



Synthesis, characterization, anti-microbial and thermal investigation study of Schiff base derived from 1,7,7-Trimethylbicyclo [2.2.1] heptan-2-one with 4-Hydroxyphenylalanine and its metal complexes

M Ali Hassan^{1*}, N P Pranamya¹, G Indira Devi¹, Susannah Seth²

¹Department of Chemistry, The Zamorin's Guruvayurappan College, Calicut, Kerala, India

²Department of Chemistry, Malabar Christian College, Calicut, Kerala, India

Abstract

Synthesis of bidentate Schiff base ligand by the condensation of 1,7,7-Trimethylbicyclo [2.2.1] heptan-2-one with 4-Hydroxyphenylalanine and its complexes of Co (III), Cu (II) and Cr (III). Synthesised ligand and its complexes were characterised by FT-IR, UV-Visible spectroscopy, Gouy method, molar conductance study and thermal analysis. Spectral data shows that distorted octahedral geometry of Cobalt (III), square planar geometry of Copper (II), and octahedral geometry of Chromium (III) complexes. The thermal stability of complex is explained on the reverse order of Irving William series. All the complexes are coloured, stable in air, non-electrolytic nature and soluble in DMSO solvent. The antimicrobial activity was studied using two bacteria such as *Klebsiella pneumoniae* and *Bacillus subtilis* and two fungi such as *Aspergillus Niger* and *Candida albicans* by agar well-diffusion method. The result shows that metal complexes have higher biological activity than the ligand and the Cu (II) complex show 79.31% antibacterial activity on *Bacillus subtilis*.

Keywords: schiff base, 1,7,7-trimethylbicyclo [2.2.1] heptan-2-one, 4-hydroxyphenylalanine, coats-redfern equation, antimicrobial activity

Introduction

The condensation reaction of primary amines with a carbonyl compound to form Schiff's base was identified by Hugo Schiff in 1864. This compound belongs to an important class of organic compound having the general formula $R-C=N-R'$ where R and R' are aryl, alkyl, cycloalkyl or heterocyclic group^[1]. Schiff's base compound contains azomethine moiety will facilitate the wider applications in analytical, medicinal, bioinorganic and inorganic chemistry. Most of the research review reveals that azomethine compounds act as chelating ligands due to the presence of the lone pair of electrons present on the nitrogen atom of the azomethine group and also due to the electron-donating nature of the double bond and electro negativity of the nitrogen atom^[1-2]. Numerous studies have shown that the azomethine group makes the Schiff base compounds so important. Transition metal complexes of Schiff-base ligands find applications in catalysis^[3-4], corrosion inhibition^[5-6] and biological activity such as antimicrobial^[7-8], antifungal^[9], anticonvulsant^[10], antitumor and antiviral studies^[11]. Schiff base ligand and their metal complexes individually exhibit varying degrees of inhibitory effect on the growth of the bacterial species tested so far. The anti-microbial result shows that the activity of the compound became more pronounced after chelation with metal ion.

Among the numerous analytical techniques, thermal studies possess significant use in the structural and kinetic studies of coordination compounds^[12]. This technique is categorized by different methods such as thermogravimetry (TG), differential thermal analysis (DTA), derivative thermogravimetry (DTG), and differential scanning calorimetry (DSC). Among these one of the oldest thermo analytical methods is thermogravimetry and it

has wide application in coordination compounds. Thermogravimetric analysis is a standard method to analyse organic, inorganic and synthetic materials using the estimated mass loss of the sample as a function of temperature under an inert atmosphere such as nitrogen. Generally, TGA contains two types of plots. The first plot is obtained by the result of a change in mass versus temperature and it gives the information about thermal stability and composition of the intermediate compound^[12-13]. In the second plot, the differential thermal analysis obtained by plotting the rate of mass change versus temperature gives the number of peaks instead of steps. In this curve, the peak area is proportional to the total change in mass. These curves can also be used to derive other parameters, such as the kinetics of the reaction including rate constant, activation energy, order of the reaction and frequency factor^[12-14]. For this commonly two approaches are possible. One is isothermal (static) and another one is non-isothermal (dynamic heating). Comparing these two methods, the determination of the degree of transformation as a function of time during a linear increase of temperature is obtained by the dynamic method.

This work deals with synthesis and characterisation of Schiff base formed from 1, 7, 7-Trimethylbicyclo [2.2.1] heptan-2-one and 4-Hydroxyphenylalanine and its metal complexes. The characterization studies of synthesised ligand and its complexes are done by using FT-IR, UV-Visible spectroscopy, molar conductance and magnetic moment measurements. Interpretation and analysis of thermal decomposition data and evaluating order of reaction, free energy and entropy of activation, enthalpy of activation and pre-exponential factor based on Coats Red fern

equation and nine Mechanistic equations in thermal analysis method. The anti-microbial activity of the synthesised complex was studied using bacteria and fungus.

