IJBPAS, September, 2021, 10(9): 3074-3086

ISSN: 2277–4998

International Journal of Biology, Pharmacy
and Allied Sciences (IJBPAS)
'A Bridge Between Laboratory and Reader'

www.ijbpas.com

ONE POT MULTI-COMPONENT SYNTHESIS AND CHARACTERIZATION OF Cd(II) COMPLEX WITH BIDENTATE SCHIFF BASE AND THIOCYANATE ION

R. SELVARANI[*], S. BALASUBRAMANIYAN, K. RAJASEKAR, C. VEERAVEL & R. GEETHA

Department of Chemistry, Govt. Arts College, Ariyalur-621713 (Affiliated to Bharathidasan University, Tiruchirappalli-620 024), Tamil Nadu, India

***Corresponding Author: Dr. R. Selvarani: E Mail: selvasekar2008yoki@gmail.com; yokkesh111@gmail.com**

Received 3rd Oct. 2020; Revised 5th Nov. 2020; Accepted 6th Dec. 2020; Available online 1st Sept. 2021

https://doi.org/10.31032/IJBPAS/2021/10.9.5620

ABSTRACT

A new schiff base ligand derived based on the condensation of orthophenylenediamine and cinnamaldehyde and coordination complex with Cd(II) have been synthesized. The resulting complex has been characterized by the elemental analysis, melting point, IR and Far-IR spectra, reflectance spectra and NMR (^{1}H & ^{13}C) spectra. The purity of the ligand and its metal complex confirmed by microanalysis and melting point studies. The monomeric and neutral nature of the complex was confirmed by the low conductance value. The electronic spectra of the schiff base and its complex support chromophoric group present in the schiff base and tetrahedral geometry of complex. The IR spectra show the involvement of azomethine nitrogen in coordination to the central metal ion and metal chelates were also confirmed by Far-IR spectra. The NMR spectra of schiff base and its diamagnetic Cd(II) complex shows the magnetic property and geometry of them. The schiff base and its complex were screened for in-vitro antibacterial activity against some gram positive and gram negative bacteria and fungus, the complex is active for some strain of microorganisms and resistant for bacterial and fungal strains. The biological activity and medicinal chemistry properties was further confirmed by pharmacokinetics study.

Keywords: Cinnamaldehyde, Schiff base, Cd(II)complex, Antibacterial, Antifungal, Pharmaceutical

INTRODUCTION

Schiff base is an effective ligand which is commonly used as a potential drug in inorganic and medicinal chemistry **[1]**. In coordination chemistry schiff base are very important due to the formation of most stable complexes with transition metal ions **[2-3]**. Nowadays active and well designed schiff base ligands are considered as privileged ligand. Schiff bases show chemical and biological properties such as oxygen binding, hydrogenation, amino group transformation, complexing ability, antibacterial, antifungal and anticancer activities **[4-5]**. Coordination metal complexes are gaining increasing important in the design of repository drug in nutrition and study of metabolism **[6-7]**. Schiff base metal complexes are very interesting in inorganic chemistry due to the physico-chemical, spectral and structural properties **[8]**. They are importance in the field of modern coordination chemistry because they have industrial, analytical, antibacterial, antifungal, anticancer, antiviral and antitubercular activities and it also shows chelating ability, catalytic and extraction properties **[9-10]**.This paper aims to synthesis of new Cd(II) complex with bio-active schiff base via green route method and characterized by various analytical, spectral and bio-potential methods.

MATERIALS AND METHODS

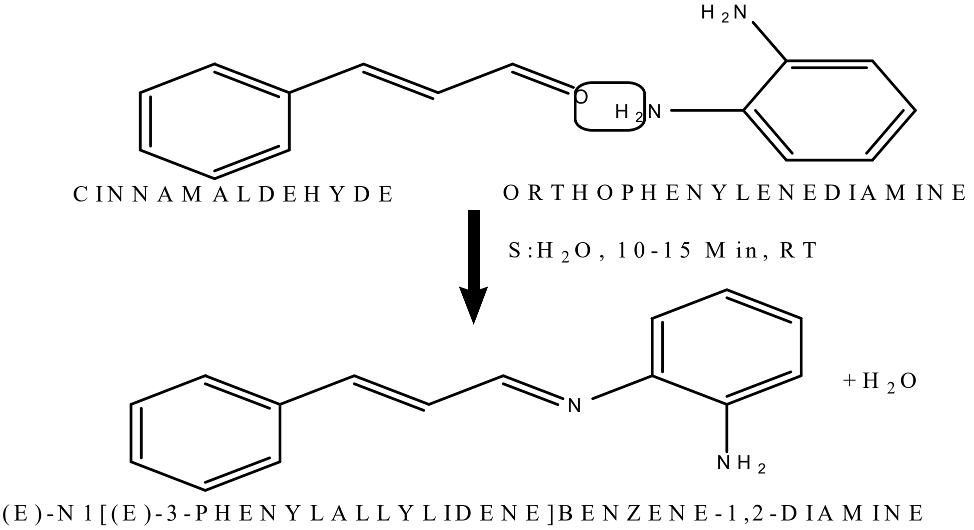
Materials: All the chemicals such as Orthophenylenediamine, cinnamaldehyde, potassium thiocyanate, cadmium nitrate, solvents and reagents were of AnalaR grade (99% pure) used as such without further purification. The synthesized schiff base and its complexes are stable and stored in long time at room temperature.

