

Investigation of Physico-chemical Properties and Antibacterial Activities of Newly Synthesised Co(II) and Cd(II) Complexes of an Ionic Liquid Tagged Schiff Base: 1-{2-(2-Hydroxybenzylideneamino)ethyl}-3-Methylimidazolium Hexafluorophosphate

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Abstract—Schiff base ligands and their transition metal complexes are well known for broad spectrum biological activities such as antiviral, antifungal and antibacterial agents. They possess excellent characteristics, structural similarities with natural biological substances. Inspired by these facts, two new Co(II) and Cd(II) complexes (1:2) of an ionic liquid tagged Schiff base, 1-{2-(2-hydroxy benzylideneamino) ethyl}-3-methylimidazolium hexafluorophosphate, were synthesized and characterized by various analytical and spectroscopic methods such as elemental analysis, FT-IR, ¹H NMR, ESI-MS, UV-Visible, TGA and magnetic susceptibility measurement. These studies suggested tetra coordinated tetrahedral geometry for the complexes. The Schiff base ligand and its complexes were tested for *in vitro* antibacterial activities against two gram positive and two gram negative bacteria which are mostly found in soil. All the tested compounds showed significant antibacterial activity against the all four bacteria.

Keywords: Ionic liquid tagged Schiff base; Co(II) complex; Cd(II) complex; Antibacterial activities.

1. INTRODUCTION

Ionic liquids (ILs) are generally defined as “designer solvents”, as their structures are based on large non-centrosymmetric organic cations and anions. In recent years, ILs have gained much attention due to their important features such as high thermal stability,¹ high density, extremely low volatility, non-flammability, high ionic conductivity² and a large number of possible variation in cation and anion conformation. A major cause for the growing interest is their negligible vapour pressure³ that decreases the risk of technological exposure and loss of solvent to the atmosphere. Due to these properties ILs are considered as a new generation of solvents for catalysis, ecofriendly reaction media for organic synthesis and a successful replacement for conventional media in chemical processes.⁴⁻⁶ Functionalized

ionic liquids (FILs) are generally recognized as ILs with functional groups in the cation. Functionalization of the cation requires in most cases only a single reaction process making them relatively easy to prepare. ILs containing functionalized cations has usually higher viscosity compared to conventional ionic liquids with same anions. Recently, many workers have focused on the preparation and application of FILs with different functional groups like hydroxyl,⁷ amino,⁸ sulfonic acid,⁹ etc.¹⁰ Compared with conventional ILs such FILs possess three advantages: (i) they can be bio-regenerated and biodegradable, (ii) chirality in bio-precursor can be maintained in IL and (iii) further functionalization is also possible.

Schiff bases are widely employed as ligand in coordination chemistry.¹¹ These ligand are readily available, versatile and depending on the nature of the starting materials they exhibit various denticities and functionalities.¹² Schiff bases and their metal complexes are also applied in biochemistry, material science, catalysis, encapsulation, activation, transport and separation phenomena and hydrometallurgy, etc.^{13,14} Transition metal complexes with oxygen and nitrogen donor Schiff base are of particular interest, because of their ability to possess unusual configuration.¹⁵ Salicylaldehyde and its derivatives are useful carbonyl precursors for the synthesis of a large variety of Schiff bases with wide variety of interesting properties. Hence in this paper the synthesis an ionic liquid grafted Schiff base 1-{2-(2-hydroxybenzylideneamino) ethyl}-3-methylimidazolium hexafluorophosphate and its Co(II) and Cd(II) complexes were discussed. The synthesized compounds were characterized by various analytical and spectroscopic methods. The ligand and its complexes were tested for their *in vitro* antibacterial activity against two gram negative bacteria and two gram positive bacteria. The complexes along with the Schiff base showed significant inhibition against all the tested bacteria.