Experimental

Materials and methods

1,7,7-Trimethylbicyclo [2.2.1] heptan-2-one, 4-Hydroxyphenylalanine, anhydrous sodium acetate, chromium acetate, cobalt acetate, copper acetate (Aldrich) and solvents (Merck) were used without further purification. The IR spectra ($4000\text{--}400\text{ cm}^{-1}$) were recorded on a Mattson-1000 FTIR spectrophotometer with samples prepared as KBr pellets. UV-Visible spectra were recorded on UNICAM-UV2-100 spectrophotometer. Gouy balance is used to measure magnetic susceptibility of the complexes. The molar conductance is measured using a Siemens WPA CM 35 conductometer. Thermal analysis is carried out by a Du Pont Instrument 951 thermal analyser used to record TG curves. The experiments were conducted in nitrogen atmosphere with a heating rate of $10\text{ }^{\circ}\text{C min}^{-1}$ in the temperature range $30\text{--}1000\text{ }^{\circ}\text{C}$. The study of antimicrobial activity was done using disk diffusion method.

Synthesis of ligands

An ethanolic solution of 1,7,7-Trimethylbicyclo [2.2.1] heptan-2-one (0.01mol) was mixed with a solution of 4-Hydroxyphenylalanine (0.01mol) in minimum hot water, containing anhydrous sodium acetate (0.5g) refluxed for 4 hrs on a water bath. The resulting solution was kept overnight and was concentrated by evaporation. The light yellow-coloured precipitate obtained was filtered and washed with 50% ethanol. It was recrystallised using ethanol and dried over desiccator (yield 80%). The formation of Schiff base is represented by scheme 1.

Synthesis of metal complexes

Complexes were synthesised by mixing an aqueous solution of metal acetate (0.001mol) with a hot aqueous solution of 4-Hydroxyphenylalanine (0.001mol) and ethanolic solution of 1,7,7-Trimethylbicyclo [2.2.1] heptan-2-one (0.002mol) in presence of sodium acetate (0.05g) solution. Then it was refluxed for 8hrs on water bath and was kept overnight. It was then filtered, washed with 50% ethanol and was dried in a desiccator. Approximately 80% yield was obtained for these complexes. Physical properties of synthesized compounds are listed in table 1.

Table 1: physical characterisation of Schiff base and its complexes.

compound	Molecular weight	colour	yield	% Metal	Conductance Ω^{-1}	Magnetic moment B.M
$\text{C}_{19}\text{H}_{25}\text{NO}_3$ [HL]	315	Yellow	80%	-	-	-
$[\text{CoL}_2(\text{H}_2\text{O})_2]$	722.93	Coffee brown	74%	8.0(8.15)	6.3	4.5
$[\text{Cu L}(\text{H}_2\text{O})_2]$	413.55	Pencil ash	83%	13.66 (12.95)	3.36	2.03
$[\text{CrL}_2(\text{H}_2\text{O})_2]$	715.996	Coffee brown	75%	12.04 (12.93)	5.93	3.96

Anti-microbial activity

The antimicrobial activity of synthesized compounds was investigated for two bacteria (*Klebsiella pneumonia* MTCC 109, *Bacillus subtilis* MTCC 2413) and two fungi (*Aspergillus Niger* MTCC 281, *Candida albicans* MTCC 227) using the agar well-diffusion method. For the determination of the vulnerability of microorganisms to antimicrobial agents, Mueller Hinton Agar M173 Himedia was used. The agar medium was prepared by dissolving 38 grams in 1000 ml distilled water. For antifungal study Rose Bengal agar M842 Himedia was used as medium by dissolving 31.55 grams in 1000 ml distilled water. The agar medium was dissolved completely by boiling. This was sterilized by autoclaving at 15 lbs pressure under 121°C for 15 minutes and then cooled to $45\text{--}50\text{ }^{\circ}\text{C}$.

About 15-20 ml of Mueller-Hinton agar (for antibacterial) or Rose Bengal agar (for antifungal) was poured on glass Petri plates of the same size and allowed to solidify. With a sterile cork borer in each plate, wells with a diameter of 8 mm (20 mm apart from one another) were punched aseptically. Standardized inoculums of the test organism were uniformly spread on the surface of these plates using a sterile cotton swab. A volume ($50\text{ }\mu\text{l}$) of the extract solution at desired concentration was added to the wells and one well with Gentamycin (for antibacterial) or Clotrimazole (for antifungal) was maintained as positive and DMSO as a negative control. Then, it incubated in agar plates under suitable conditions depending on the test microorganism. After incubation, a clear zone was observed. Inhibition of the bacterial or fungal growth was measured in mm and activity is measured using MIC value.

