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Green Route Synthesis of Bio-active Cd(II) and Hg(II) Complexes With 'N' Donor Novel Schiff base and Oxalate ion

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ABSTRACT

Green route synthesis of bio-active diamagnetic Cd(II) and Hg(II) complexes with Schiff base and oxalate ion were synthesized using water as a solvent and characterized by using electronic spectra (UV-visible), Fourier transforms infrared (FT-IR), ^{1}H and ^{13}C-NMR spectroscopy, mass spectra and physical characterization such as CHN analysis, metal estimation and molar conductivity. ^{1}H- and ^{13}C-NMR spectra of ligand complex compared with Schiff base. The complexes have the general formula of ML_2X (M= Cd(II) & Hg(II), L-$C_{15}H_{13}N$, X-C_2O_4) confirmed based on the results of elemental analysis, metal estimation and the reasonable shift of mass spectra, FT-IR and NMR spectral signals of the complexes compared with free Schiff base. The coordination of Schiff-base and anionic ligands through an inner-sphere coordination mode by imine nitrogen and the oxygen atom of oxalate ion. The conductivity measurements of metal complexes indicate that they are non-electrolyte. The Schiff base and its metal chelates were tested *in-vitro* bio-potential activity against bacterial strain such as *E. coli, S. aureus,B. subtilis, P. aeruginosa* and fungal strain *viz.,C Albicans, A. Niger* by Agar disc diffusion method using chloramphenicol and fluconazole as bacterial and fungal standard. The results revealed that the metal (II) chelates exhibited higher antibacterial activity than the free Schiff base.

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INTRODUCTION

Compounds with C=N (azomethine group) is known as Schiff bases, which were synthesized from the condensation of primary amines and compounds with active carbonyl groups (Aldehyde or Ketone) (Abu-Hussen, 2006). Literature reports show analytical and industrial applications of Schiff bases and their metal complexes (Thomas *et al.*, 2012; Rama and Selvameena, 2015). They show a variety of biological applications (da Silva *et al.*, 2011; Sridhar *et al.*, 2001), including antibacterial (Etaiw *et al.*, 2011), antifungal (Panneerselvam *et al.*, 2005) and anticancer properties (Ganeshpandian *et al.*, 2014). It is an important intermediate for enzymatic reactions. In medical chemistry, Schiff base complexes are known as a new anti-cancer agent (Qin *et al.*, 2010) because of their abilities of the cleavage of DNA strands and destruction of cancer cell (Shahabadi *et al.*, 2010).

Cadmium Schiff base metal complexes have shown various properties such as luminescent potential (Montazerozohori *et al.*, 2015), antimicrobial activity (Montazerozohori *et al.*, 2014), anticancer (Saedi *et al.*, 2019), urease inhibitory activity, (You *et al.*, 2008) corrosion inhibitory effect (Das *et al.*, 2017) and photo catalytic activity (Roy *et al.*, 2017).

The present studies Aim to synthesis of Cd(II) & Hg(II) complexes with monodentate Schiff base ((E-N-((E)-3-phenylallylidene)aniline) and characterized by analytical, spectral, and Bio-potential activities.

MATERIALS AND METHODS

The chemicals and solvent used as such without further purification. Aniline, Cinnamaldehyde, sodium oxalate, Cadmium nitratetetrahydrate and Mercury chloride were of AnalaR grade. Using Thermo Finnegan make, Flash EA1112 series CHNS(O) analyser instrument, the elemental analysis of the complexes were carried out. The molar conductance 10^{-3} M complex solution in acetonitrile was measured using Systronic Conductivity Bridge at 30°C.

Electronic spectra of the Schiff base and the metal(II) complexes were obtained by solid-state diffused reflectance method spectra (DRS-method) using JASCO model No: V-650 make UV-VIS spectrophotometer. The IR-spectra of Schiff base and its metal complexes were recorded in the range of 4000-400cm^{-1} using KBr pellet technique by Perkin Elmer spectrum, ONE-NO17-1159 Spectrometer and the ^{1}H & ^{13}C NMR spectra of Cd(II) & Hg(II) complexes were also recorded in DMSO-d$_6$ using BRUKER AS-3590-I spectrometer.