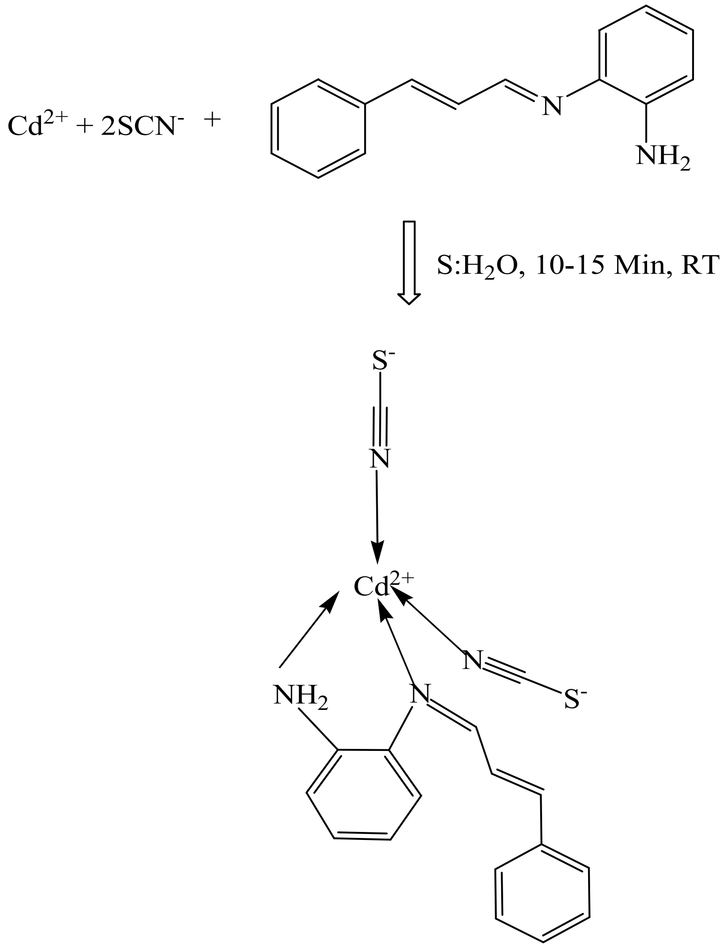
Methods: Elemental analysis was carried out using elemental Vario make EL-III model instrument at 950-1200°C temperature. The metal ions were estimated after decomposing a known weight of complex in acids by gravimetric/ colorimetric method. Melting point (°C) were recorded on a Ajay melting point instrument in open capillary tube. Molar conductance of the schiff base and complex was measured in acetonitrile solution at 10^{-3} M concentration at room temperature by the use of Systronic Conductivity Bridge with dip-type conductivity cell made of platinum black. UV-Visible spectra were recorded in solid state spectra (DRS method) on JASCO-V650 made spectrometer in the range of 200-800 nm. Using Schimadzu, FT-IR,-4100 type-A model IR spectrometer, IR spectra of Schiff base and its metal complex were recorded in the range of 4000 to 400cm^{-1} as KBr pellet method. The Far IR spectra of the complex were recorded in a Bruker, Germany make, 3000 Hyperion Microscope with Vertex 80 FTIR system model instruments. The ^{1}H and ^{13}C-NMR spectra of schiff base and its diamagnetic Cd(II) complex were carried out by Bruker instrument in DMSO-d6.

Synthesis

Synthesis of Schiff base: The goal of green chemistry is to develop Eco-friendly synthetic reactions. Green chemistry involves the use of microwave technology, sonochemistry, phase transfer catalysis, ionic liquids, and many other techniques. Green chemical one-pot multi component condensation reaction of 0.486g (4.40 m mol) of Orthophenylenediamine (15 ml ethanol) and 0.624g (4.70 m mol) of cinnamaldehyde (15 ml diethyl ether) using water as a green solvent and stirred continuously for about 10-15 min at room temperature, shiny powdered yellow color precipitate was formed **[11]**. The product was purified by simple filtration followed by washing with water and drying in desiccators and the yield was (73.33%). This method is experimentally simple, clean, high yielding, and green, with reduced reaction times.

Synthesis of Cd(II) complex: Schiff base, 0.720g, (3.24 mmol) in 25 ml ethanol solution was mixed with cadmium nitrate (1g, 3.24 mmol in 10 ml of methanol) and add anionic ligand viz., potassium thiocyanate (0.630g, 6.48 mmol in 10 ml of water) was added. Then 10 ml of water used as a green solvent and stirred continuously for 10-15 min at room temperature yellow color precipitate was formed. The product was purified by simple filtration followed by washing with water and drying in desiccators and the yield was (81.25%).