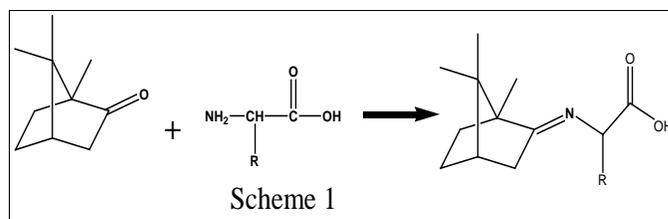


Fig 1

Result and discussion

IR spectral data

Ligand

The intense band of $>\text{C}=\text{O}$ of 1,7,7-Trimethylbicyclo [2.2.1] heptan-2-one at 1780 cm^{-1} is absent in the ligand. Also, the weak absorption at 1609 cm^{-1} due to NH_2 scissoring is replaced by an intense one at 1614 cm^{-1} in the ligand indicating the formation of $\text{C}=\text{N}$ [12-14]. Similarly, the doublet at 3500 cm^{-1} which is typical of primary amines is also absent in the ligand indicating the condensation reaction between the $-\text{NH}_2$ group and $\text{C}=\text{O}$ of 1,7,7-Trimethylbicyclo [2.2.1] heptan-2-one. The $-\text{NH}_2$ wagging in 4-Hydroxyphenylalanine at 850 cm^{-1} is also absent in the ligand [15]. The typical OH band, broad with small spikes, of $-\text{COOH}$ in 4-Hydroxyphenylalanine is remaining as such in the ligand also indicating that the carboxyl group is not involved in any condensation reaction.

Complexes

In the spectra of the complexes, the position of bands due to carbonyl group $\nu\text{C}=\text{O}$ at 1614 cm^{-1} in the ligand is shifted to 1587 cm^{-1} in the complexes. The broadband of $-\text{OH}$ with spikes

typical for -COOH was missing in the complexes showing the involvement of -COOH in complex formation [14-15]. The replacement of the carboxylic group hydrogen with a metal ion brought about characteristic changes in the IR spectra of the metal complexes in comparison with the spectra of ligand. Broadband at 3400-3100cm⁻¹ in the spectra of several complexes is due to the hydroxyl stretching mode of water molecule [15-16]. In addition, a medium band approximately at 870-950cm⁻¹ suggest that the water molecule is coordinated. One can observe the disappearance of bands of the symmetric and asymmetric valence vibrations of carboxylic group and appearance of bands of the asymmetric and symmetric vibrations of the carboxylate group $\nu_{\text{asym}}(\text{COO})$, $\nu_{\text{sym}}(\text{COO})$, as well as $\beta_{\text{asym}}(\text{COO}^-)$, $\beta_{\text{sym}}(\text{COO}^-)$.

In the IR spectra of imine ligand, the wave numbers of asymmetric ($\nu_{\text{asym}}\text{COO}^-$) and symmetric ($\nu_{\text{sym}}\text{COO}^-$) stretching vibrations of carboxylate occur in the range of approximately 1520cm⁻¹ and 1330-1420 cm⁻¹ respectively [16]. Asymmetric and

symmetric deformation vibrations of the carboxylate group ($\beta_{\text{asym}}\text{COO}^-$) and ($\beta_{\text{sym}}\text{COO}^-$) are located respectively, in the range of 483-531cm⁻¹ and 817-851 cm⁻¹ in the IR spectra of salts of the acid [17].

Based on the differences between the wave numbers of the asymmetric and symmetric stretching vibrations of the carboxylate group -COO⁻, some assumptions about the type of metal-ligand coordination might be stated. For the mono-dentate geometry, the bands for ($\nu_{\text{asym}}\text{COO}^-$) and ($\nu_{\text{sym}}\text{COO}^-$) in the complex are shifted to higher and lower wave numbers, respectively, or ($\Delta\nu\text{COO}^-$)_{studied complex} >> ($\Delta\nu\text{COO}^-$)_{sodium salt}. This coordination has been observed for all other complexes. This indicates that -COO⁻ is covalently bonded to metal through oxygen of deprotonated -OH. Further evidence for bonding by nitrogen and oxygen atom is provided by far IR Spectrum of the complex. Complex shows an intense broadband at 495cm⁻¹ corresponds to M-N and bond at 413cm⁻¹ at M-O linkages [12].

