IJPSR (2014), Volume 5, Issue 10 **(Research Article)**

INTERNATIONAL JOURNAL
OF
PHARMACEUTICAL SCIENCES
AND
RESEARCH

Received on 26 March 2014; received in revised form, 15 May 2014; accepted, 13 July 2014; published 01 October 2014

SYNTHESIS AND CHARACTERISATION OF BIO-INORGANIC TRANSITION METAL COMPLEXES DERIVED FROM NOVEL BIGINELLI ADDUCT COUPLED SCHIFF'S BASES

Rohini Chandran [1] and S. Arul Antony [* 2]

Department of Chemistry [1], Sriram Engineering College, Perumalpattu, Thiruvallur - 602024, Tamil Nadu, India.
PG and Research Department of Chemistry [2], Presidency College, Chennai - 600005, Tamil Nadu, India.

Keywords:

Schiff base, 4-aminoantipyrine, Biginelli reaction, Metal complexes, Spectral studies, *In-vitro* antimicrobial activity

Correspondence to Author:
Dr. S. Arul Antony

PG and Research Department of Chemistry, Presidency College, Chennai - 600005, Tamil Nadu, India.

E-mail: aruantsam@gmail.com

ABSTRACT: Novel Schiff base comprising 4-aminoantipyrine with Biginelli adducts of salicylaldehyde has been designed and synthesized. Solid metal complexes of this Schiff base with Ni(II), Zn(II), Cd(II) and Hg(II) metal ions were synthesized and characterized by elemental analysis, magnetic susceptibility, molar conductance, ESI mass, IR, NMR, and UV-Vis spectral studies. From the data, it has been observed that the complexes had the composition of ML_2 type, diamagnetic nature and a tetrahedral geometry around the metal ion except for Ni(II) complex which has square planar geometry. The Ligand and its complexes have been screened for their *in-vitro* antifungal and *in-vitro* antibacterial activities against the fungi *i.e.*, *Candida albicans*, *Aspergillus flavus*, *Penicillium* spp., *Aspergillus niger and Trichophyton* and the gram-negative bacteria *Escherichia coli*, *Vibrio* spp., *Pseudomonas aeroginosa*, *Vibrio para haemolytic*, *Salmonella* spp., *Aeromonas* spp., *Klebsiella* spp., *Proteus* spp. and gram-positive bacteria *Bacillus spp* and *Staphylococcus aureus*. The *in-vitro* antimicrobial activities of these metal complexes found to be stronger than the ligand.

INTRODUCTION: Schiff base transition metal complexes possess excellent characteristics, structural similarities with natural biological substances, prepared by relatively simple preparatory procedures and the synthetic flexibility that enables the design of suitable structural properties [1]. Schiff base is derived by the condensation reaction of aldehyde or ketones or primary amine and these containing azomethine (RCH=N) group. Many Schiff base ligands have been synthesized from heterocyclic compounds [2]. The heterocyclic ring contained sulphur, nitrogen, and oxygen import special biological activity [3-8] to Schiff base and their metal complexes. The coordinating property of Schiff base with 4-aminoantipyrine has a variety of applications in the biological, clinical, analytical, and pharmacological areas [9-10]. Aminoantipyrine is very much used in medicine [2,] and it is believed that its amino derivative would equally be of much use in medicine possibly as intermediate in antipyretic and analgesic drugs [11]. A thorough search of the literature reveals that no work has been done on the transition metal complexes of Schiff base condensed by 4-aminoantipyrine with Biginelli reaction through salicylaldehyde which is a characteristic aroma component of buckwheat [12] and has good antimicrobial activity against certain bacteria or fungi [13].

QUICK RESPONSE CODE

DOI:
10.13040/IJPSR.0975-8232.5(10).4339-50

This article can be accessed online on
www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.5(10).4339-50

Moreover, Biginelli reactions (Multicomponent reactions) are of increasing importance in the organic and medicinal chemistry due to their high degree of atom economy, applications in the combinatorial chemistry and diversity-oriented synthesis [14].

In the present context, bidentate ligand from condensing 4-amionoantpyrine with Biginelli adduct of salicylaldehyde was synthesized. The synthesized compound and its chelation behavior with metal ions were studied through physical parameters and spectral analysis. The *in-vitro* antimicrobial properties of ligand and metal complexes were also investigated.

MATERIAL AND METHODS:

Chemicals and Reagents: All the chemicals and solvents were of analytical grade procured from Spectrochem Pvt Ltd, Mumbai, the solvent ethanol was dried by the standard procedures [15].

Reagents Required: Salicylaldehyde, Urea, Ethyl acetoacetate, acetic acid, 4-aminoantipyrine, Ethanol.

Instrumental Analysis: The molar conductance was measured in ELICO – CM 180 instrument using a 10^{-3} M Solution of DMSO as the solvent at room temperature. The elemental analysis was performed at IIT, Madras, India using analyzer Perkin Elmer 2400 for C, H, and N. The metal contents were determined by standard gravimetric method [16].

IR characteristic vibrations were recorded in JASCO FTIR/4100 spectrometer in the range of 4000-400 cm^{-1} using KBr pellet. UV visible spectra were recorded in JASCO UV spectrometer in the wave length range of 200-800 nm. H^1NMR and C^{13} NMR were recorded in $CDCl_3$ on a JASCO FTNMR Spectrometer. ESI mass spectra were recorded in Mass QTOFmicro mass spectrometer using nitrogen (CE-8ev, CV-27ev).

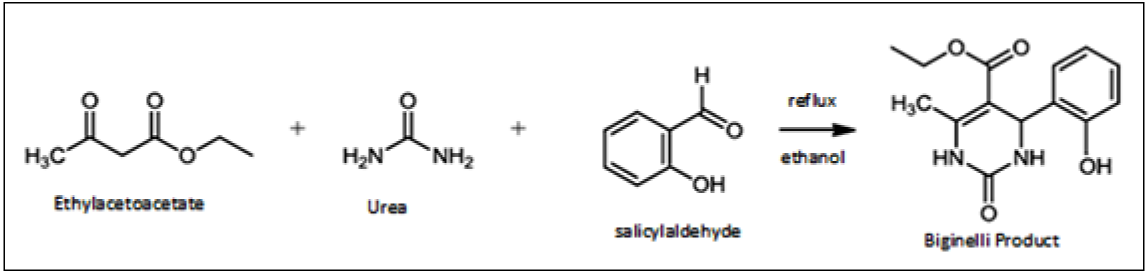
Magnetic susceptibility measurements of the complexes in the solid-state were determined by the Faraday method at room temperature using Lake Shore Model 7410 VSM, Std Ni as calibrant. Diamagnetic corrections were applied in compliance with Pascal's constant.

The *in-vitro* antimicrobial activities were carried out using disc and well diffusion method. All the spectral activities carried out at IIT, Madras, India.

Synthesis of Schiff Base Ligand: The synthesis of Schiff base ligand consisted of two steps described as follows and is shown in **Scheme 1**.

