts allow the formation of three mononuclear metal complexes having composition [$M^{II}(L)$] [M^{II} = Zn, Cd, Cu]. Salen-type ligand (H_2L) and its corresponding metal complexes **(1-3)** were successfully characterized using different important analytical tools like elemental analysis (CHN), FT-IR, UV-Vis and mass spectroscopic method. Analysis of the structure revealed that all three M(II) complexes possess a 4-membered MN_2O_2 structural motifs fastened by the combined coordination action of a doubly deprotonated ligand (H_2L).The antibacterial efficacy of M(II) transition metal complexes **(1-3)** were successfully investigated against some important Gram-positive and Gram-negative bacterial strains like Escherichia coli, Bacillus subtilis. In addition to that, the fungus activities of complexes **(1-3)** towards Candida albicans were also examined very carefully.*

Keywords: *Antibacterial, Schiff base, M(II) complex, Fungus*

INTRODUCTION

During 19th century Prof. Hugo Schiff [1] opened the flourishing door of Schiff base chemistry and since then it has become one of the important pillars in the development of modern coordination chemistry.[2,8] Generally Schiff bases are the condensation product of a carbonyl compound (substituted aldehyde/keto) with an amine which may be of primary in nature. Schiff bases chemistry studied extensively in the field coordination chemistry as potential ligands since it strongly coordinate with several metal ions through the azomethine nitrogen and oxygen atom to form mono, di or polynuclear metal complexes. Such category of metal complexes formation strongly depend on various factors like donor atom, denticity and flexlibilty of ligands, ligand size, metal charge, coordination number.[9] The chemistry of Schiff base complexes is very diverse with several applications in the field of biological, medicinal, pharmaceutical, optical, gas storage, sensing and finally strong active potential applications as functional materials.[10,24] Such kind of complexes till date is reported to show characteristic biological activities including antibacterial, antifungal and anticancerous.

In this manuscript, we have reported briefly the novel syntheses, their characterization and antimicrobial, fungus activities on a family of M(II) metal complexes **(1-3)**.

EXPERIMENTAL

Materials

All the chemicals were of reagent grade, purchased from commercial sources and used as received. 5-chloro-2-hydroxy acetophenone, 1,3-Diaminopropane and hydrated copper(II) nitrate metal salts were purchased from Aldrich Chemical Company, USA. $Cd(OAc)_2.4H_2O$ and $Zn(OAc)_2.2H_2O$ was purchased from E Merck, India. Solvent CH_3OH used high purity grade quality.

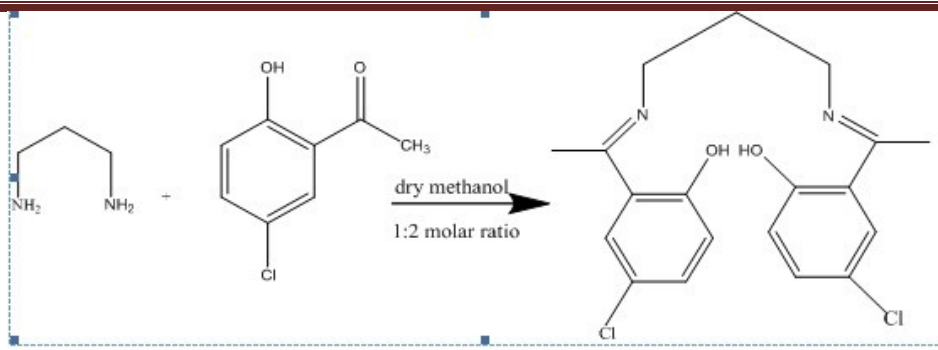
Physical Measurement

The electronic spectra of M(II) metal complexes (**1-3)** in methanol solution was recorded on a Hitachi model U-3501 spectrophotometer. FT-IR spectra (KBr Pellet, 400-4000 cm^{-1}) were recorded on a Perkin-Elmer model 883 infrared spectrophotometer. Elemental analyses (CHN) of metal complexes (**1-3)** were determined with a Perkin–Elmer CHN analyzer 2400. ESI-MS of complexes (**1-3)** were measured on LC-MS Varian Saturn 2200 Spectrometer.