(E)-N1[(E)-3-phenylallylidene]benzene-1,2-diaminedithiocyanato-KN-cadmium(II)

RESULTS AND DISCUSSION

Micro analysis

The synthesized schiff base and its metal complex were subjected to microanalysis. The elemental analysis of schiff base and its complex are present in **Table 1**. The experimental elemental analysis data were in good agreement with calculated values and the % of metal ion by metal estimation was confirmed by the formation of 1:1 (M:L) ratio metal complex. It is also predicted that the complex molecular formula $[Cd(SB)(SCN)_{2}]$ where SB is schiff base, SCN is thiocyanate ion. The conductance of synthetic complex illustrated in **Table 1** which reveal that the non-electrolytic (1:0) type of complex **[12]**.

ESI Mass spectra

ESI mass spectrum of schiff base recorded at room temperature. It is proposed that the empirical formula of the schiff base and also support the stability of them. From the data of m/z the value at 222 confirmed the molecular formulae of schiff base ($C_{15}H_{14}N_2$) but the fragments at 105and 117 corresponds to the $C_6H_6N_2^-$ and $C_9H_8^+$ respectively **[13]**.

UV-spectral study

The Cd(II) complex did not show any d-d transition because of its diamagnetic nature and the UV spectra were diminated, only for the charge transfer transition (CT band) 397 nm (5188 cm^{-1}) in the absence of d-d transition they show colorless or pale yellow due to completely filled ‘d’ sub shell. The diamagnetic Cd(II) complex is tetrahedral geometry predominantly confirmed by its UV spectral data **[14]**.

IR & Far-IR spectral studies

The IR spectrum of schiff base shows a strong band at 1595$cm^{-1}$and 3500 cm^{-1} region which are attributed to imine (C=N) and amino group (N-H) stretching frequencies. There are two aromatics rings present in the schiff base which shows the aromatic (C-H) and (C-C) stretching frequency at 3371 cm^{-1} 3142 cm^{-1}, 3020 cm^{-1} and 2750 cm^{-1} respectively. The aromatic C-N stretching frequency at 1398 cm^{-1} and allylic group (C-H), (C=C) and (C-C) stretching frequencies at 1850 cm^{-1}, 1960 cm^{-1} and 1780 cm^{-1}. In Cd(II) complex the imine (C=N) stretching frequency was shifted to higher frequency at 1627 cm^{-1} where as the amine (N-H) stretching frequency of schiff base shifted to lower region at 3467 cm^{-1}, due to the complexation by deprotonation moreover all the aromatic and allylic stretching frequencies are shifted to lower and higher values after complexation. The stretching frequency at 2053 cm^{-1} in complex which is absent in the free ligand indicating the thiocyanate ion coordinated to the metal ion through its nitrogen atom **[15-16]**. The new peak at 421 cm^{-1}, 526 cm^{-1} and 498 cm^{-1} region due to the formation of (M-N) bond of azomethine, (M-N) of amino group and (M-N) thiocyanate ion bond respectively which are absent in schiff base ligand confirmed by the effective coordination of schiff base through its imine and amino nitrogen and nitrogen atom of mixed anionic thiocyanate ion **[17] (Figure 1)**.

NMR spectral study (^{1}H & ^{13}C)

^{1}H-NMR spectra of schiff base and its diamagnetic Cd(II) complex were recorded in DMSO-d6. The spectrum of schiff base demonstrated amino and azomethine proton chemical shift at 5.05 ppm and 8.41-8.43 ppm respectively. The orthophenylenediamine aromatic (C-H) were founded at 6.69-6.70 ppm, 6.57-6.58 ppm, 6.97-6.98 ppm and 7.022-7.03 ppm respectively. Cinnamaldehyde three aromatic proton of schiff base were observed at 7.44ppm, 7.38ppm and 7.65-7.66 ppm as multiplet. The coordination of azomethine and amino nitrogen were assigned at downfield shift in the Cd(II) complex. This downfield shift is attributed to the deprotonation and discharging of electrons towards the Cd(II) ion and also increase the conjugation on complexation of schiff base with the metal ion **[18]**.

^{13}C-NMR spectra of schiff base and its diamagnetic Cd(II) complex were recorded in DMSO-d6. The spectral data reported and the experimental evidence confirmed all the carbon atoms were found to be in expected region of chemical shift values. The schiff base shows carbon chemical shift value of azomethine carbon (CH=N) and amino carbon (C-NH_2) at 158.79 ppm and 144.02 ppm. The condensed moiety of cinnamaldehyde show aromatic carbon atom chemical shift in schiff base 127.98 ppm, 129.43 and 129.82 ppm, the another moiety orthophenylenediamine in schiff base also show the aromatic carbon atoms chemical shift values at 143.10 ppm, 116.89 ppm, 129.33 ppm, 117.21 ppm and 17.85 respectively. The downfield shift of azomethine and amino nitrogen atom at 158.96 ppm and 143.83 ppm in Cd(II) complex was due to the change of electron density and also the increase of conjugation which favor the down field/up field shifts at 0.17 ppm to 0.19 ppm. All the other chemical shift values of carbon atoms in the schiff base were shifted to downfield/up field shift in Cd(II) complex after complexation **[19] (Figure 2-5)**.