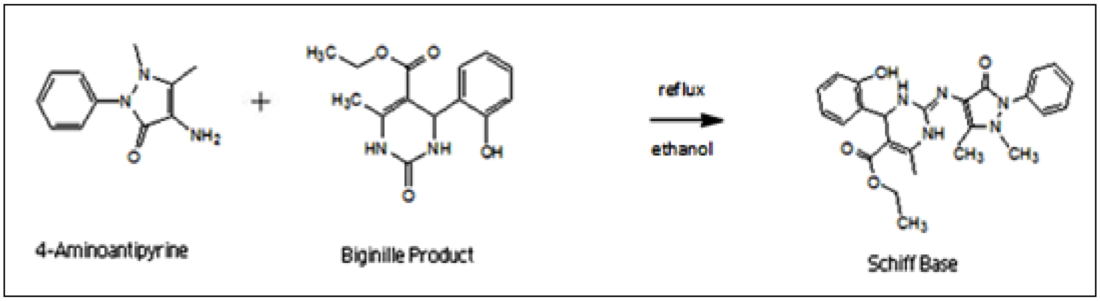
Step 1: Preparation of 4-(2-Hydrophenyl)-6-mehtyl-2-oxo-1, 2, 3, 4-tetrahydropyrimidine-5-carboxylate by Biginelli reaction: A mixture of urea (1.32g. 22mmol), salicylaldehyde (1.20ml, 10mmol), ethylaceto acetate (1.60ml, 12mmol), ethanol (25ml) and acetic acid (2ml) was heated under reflux for six hours until the completion of the reaction (60 ºC, mp-180, monitored by TLC).

The solvent was removed under reduced pressure; the yellow colored solid obtained was treated with 50ml of water, filtered, washed with water, dried and crystallized from ethanol [17].



SCHEME 1(a): SYNTHETIC ROUTE FOR BIGINELLI REACTION

Step 2: Preparation of 2-ethyl 2-(2,5-dihydro-2,3-dimethyl-5-oxo-1-phenyl-1H-pyrazol-4-ylimino)-1,2,3,4-tetrahydro-4-(2-hydroxyphenyl) -6 methyl pyrimidine-5-carboxylate: The Schiff base ligand was prepared by adding an ethanolic solution (50ml) of 4-aminoantipyrine (2.03g, 0.01 mol) to Biginelli product (2.76, 0.01 mol). The equimolar mixture was stirred and refluxed for 8-12 h until the completion of the reaction (60 ºC, mp-232, monitored by TLC). This was then filtered and kept aside for 24 h to facilitate crystallization. The crystal formed was recrystallized with hot ethanol and dried in a desiccator over $CaCl_2$ vacuum [2]. The yellow colored yield was measured.



SCHEME 1 (B): SYNTHESIS OF PROPOSED SCHIFF BASE LIGAND

Preparation of Metal Complexes: The complexes were prepared by the reaction of the ligand (9.23g, 0.02 mol) with the respective 0.01M metal (II) salts in ethanol medium (2.34g $NiCl_2.6H_2O$, 1.36 g $ZnCl_2$, 2.88g $CdCl_2$, and 2.71g $HgCl_2$).

The various metal salts and ligand in 1:2 ratios were refluxed and washed several times with ethanol after which kept aside for 24 hrs to facilitate crystallization [2]. The resulting crystals were then dried. The proposed structure of the complex is as shown in **Fig. 1**.

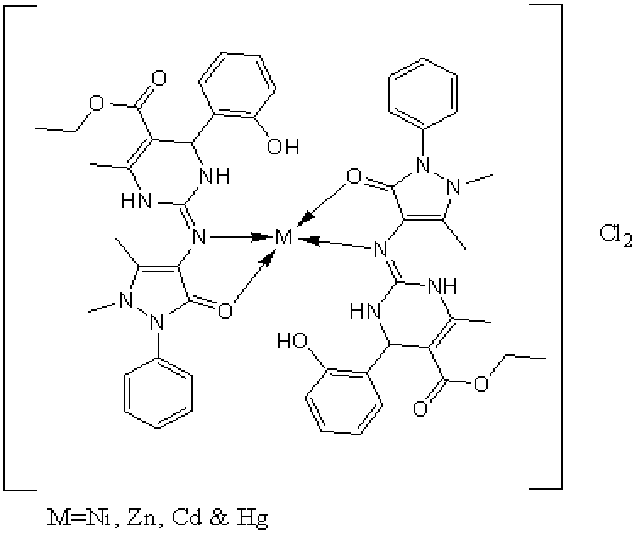


FIG. 1: PROPOSED STRUCTURE OF METAL COMPLEX

Pharmacological Assays:

Antimicrobial Assays: The biological activities of the synthesized Schiff base ligand and its Ni (II), Zn(II), Cd(II), and Hg(II) complexes were screened for their antibacterial and antifungal activities by the disc diffusion [18-19] and agar plate [20-21] method respectively. The *in-vitro* antibacterial activities of the compounds were tested against eight gram-negative bacteria like *Escherichia coli*, *Vibrio* spp., *Pseudomonas aeroginosa*, *Vibrio parahaemolytics*, *Salmonella* spp., *Aeromonas* spp., *Klebsiella* spp., *Proteus* spp. and two gram-positive bacteria like *Bacillus spp* and *Staphylococcus aureus*.

The *in-vitro* antifungal activities were carried out against *Candida albicans*, *Aspergillus flavus*, *Penicillium* spp., *Aspergillus niger*, and *Tricho - phyton* fungi [22-23]. The stock solutions of the test chemicals (1 mg mL^{-1}) were prepared by dissolving 10 mg of each test compound in 10 mL of distilled DMSO solvent. The different concentrations of the test compounds (100, 75, 50, and 25 μg mL^{-1}) were prepared by diluting the stock solution with the required amount of freshly distilled DMSO. Further, the controlled experiments were carried out by using freshly distilled DMSO solvent alone.

Antibacterial and Antifungal Screening: Muller-Hinton agar media was used for antibacterial studies.

The pure dehydrated Muller-Hilton agar (38 g) was dissolved in 1000 mL distilled water. The pure cultures of the bacterial strains *E. coli*, *Vibrio* spp., *Staphylococcus aureus, Pseudomonas aeroginosa, Bacillus* spp., *Vibrio parahaemolytics*, *Salmonella* spp., *Aeromonas* spp., *Klebsiella* spp., *Proteus* spp. were subcultured by inoculating in the nutrient broth, and they were incubated at 37 °C for about 18 h. The agar plates were prepared by using Muller-Hinton agar media, and wells were dug with the help of 6 mm sterile metallic cork borer.

Each plate was inoculated with 18-h-old bacterial culture (100 μL) using a micropipette and spread uniformly using a bent glass rod on each plate. The drug gentamycin was used as standard. Different concentration of the test compounds was incorporated into the wells using micropipette, and the plates were kept for incubation at 37 °C for 24 h. Soon after the completion of the incubation period, the diameter of the inhibition zone generated by each test compound against bacterial growth was measured using the antibiogram zone measuring scale. A similar procedure was followed for antifungal screening using Potato dextrose agar (PDA) media and Fluconazole drug as standard.

RESULTS AND DISCUSSION: All the complexes were characteristically colored, crystalline solid, non-hygroscopic, and air-stable at room temperature and could be stored for months without any appreciable changes. These were soluble in common organic solvents like Ethanol, Chloroform, DMSO, DMF, *etc*. but insoluble in water and decomposed on heating at a high temperature around equal or greater than 250 ºC.

Molar Conductance: The conductance measurements of the complexes were carried out in DMSO at room temperature and listed along with other parameters in **Table 1**. The obtained values were taken as good evidence for the existence of a non-electrolyte nature [22-23] of the complexes, and the values were too low to account for any dissociation.

Elemental analysis or Microanalysis: Analytical data of the compound together with their physical properties are consistent with the proposed molecular formula as given in **Table 1**. The data found are in good agreement with the theoretical calculation. The results showed that all the metal chelates have 1:2 (M: L) stoichiometry. Sharp melting point and consistency of both experimental and calculated percentage of C, H, N, and M show the purity of the Schiff base complexes. Further, the purity is further supported by TLC technique.