2. EXPERIMENTAL

Materials and measurements

All the reagents used were of analytical grade and used without further purification. 1-methyl imidazole, 2-bromoethylamine hydrobromide and potassium hexafluorophosphate were procured from Sigma Aldrich, Germany. Salicylaldehyde, $\text{Co}(\text{CH}_3\text{COO})_2 \cdot 4\text{H}_2\text{O}$, $\text{Cd}(\text{CH}_3\text{COO})_2 \cdot 2\text{H}_2\text{O}$ and all other chemicals were purchased from SD fine Chemicals, India. All the chemicals were used as received. IR spectra were recorded in KBr pellets with a Perkin-Elmer Spectrum RX I FT-IR spectrometer, operating in the region 4000 to 400 cm^{-1} . Proton NMR spectra were recorded at room temperature on a FT-NMR BRUKER ADVANCE II 300 MHz spectrometer by using $\text{DMSO-}d_6$ and D_2O as solvents. Chemical shifts are quoted in ppm downfield of internal standard tetramethylsilane (TMS). Melting points were recorded by open capillary method. Elemental micro-analyses (C, H and N) were conducted by using Perkin-Elmer (Model 240C) analyzer. Mass spectra were recorded on a JMS-T100LC spectrometer. The purity of the Schiff base and its complexes were confirmed by thin layer chromatography (TLC) on silica gel plates and TLC visualization was done by UV-light and iodine. Thermal analysis (TGA) was performed with 4000 Perkin-Elmer. Antibacterial activities (*in vitro*) of the synthesized ligand and the complexes were studied by disc diffusion method against commonly known bacteria, *viz.*, *Bacillus subtilis*, *Bacillus cereus*, *Proteus vulgaris* and *Enterobacter aerogenes* with respect to the standard drug *Ampicilin*.

Synthesis of ionic liquid [2-aemim]PF₆

The amino functionalized ionic liquid was prepared by following a literature procedure.¹⁶

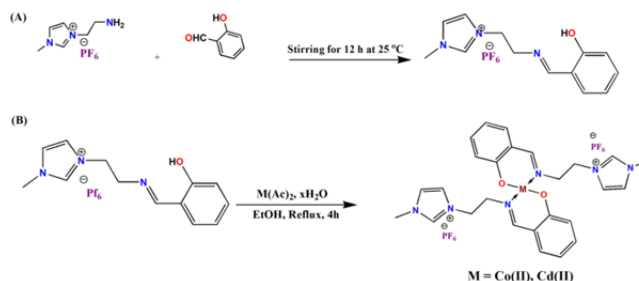
[2-aemim]PF₆: Yellow oil; Yield 67 %; Anal. Calcd. (%) for $\text{C}_6\text{H}_{12}\text{F}_6\text{N}_3\text{P}$: C, 57.11; H, 9.59; N, 33.30. Found: C, 57.02; H, 9.42; N, 32.88; FT-IR (KBr, cm^{-1}): 3412, 3086, 2896, 1581, 1452, 1175, 847 cm^{-1} ; ¹H-NMR (300 MHz, D_2O , δ/ppm): 3.25 (2H, *m*, $\text{NH}_2\text{-CH}_2$), 4.12 (3H, *s*, CH_3), 4.49 (1H, *t*, N-CH_2), 4.52 (1H, *t*, N-CH_2), 7.68 (1H, *s*, NCH), 7.75 (1H, *s*, NCH), 8.63 (2H, *s*, NH_2), 8.99 (1H, *s*, N(H)CN); The ESI-MS (*m/z*, relative abundance, %): 126.20 (M^+ , 92.6).

Synthesis of ionic liquid grafted Schiff base

The ionic liquid based Schiff base ligand (L) was synthesized by slight modification of a literature procedure.¹⁷ A mixture of salicylaldehyde (1.22 g, 10 mmol) and [2-aemim]PF₆ (2.71 g, 10 mmol) in 10 mL methanol was stirred at room temperature for 1 h. After completion of the reaction, as indicated by TLC, the reaction mixture was diluted with MeOH (10 mL). The precipitate was then filtered and dried to afford the expected ligand as a pale yellow solid in good yield.