Table 2: IR data of ligand and complexes.

compound	ν_{OH} phenolic	$\nu\text{C}=\text{N}$ azomethine	In-plane deformation	Out of plane deformation	$\nu\text{M-N}$	$\nu\text{M-O}$
HL		1608m	834m	760,704 m	-	-
[Co L ₂ (H ₂ O) ₂]	3400-3100br	1567m	812m	710,657m	475w	434w
[Cu L (H ₂ O) ₂]	3400-3100br	1580m	846m	710,682m	491w	418w
[Cr L ₂ (H ₂ O) ₂]	3300-3100br	1573m	872m	738,710m	495w	434w

Electronic spectroscopy

In the UV spectra of Schiff base ligands observed two absorption bands at 259nm and 358nm indicates $\Pi \rightarrow \Pi^*$ transition of C=C and $n \rightarrow \Pi^*$ transition of azomethine group respectively. During the formation of complexes, the azomethine linkage is shifted to 357-369nm and $\Pi \rightarrow \Pi^*$ transition is observed at 287-330nm [16-17]. The UV and magnetic susceptibility data show cobalt complexes are mixed oxide types. Here, cobalt (III) complex, three bands are observed at 535nm, 360nm and 265nm. In low spin cobalt (III) complex is expected to show two spins allowed d-d transition, which is $^1\text{A}_{1g} \rightarrow ^1\text{T}_{1g}$ and $^1\text{A}_{1g} \rightarrow ^1\text{T}_{2g}$. At 535nm, the absorption band is assigning as $^1\text{A}_g \rightarrow ^1\text{T}_{1g}$. The other one is blurred due to intense LMCT transition at 330nm and also the characteristic cobalt (II) spectral band cannot be seen in the spectrum due to the same reason [18]. The magnetic moment value

shows good agreement with the above conclusion. Room temperature mixed-valence cobalt (III)/cobalt (II) complex has a magnetic moment value is 4.54 B.M which corresponds to high-spin cobalt (II). These values show distorted octahedral geometry of cobalt complex [18].

Electronic spectra of Cu (II) complex exhibit three bands at 562nm, 380nm and 283nm corresponds to d-d transition, LMCT ($n \rightarrow \Pi^*$) transition and $\Pi \rightarrow \Pi^*$ transition respectively. These values close to indicates the square planar nature of the complex [19]. Cr (III) complexes exhibit three-band at 309nm, 368nm, and 499nm corresponding to $^4\text{A}_{2g} \rightarrow ^4\text{T}_{1g}$ (F), $^4\text{A}_{2g} \rightarrow ^4\text{T}_{2g}$, and $^4\text{A}_{2g} \rightarrow ^2\text{T}_{2g}$ respectively. The magnetic moment value 3.14BM suggest the high spin octahedral geometry of the complex [13].

Thermal study

Table 3: Thermal decomposition data of ligand and complexes.

Complexes	T _{DTG} (°C)	Temperature range (°C)	TG weight loss Obs/Calc	Assignments
[Co L ₂ (H ₂ O) ₂]	216	40- 250	28.08(30.71)	Eliminate two water molecules and a phenolic group from amino acid.
	342, 545	250- 640	25.55(25.18)	Part of ligand
	739, 831	640-1000	25.26(25.45)	Remaining part of the ligand and leaving Co ₃ O ₄ .
[Cu L (H ₂ O) ₂]	49, 167	40 - 170	3.19(3.63)	Elimination of methyl group
	199, 322	170 -700	46.16(47.64)	Elimination of two water molecule and a part of amino acid.
	866	700-1000	25.39(25.63)	Remaining part of ligand and leaving CuO.
[Cr L ₂ (H ₂ O) ₂]	50	40- 170	20.80(21.23)	Elimination of water, -CO, -OH and -CH group of ligands.
	236,398	170- 570	30.71(32.84)	Part of ligand
	847	570- 960	27.72(29.05)	Remaining part of ligand and leaving Cr ₂ O ₃ .

Thermogravimetry is a tool to study the weight loss of a substance is recorded as a function of temperature or time. The result

obtained from the instrument either by thermogravimetric curve (by plotting weight loss recorded as a function of temperature or

time) or by derivative thermogravimetric curve (the first derivative of TGA curve plotted concerning temperature or time). The thermogravimetric analysis gives the idea about the thermal stability of complexes, get information about the presence of water molecules are inside or outside of the coordination sphere and the mechanism of thermal decomposition [12-13]. Generally thermal decomposition involves three steps. First one is the elimination of lattice water, followed by remove coordinated water and finally the main components from ligand. The TGA and DTG curves of Co (III), Cu (II) and Cr (III) are shown in fig.1, fig. 2and fig. 3 respectively and the data are listed in table3. The Co (III) complex of the thermogram shows a three-stage decomposition within the range of temperature from 30 to 1000°C. The first step involves the decomposition of the coordinated water molecule and phenyl group from amino acid with mass loss of 28.08% (calculated. 4.98% and 25.73%) with temperature 40 – 250°C. The second step occurs at a temperature range between 250– 640 °C involve elimination of the remaining part of amino acid and three methyl group from each 1, 7, 7-Trimethylbicyclo [2.2.1] heptan-2-one part with mass loss of 25.55% (calculated. 25.45%). The subsequent step contains the removal of the remaining part of the ligand leaving metal oxide as residue about the temperature 640 – 1000°C. From DTG it is clear that mass losses are accompanied by temperature at 216, 342, 545, 739 and 831 °C.