Bio-potential activity

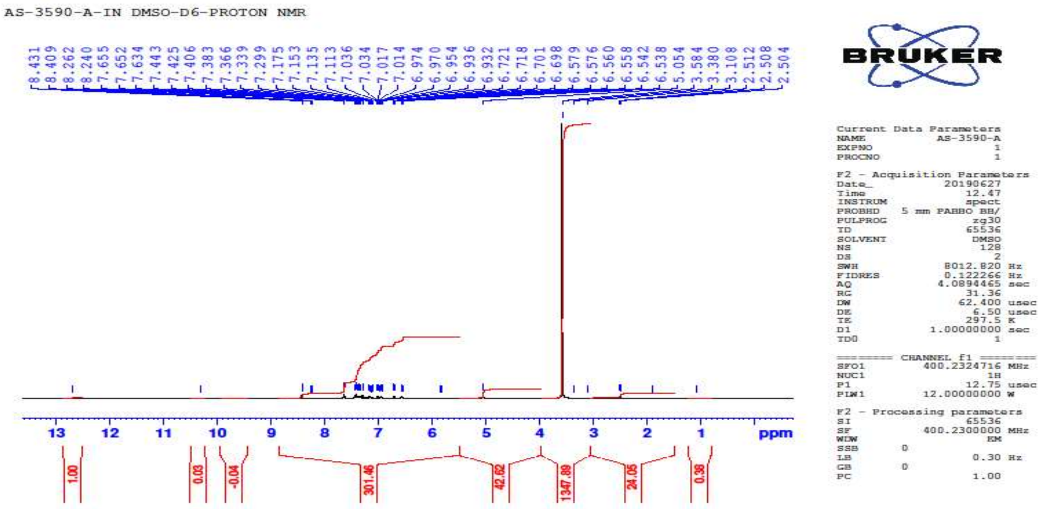
The in-vitro biological screening effect of the investigated complex were tested against two gram positive bacteria *S. aureus* and *Enterococcus* and three gram negative bacteria *viz., E. coil, P. aeruginosa* and *Vibrio parahaemolyticus* and then one fungus *C. Albicance*. The results shows the metal complex have higher activity than the schiff base because of the results have been suggested that the Schiff base with the nitrogen donor system having inhibited enzyme protection. The enzyme protection deactivates the metal ion in the complex after complexation chelates effect reduces the polarity of metal ions. Due to the partial sharing of positive charge to the donor group and also π electrons delocalization with whole chelates ring. This chelates effect increase the lipophilicity of metal ion which favors the cell permeation through lipid layer of cell membrane **[20-21] (Figure 6)**.

Physico-chemical and general computational studies

The computational study of schiff base and Cd(II) complex generate structure file generator from online tool Swiss ADME web page. Using the web tool the physico-chemical parameters, such as molecular weight, molecular refractivity, count of specific atom types and the topological polar surface area were predicted. The latter proven as a useful descriptor in many models for estimation of membrane diffusion, ADME and pharmacokinetic behavior. The lipophilicity was assessed by means of five alternative predictive models; i.e. XlogP; WlogP; MlogP; SILICOS-IT and ilogP, together with consensus logP estimation, based on the average value of the different computational parameters. The medicinal chemistry and drug properties of the compounds also assessed and the results indicating the schiff base and its complex are used as drug in the field of medicinal chemistry **(Table 2 to 4)**.

Table 1: Analytical data

S. No.	Schiff base/ complex	Molecular weight (g/mol)	MP (°C)	Color	Elemental analysis					Molar conductance (Ohm^{-1}cm^{2}mol^{-1}
					%C	%H	%N	%S	%M	
1	**Schiff base**	**222.30**	**117**	**Shiny yellow**	**80.97 (80.19)**	**6.29 (6.30)**	**12.59 (12.52)**	**-**	**-**	**20.00**
2	**[Cd(SB)(SCN)$_2$]**	**450.89**	**137**	**Yellow**	**45.24 (46.00)**	**3.10 (3.45)**	**12.41 (12.50)**	**14.19 (14.89)**	**24.94 (24.90)**	**04.00**



```
Current Data Parameters
NAME             AS-3590-A
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
Date_             20190627
Time                 12.47
INSTRUM              spect
PROBHD    5 mm PABBO BB/
PULPROG               zg30
TD                   65536
SOLVENT               DMSO
NS                     128
DS                       2
SWH               8012.820 Hz
FIDRES            0.122266 Hz
AQ               4.0894465 sec
RG                   31.36
DW                  62.400 usec
DE                    6.50 usec
TE                   297.5 K
D1              1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
SFO1           400.2324716 MHz
NUC1                    1H
P1                   12.75 usec
PLW1           12.00000000 W

F2 - Processing parameters
SI                   65536
SF             400.2300000 MHz
WDW                     EM
SSB       0
LB                    0.30 Hz
GB        0
PC                    1.00
```

