

SYNTHESIS, SPECTRAL CHARACTERIZATION AND ANTIMICROBIAL ACTIVITIES OF Ni(II) AND Cu(II) SCHIFF BASE COMPLEXES

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ABSTRACT: Ni(II) and Cu(II) mono nuclear metal complexes of symmetrical Schiff-base ligands derived from 4,6-diacetyl resorcinol and 2-aminophenol or 4-nitro-2-aminophenol were synthesized. The structure of Schiff-base ligands and their metal complexes were characterized by elemental analysis, ¹H & ¹³CNMR, electronic spectroscopy, FT IR, mass, magnetic susceptibility and conductance measurements. The free ligand being tetradentate in nature coordinates through its two nitrogen donors and two oxygen donors in equatorial position, the ligand act as dianionictetradentatedioxadiaza moiety. Both the ligands and the complexes were screened for their antimicrobial activities against Gram positive, Gram negative bacteria and antifungal activities against candida albicans.

KEY WORDS: Schiff-base ligands, Metal complexes, Diacetyl resorcinol, tetradentate ligand Antimicrobial activity.

INTRODUCTION:

The Schiff bases are widely studied because of the increasing recognition of their role in biological systems. Mononuclear complexes of acyclic ligand have been reported¹. Schiff-base complexes play important roles in antibacterial, antifungal and antiviral activities^{2,3}. Tetradentate Schiff-base complexes have shown high stability when coordinated to metal ion using the N₂O₂donar atoms^{4,5}. Alkyl resorcinol and aromatic resorcinol are reported to possess valuable therapeutic and antiseptic properties. Phenolic compounds are reported to exhibit analgesic, antibacterial antifungal activities and antioxidants⁶. In the presence of metal ions these phenolic compounds are believed to damage the cytoplasmic membrane, which is related to their activity⁷. This prompted us to synthesis a new series of Schiff bases containing the phenolic moiety. In this article we describe the synthesis, characterization and anti-microbial activities of Ni(II) and Cu(II) complexes of Schiff bases derived from 4,6-diacetyl resorcinol and 2-amino phenol/2-amino-4-nitro phenol in molar ratio 2:1.

EXPERIMENTAL:

MATERIALS AND METHODS:

4,6-Diacetylresorcinol was synthesized according to the literature method. Aminophenol and 2-amino-4-nitrophenol and metal salts were obtained from Sigma and Merck. Organic solvents methanol, diethyl ether, dimethylformamide and acetone were analytical grade and used as without any further purification.

ANTIMICROBIAL ACTIVITY (DISC DIFFUSION METHOD):

DISC PREPARATION:

The sterile filter paper discs were impregnated with the ligand and complexes usually consisting of absorbent paper. It is most convenient to use Whatman No.1 filter paper for preparing the discs. Dried disc size was 6 mm diameter

TESTED MICROORGANISMS:

Antimicrobial activity of ligand and complexes were investigated against both gram positive (*Bacillus cereus*) and gram negative (*Serratia marcescens* and *Klebsiella pneumoniae*) and fungal (*Candida albicans* and *Cryptococcus neoformans*). The species that were purchased from Department of Microbiology, K.A.P Viswanatham medical college, Tiruchirappalli, Tamil Nadu

PROCEDURE:

Sterile liquid nutrient agar/potato dextrose agar medium (pH 7.4 ± 2) was poured (10-15ml) into each sterile petriplates. These growth media an important role in the determination of the antimicrobial activity after solidification, 100µl of suspension containing 10⁸ CFU/ml of each test bacteria/fungi were spread over nutrient agar/potato dextrose agar plates. The sterile filter paper discs (6 mm in diameter) were impregnated with ligand and complexes placed on the inoculated agar. Negative controls were prepared in using the same solvents employed. Chloramphenicol (30mcg/disc)/Amphotericin (100mcg/disc) were used as positive reference control to determine the sensitivity of the ligand and complexes on each pathogen. The inoculated plates were

incubated 37°C at 24hrs for bacteria/ 37°C at 48-72hrs for fungi. Antimicrobial activity was evaluated by measuring the diameter of the inhibition zones. Each assay was conducted in triplicate.

4,6-DIACETYL RESORCINOL:

It was synthesized according to the method reported in literature⁸

SYNTHESIS OF SCHIFF BASES:

The Schiff base (L¹ and L²) Ligands were prepared by adding 4,6-diacetylresorcinol (5 mmol) dissolved in hot absolute ethanol (20 ml) to aminophenol (10 mmol)/2-amino-4-nitrophenol (10 mmol) respectively in absolute ethanol (20 ml). The reaction mixtures were refluxed for 6 hours. The resulting brownish yellow solution was cooled to 0°C. The solid product formed was removed by filtration and washed with a few amounts of cold absolute ethanol and air dried. Yield (L¹) 75% and (L²) 67%.