LH (2): Yellow solid; yield: 65-70 %; m. p. 132-133 °C, Anal. Calcd. (%) for $\text{C}_{13}\text{H}_{16}\text{N}_3\text{OPF}_6$: C, 40.81; H, 4.19; N, 10.99.

Found: C, 41.61; H, 4.29; N, 11.20; FT-IR (KBr, cm^{-1}): 3430, 3151, 2923, 2866, 1640, 1616.2, 1569.9, 1508.2, 1465.50, 1278.31, 1167.87, 837; ¹H NMR (300 MHz, $\text{DMSO-}d_6$, δ/ppm): δ 3.82 (*s*, 3H, CH_3), 3.99 (*t*, 2H, CH_2), 4.52 (*t*, 2H, CH_2), 6.85–7.42 (*m*, 4H, Ar-H), 7.67 (*s*, 1H, NCH), 7.33 (*s*, 1H, NCH), 9.29 (*s*, 1H, N=CH), 8.31 (*s*, 1H, OH); ESI-MS (*m/z*, relative abundance, %): 231, [$\text{M}+1$, 30.6].



Scheme 1. Syntheses of the M(II) complexes (3 and 4) from the ionic liquid based Schiff base, [1-{2-(2-hydroxybenzylideneamino)ethyl}-3-methylimidazoliumhexafluorophosphate (LH).

Synthesis of Complexes (3 and 4)

To a solution of ligand (HL) (0.50 g, 1.30 mmol) in EtOH (20 mL), metal salts, *viz.*, $\text{Cd}(\text{CH}_3\text{COO})_2 \cdot 2\text{H}_2\text{O}$, (0.17 g, 0.65 mmol) or $\text{Co}(\text{CH}_3\text{COO})_2 \cdot 4\text{H}_2\text{O}$ (0.16 g, 0.65 mmol) was added and the reaction mixture was refluxed for 4h until the starting material was completely consumed as monitored by TLC. On completion of the reaction, the reaction mixture was cooled to room temperature. The precipitate was collected by filtration, washed with cold $\text{C}_2\text{H}_5\text{OH}$ (10 mL x 3), and dried to get the compound as yellow and brown solid. A schematic representation of the synthesis is shown in Scheme 1.

Co(II) complex (3): Brown solid; Yield: (0.47gms) 71%; m.p. 96-97 °C; Anal. Calcd for $\text{C}_{26}\text{H}_{30}\text{CoF}_{12}\text{N}_6\text{O}_2\text{P}_2$: C, 38.68; H, 3.75; N, 10.41. Found: C, 38.55; H, 3.46; N, 10.22; FT-IR (KBr, cm^{-1}): 3447, 3162, 2926, 1620, 1526, 1448, 1130, 843.5, 620, 555; ESI-MS (*m/z*, relative abundance, %): 517, [M , 35].

Cd(II) complex (4): Yellow solid; Yield: (0.44gms) 65%; m.p. 85-87 °C; Anal. Calcd for $\text{C}_{26}\text{H}_{30}\text{CdF}_{12}\text{N}_6\text{O}_2\text{P}_2$: C, 36.27; H, 3.51; N, 9.76. Found: C, 36.12; H, 3.43; N, 9.69; FT-IR (KBr, cm^{-1}): 3448.5, 3152, 2863, 1634, 1545, 1459, 1159, 842.49, 618, 548; ¹H NMR (300 MHz, D_2O , δ/ppm): δ 3.99 (*s*, 3H, CH_3), 4.11 (*t*, 2H, CH_2), 4.38 (*t*, 2H, CH_2), 6.98–6.85 (*m*, 4H, Ar-H), 7.43 (*s*, 1H, NCH), 7.31 (*s*, 1H, NCH), 7.68 (*s*, 1H, N=CH), 8.41 (*s*, 1H, OH) ESI-MS (*m/z*, relative abundance, %): 572, [M , 46].

3. RESULTS AND DISCUSSION

All the isolated compounds were found to be air stable and were characterized by different analytical and spectroscopic methods.