Figure 1: ^{1}H-NMR spectrum of Schiff base

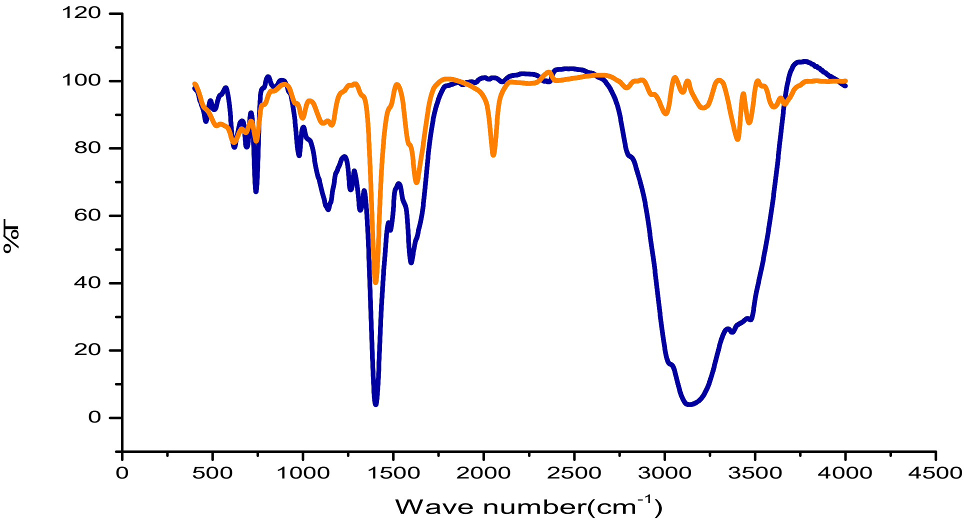
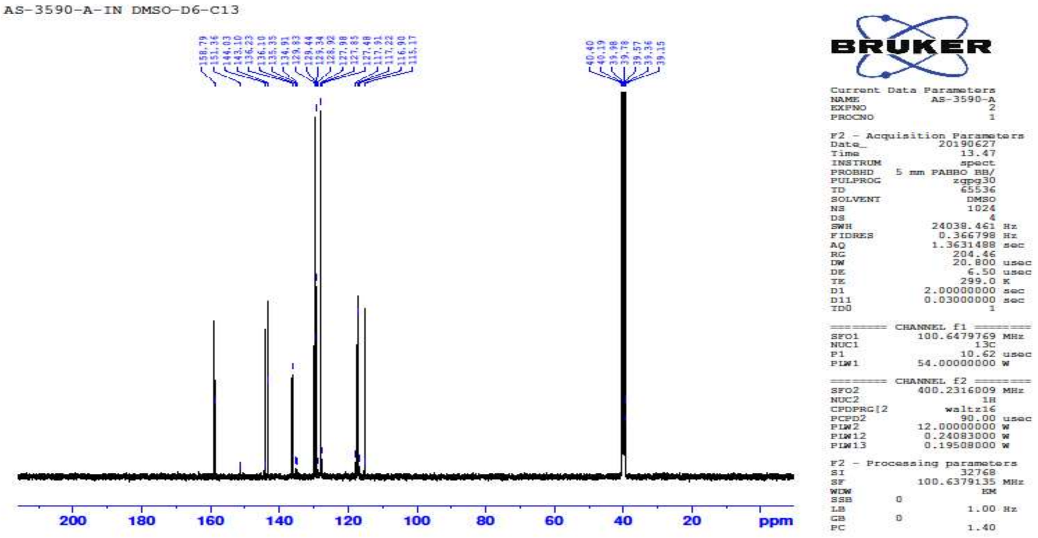
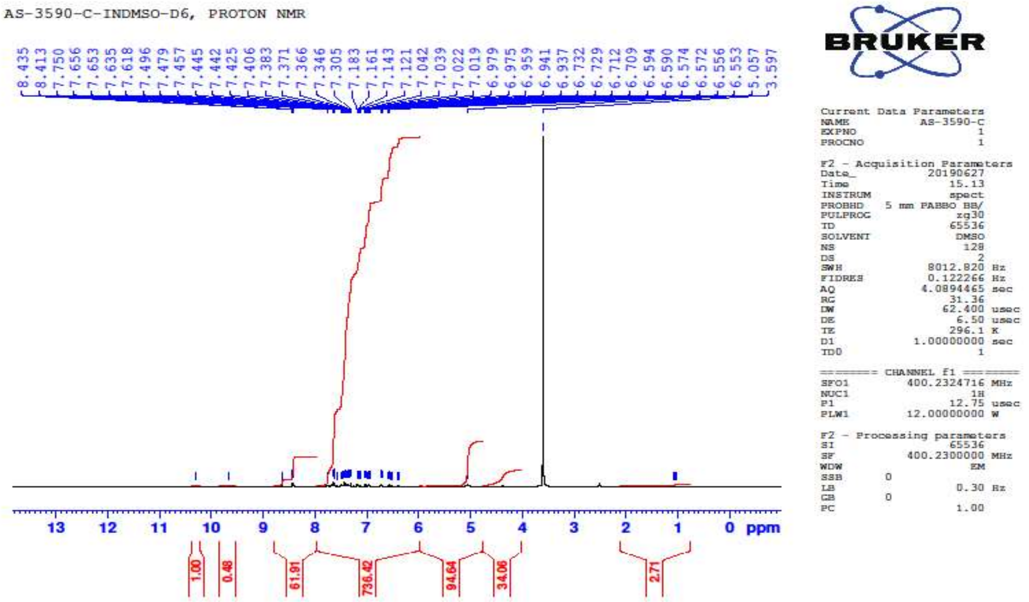