TABLE 1: PHYSICAL PROPERTIES AND ELEMENTAL ANALYSIS OF PROPOSED LIGAND AND ITS COMPLEXES

Compound	Colour	Melting point ◦C	Yield (%)	Elemental analysis found / (Calcd) %				Molecular Weight found/ (Calcd)	Molecular Formula	Molar Conductance
				C	H	N	M			
L	Yellow	220	82.4	65.78 (65.06)	5.72 (5.90)	15.66 (15.17)	-	461.24 (461.51)	$C_{25}H_{27}N_5O_4$	-
$(NiL_2)\ Cl_2$	Yellow Orange	250	66.2	57.31 (57.05)	4.90 (5.17)	13.12 (13.31)	5.78 (5.58)	1052.29 (1052.63)	$C_{50}H_{54}Cl_2N_{10}NiO_8$	1.88
$(ZnL_2)\ Cl_2$	Sandal Yellow	255	59.1	56.58 (56.69)	5.28 (5.14)	13.08 (13.22)	6.14 (6.17)	1059.28 (1059.32)	$C_{50}H_{54}Cl_2N_{10}O_8Zn$	1.56
$(CdL_2)\ Cl_2$	Wood Yellow	258	54.6	54.16 (54.28)	5.00 (4.92)	12,89 (12.66)	10.25 (10.16)	1106.35 (1106.34)	$C_{50}H_{54}CdCl_2N_{10}O_8$	1.46
$(HgL_2)\ Cl_2$	Brownish Yellow	262	52.9	50.37 (50.27)	4.63 (4.56)	11.94 (11.73)	16.83 (16.79)	1194.32 (1194.52)	$C_{50}H_{54}Cl_2HgN_{10}O_8$	1.28

*L – Schiff Base Ligand, *Molecular Weight- g/mol, *Molar Conductance ($ohm^{-1}\ Cm^2\ Mol^{-1}$)

ESI Mass Spectra: ESI mass spectra provide a vital clue for elucidating the structure of complexes, and the mass spectrum of the ligand is presented in **Fig. 2**.

It shows a molecular ion peak (M^+) m/z at 461.24 which is equivalent to its molecular weight and the isotopic peak at (M^++1) at m/z = 462.24 due to C^{13} and N^{15} isotopes. The base peak at m/z = 187 was due to 4-Aminoantipyrine $(C_{11}\ H_{11}\ N_2O)^+$ ion.

Another intense peak at m/z= 274 is due to $(C_{14}H_{16}N_3O_3)^+$ ion. The different competitive fragmentation pathways of ligand give the peaks at different mass numbers at 257, 185, 173, 171, 147, 132, 82, 77 and 56 due to $(C_{14}H_{15}N_3O_2)^{+,}$ $(C_{11}H_{11}N_3)^+$, $(C_{10}H_9N_2O)^+$, $(C_{10}H_9N_3)^+$, $(C_8H_9N_3)^+$, $(C_8H_8N_2)^+$, $(C_3H_2N_2O)^+$, $(C_6H_5)^+$, $(C_2H_4N_2)^+$ ions respectively. The intensity of these peaks reflects the stability and abundance of the ions [24-25].

The Spectrum of $(NiL_2)\ Cl_2$, $(ZnL_2)\ Cl_2$, $(CdL_2)\ Cl_2$ and $(HgL_2)\ Cl_2$ show a molecular ion peak (M^+) at m/z 1052.29, 1059.28, 1106.35 and 1194.32 respectively that is corresponding to their molecular weight. All these fragments lead to the formation of the species $(ML_2)^+$ which further undergo demetallation to yield the species $(L)^+$ which gives the fragment ion peak at m/z 461.

Thus, the data obtained from mass spectra confirm the stoichiometry of metal (1:2) ratio and in good agreement with the micro-analytical data.

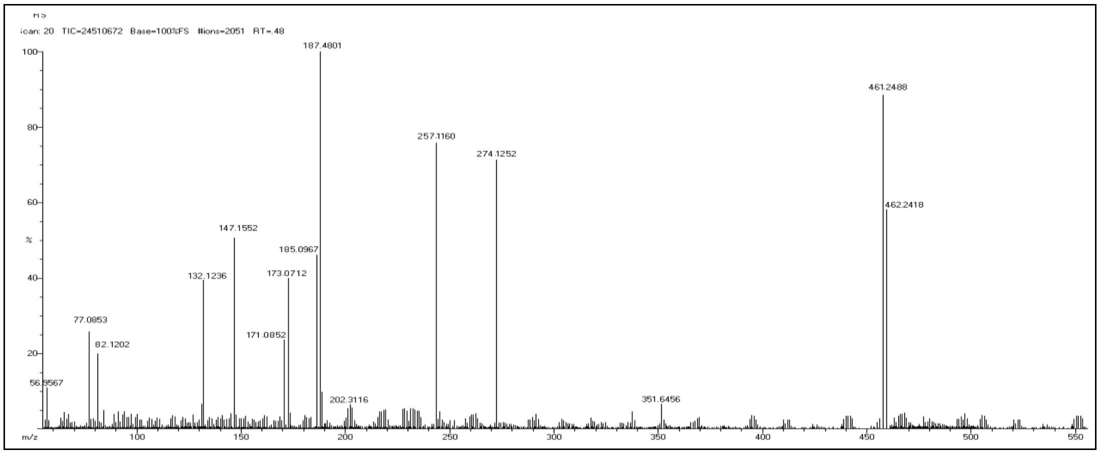


FIG. 2: MASS SPECTRUM OF SCHIFF BASE LIGAND

IR Spectrum: The IR spectra of complexes are compared with those of the free ligand to determine the involvement of co-ordination sites in chelation **Table 2** and **Fig. 3**.

The IR spectrum of the Schiff base exhibited characteristic band due to $\nu_{(C=N)}$ & $\nu_{(C=O)}$ at 1620 cm^{-1} and 1684 cm^{-1} respectively [26]. Also, the strong band at 3372cm^{-1} and a characteristic intensity band at 3355cm^{-1}were assigned to $\nu_{(N-H)}$ and $\nu_{(phenolic - OH)}$ group respectively [26]. In comparison with the spectra of the Schiff base, all the metal complexes exhibit the band of $\nu_{(C=N)}$ in the region of 1618-1602cm^{-1} showing the shift of band to lower wave numbers indicates that the azomethine nitrogen coordinated to the metal ion [27]. The band of $\nu_{(C=O)}$ in the region of 1680-1658 cm^{-1} in the metal complexes showing the shift of band to lower wave numbers confirmed that the carbonyl oxygen is coordinated to the metal ion [27].