IR spectral studies

IR spectra of the free Schiff base (HL) and its metal (II) complexes are given in Fig 1. The IR spectra of the complexes were compared with the free ligand in order to determine the co-ordination sites that may be involved in complexation. IR spectra of the ligand showed a strong broad band at 3430.12-3151 cm^{-1} ; this band was attributed to the hydrogen bonded –OH of the phenolic group with –NH group of the ligand (OH...N=C).^{18,19} The –OH stretching frequency appearing in the spectra of two complexes studied as a broad band in the range 3449-3152 cm^{-1} was due to the presence of water of hydration/or coordinated water.²⁰ A weak band at 3101-2923 cm^{-1} in the spectra of the ligand was assigned to –NH stretching vibrations. The involvement of deprotonated phenolic moiety in metal complexes was confirmed by the shift of (–CO) stretching band at 1465.5 cm^{-1} to lower frequency region of 1449-1448 cm^{-1} for the complexes.²¹ The Schiff base displayed the –C=N band at 1640 cm^{-1} . On complexation, this band shifted to lower wave number range of 1634-1620 cm^{-1} has been observed. This indicated the involvement of N atom of azomethine (–C=N) group in the complex formation²² and the band at 843.5-842.49 cm^{-1} was assigned for P-F stretching frequency.

Therefore, from the IR spectra data, it is concluded that the coordination of ligand to metal ion occurred through the N-atom of azomethine (–C=N) group and the O-atom of phenolic (O-Ar) group. The new bands appearing in the region 620-618 cm^{-1} and 559-557 cm^{-1} were assigned to M-O and M-N stretching frequencies respectively.²³

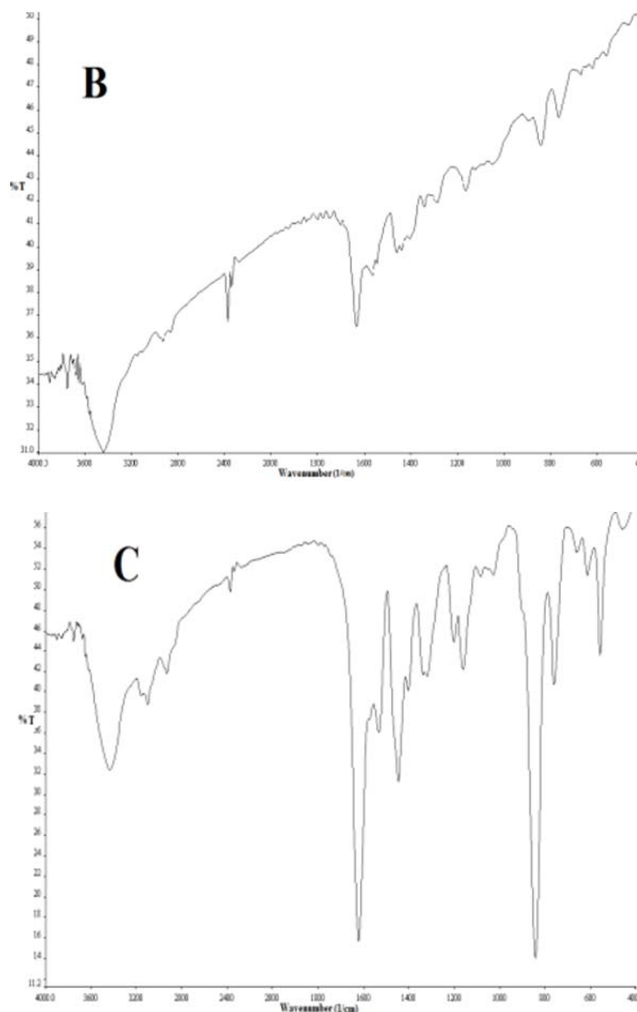
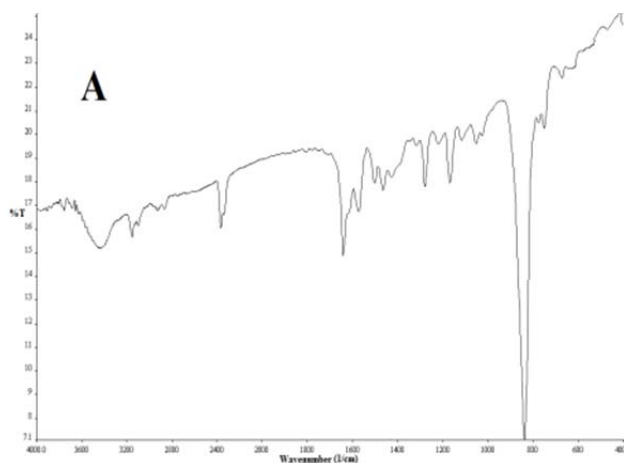