Figure 2: IR spectrum of Schiff base and Cd(II) complex



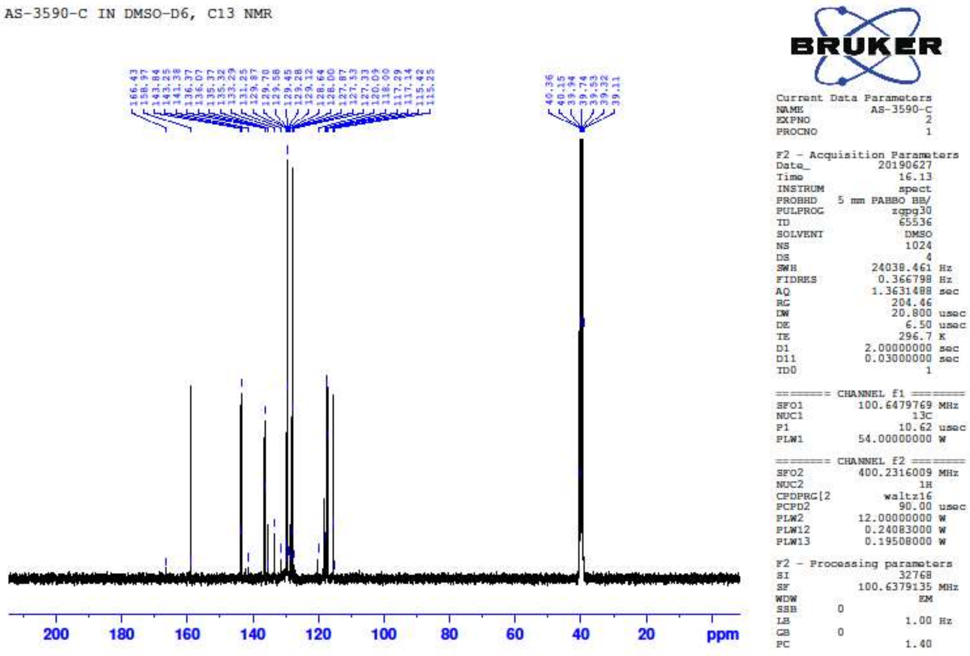
```
Current Data Parameters
NAME              AS-3590-A
EXPNO                     2
PROCNO                    1

F2 - Acquisition Parameters
Date_              20190627
Time                  13.47
INSTRUM               spect
PROBHD   5 mm PABBO BB/
PULPROG             zgpg30
TD                    65536
SOLVENT                DMSO
NS                     1024
DS                        4
SWH               24038.461 Hz
FIDRES             0.366798 Hz
AQ                1.3631488 sec
RG                   204.46
DW                   20.800 usec
DE                     6.50 usec
TE                    299.0 K
D1               2.00000000 sec
D11              0.03000000 sec
TD0                       1

======== CHANNEL f1 ========
SFO1            100.6479769 MHz
NUC1                    13C
P1                    10.62 usec
PLW1            54.00000000 W

======== CHANNEL f2 ========
SFO2            400.2316009 MHz
NUC2                     1H
CPDPRG[2            waltz16
PCPD2                 90.00 usec
PLW2            12.00000000 W
PLW12            0.24083000 W
PLW13            0.19508000 W

F2 - Processing parameters
SI                    32768
SF              100.6379135 MHz
WDW                      EM
SSB         0
LB                     1.00 Hz
GB          0
PC                     1.40
```

Figure 3: ^{13}C-NMR spectrum of schiff base



```
Current Data Parameters
NAME              AS-3590-C
EXPNO                     1
PROCNO                    1

F2 - Acquisition Parameters
Date_              20190627
Time                  15.13
INSTRUM               spect
PROBHD   5 mm PABBO BB/
PULPROG                zg30
TD                    65536
SOLVENT                DMSO
NS                      128
DS                        2
SWH                8012.820 Hz
FIDRES             0.122266 Hz
AQ                4.0894465 sec
RG                    31.36
DW                   62.400 usec
DE                     6.50 usec
TE                    296.1 K
D1               1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
SFO1            400.2324716 MHz
NUC1                     1H
P1                    12.75 usec
PLW1            12.00000000 W

F2 - Processing parameters
SI                    65536
SF              400.2300000 MHz
WDW                      EM
SSB         0
LB                     0.30 Hz
GB          0
PC                     1.00
```