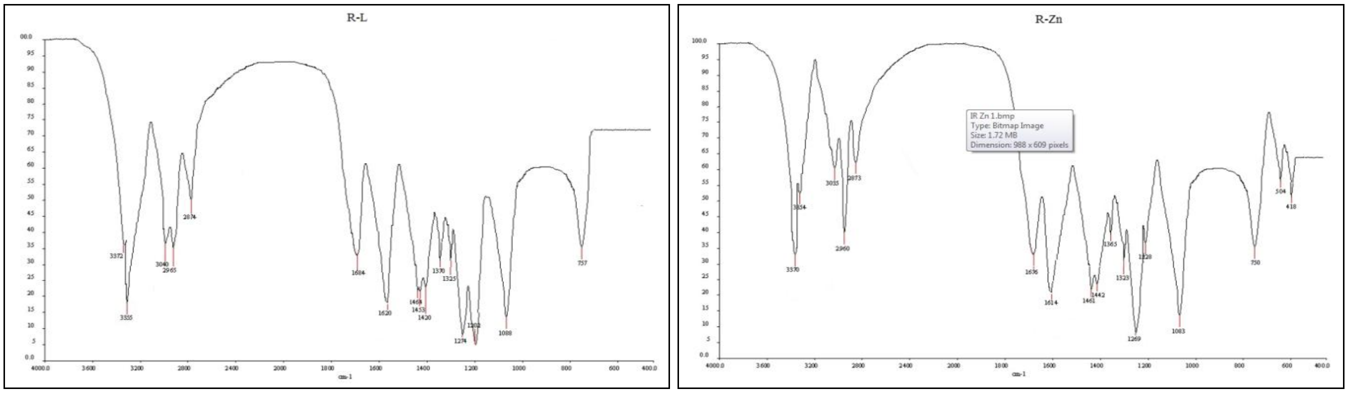
The unaltered position of a band due to $\nu_{(N-H)}$ and $\nu_{(phenolic\ OH)}$ in all-metal complexes indicate that these groups are not involved in co-ordination. The new bands in the region of 410-458 cm^{-1} and 498-552 cm^{-1} in the spectra of the complexes are assigned to stretching frequencies of M-O and M-N bonds respectively [28].

Thus, the IR spectral results provided strong evidence for the complexation of Schiff base with metal ions through bidentate mode by azomethine and carboxyl oxygen groups.

TABLE 2: IR SPECTRAL DATA FOR THE PROPOSED LIGAND AND ITS COMPLEXES

Compound	ν_{NH}	ν_{OH}	$\nu_{C=N}$	$\nu_{C=O}$	ν_{M-N}	ν_{M-O}
L	3372	3355	1620	1684	-	-
NiL_2	3371	3353	1602	1658	552	458
ZnL_2	3370	3354	1614	1676	504	418
CdL_2	3369	3352	1616	1679	500	415
HgL_2	3370	3350	1618	1680	498	410

*L – Schiff Base Ligand



(a) Ligand **(b) Zn Metal Complex**

FIG. 3: IR SPECTRA OF LIGAND AND ZINC METAL COMPLEX

NMR Spectra:

H^1 NMR Spectra: The H^1NMR spectra of the Schiff base and its metal complexes were recorded at room temperature in $CDCl_3$ **Fig. 4**.

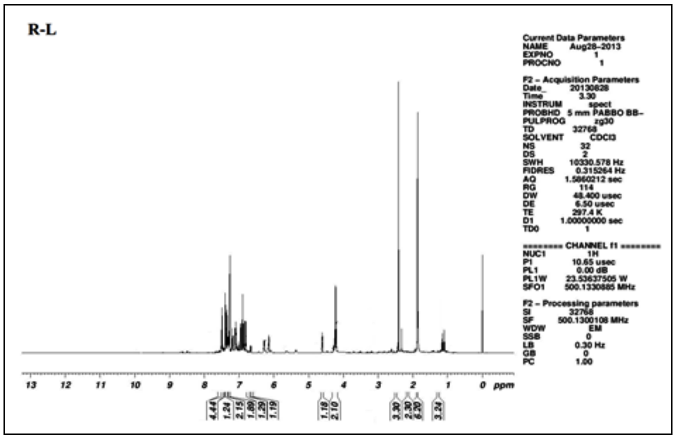


FIG. 4: H^1 NMR SPECTRUM OF SCHIFF BASE LIGAND

The ligand shows the following signals: C_6H_5 as multiplet at 6.10-7.50 ppm (10H); N-CH_3 as single at 2.42 ppm (3H); -NH as singlet at 2.34 ppm (2H), H_3C-C as singlet at 1.85ppm (6H); H_3C-CH_2as triplet at 1.32ppm (3H) and H_2C-CH_3 as quartet at 4.21-4.25 ppm (2H) and CH as singlet at 4.58 ppm [29].

The H^1-NMR of metal complexes compared with Schiff base ligand infers that there is no appreciable change in the signals of the complex as no hydrogen involves in chelation process.

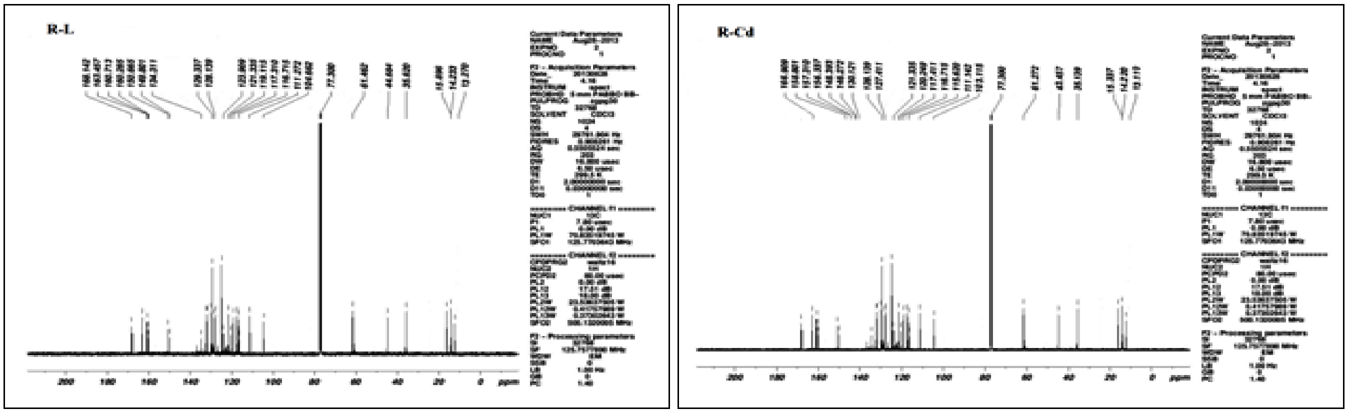
C^{13} NMR Spectra: C^{13} NMR spectra of Schiff base ligand and metal complexes are summarised in **Table 3** and given in **Fig. 5**.

In the ligand, the C=O carbon resonated at 160 ppm, but in the complexes, C=O band shifted down the field due to complexation [30]. The azomethine carbon C=N appears at 163ppm in ligand while in the complexes, C=N band shifted downfield due to chelation [31]. There is a prominent peak that appeared in all spectra at 77ppm; this resulted from the solvent $CDCl_3$used in the analysis. There are a total number of 22 peaks which confirmed the structure of the ligand. There is also a concentration of peaks between 104-150ppm which indicate sp^2 hybridized carbons and they consist of azomethine carbons, C=C carbons, benzylic carbons and aromatic carbons [29]. Thus, NMR information further supports the apprehension of IR results.

TABLE 3: C^{13} NMR SPECTRAL DATA FOR THE PROPOSED LIGAND AND ITS COMPLEXES

Compound	C=O	C=N	Aromatic Carbon	N-CH_3
	(pyrazole ring)	(azomethine group)		
L	160	163	116-149	44
NiL_2	159	160	115-145	43
ZnL_2	155	158	116-145	44
CdL_2	157	158	114-146	43
HgL_2	155	157	115-148	43

* L – Schiff Base Ligand



(a) Ligand (b) Cd Metal Complex

FIG. 5: C^{13} NMR SPECTRA OF LIGAND AND CADMIUM METAL COMPLEX

Electronic Spectra and Magnetic Moment: The electronic spectra and magnetic measurements are performed to obtain information regarding the geometry of the complexes.

The nature of the ligand field around the metal ion has been deduced from the electronic spectra **Table 4** and **Fig. 6**. The ligand spectral data displays two bands at 32258 cm^{-1} and 25445 cm^{-1} due to л →л* (C=O in pyrazole) and n→л*(C=N) transitions [32].