SYNTHESIS

Synthesis of salen-type N_2O_2 donor ligand (H_2L)

To a solution of 5-chloro-2-hydroxy acetophenone (1.19g, 7mmol) in methanol (20 ml), propylene diamine (0.511g, 3.5 mmol) in methanol (5ml) was added with constant stirring. The color of the solution immediately turned yellow and it was refluxed for four hours. A yellow solid was separated and collected by filtration after cooling the solution at room temperature (Scheme 1). Then the yellow solid was dried and preserved in desiccators. (Yield 0.575 g). Exact Mass: 378, m/e 378.09, Anal. Calc. for $C_{19}H_{20}Cl_2N_2O_2$: C, 60.17; H, 5.32; N, 7.39; Found: C, 61.01; H, 5.09, N, 7.28 %. IR (KBr, ν_{max}/ cm^{-1}): $\nu_{(C=N)}$ =1611



Scheme1. Synthetic route of N,O donor salen-type Schiff base ligand (H_2L)

Synthesis of mononuclear M(II) complexes (1-3)

Synthesis of complex [Zn^{II}(L)] (1)

To a hot solution of Schiff base ligand (0.075g, 0.2mmol) in methanol (25 ml), $Zn(OAc)_2.2H_2O$ (0.439g, 0.2mmol) taken in same solvent was added drop wise with constant stirring for 3 hours. A light yellow colored complex was immediately precipitated out and this was filtered under suction, washed with methanol, dried and preserved in desiccators. Exact Mass: 441, m/e 442, Anal. Calc. for $C_{19}H_{19}ZnCl_2N_2O_2$: C, 51.44; H, 4.32; N, 6.31; Found: C, 50.91; H, 4.30, N, 6.25 %. IR (KBr,ν_{max}/ cm^{-1}): $\nu_{(C=N)}$ 1627.

Synthesis of complex [Cd^{II}(L)] (2) and complex [Cu^{II}(L)] (3)

For complex (2) and complex (3) synthesis purpose we consider the similar procedure except $Cd(OAc)_2.4H_2O$, hydrated copper(II) nitrate metal salts are used in place of $Zn(OAc)_2.2H_2O$. In case of complex **(3)** bluish green type precipitate was only received.

For [Cd^{II}(L)] **(2)** Exact Mass: 490, m/e 490.1, Anal. Calc. for $C_{19}H_{19}CdCl_2N_2O_2$: C, 46.51; H, 3.90; N, 5.71; Found: C, 47.01; H, 3.88, N, 5.68 %. IR (KBr,ν_{max}/ cm^{-1}): $\nu_{(C=N)}$ 1628.

For [Cu^{II}(L)] **(3)** Exact Mass: 441.82, m/e 442, Anal. Calc. for $C_{19}H_{19}CuCl_2N_2O_2$: C, 51.65; H, 4.32; N, 6.34; Found: C, 50.91; H, 4.30, N, 6.25 %. IR (KBr, ν_{max}/ cm^{-1}): $\nu_{(C=N)}$ 1627.

Characterizations of Ligand (H_2L) and M(II) complexes (1-3)

Both Schiff base ligand and its corresponding complexes **(1-3)** were fully characterized by FT-IR, UV-Vis and mass spectroscopic study. Presence of strong FT-IR band near ν= 1611 cm^{-1} provides the evidence of azomethine functional group (C=N) formation in the compartmental Schiff base ligand [see Figure **1**]. The absence of ν (CO) IR stretching value strongly support C=N bond formation in the ligand. The UV-Vis spectrum of the ligand in methanol solvent exhibited three bands near at 272.89 nm,334.10 nm and 400.08 nm which are assigned to the π-π* and n-π* transitions respectively [see Figure **2**]. An intense strong band near at 1632, 1631 [1] and 1627 cm^{-1} for complexes (**1-3)** respectively is shifted considerably towards lower frequencies compared to that of the free Schiff base ligand (H_2L) that further confirmed the coordination binding mode of the imino nitrogen atoms with Cd^{II}/Zn^{II}/ Cu^{II} metal centers. Ar-O stretching frequencies of complexes (**1-3)** observed nearly at 1210-1293 cm^{1} which is similar to the other reported salen-type ligands.[25] Complexes (**1-3)** exhibit mainly ligand-based transition near at 380, 372.11 and 379.77 nm due to $\pi\rightarrow\pi^*$ or $n\rightarrow\pi^*$ transitions. Further mass spectroscopic study conclusively confirmed the complexes **(1-3)** chemical compositions.