In [Cu L (H₂O)₂] complex also exhibits three-stage of decomposition. The first step involves decomposition of the methyl group from ligand at a temperature 40 to 170°C with mass loss corresponds to 3.19% (calculated. 3.63%). Water molecules and part of ligand are dissociated at a temperature range between 170°C to 700°C with a mass loss per cent 46.16% (calculated. 47.64%). Overall mass loss percentage is found to be 74.73(calculated. 76.89%), leaving CuO as residue. From DTG data clear that mass loss is accompanied at temperature 49, 167, 199, 322 and 866°C. In the case of [Cr L₂ (H₂O)₂] complex first step involves 20.80% (calculated. 21.23%) mass loss by the elimination of -CO, -CH-, -OH group from ligand and two water molecules with temperature range is 40- 170°C. The remaining two step involves the degradation of other part of ligand with temperature ranges from 170- 570and 570-960 °C having mass loss 30.71% and 27.72% (calculated. 32.84% and 29.05%) respectively. Overall mass loss percentage is 79.23% (calculated 83.12%), leaving Cr₂O₃ as residue. The above-mentioned mass loss corresponds to DTG temperature are 50, 236, 398 and 849 °C. All the thermal decomposition reaction has order 2/3.

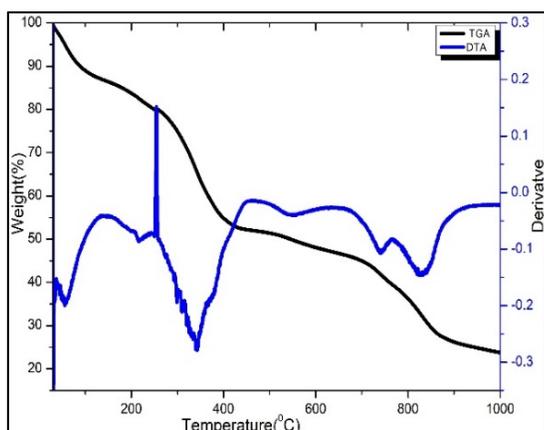


Fig 1: TGA/DTG curve of Co complex

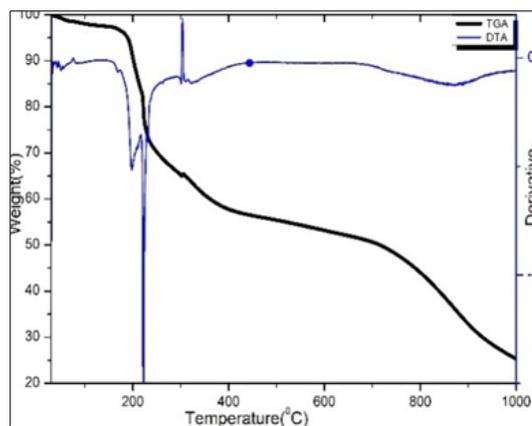


Fig 2: TGA/DTG curve of Cu complex

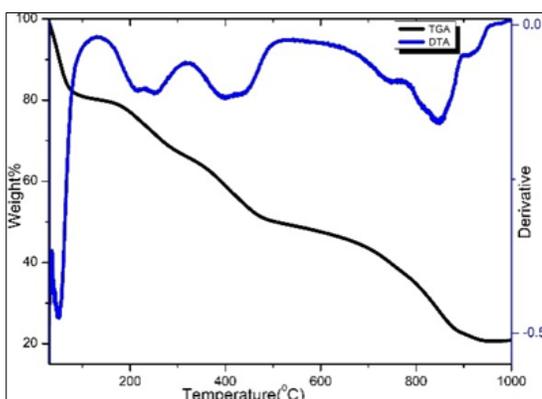


Fig 3: TGA/DTG curve of Cr complex

Calculation of thermodynamic parameters.

Thermodynamic activation parameters such as activation energy (E^*), enthalpy (H^*), entropy (S^*) and free energy (G^*) of decomposition processes are graphically by using Coats-Redfern equation [20] and nine equations.

$$\log \left[\frac{\log \left\{ \frac{w_f}{(w_f - w)} \right\}}{T^2} \right] = \log \left[\frac{AR}{\theta E^*} \left(1 - \frac{2RT}{E^*} \right) \right] - \frac{E^*}{2 \cdot 303RT}$$