The Ni (II) complex showed two absorption bands at 16501 and 21459 cm^{-1} due to $^1A_{1g} \rightarrow {}^1A_{2g}$ and $^1A_{1g} \rightarrow {}^1B_{1g}$ d-d transition respectively supporting the square planar structure of Nickel complex [33]. Besides this, diamagnetic nature [34-35] as well as the absence of absorption band at 16000 cm^{-1} for $^3T_1$ (F) →$^3T_1$ (P) transition, which again confirmed the square planar geometry [36]. Zn (II), Cd (II) and Hg (II) complexes are diamagnetic evidenced by the absence of characteristic d-d transition except for INCT bands as expected for d^{10} systems in the visible region. The electronic spectral studies also confirm the tetrahedral geometry to these complexes [37].

Structural Interpretation: The structure of the complexes of the Schiff base derived from condensing 4-aminoantipyrine by Biginelli adduct of salicylaldehyde with Ni(II), Zn(II), Cd(II) and Hg(II) are confirmed by the elemental analysis, IR, UV-Vis, NMR, ESI mass spectra, molar conductance and magnetic data. From the IR spectra it is concluded that the ligand behaves as a bidentate ligand in all the complexes through the azomethine 'N' and pyrazole'O' and further this results are supported by NMR data.

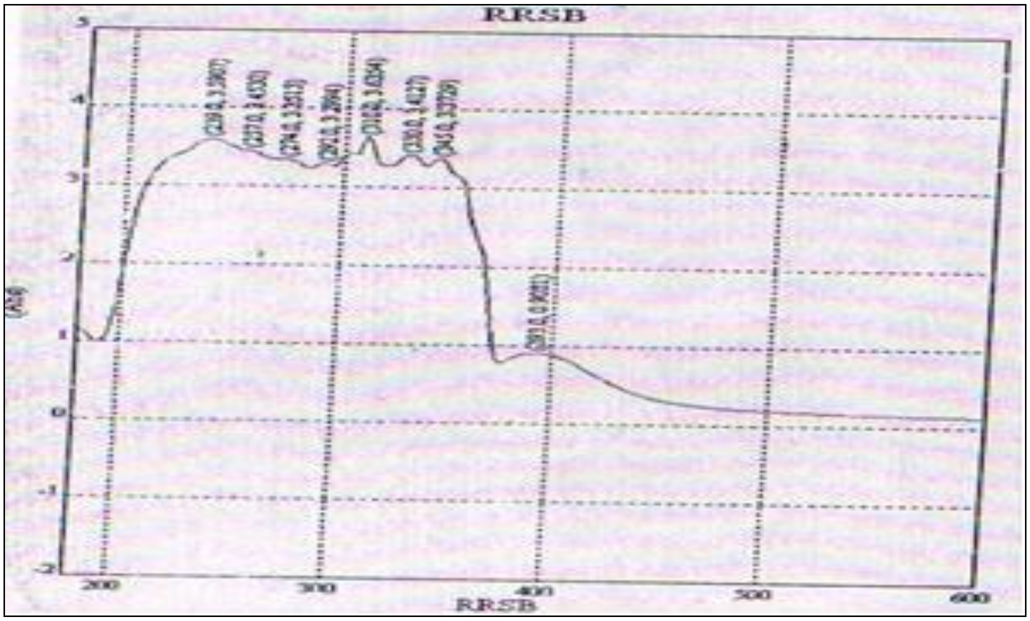
The mass spectra data are correlated with elemental analyses and from the molar conductance data; it is found that all the complexes are non-electrolytes.

On the basis of the above observations and from the diamagnetic nature, UV-Vis data, the structure for the complexes could be proposed as follows: a square planar geometry for Ni (II) and a tetrahedral geometry for Zn (II), Cd (II) and Hg (II) complexes **Fig. 7**.

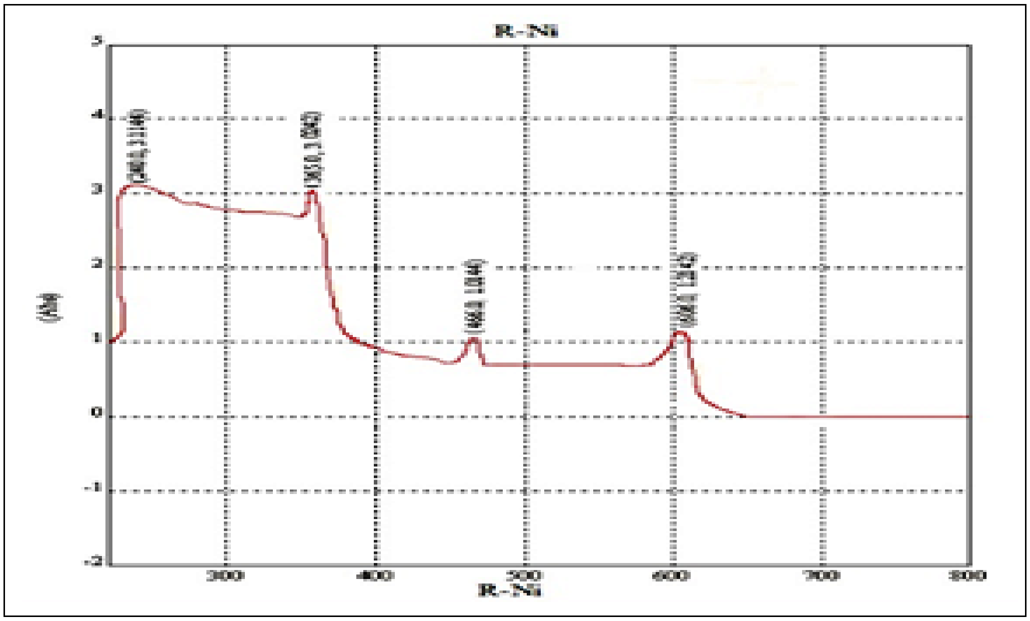
TABLE 4: UV-VIS SPECTRAL DATA FOR THE PROPOSED LIGAND AND ITS COMPLEXES

Compound	Solvent	Absorption region		Assignment	∑max	Magnetic moment	Geometry
		Nm	cm^{-1}			(BM)	
L	EtOH	310	32258	π→ π*	3635.4	-	-
		393	25445	n → π*	903.1		
NiL$_2$	DMF	606	16501	$^1A_{1g} \rightarrow {}^1A_{2g}$	1214.2	Diamagnetic	Square planar
		466	21459	$^1A_{1g} \rightarrow {}^1B_{1g}$	1014.4		
		365	27397	INCT	3024.2		
		240	41666	INCT	3114.4		
ZnL$_2$	DMF	308	32467	INCT	3306.3	Diamagnetic	Tetrahedral
		400	25000	INCT	1144		
CdL$_2$	DMF	306	32679	INCT	3316.3	Diamagnetic	Tetrahedral
HgL$_2$	DMF	306	32679	INCT	3374.4	Diamagnetic	Tetrahedral
		316	31645	INCT	2886.3		