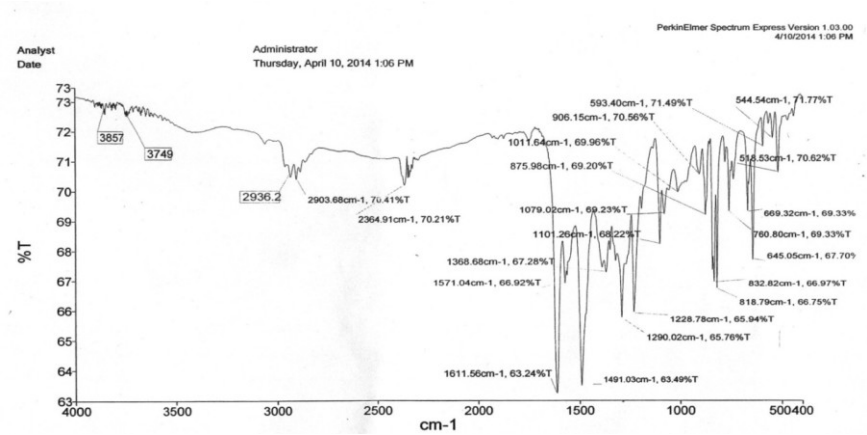


Fig.1. FT-IR spectra of Schiff base ligand(H_2L)

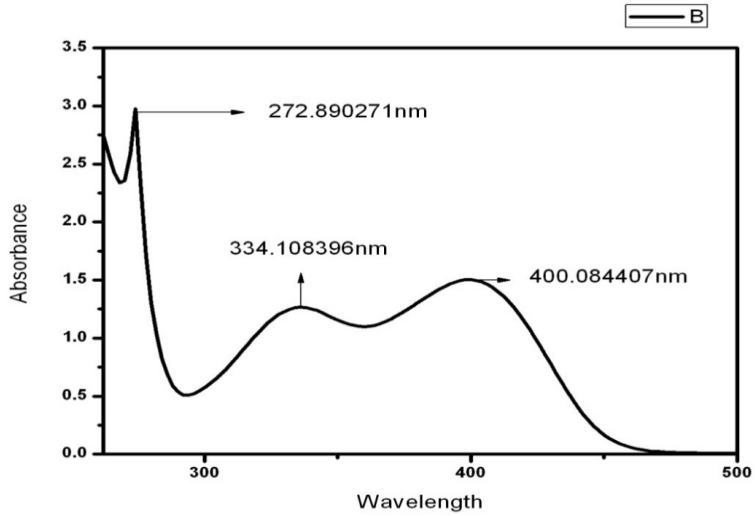


Fig.2. UV-Vis spectra of Schiff base ligand (H_2L)

Experimental of Antimicrobial and Fungus assay of M(II) complexes (1-3)

Schiff base M(II) metal complexes **(1-3)** was screened strongly for antimicrobial assay against one gram positive BS-*Bacillus subtilis* and one gram negative EC- *Escherichia coli*, bacterial stains along with and one fungus CA- *Candida albicans* using the common well diffusion method [26].Two hundred milliliters of nutrient agar growth medium was dispensed into sterile conical flasks; these were then inoculated with 20 µl of cultures mixed gently and poured into sterile petri-dish. After setting a borer with 6 mm diameter was properly sterilized by flaming and used to make three uniform wells in each petri-dish. The wells were loaded with 50 µl of synthesized bivalent metal complexes **(1-3).**The solvent DMSO used for reconstituting the solvent for diluting the complexes **(1-3)** was similarly analyzed for control. The plates were incubated at 37^0C for 24 h similar procedure is adopted also for fungal assay and the medium in that case is potato dextrose agar instead of nutrient agar and incubated at 27^0C for 48 h. The zone of inhibition was measured with a Hi Antibiotic Zone Scale in mm and all experiments were carried out in triplicate.