Where W_f is the mass loss after the reaction, W is the mass loss at a temperature T , R is the universal gas constant, E^* is the activation energy in KJ/mol, A is Arrhenius constant and θ is the heat rate. A plot of $\log \left[\frac{\log \left\{ \frac{w_f}{(w_f - w)} \right\}}{T^2} \right]$ verses $1/T$ gives a straight line with slope is $-\frac{E^*}{2 \cdot 303RT}$, from which E^* is calculated. The entropy of activation is calculated by $\Delta S^* = 2 \cdot 303 \left[\log \left(\frac{Ah}{kT} \right) R \right]$, where k and h are Boltzmann's constant and Plank's constant respectively. The enthalpy of activation is calculated by using an equation $\Delta H^* = E^* - RT$ and free energy change obtained from $\Delta G^* = \Delta H^* - T\Delta S^*$ [13]. The activation energies of decomposition are in the ranges between 0.084 to 8.736 kJ/mol. The positive values of E^* involves the processes of translational, vibrational, rotational state and mechanical potential energy of the complexes. Higher the value of activation energy means higher the thermal stability of the complexes [14]. The entropy of

activation is negative for all complexes indicates the decomposition reaction proceed with a lower rate than the normal ones and also indicates the activated complexes have more ordered than reactant. In addition, the positive values of ΔH^* means the endothermic and negative values indicates exothermic decomposition process. All the ΔG^* values are positive which

indicates all steps are nonspontaneous [21]. From the table 4 can easily understand that Cu complex has least stable, while Cr complex is most thermally stable. The thermal stability of complex is explained on the reverse order of Irving William series. i.e., $[\text{CrL}_2(\text{H}_2\text{O})_2] > [\text{CoL}_2(\text{H}_2\text{O})_2] > [\text{CuL}(\text{H}_2\text{O})_2]$.

Table 4: thermodynamic data of thermal decomposition of complexes.

complex	Decomposition temperature (°C)	Order of reaction	E* (kJ/mol)	ΔS^* (kJ/mol)	ΔH^* (kJ/mol)	ΔG^* (kJ/mol)
[CoL ₂ (H ₂ O) ₂]	40 - 250	2/3	4.438	-330.52	2.597	233.188
	250 - 640		0.360	-364.75	5.113	224.316
	640 - 990		0.828	-363.85	9.178	401.699
[CuL(H ₂ O) ₂]	40 - 170	2/3	8.736	-769.64	3.649	338.645
	170 - 700		1.981	-378.33	3.257	148.309
	700 - 960		5.579	-345.03	9.464	392.998
[CrL ₂ (H ₂ O) ₂]	40 - 170	2/3	3.552	-67.941	2.682	21.948
	170 - 570		0.084	-374.36	4.231	190.553
	570-960		0.327	-371.69	9.311	416.302

Antimicrobial studies

The antimicrobial result shows that ligand has less active than metal complexes because of Overtone's concept of cell permeability and Tweedy's chelation theory [7-8]. According to Overtone's concept cells favours only the transport of lipid-soluble material through lipid membrane. Hence lipophilicity is an important tool to control antimicrobial activity. On chelation polarity of the metal ions is reduced due to sharing of electrons from donor groups to metal and overlapping of ligand orbitals. So, chelation increase, delocalisation of pi-electron is increasing and hence lipophilicity of the complex was increased. That is metal atom from the complex can block metal-binding site in enzymes of microorganisms. The below table 5 indicated the antibacterial activities of Schiff base ligand and some complexes at their two concentrations (400mcg and 800mcg). From the table Cu complex found inhibitory to Klebsiella pneumonia at both the test concentrations at the range of 38.71% and 48.38% compared to control (standard), whereas Bacillus subtilis found inhibited

62.06% and 79.31%. It indicated that this Cu complex is effective to control both the bacterial pathogens significantly and activity is shown in the figure 4.

The Co complex was found to resist the growth of Bacillus Subtilise at a range of 39.28% and 50.00% at both the test concentrations. But it was found ineffective in K. Pneumonia. The same trend was noticed in the Cr complex. Both the concentrations of Cr complex found inhibitory to B. Subtilise at a range of 40.74% and 44.44% shown in the figure 5. From the table 5, it was evident that B. Subtilise was sensitive to three complexes at the two concentrations tested and only the Cu complex was found inhibitory to both the bacterial pathogens tested, whereas, in the antifungal assay, all the samples at their two concentrations, only the cobalt complex at 800mcg showed inhibitory effect on Candida albicans at a range of 61.11% compared to standard as shown in figure 6. The overall antimicrobial activity is summarised in chart representation by figure 7.

Table 5: Antimicrobial activity of HL ligand and its complexes.

Name of pathogen	Zone of inhibition (mm)								Gentamycin	Clotrimazole	DMSO
	HL		[CoL ₂ (H ₂ O) ₂]		[CuL(H ₂ O) ₂]		[CrL ₂ (H ₂ O) ₂]				
	400	800	400	800	400	800	400	800			
K. Pneumonia	-	-	-	-	12	15	-	-	31	-	-
B. Subtilise	-	-	11	14	18	23	11	12	27	-	-
A. Niger	-	-	-	-	-	-	-	-	-	18	-
C. albicans	-	-	-	11	-	-	-	-	-	19	-



Fig 4: anti-bacterial activity of Cu complexes.