Figure 4: 1H-NMR spectrum of Cd(II) complex



```
Current Data Parameters
NAME          AS-3590-C
EXPNO                 2
PROCNO                1

F2 - Acquisition Parameters
Date_          20190627
Time              16.13
INSTRUM           spect
PROBHD   5 mm PABBO BB/
PULPROG         zgpg30
TD                65536
SOLVENT            DMSO
NS                 1024
DS                    4
SWH           24038.461 Hz
FIDRES         0.366798 Hz
AQ            1.3631488 sec
RG               204.46
DW               20.800 usec
DE                 6.50 usec
TE                296.7 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
SFO1        100.6479769 MHz
NUC1                13C
P1                10.62 usec
PLW1        54.00000000 W

======== CHANNEL f2 ========
SFO2        400.2316009 MHz
NUC2                 1H
CPDPRG[2        waltz16
PCPD2             90.00 usec
PLW2        12.00000000 W
PLW12        0.24083000 W
PLW13        0.19508000 W

F2 - Processing parameters
SI                32768
SF          100.6379135 MHz
WDW                  EM
SSB      0
LB                 1.00 Hz
GB       0
PC                 1.40
```

Figure 5: 13C-NMR spectrum of Cd(II) complex

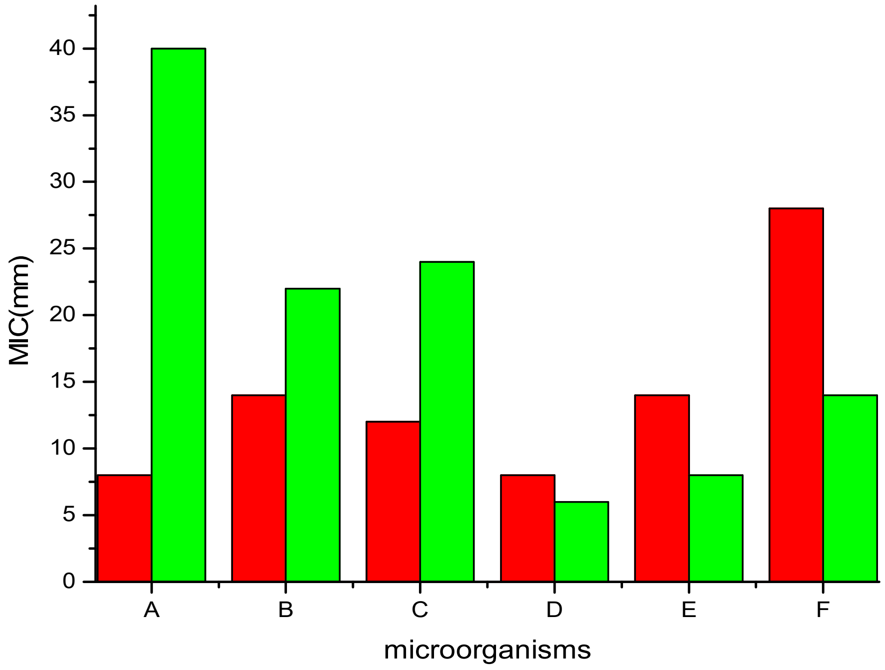


Figure-6: Comparative bio-potential activities of Schiff base & Cd(II) complex
A- *S. aureus*, B- *E. Coli*, C- *V.parahaemolyticus*, D- *P. aeruginosa*, E- *Enterococcus*, F- *C. albicans*

Table 2: Physico-chemical data's

S. No.	Parameters	Schiff base	$[Cd(SB)(SCN)_2]$
1	Formula	$C_{15}H_{14}N_2$	C17H14CdN4S2
2	Molecular weight	222.29 g/mol	450.86 g/mol
3	Num. heavy atoms	17	24
4	Num. atom. heavy atoms	12	12
5	Fraction Csp3	0.00	0.00
6	Num. rotatable bonds	3	3
7	Num. H-bond acceptors	1	3

Table 3: Lipophilicity data's

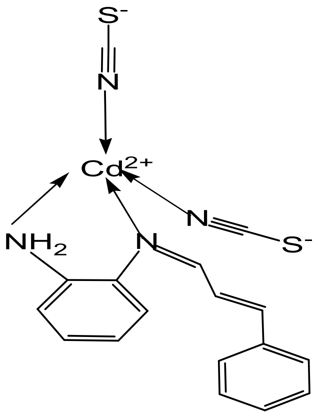
1	GI absorption	High	High
2	BBB permeant	Yes	No
3	P-gp substrate	No	No
4	CYP1A2 inhibitor	Yes	Yes
5	CYP2C19 inhibitor	Yes	Yes
6	CYP2C9 inhibitor	Yes	Yes
7	CYP2D6 inhibitor	No	No
8	CYP3A4 inhibitor	Yes	Yes
9	Log K_p (skin permeation)	-5.55 cm/s	-6.14 cm/s