* L – Schiff Base Ligand; *INCT- Intraligand Charge Transfer Band

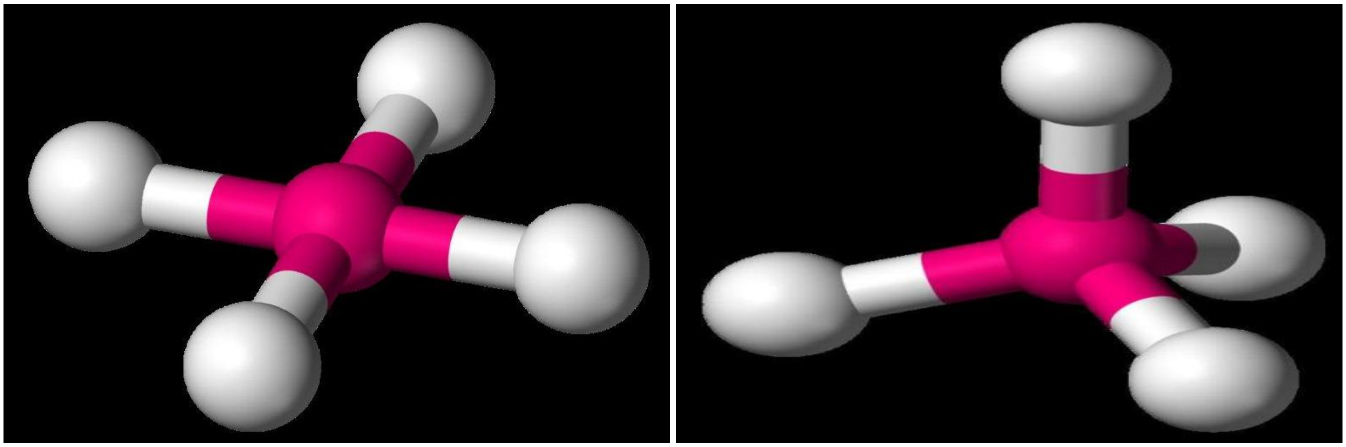


(a) Ligand



(b) Nickel Metal Complex

FIG. 6: ELECTRONIC SPECTRA OF LIGAND AND NICKEL METAL COMPLEX



(a) Ni Metal Complex **(b) Zn, Cd & Hg Metal Complexes**

FIG. 7: OPTIMISED STRUCTURAL GEOMETRY OF METAL COMPLEXES

*Red – Metal; *White – 'N' and 'O' of ligand

Pharmacological Results:

***In-vitro* Antimicrobial Activity:** The *in-vitro* antimicrobial activity of all the synthesized complexes are screened against eight gram-negative bacteria like *Escherichia coli, Vibrio* spp., *Pseudomonas aeroginosa*, *Vibrio parahaemolytics, Salmonella* spp., *Aeromonas* spp., *Klebsiella* spp., *Proteus* spp. and two gram-positive bacteria like *Bacillus* spp and *Staphylococcus aureus* and fungi like *Candida albicans, Aspergillus flavus, Penicillium* spp., *Aspergillus niger* and *Trichophyton* fungi fungal strains by minimum inhibitory concentration (MIC) method. The minimum inhibitory concentration (MIC) profiles of all the complexes against bacteria and fungi are summarized in **Table 5** and **6**.

The MIC values indicate that all the complexes exhibited promising results than the ligand against the mentioned microorganisms, and this activity is enhanced on coordination with the metal ions. This enhancement in the activity may be rationalized on the basis that ligands mainly possess C=N bond. The enhanced activity of the complexes over the ligand can be explained based on chelation theory [38-39]. It is observed that, in a complex, the positive charge of the metal is partially shared with the donor atoms present in the ligand, and there may be π-electron delocalization over the whole chelating [40]. This increases the lipophilic character of the metal chelate and favors its permeation through the lipid layer of the bacterial membranes.

The heterocyclic Schiff bases with different functional groups have greater tendency to interact with nucleoside bases even after complexation with metal ion or with the essential metal ions present in the biosystem can act as promising bactericides because they always tend to interact with enzymatic functional groups, to achieve higher coordination numbers [41]. There are also other factors which increase the activity, namely, solubility, conductivity, and bond length between the metal and the ligand.

TABLE 5: *IN-VITRO* ANTIBACTERIAL ACTIVITY OF PROPOSED SCHIFF BASE LIGAND AND ITS COMPLEXES

Compound	Anti-Bacterial Activity									
	Gram +ve		Gram –ve							
	***Ba.* Spp**	***Stap.* Aurs**	***E. coli***	***Vib.* Spp**	***Pseu. Aero***	***Vib. Para***	***Sal.* Spp**	***Aero.* Spp**	***Kleb.* Spp**	***Proteus* Spp**
L	-	+	+	+	+	-	-	+	-	+
NiL_2	+++	+++	++++	+++	+++	+++	+++	+++	+++	+++
ZnL_2	++	++	+++	++	++	++	++	++	++	++
CdL_2	+	++	++	++	++	+	+	++	+	++
HgL_2	+	++	++	++	++	+	+	++	+	++

*Ba. spp - *Bacillus* spp *Stap. aurs - Staphylococcus aureus**E. coli - Escherichia coli,* *Vib. Spp -*Vibrio* spp. **Pseu. aero - Pseudomonas aeroginosa, *Vib. para - Vibrio parahaemolytics,* * Sal. Spp - *Salmonella spp.,** Aero. Spp - *Aeromonas* spp.,*Kleb. Spp - *Klebsiella* spp.* Proteus Spp - *Proteus* spp.

*C = 5 mg/L. Inhibition zone diameter mm (% inhibition): +, 6-10 (27-45 %); ++, 10-14 (45-64 %); +++, 14-18 (64-82 %); ++++, 18-22 (82-100 %). Percent inhibition values are relative to the inhibition zone (22 mm) of the most active compound with 100 % inhibition.

TABLE 6: *IN-VITRO* ANTIFUNGAL ACTIVITY OF PROPOSED SCHIFF BASE LIGAND AND ITS COMPLEXES

Compound	Anti-Fungal Activity				
	Cand. albi	***Asper. flav***	***Pen. spp***	***Asper. nig***	***Trichophyton***
L					
NiL_2	++++	+++	++	+++	++
ZnL_2	+++	++	+	++	++
CdL_2	++	+	+	++	+
HgL_2	++	+	+	++	+

*Cand. Albi - *Candida albicans,* *Asper. Flav - *Aspergillusflavus,* *Pen. Spp -*Pencillium spp.,**Asper. Nig –*Aspergillus niger* *Trichophyton - *Trichophyton.*

*C = 5 mg/L. Inhibition zone diameter mm (% inhibition): +, 6-10 (27-45 %); ++, 10-14 (45-64 %); +++, 14-18 (64-82 %); ++++, 18-22 (82-100 %). Percent inhibition values are relative to the inhibition zone (22 mm) of the most active compound with 100 % inhibition.

Antibacterial Activity: It has been observed that the antibacterial activity of the complexes followed the order: Ni (II) >Zn (II)>Cd (II) ~Hg (II)). The antibacterial activity of metal complexes is graphically represented in **Fig. 8**. The data reveal that *E. coli* is inhibited to a greater degree by almost all complexes and so they could be reasonably used for the treatment of some common diseases caused by *E. coli* **Fig. 9**.