Antimicrobial assay

The newly synthesized metal chelates were screened for their antibacterial and antifungal activity against four bacterial strains, namely *E. coli*, *S.aureus*, *B.subtilis* and *P.aeruginos* and *C.Albicans*, *A.Niger* for fungal strains were obtained from Microbial type culture collection at the Institute of Microbial Technology, Chandigarh, India. Petri plates were prepared by pouring 30 ml of Nutrient agar (NA) and Potato dextrose agar (PDA) medium. The plates were incubated at 37 ºC for 24 hours for the bacteria and 48 hours for fungal strains. Each sample was tested in triplicate. Each disc was added 100μl of test samples, chloramphenicol for bacteria and Fluconazole for fungi used as standard drug separately. The zone of inhibition was measured in millimetres.

Synthesis of Schiff base

The Schiff base were synthesized by mixing 0.462g (4.90 mmole) of aniline in 10 ml ethanol, 0.668g (5.05 mmole) of cinnamaldehyde in 10 ml diethyl ether was mixed in a beaker, add 15ml of water as a catalyst. The whole mixture was stirred for 10 min at room temperature. The pale-yellow precipitated powder was formed and filtered, washed with water, dried in desiccators, kept in a glass container (Figure 1).

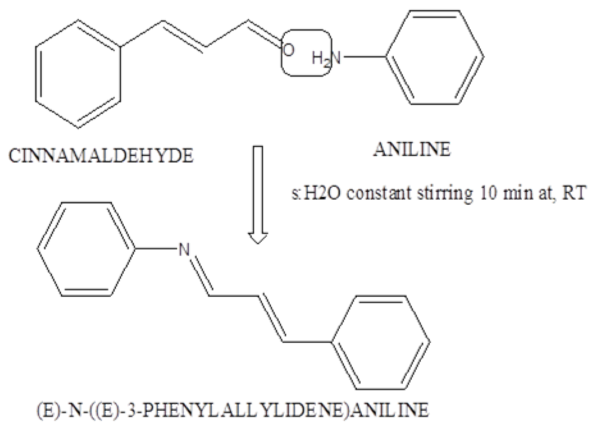

Figure 1: The Schiff base is soluble in ethanol

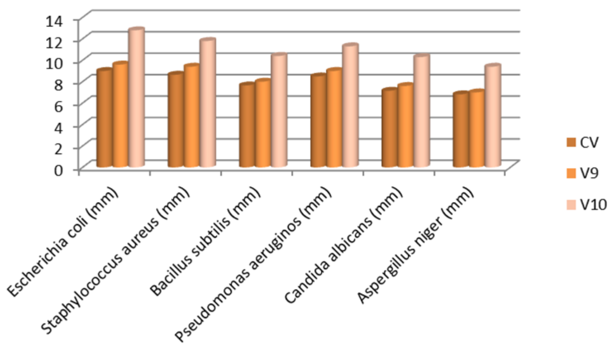

Figure 2: The Schiff base ligand has moderate activity against C. Albicans, B. Subtilis and showed no activity against *A.niger*

Synthesis of Cd(II) Complexes

1.00g (3.20 mmole) of Cadmium nitrate was dissolved in 10ml of methanol and 1.34g (6.44 mmole) of Schiff base in 10ml ethanol and 0.434g (3.20 mmol) oxalate in 20ml water. The mixture was stirred at room temperature for about 20 min after adding 15 ml water used as a green catalyst. The obtained colourless precipitate was filtered, washed and dried in a desiccator.

Synthesis of Hg(II) Complexes

1.00g (3.60 mmol) mercury chloride was dissolved in 10ml of methanol and the 1.526g (7.30mmol). Schiff base in 20ml ethanol and oxalate ion 0.493g (3.60 mmole) in 20ml water stirred at room temperature for about 20 min after adding 15 ml water used as a green catalyst. The obtained fly-ash colour precipitate was filtered, washed and dried in a desiccator.