Table 4: Pharmacokinetics data's

1	Log $P_{o/w}$ (ilogP)	2.61	0.00
2	Log $P_{o/w}$ (XlogP3)	2.97	4.10
3	Log $P_{o/w}$ (WlogP)	3.58	3.61
4	Log $P_{o/w}$ (MlogP)	3.05	1.66
5	Log $P_{o/w}$ (SILICOS-IT)	3.67	3.67
6	Consensus log $P_{o/w}$	3.18	2.61

CONCLUSION

The present study reveals that the schiff base (E)-N1[(E)-3-phenylallylidene]benzene-1,2-diamine contains two potential sites for coordination of metal ions. Thus it behaves as bidentate ligand coordinating through imine and amino nitrogen atoms. On the basis of UV visible and NMR spectral data, they are found to be tetrahedral geometry. On the basis of conductivity the complex is neutral and they show enhanced biological screening activities against tested microorganisms. The structure of the complex may be given as following:



ACKNOWLEDGEMENTS

The authors are very much grateful to the Principal, and Head Department of Chemistry, Govt. Arts College, Ariyalur for providing facilities available at the Department. We are indebted to the Head and Staff members of SAIF Chennai, Mumbai, STIC Cochin, Harman Research Institute, for providing spectral and biological activities of compounds.

REFERENCES

[1] Muneera Fatin Manan, Karimah Kassim and Mohd Abdul Fatah Abdul Manan, *The Malaysian Journal of Analytical Science*, **16**(3), 318-324 (2012).

[2] Tolulope M. Fasina, Olorunfemi O. Ogundele and Isaac Ayeni, *Journal of Chemical and Pharmaceutical Research,* **6**(6), 816-819 (2014).

[3] Zong Chin Khor, May Lee Low and Irene Ling, *Journal of Transition Metal Complex*, **3**, 1-9 (2020).

[4] Rakesh Chandra Ray, Md. Kudrata-E-Zahan, M. M. Haque, Md. Abdul Alim, Md. Mofasseral Alam, Md. Sher Ali, J. A. Shompa and Md. Akhter Farooque, *Int. J. of Chemical Studies.,* **3**(2), 17-19 (2015).

[5] N. Raman, S. Johnson Raja, J. Joseph, A. Sakthivel and J. Dhaveethu Raja, *J. Chil. Chem. Soc,* **53**(3), 1599-1604 (2008).

[6] R. Ramesh and S. Maheswaran, *Journal of Inorganic Biochemistry*, **96**, 457-462 (2003).

[7] Nanishankar V Haro Hally, Chris Chereta, Praveena Bhatp and Ka Anu Apparah, *Journal of Agriculture and Food Chemistry*, **65**(40), 8773-8778 (2017).

[8] Hamdi Temel, Salih Ilhan and Memet Sekerci, *Synthesis and Reactivity in Inorganic and Metal - organic Chemistry*, **32**(9), 1625-1634 (2002).

[9] R. Nair, A. Shah, S. Baluja and S. Chanda, *J. Serb. Chem. Soc*, **71**(7), 733-744 (2006).

[10] J. T. Makode and A. S. Aswar, Indian Journal of Chemistry, 43A, 2120-2125 (2004).

[11] V. K. Rao, S. S. Reddy, B. S. Ktishna M.K. R Naidu, C.N Raju and S. K. Ghosh, *Green Chem. Lett. Rev*, **3**(3), 217-223(2010).

[12] Morteza Montazerozohori, Kimia Nozarian and Hamid Reza Ebrahimi, Journal of Spectroscopy, 2013, 1-9 (2013)

[13] A.P. Mishra, R. K. Mishra and S. P. Shrivastava, *J. Serb. Chem. Soc.* **74**(5), 523-535(2009).

[14] G. G. Mohamed, M. M. Omar, and A. M. Hindy, *Turkish Journal of Chemistry*, **30**(3) 361–382, (2006).

[15] N. Raman, Y. Pichaikani Raja, and A. Kulanthaisamy, Indian Acad. Sci.(Chem. Sci), 1113(3), 183-189 (2001).

[16] A. Nagajothi, A. Kiruthika, S. Chitra and K. Parameshwari, Research Journal of Chemical Science, 3(2), 35-43 (2013).

[17] Adeola A. Nejo, Gabriel A. Kolawole and Ayorinde O. Nejo, Journal of Coordination Chemistry, 63(24), 4398-4410 (2010).

[18] Aliakbar Dehno Khalaji and Debasis Das, J. Therm. Anal Calorim, 114, 671-675 (2013)

[19] M. EL-Ajaily, M. Abou-Krisha, A. Etorki, F. AL-Assbaly and A. Maihub, J. Chem & Pharmaceutical Research, 5(12), 933-938 (2003).

[20] Pearly Sebastian Chittilappilly and K. K. Mohommed Yusuff, Indian Journal of Chemistry, 47A, 848-853 (2008).

[21] Md. Kutrat-E-Zahan, MS. Islam and Md. Abul Bashar, Russian Journal of General Chemistry, 85(3), 667-672(2015).