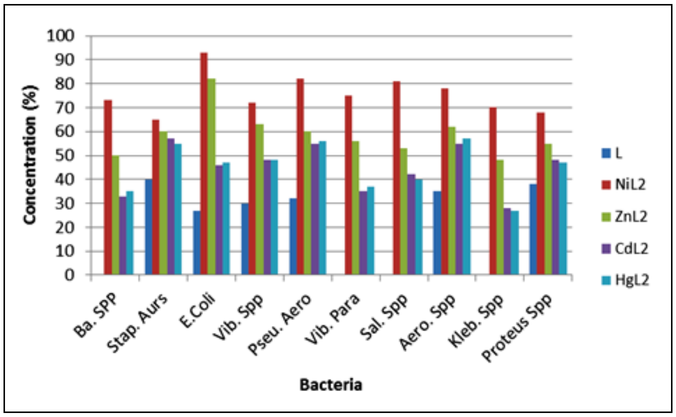


FIG. 8: EFFECT OF LIGAND AND IT'S METAL COMPLEXES TOWARDS BACTERIA

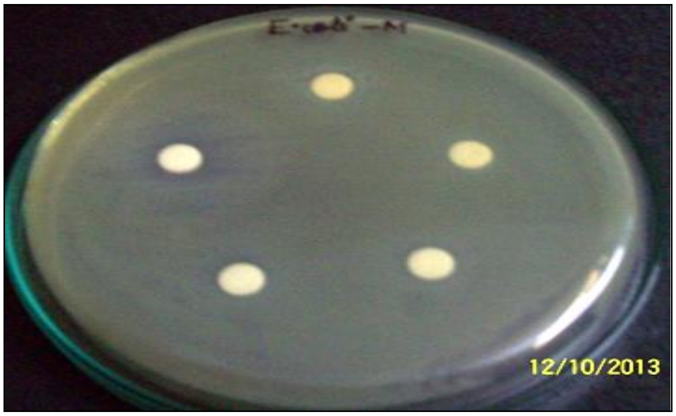


FIG. 9: ANTIBACTERIAL ACTIVITY AGAINST *E-COLI* OF NICKEL METAL COMPLEX

Antifungal Activity: It has been observed that the antifungal activity of the complexes follows the order: Ni(II) >Zn (II)>Cd (II) ~Hg (II). The antifungal activity of metal complexes is graphically summarized in **Fig. 10**. The data showed that all metal complexes have great MIC towards *Candida albicans* and concluding that the complexes prepared with the new Schiff base could reasonably be used for the treatment of skin diseases caused by *Candida albicans* **Fig. 11**.

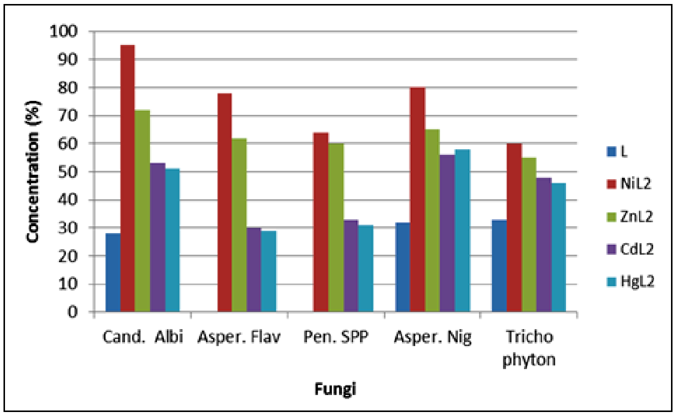


FIG. 10: EFFECT OF LIGAND AND IT'S METAL COMPLEXES TO.WARDS FUNGI

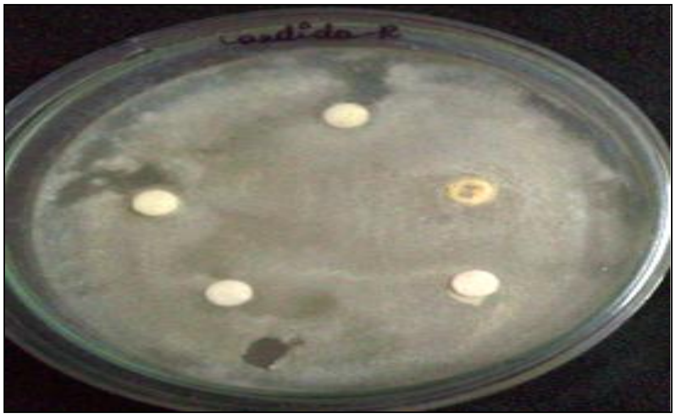


FIG. 11: ANTIBACTERIAL ACTIVITY AGAINST *CANDIDA ALBICANS* OF NICKEL METAL COMPLEX

CONCLUSION: Ni (II), Zn (II), Cd (II) and Hg (II) complexes of the Schiff base derived from condensing 4-aminoantipyrine with Biginelli adduct of salicylaldehyde were prepared and characterized. The study revealed that;

1. All the complexes are non-electrolytes.
2. The Schiff base behaves as a bidentate ligand and is co-ordinated to the central metal ion through azomethine 'N' and pyrazole 'O'.
3. Ni (II) complex has square planar geometry while Zn (II), Cd (II) and Hg (II) complexes have tetrahedral geometry.
4. The *in-vitro* antimicrobial activity of all the complexes are higher than that of the free Schiff base ligand and follows order: Ni (II)>Zn(II)>Cd (II)>Hg (II).
5. This means that metal chelation significantly enhances the antimicrobial behavior of organic ligand.

ACKNOWLEDGEMENT: The author expresses their sincere thanks to The Principal, HOD and faculty members of Department of Chemistry, Sriram Engineering College, Thiruvallur and The Principal, HOD, PG and Research Department of Chemistry, Presidency College, Chennai for providing the research facilities.

CONFLICT OF INTEREST: Nil

REFERENCES:

1. Rai A, Kumar A and Sirohi R: Synthesis & characterisation of schiff base legends derived from 4-aminoantipyrine & 4-nitro salicylaldehyde, benzene-1,2-diamine & its complex with molybdenum tricarbonyl. VSRD Technical & Non-Technical Journal 2011; 2(8): 352-57.
2. Elemike EE, Oviawe AP and Otuokere IE: Potentiation of the Antimicrobial activity of 4- Benzylimino - 2, 3 – Dimethyl - 1 – Phenylpyrazal - 5- One by Metal Chelation. Research Journal of Chemical Sciences 2011; 1(8): 6-11.
3. Lashanizadegan M and Jamshidbeigi M: Synthesis of n, n'-bis[4-(benzeneazo) salicylaldehyde]4 – methyl-1 – 2-phenylenediamine and its transition metal complexes. Synthesis and Reactivity in Inorganic, Metal-Organic, andNano-Metal Chemistry 2012; 42: 507-12.
4. Mitu L, Ilis M, Raman N, Imran M and Ravichandran S: Transition metal complexes of isonicotinoyl –hydrazone – 4-diphenylaminobenzaldehyde: synthesis, characterization and antimicrobial studies. E-Journal of Chemistry 2012; 9: 365-72.
5. Chandr S and Kumar A: Spectral, thermal and morphological studies on chromium nanoparticles. SpectrochimActa A: Molecular and Biomolecular Spectroscopy 2013; 102: 250-55.
6. Chandra S, Bargujar S, Nirwal R and Yadav N: Synthesis, spectral, characterization and biological evaluation of copper(ii) and nickel(ii) complexes with thiosemicorbazone derived from a bidentate schiff base. Spectrochim Acta A: Molecular and Biomolecular Spectroscopy 2013; 106: 91-98.
7. Chandra S and Ruchi: Synthesis, spectroscopic characterization, molecular modelling and antimicrobial activities of Mn(II), Co(II), Ni(II) Cu(II) complexes containing the tetra dentate aza schiff base ligand. Spectrochim Acta A: Molecular and Biomolecular Spectroscopy 2013; 103: 338-48.