Fig. 1: The FT-IR spectra of: (A) the ligand (LH), (B) the Co(II) complex (3) and (C) the Cd(II) complex (4).

Mass spectra

The mass spectra of the ligand, LH showed a molecular ion peaks (m/z) at 231, these corresponds to $M+1$, $[\text{C}_{13}\text{H}_{16}\text{N}_3\text{O}+1]^+$ peak. The observed mass spectra confirmed the formation of the proposed ligand. Again the mass spectra of the Co(II) complex (3) and Cd(II) complex (4) showed molecular ion peaks (m/z) at 519 and 573, respectively. These molecular ion peaks were assigned for ($M'+2$) (where $M' = [\text{CoC}_{26}\text{H}_{30}\text{N}_6\text{O}_2]^+$) and ($M''+1$) (where $M'' = [\text{CdC}_{26}\text{H}_{30}\text{N}_6\text{O}_2]^+$) peaks, respectively.

^1H NMR spectra

The ^1H -NMR spectra of ligand and complexes were recorded in $\text{DMSO-}d_6$ and D_2O respectively. The chemical shifts to the different types of protons for the LH and its diamagnetic Cd(II) complex showed well resolved signals as expected. The spectrum of the complex was examined in comparison with those of the parent Schiff base. The $-\text{OH}$ signal, appeared in the spectrum of ligand at 9.29 ppm, completely disappeared in the spectrum of its Cd(II) complex indicating that the $-\text{OH}$ proton was removed by the chelation with the metal ion.²⁴⁻²⁶ The signal observed at 8.52ppm, (presumably due to the effect of the *ortho*-hydroxyl group in the aromatic ring) for HL was assigned to azomethine protons. This signal was found at 7.68 for Cd(II) complex. This indicated that the azomethine ($-\text{C}=\text{N}$) group was coordinated to the Cd(II) ion without proton displacement.^{27, 28} We were unable to record the NMR spectra of Co(II) complex due to its paramagnetic nature.²⁹

Electronic absorption spectral and magnetic moment studies

The electronic absorption spectra of the metal complexes were recorded in freshly prepared solutions in methanol at room temperature shown in Fig.2. The UV-Vis spectrum of ligand exhibited high intense absorption peak at 319 nm, with a shoulder at 255 nm, assigned to $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$, respectively.^{30, 31} The electronic spectra of the Co(II) complex (3) showed high intense peaks at 212 and 272nm, respectively, due to ligand field. The spectra exhibited band at 346 nm which can be attributed to $^4\text{T}_{1g}^{(F)} \rightarrow ^4\text{A}_{1g}^{(F)}$ transition, corresponding to tetrahedral Co(II) complex.³² The observed room temperature magnetic moment values 3.87 B.M for Co-complex assigned to tetrahedral geometry. The slightly lower magnetic moment might be due to the slight deviation from the regular tetrahedral geometry. The spectra of the Cd(II) complex (4) exhibited bands at 254 and 318nm assigned to ligand $\pi \rightarrow \pi^*$ and $\text{L} \rightarrow \text{M}$ charge transfer.³³ The metal normally prefers tetrahedral coordination.