Table 1: Elemental Analysis

S. No.	Compound	% C	% H	% N	% O	% Metal
1.	($C_{15}H_{13}N$)	86.86 (86.90)	06.27 (06.30)	06.75 (06.00)	-	-
2.	[$Cd(C_{15}H_{13}N)_2(C_2O_4)$]	58.18 (58.20)	03.93 (03.50)	04.24 (04.60)	09.99 (10.00)	17.00 (17.10)
3.	[$Hg(C_{15}H_{13}N)_2(C_2O_4)$]	51.25 (51.21)	03.47 (03.30)	03.73 (03.40)	08.54 (08.12)	26.77 (27.00)

*Theoretical values are given in parenthesis

Table 2: Physical and spectral data

S. No.	Compound	Color	MP (°C)	Molar Conductance (Ohm^{1}cm^{2}mole^1	λ_{max} (nm)	Yield
1.	($C_{15}H_{13}N$)	Pale yellow	125	20.00	261 388	71.42
2.	[$Cd(C_{15}H_{13}N)_2(C_2O_4)$]	Colourless	190	20.00	259 354	68.75
3.	[Hg ($C_{15}H_{13}N)_2(C_2O_4)$]	Fly-ash	195	09.09	383	77.77

Table 3: Antimicrobial data

Sample does (100 μl)	*E. coli* (mm)	*S. aureus* (mm)	*B. subtilis* (mm)	*P. aeruginos* (mm)	*C. Albicans* (mm)	*A. Niger* (mm)
Control	01.66	01.33	01.00	01.33	01.0	00.66
CV	09.00	08.65	07.65	08.49	07.15	06.82
V9	09.60	09.40	08.00	09.00	07.60	07.00
V10	12.80	11.80	10.40	11.30	10.30	09.40
Std	15.60	15.00	14.30	14.80	13.60	13.40

CV-Schiff base, V9- Cd(II) complex & V10-Hg(II) complex

Table 4: ^{1}H NMR Spectral Data

S. No.		Chemical shift (ppm)		
	Complex/Ligand	Azomethine proton	Aromatic Phenyl	Aliphatic proton
1.	Schiff base	7.43 - 7.44	7.342-7.359	6.58-6.58 & 7.40-7.41
2.	Cd(II) complex	7.67-7.68	8.38-8.40	7.40-7.41
3.	Hg(II) complex	8.44-8.61	7.70-7.76	7.44-7.45

RESULTS AND DISCUSSION

Elemental analysis and Molar Conductance

The Schiff base is pale-yellow in color whereas metal complexes are colorless and fly ash color respectively. They are soluble in common organic solvents such as DMSO, ethanol and methanol but insoluble in water. They are stable under ordinary conditions. The elemental analysis and metal estimation data show the complexes stoichiometry's as 1:1 metal and ligand ratio based on the literature of Geary *et al.,* the low values of molar conductance indicate that they are non-electrolytes (1:0 type) (Desai *et al.*, 2016). The physicochemical and analytical data's are given in Table 1 and Table 2.

Mass spectrum of Schiff base

The ESI mass spectral fragmentation of Schiff base shows the m/z value at 207 indicating the formula

Table 5: ^{13}C NMR Spectral Data

S. No.	Complex/ Ligand	Chemical shift (ppm) C_1	C_2	C_3	C_4	C_5	C_6	C_7	C_8	C_9	C_{10}	C_{11}
1.	Schiff base	128.04	128.69	126.50	135.85	144.81	120.31	162.51	151.79	121.63	130.11	127.69
2.	Cd(II) complex	128.66	129.71	129.46	144.86	135.84	121.34	162.58	151.76	128.05	130.14	126.52
3.	Hg(II) complex	128.81	129.42	129.46	145.07	135.72	119.26	158.86	156.60	128.28	130.12	126.99

and molecular weight of them, the other two m/z values of 115 and 89 indicating the fragment of $C_9H_8^+$ and $C_6H_7N^-$ (Tumer, 2007).

IR spectrum

To predict binding mode and complex formation ability of Schiff base towards metal ions, IR spectral data of Schiff base compared with metal chelates. The IR spectrum of free Schiff base exhibit peak at 1621cm^{-1} indicates the azomethine group (-CH=N) which are shifted to the lower frequency at 1572 cm^{-1} in Cd(II) complex and higher frequencies at 1631cm^{-1} in Hg(II) complex indicates the coordination of Schiff base to the metal through its azomethine nitrogen atom. The increasing stretching Frequency based on the electron density of that particular group. A broad peak at 3053 cm^{-1} is assigned to hydrogen-bonded aromatic C-H of ligand, which is appeared at 3047cm^{-1} in Cd(II) and 3063cm^{-1} in Hg(II) complexes due to the involvement of aromatic ring in coordination. The other frequencies of C=C, C-C, C-H, C-N at 1953cm^{-1}, 2979cm^{-1}, 3456cm^{-1} and 1300cm^{-1} respectively in Schiff base which are shifted to higher/lower frequencies at 1963cm^{-1}, 2920 cm^{-1}, 3420 cm^{-1} &1310 cm^{-1} in Cd(II) complex while 1980 cm^{-1}, 2980 cm^{-1}, 3562 cm^{-1}, 1321 cm^{-1} in Hg(II) complex. The very weak band which is absent in Schiff base but present in metal complexes are in the ranges of 476 cm^{-1}for Cd(II) complex and 467 for Hg(II) complex, 364-343 cm^{-1}Hg(II) complex assigned to stretching frequencies of both C-O bond in oxalate by ν(M-O) mode (Montazerozohori *et al.*, 2009; Chang *et al.*, 2016; Aghatabay *et al.*, 2007).