Analysis of Antimicrobial and Fungus assay towards M(II) complexes (1-3)

The systematic analysis of antimicrobial assay, it was observed that complexes **(1-3)** was found to be more active against one gram negative bacteria EC- *Escherichia coli* followed by against one gram positive BS-*Bacillus subtilis* bacterial strains [see Figure **3-4**]. The increased biological assay of M(II) Schiff base metal complexes **(1-3)** can be explained with the help of 'chelation theory' according to Odds, 1989.[27] According to that theory the lipid membrane surrounding the cell favors the passage of only lipid-soluble materials due to that better antimicrobial assay was exhibited. In addition to 'chelation theory' concept the polarity of the M(II) metal ion will be reduced to maximum extent and thereby expected to be hydrogen bond formation will be strongly. This is due to the overlapping of the compartmental N,O donor ligand (H_2L) specified orbital and partial sharing of positive charge of the Cu(II)/Zn(II)/Cd(II) transition metal ion with N,O donor centers of reference type of ligand. Apart from, complexes 1-3 may also involved the formation of a hydrogen bond through the azomethine group of the N,O donor ligand. The week antifungal assay exhibited by the complexes **(1-3)** could be attributed to their strong resistant nature to fungus. The zone of inhibition of the synthesized M(II) metal complexes **(1-3)** for antibacterial and antifungal assay at 10 µg/mL concentrations is clearly shown in Table **1**.

Table 1

Symbols stand for: EC**- Escherichia coli, BS- Bacillus subtilis, CA-Candida albicans**

Complexes	EC	BS	CA
1	22-24	15	5
2	22-21.8	14	5.2-5.3
3	21-22.4	17	4.05

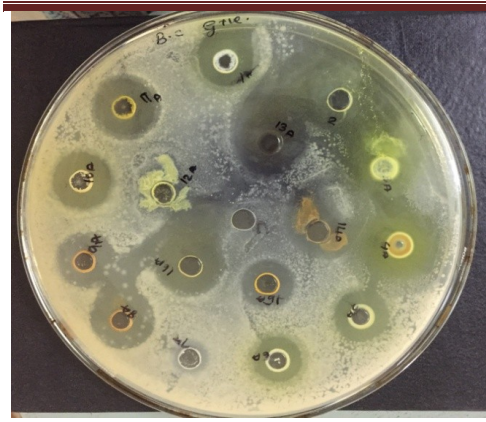


Fig.3. Samples [1,2,3] coded for complexes **(1-3)**

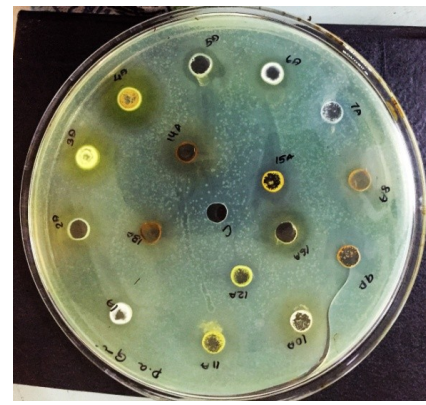


Fig.4. Samples [2A,3A,4A] coded for Complexes **(1-3)**

CONCLUSION

In this communication the antimicrobial efficacy of important M(II) [Zn^{II}/Cd^{II}/Cu^{II}] metal complexes (**1-3)** with N_2O_2 donor Schiff base ligand (H_2L) were successfully investigated. Apart from this analysis, one important fungus 'Candida albicans' activities towards complexes **(1-3)** were also examined very carefully. The combined results suggest strongly that these M(II) complexes are screened against one impotant Gram + ve and one Gram –ve bacterial strains along with fungus implying their prospective use as bacteriostatic agents.

ACKNOWLEDGEMENT

Dr. Dipankar Mishra gratefully acknowledges the financial grant sanctioned by UGC, New Delhi; in his favour vide Minor Research Project (F.PSW-232/15-16(ERO).

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