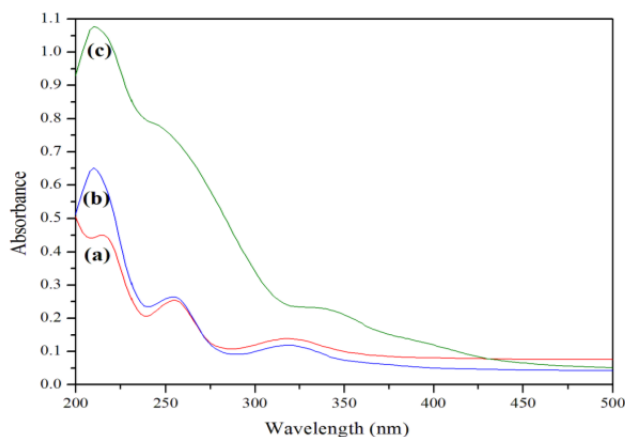


Fig. 2: UV-Vis spectra of (a) ligand (2) (b) Co(II) complex (3) and (c) Cd(II) complex (4)

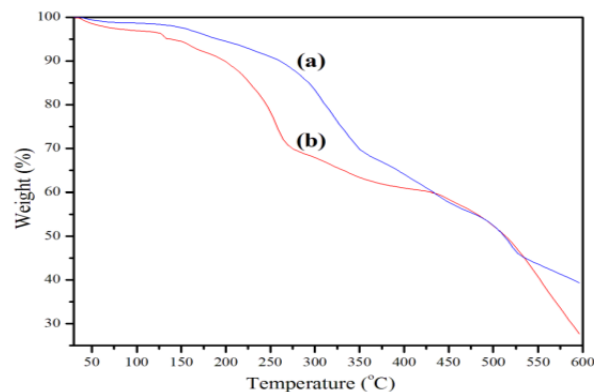


Fig. 3: TGA spectra of (a) Co(II) complex (3) and (b) Cd(II) complex (4)

Thermal analysis:

The thermal behaviour of ionic liquid based Schiff base metal complexes were characterized by thermo gravimetric analysis (TGA) given in Fig.3. The sample was analysed in a platinum pan under air atmosphere and the temperature was linearly increased at $10\text{ }^\circ\text{C}/\text{min}$ over a temperature range of 25-600 $^\circ\text{C}$. In case of Cd(II) complex (4) the hydrated water molecules was eliminated in the temperature range 100 -150 $^\circ\text{C}$. The thermal decomposition profile showed a catastrophic weight loss around 150 – 250 $^\circ\text{C}$, followed by gradual 35% weight loss between 250 – 500 $^\circ\text{C}$. For Co(II) complex (3) a mass loss occurred within the temperature range 150 -325 $^\circ\text{C}$ corresponding to a loss of organic fragments. At the temperature range 325-540 $^\circ\text{C}$ mass losses occurred due to the formation of intermediate species through the decomposition of the organic moiety of the complexes.

Antibacterial activities

The antibacterial activity of the ligand and its newly synthesized Cd(II) , Co(II) complexes against the gram positive bacteria *Bacillus subtilis*, *Bacillus cereus* and gram negative bacteria *Proteus vulgaris* and *Enterobacter aerogenes* were studied. The different concentrations were made by adding with DMSO . Throughout the solvent control (DMSO) was used that showed no inhibition zone. The concentrations of the tested compounds were 10, 20, 30, 40 and $50\text{ }\mu\text{g}/\text{mL}^{-1}$ in comparison to the standard drug *Ampicilin*. Minimum inhibitory concentration (MIC) was evaluated for all the compounds. The nutrient agar medium was poured into 0.5 ml culture containing Petri plates. Then well diffusion technique^{34, 35} was performed. Petri plates were placed in incubator at 37°C for 24 hrs. The ligand along with the complexes showed very significant result against the tested bacteria. The result is shown in Fig.4.