UV-Visible spectra

UV-visible absorption spectrum of the Schiff base show two absorption broad bands at 261 nm and 388 nm corresponding to the $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions (Back *et al.*, 2015). The bivalent Cd^{2+}complex are diamagnetic with filled d^{10} electronic configuration, and the d-d transition is not expected for this filled configuration. The complex show only charges transfer transitions (C-T) band MLCT & LMCT at 259nm & 354nm respectively suggested that the tetrahedral geometry (Alaghaz *et al.*, 2015). The same conclusion is in Hg(II) complex, which shows only one broad peak at 383nm also indicates the (C-T) charge transfer transition confirming the tetrahedral geometry around the Hg(II) (Sasikumar and Manisankar, 2012).

^{1}H and ^{13}C NMR studies

^{1}H NMR spectrum of (E-N-((E)-3-phenylallylidene)aniline and its diamagnetic complexes was recorded in DMSO-d6 using TMS as an internal standard. A signal at 7.43-7.44 ppm confirms the presence of azomethine proton (−HC=N) group (Sumrra *et al.*, 2014; Kumaran *et al.*, 2013). The signal at 7.67-7.68 ppm (multiplet) corresponding to the protons of the aromatic phenyl ring in the Schiff base. The signals observed at δ 6.58-6.589 and 7.40-7.41 ppm were due to the aliphatic protons of the Schiff base.

^{13}C –NMR spectrum of Schiff base gives eleven different carbon atoms corresponds to aromatic –C_1, ortho-C, meta C-C-H, allylic-C_1, allylic-C_2, imine-C, C-N, meta-C, ortho-C, para-C respectively in indicating the complex. All the ^{1}H and ^{13}C –NMR spectral data of Schiff base shifted to downfield/up-field upon coordination to metal ion in metal chelates (Table 4 and Table 5).

In-vitro Biological activity studies

Bio-potential activities of *E.coli, S. aureus, B. subtilis, P.aeruginos, C. Albicans & A. Niger* were assessed by the Schiff base and metal complexes by agar well diffusion method using *in-vitro.* The enhancement of the biological activity of the complexes than the free ligand due to the lipophilicity, which are the major factor for the enhancement, the positive charge on the metal ion attracted to the ligand and sharing of electrons favour the lipophilicity. The cell growth of the bacteria is reduced by the lipid membrane, the other factors which favour the biological activity such as chelation, neutral nature, molecular weight and metal ions nature. The results revealed that the Schiff base ligand has moderate activity against *E coli, S. aureus P. aeruginosa*. The activity follows the order *E.coli* > *S. aureus* > *P.aeruginos*. The Schiff base ligand has moderate activity against *C. Albicans, B. Subtilis* and showed no activity against *A.niger* (Figure 2). The bio-potential activity of the complexes was found to be in the order of *E.coli* > *S. aureus* > *P.aeruginos* > *B. Subtilis* (Zaky *et al.*, 2014). The MIC values are given in Table 3.

CONCLUSION

The Schiff base metal complexes prepared by the green route method. The ligands Schiff base is monodentate whereas oxalate ion as bidentate in nature, so they can form chelate complexes. The binding mode and complex formation nature was concluded from the stretching frequencies of IR spectral data and the molecular formula was also concluded by mass spectra. Electronic absorption spectra suggested that the tetrahedral and square planar geometry of the complex. The complexes are non-electrolyte, stable they show potent antibacterial and antifungal activities against tested bacterial and fungal strains.

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Conflict of Interest

The authors declare that they have no conflict of interest for this study.

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