Fig 5: antibacterial activity of Cr and Co complexes.



Fig 6: antifungal activity of Co complexes.

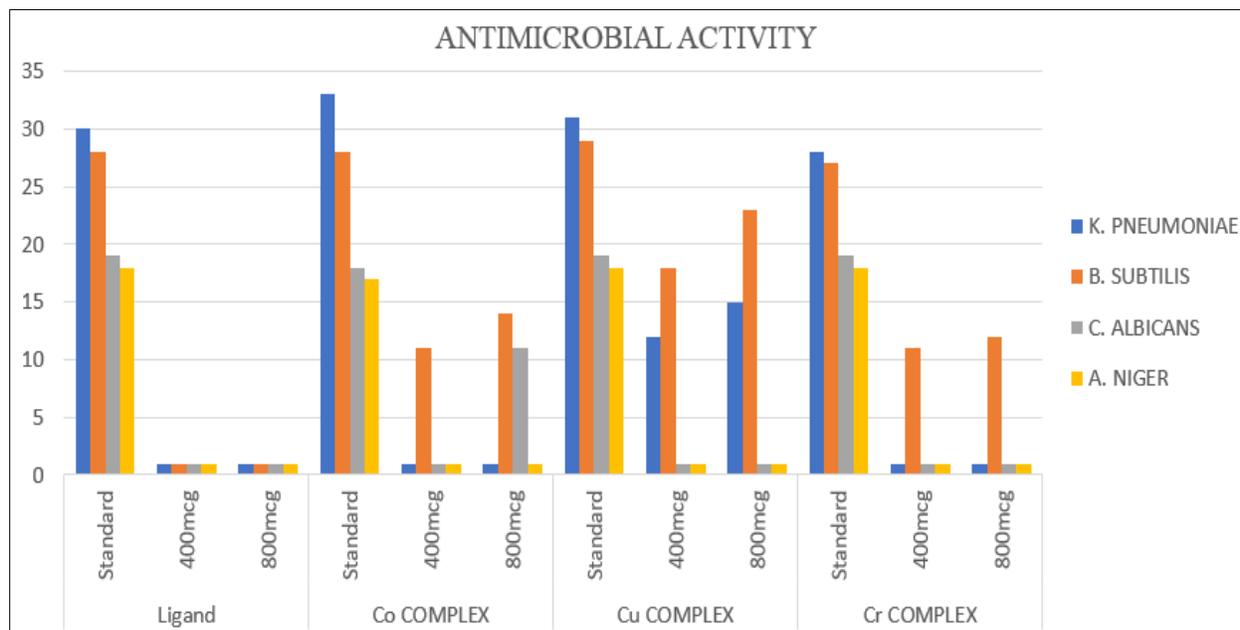


Fig 7: chart representation of antimicrobial activity of ligand and complexes.

Conclusion

The Schiff's base ligand and its metal complexes were prepared and characterized by various techniques such as IR, UV-Visible spectroscopy, molar conductance measurement, magnetic moment studies and thermal studies. With the help of all these techniques, distorted octahedral geometry around Co (III) complex, octahedral geometry around Cr (III) and square planar geometry around Cu (II) complexes are proposed. The order of thermal stability was observed in reverse form of Irvin William series. i.e., $[\text{CrL}_2(\text{H}_2\text{O})_2] > [\text{CoL}_2(\text{H}_2\text{O})_2] > [\text{CuL}(\text{H}_2\text{O})_2]$. This study reveals that ligand does not possess any antimicrobial activity but on complexation it acquires enhanced anti-microbial activity. Among these complexes Copper complex shows greater bacterial inhibition potential than others and is actively inhibit

both K. Pneumonia and B. Subtilise bacteria with efficiency up to 80%. Antimicrobial activity of synthesised compounds was observed in the reverse order of stability of complexes. i.e., $[\text{CuL}(\text{H}_2\text{O})_2] > [\text{CoL}_2(\text{H}_2\text{O})_2] > [\text{CrL}_2(\text{H}_2\text{O})_2] > \text{HL}$. Only the cobalt complex shows anti-fungal activity against C. Albicans at 61% efficiency at a concentration 800mcg, below this concentration it is found to be ineffective.

References

- Deivanayagam P, R Pa, Bhoopathy, S Thanikaikarasan. Synthesis, characterization, anti-microbial, analgesic and CNS studies of Schiff base Cu (II) complex derived from 4-chloro-o-phenylene Diamine. International Journal of Advanced Chemistry, 2014;2(2):166-170.