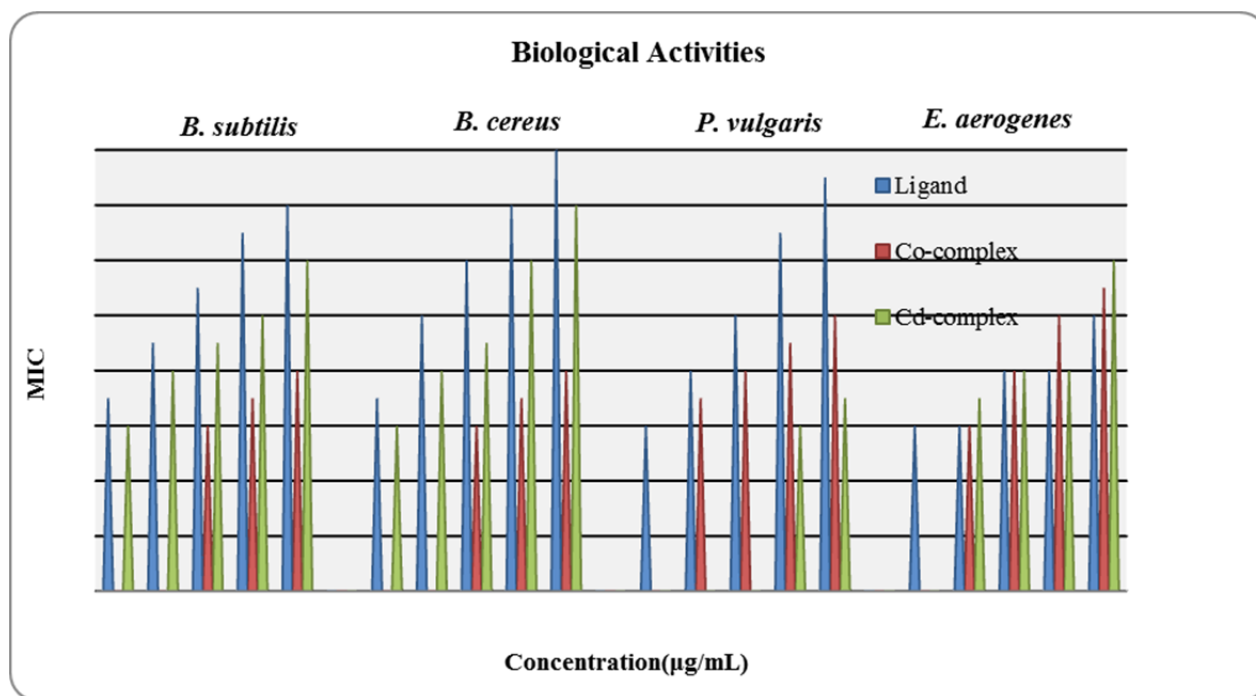


Fig. 4: Antibacterial activities of ligand(2), Co(II) complex(3) and Cd(II) complex(4).

4. CONCLUSION

The physico-analytical data showed that both the complexes were formed from the reaction of the ligand and the metal salts. The 1:2 (M:L) of the Schiff base metal complexes were suggested by the elemental analysis and mass-spectra, FT-IR, ¹H-NMR, TGA and magnetic moment analysis. The minimum inhibition zone data suggested that the Schiff base and its Co (II), Cd (II) complexes have significant antibacterial activity on the tested bacteria.