8. Chandra S and Pipil P: Synthesis, spectral characterization and biological evaluation of Chromium(III) complexes of schiff base. Open Journal of Inorganic Chemistry 2014; 4: 30-40.
9. Wang Y, Liu Y, Luo J, Qi H, Li X, Nin M, Liu M, Shi D, Zhu W and Cao Y: Mettallomesogens based on Platinum(ii) complexes: synthesis, luminescence and polarized emission. Dalton Transactions 2011; 40: 5046-5051.
10. Anupama B and Kumari CG: Synthesis, Characterization, DNA binding and antimicrobial activity of 4 – amino antipyrine schiff base metal complexes. Research Journal of Pharmaceutical, Biological and Cehmical Sciences 2011; 2(4): 140-59.
11. Scovill JP, Klayman DL and Franchino CF: 2-acetylpyridine thiosemicarbazones complexes with ttransition metals as antimalarial and antileukemic agents. J of Med Chem 2009; 25(10): 1261-64.
12. Janes D and Kreft S: salicylaldehyde is a characteristic aroma component of buck wheat groats. Food Chem 2008; 109(2): 293-98.
13. Shanmugapriya M, Jameel A and Padusha MSA: Synthesis, characterisation and antimicrobial activities of salicylaldehyde derivatives. Int J Chem Tech Res 2012; 4(1): 12-15.
14. Thakur K and Trivedi J: Spectroscopic (FTIR, Ih-NMR and Mass) studies of new dihydropyrimidine derivatives. Int J Theo and Appli 2011; 3(2): 13-14.
15. Argarego WLF and Pernin DD: Purification of Laboratory Chemicals. Butter Worth, Henemann & Oxford, Fourth Edition 1997.
16. Vogel AI: A Textbook of Quantitative Inorganic Chemistry. JohnWiely, Third Edition1971.
17. Hassan EM, Mahmoud S, Hakim M, Awadhall TH and Salih W: Behaviour of salicylaldehyde and some of its derivatives in the biginelli reaction for the preparation of any tetra hydropyrimidines. Turk J Chem 2008; 32: 297-04.
18. Chandra S, Jain D and Sharma AK: Coordination modes of a schiff base pentadentate derivative of 4-aminoantipyrinewith Cobalt(II), Nickel(II) and Copper(II) Metal Ions: Synthesis, Spectroscopic and Antimicrobial Studies. Molecules 2009; 14: 174-90.
19. Singh, DP, Kamboj M, Kumar K, Jain K and Sharma C: Divalent metal macrocyclic complexes derived from acetonylacetone and carbohydrazide with their spectroscopic and antibacterial studies. Journal of Coordination Chemistry 2011; 64: 502-10.
20. Grurumoorthy P, Ravichandran J, Karthikeyan N, Palani P and Kalilur RA: Template synthesis of polyaza macrocyclic Copper (II) and Nickel(II) complexes. Spectral Characterization and Antimicrobial Studies. Bulletin ofthe Korean Chemical Society 2012; 33: 2279-92.
21. Chandra S and Pipil P: EPR, IR, Mass and Electronic Spectroscopic Studies on Newly Synthesized 23,24-Dioxo-1,6,9,12,17,20-Hexaazacyclotracosa-1,5,12,16-Tetraene Macrocyclic Ligand (L) and Its Transition Metal Complexes. Journal of Chemical and Pharmaceutical Research 2013; 5: 99-104.
22. Geary WJ: The use of conductivity measurements in organic solvents for the characterization of co-ordination compounds. Coordination Chemistry Reviews1971; 7(1):81-122.
23. Abdlseed FA and El-ajaily MM: Preparation and Spectroscopic Investigation of a Schiff base Metal Complex. Int J Pharma Tech Res 2009; 1(4): 1097-03.
24. Chandra S, Jain D, Sharma AK and Sharma P: Co-ordination modes of a schiff base pentadentate derivative of 4-aminoantipyrine with Cobalt (II), Nickel (II) and Copper(II) metal ions: synthesis, spectroscopic and antimicrobial studies. Molecules 2009; 14: 174-90.
25. Kumar U and Chandra S: Synthesis, spectral and antifungal studies of some coordination compounds of cobalt (II) and copper (II) of a novel 18-membered octaaza [N8] tetradentate macrocyclic ligand. Journal of Saudi Chemical Society 2011; 15: 187–193.
26. Nakamoto K: Infrared and Raman Spectra of Inorganic and Co-ordination Compounds. John Wiley& Sons, Interscience, New York, USA, Fourth Edition 1986.
27. Raman N, Sobha S and Selvaganapathy M: Probing the DNA binding mode of transition metal-based biologically active compounds: Validation by Spectroscopic methods. In. J. Phar and Bio Sci 2012; 3(1): 251-68.
28. Mahapatra BB and Panda SK: Coordination Compounds of CoII, NiII, CuII, ZnII, CdII and HgII with Tridentate ONS Donor Azo dye Ligands. Biokem 2010; 22(2): 71-75.
29. Kemp W: Organic Spectroscopic. PALGRAVE, New York, Third Edition 1991.
30. Singh GS and Pheko T: Spectroscopic Characterization of the 1-Substituted 3,3' – Diphenyl-4- (2' hydroxyl phenyl) azetidine-2-Ones; Application of C NMR, ^{1}H-^{13}C COSY NMR and Mass Spectroscopy. Spectrochim. Acta 2008; PartA 70: 595-00.
31. Dilip CS, Manikandan K, Rajalaxmi D, Subahashini and Thiruneelakandan R: Synthesis, spectroscopic characterisation, and biopotential and DNA cleavage applications of mixed ligand4-n, n-dimethylaminopyridine metal complexes. Journal of Chemistry 2013; 1-16.
32. Lever ABP: Inorganic Electronic Spectroscopy. Elsevier, Amsterdam, The Netherland, Second Edition 1984.
33. Cotton FA and Wilkinson G: Advanced Inorganic Chemistry. Willey, New Delhi, Third Edition1992.
34. Singh BK and Adhikari D: Complexion behaviour of schiff base ligands with transition metal ions. International Journal of Basic and Appl Chem Sci2012; 2(1): 84-107.
35. Duta RL and Syama A: Elements of Magneto Chemistry. Elsevier, New Delhi, Second Edition 1992.
36. Lashanizadegan M and Boghaei DM: Template synthesis and X-ray structure determination of unsymmetrical tetradentate schiff base complexes of Nickel (II) and Copper (II). Synth. React. Iorg Met-Org Chem 2001; 31(8): 1519-29.
37. Reiss A: Theodor Ca Proiu Nicolae Stanica: Synthesis, characterisation and antibacterial studies of some metal complexes with the schiff base of a hetrocyclic aldehyde. Bull Chem Soc Ethiop 2009; 23(1): 63-68.
38. Sharma AK and Chandra S: Complexation of nitrogen and sulphur donor schiff's base ligand to Cr (III) and Ni(II) metal ions: synthesis, spectroscopic and antipathogenic studies. Spectrochimica Acta A 2011; 78(1): 337-42.
39. Gopalakrishnan S and Joseph J: Antifungal activities of Copper (II) with biosensitive macrocyclic schiff base ligands derived from 4-aminoantipyrine derivatives. Mycobiology 2009; 37(2): 141–146.
40. Raman N, Mitu L, Sakthivel A and Pandi MSS: Studies on DNA cleavage and antimicrobial screening of transition metal complexes of 4-aminoantipyrine derivatives of N_2O_2 type. J Iran Chem Soc 2009; 6(4): 738-48.
41. Reddy KRK, Suneetha P, Karigar CS, Manjunath NH and Mahendra KN: Cobalt(II), Ni(II), Cu(II), Zn(II), CD(II), Hg(II), U02(VI) and th(IV) complexes from ONNN Schiff base ligand. Journal of the Chilean Chemical Society 2008; 53(4): 1653-57.

How to cite this article:

Chandran R and Antony SA: Synthesis and characterisation of bio-inorganic transition metal complexes derived from novel biginelli adduct coupled schiff's bases. Int J Pharm Sci & Res 2014; 5(10): 4339-50. doi: 10.13040/IJPSR.0975-8232.5(10).4339-50.