2. Abu-Dief AM, IMA Mohamed. A review on versatile applications of transition metal complexes incorporating Schiff bases. Beni-Suef University Journal of Basic and Applied Sciences, 2015;4(2):119-133.
3. Tulu MM, AM Yimer. Catalytic studies on Schiff base complexes of Co (II) and Ni (II) Usingbenzoylation of phenol. Modern Chemistry Applications,2018;6(3):260-266.
4. Gupta KC, AK Sutar. Catalytic activity of Schiff base transition metal complexes. Coordination Chemistry Reviews,2008;252:1420-1450.
5. Singh AK. Inhibition of Mild Steel Corrosion in Hydrochloric Acid Solution by 3-(4-((Z)-Indolin-3-ylideneamino) phenylimino) indolin-2-one. Industrial & Engineering Chemistry Research,2012;51:3215-3223.
6. Daoud DT, Douadi S, Issaadi, S Chafaa. Adsorption and corrosion inhibition of new synthesized thiophene Schiff base on mild steel X52 in HCl and H₂SO₄ solutions. Corrosion Science,2014;79:50-58.
7. Singh K, R Thakur, V Kumar. Co (II), Ni (II), Cu (II), and Zn (II) complexes derived from4-[[3-(4-bromophenyl)-1-phenyl-1H-pyrazol-4-ylmethylene]-amino]-3-mercapto-6-methyl-5-oxo-1,2,4-triazine. Beni-Suef university journal of basic and applied sciences,2016;5:21-30.
8. Tuemer M, H Koeksal, MK Sener, S Serin. Antimicrobial activity studies of the binuclear metal complexes derived from tridentate Schiff base ligands. Transition Met. Chem,1999;24:414-420.
9. Joseyphus RS, S Nair. Antibacterial and Antifungal Studies on Some Schiff Base Complexes of Zinc (II). Mycobiology,2008;36(2):93-98.
10. Prakash CR, S Raja, G Saravanan. Synthesis, characterization and anticonvulsant activity of novel Schiff base of isatin derivatives. Int J Pharm Pharm Sci,2010;2(4):177-181.
11. Jarrahpour A, D Khalili, ED Clercq, C Salmi, JM Brunel. Synthesis, Antibacterial, Antifungal and Antiviral activity Evaluation of some new bis-Schiff bases of Isatin and their derivatives. Molecules,2007;12:1720-1730.
12. Mahmoud WH, RG Deghadi, GG Mohamed. Novel Schiff base ligand and its metal complexes with some transition elements. Synthesis, spectroscopic, thermal analysis, antimicrobial and *in vitro* anticancer activity. Applied Organometallic Chemistry,2016;30:221-230.
13. Alghool S, HF Abd El-Halim, A Dahshan. Synthesis, spectroscopic thermal and biological activity studies on azo-containing Schiff base dye and its Cobalt (II), Chromium (III) and Strontium (II) complexes, Journal of Molecular Structure,2010;983:32-38.
14. Omar MM, GG Mohamed, AA Ibrahim. Spectroscopic characterization of metal complexes of novel Schiff base. Synthesis, thermal and biological activity studies, *Spectrochimica Acta Part A*,2009;73:358-369.
15. Cinarli A, D Gurbuz, A Tavman, AS Birteksoz. Synthesis, spectral characterizations and antimicrobial activity of some Schiff bases of 4-chloro-2-aminophenol., Bull. Chem. Soc. Ethiop,2011;25:3:407-417.
16. Sakiyan I, N Gunduz, T Gunduz. Synthesis and characterization of Manganese (III) complexes of Schiff bases derived from amino acids and 2-hydroxy-1-naphthaldehyde., Synthesis and Reactivity in Inorganic and Metal-Organic Chemistry,2001;31:7:1175-1187.
17. Rahmouni NT, NH Bensiradi, SA Megatli, S Djebbar, OB Baitich. New mixed amino acids complexes of Iron (III) and Zinc (II) with isonitrosoacetophenone: Synthesis, spectral characterization, DFT study and anticancer activity. *SpectrochimicaActa Part A: Molecular and Biomolecular Spectroscopy*,2019;213:235-248.
18. Abhisek B, C Shouvik. A benzoate bridged binuclear mixed valence cobalt(III/II) complex with Co (III)O₄Co (II) core: Synthesis, Structural and investigation of its phenoxazinone synthase mimicking activity., *Polyhedron*,2019.
19. Al-Sha'alan NH. Antimicrobial activity and spectral, magnetic and thermal studies of some transition metal complexes of a Schiff base hydrazone containing a quinoline moiety., *Molecules*,2007;12(5):1080-1091.
20. Coats AW, JP Redfern. Kinetic parameters from thermogravimetric data., *Nature*,1964;201(4914):68-69.
21. Ebrahimi HP, JS Hadi, ZA Abdunabi, Z Bolandnazar. Spectroscopic, thermal analysis and DFT computational studies of salen-type Schiff base complexes, *SpectrochimicaActa Part A*,2014;117:485-492.