5. ACKNOWLEDGEMENTS

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REFERENCES

- [1] Rogers RD, Seddon KR. *Science*. 2003; **302**: 792-793.
- [2] Sakaebe H, Matsumoto H. *Electrochem. Commun.* 2003; **5**: 594-598.
- [3] Earle, MJ, Esperanc JMSS, Gilea, MA, Lopes JNC, Rebelo, LPN, Magee J, Seddon KR, Widegren JA. *Nature*. 2006; **439**: 831-834.
- [4] Freemantle M. *Chem. Eng. News*. 1998; **76**: 32-37.
- [5] Welton T. *Chem. Rev.* 1999; **99**: 2071-2083.
- [6] Holbrey J, Seddon KR. *Clean. Prod. Proc.* 1999; **1**: 223-236.
- [7] Yi F, Peng Y, Song G. *Tetrahedron Lett.* 2005; **46**: 3931-3933.
- [8] Cole AC, Jensen JL, Ntai I, Tran K L T. *J. Am. Chem. Soc.* 2002; **124**: 5962-5963.
- [9] Li J, Peng Y, Song G. *Catal. Lett.* 2005; **102**: 159-162.
- [10] Wasserscheid P. *Chem. Commun.* 2003; **16**: 2038-2039.
- [11] Chandra S, Gupta K. *Trans. Metal. Chem.* 2002; **27**: 196-197.
- [12] Atkins A J, Black D, Blake AJ, Marin-Becerra A, Parsons S, Ruiz-Ramirez L, Schröder M. *J. Chem. Soc, Chem. Commun.* 1996; **4**: 457-464.
- [13] Hadjikakou SK, Hadjiliadis N. *Coord. Chem. Rev.* 2009; **253**: 235-249.
- [14] Garoufis A, Hadjikakou SK, Hadjiliadis N. *Coord. Chem. Rev.* 2009; **253**: 1384-1397.
- [15] Goku A, Tumer M, Demirelli H, Wheatley RA. *Inorg. Chim. Acta.* 2005; **358**: 1785-1797.
- [16] Song G, Cai Y, Peng Y. *J. Comb. Chem.* 2005; **7**: 561-566.
- [17] Peng YQ, Cai YQ, Song GH, Cheng, J. *Synlett.* 2005; **14**: 2147.
- [18] Yıldız M, Kılıç Z, Hökelek T. *J. Mol. Struct.* 1998; **441**: 1-10.
- [19] Yeap G-Y, Ha S-T, Ishizawa N, Suda K, Boey P-L, Mahmood WAK. *J. Mol. Struct.* 2003; **658**: 87-99.
- [20] Abdel-Latif SA, Hassib HB, Issa YM. *Spectrochimica. Acta. Part A.* 2007; **67**: 950-957.
- [21] Canpolat E, Kaya M. *Turk. J. Chem.* 2005; **29**: 409-415.
- [22] Kohawole GA, Patel KS. *J. Chem. Soc, Dalton. Trans.* 1981; **6**: 1241-1245.
- [23] Tai X, Yin X, Chen Q, Tan M. *Molecules.* 2003; **8**: 439-443.
- [24] Rezvani Z, Dinband B, Abbasi AR, Nejati K. *Polyhedron.* 2006; **25**: 1915-1920.
- [25] Rezvani Z, Abbasi AR, Nejati K, Seyedahmadian M, *Polyhedron.* 2005; **24**: 1461-1470.

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- [26] Kakanejadifard A, Zabardasti A, Kooshki H. *J. Coord. Chem.* 2009; **62**: 3552–3558.
- [27] Kakanejadifard A, Zabardasti A, Ghasemian M, Niknam E. *J. Coord. Chem.* 2008; **61**:1820–1826.
- [28] Yilmaz I, Temel H, Alp H. *Polyhedron.* 2008; **27**: 125–132.
- [29] Yeap G. –Y, Heng B. –T. *J. Chem. Sci.* 2014; **126**: 247-254.
- [30] Peral F, Gallego E. *J. Mol. Struc.* 1997; **415**: 187-196.
- [31] Silverstein RM. *Spectrometric Identification of Organic Compounds*; John Wiley & Sons: 7th edition, 2005.
- [32] Lever AP. *Inorganic Electronic Spectroscopy*; Elsevier: New York, NY, USA, 2nd edition, 1984.
- [33] Figgis BN. *Introduction to Ligand Fields*; Interscience Publishers, JohnWiley & Sons: New York, USA, 1967.
- [34] Clinical and Laboratory Standards Institute (NCCLS), *Performance Standards for Antimicrobial Disk Susceptibility Tests*; Approved Standard, 9th edition, M2-A9, Wayne, PA, USA, 2006.
- [35] Clinical and Laboratory Standards Institute (NCCLS) (2006), *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically*; Approved Standard. 7th edition, M7-A7, Wayne, PA, USA, 2006.