L¹

Anal. Cal. (C₂₂H₂₀N₂O₄): C (70.20), H (5.36), N (7.44).

Found: C (69.90), H (5.23), N (7.28).

IR (KBr Pellets) (C=N) 1635 cm⁻¹, (C=C)_{aro} 1550 cm⁻¹, (C-O) 1254 cm⁻¹, (OH) 3331 cm⁻¹, (OH) 3253 cm⁻¹.

¹H NMR: 12.71(s, 2H, OH), 9.49 (s, 2H, OH), 8.41, 8.20 (d, 2H, Ph), 6.3-7.0 (m, 6H, Ph), 2.37 (s), 6H, CH₃.

Mass value m/z = 377.

L²

Anal. Cal. (C₂₂H₁₈N₄O₈): C (56.65), H (3.89), N (12.01).

Found: C (56.25), H (3.76), N (11.91).

IR (KBr Pellets) (C=N) 1621 cm⁻¹, (C=C)_{aro} 1505 cm⁻¹, (C-O) 1250 cm⁻¹, (OH) 3448 cm⁻¹, (OH) 3343 cm⁻¹.

¹H NMR: 12.87 (s, 2H, OH), 9.85 (s, 2H, OH), 8.51, 8.46 (d, 2H, Ph), 6.3-7.0 (m, 6H, Ph), 2.57 (s), 6H, CH₃.

Mass value m/z = 467.

The synthesis of the ligand (L¹ and L²) is depicted in **Scheme-1**.

SYNTHESIS OF METAL COMPLEXES:

Metal complexes were synthesized by mixing 1:1 methanolic solution of L¹/L² and the appropriate metal perchlorate salts. The resulting mixture was refluxed for 6 hours. The coloured precipitates were obtained by filtration, washed with diethyl ether and dried over calcium chloride in vacuum. The nature of bonding exhibited by metal ions with the ligand is depicted in **Scheme-2**.

RESULT AND DISCUSSION:

SYNTHESIS AND CHARACTERIZATION OF THE LIGAND: The dioxadiaza tetradentate acyclic ligands (L¹/L²) were synthesized by the reaction of 4,6-diacetyl resorcinol and 2-aminophenol / 4-nitro-2-aminophenol in 1: 2 mole ratio by both conventional and under microwave assisted reaction conditions. The microwave assisted reaction resulted in high yield and increased purity of the ligand. The corresponding metal perchlorate complexes were synthesized by the reaction of the preformed ligand with the corresponding perchlorate metal salts in 1:1 mole ratio in ethanol, by conventional method. The synthesized dioxadiaza tetradentate Schiff base ligand (L) and their metal perchlorate complexes were characterized by elemental analysis, infrared, electronic spectroscopy, NMR, Conductance, and Magnetic measurements. The Elemental analysis, colour, Conductance, and Magnetic measurements of the ligand and the complexes were furnished in **Table -1**. The infrared spectral data of the ligand and the complexes are furnished in **Table-2**. The electronic spectral data of the ligand and the complexes are furnished in **Table -3**.

INFRA-RED SPECTRAL STUDY OF LIGANDS AND METAL COMPLEXES:

The infrared spectra provide valuable information regarding the formation the dioxadiaza tetradentate acyclic ligands and the coordination behavior of the ligands to the metal ions. The (C=O) peak around 1700 cm⁻¹ observed in the 4,6-diacetyl resorcinol is absent in the ligand and instead the a sharp peak appears at 1635-1621cm⁻¹ corresponds to the ν (C=N) stretching of newly formed azomethine groups. The infrared spectrum of the ligand L¹ is depicted in **Fig.1**. The azomethine band is shifted to lower frequencies in the spectra of the metal complexes (1620-1582 cm⁻¹). The ligands show two broadened bands in the region 3331-3404 cm⁻¹ and 3343-3448 cm⁻¹ has been assigned to ν (O-H) stretching of phenolic groups of 4,6-diacetyl resorcinol and that of the phenolic group comprising the 2-amino phenol moiety. The broad hydroxyl band present in the ligand corresponding to the amino phenol moiety disappears in the spectra of the complexes indicating that the hydroxyl groups are coordinated to metal through the deprotonated form⁹. The other band at 3448-3393 cm⁻¹ indicates the presence of-OH group from the resorcinol phenolic group are present in the ligand as well as metal complexes¹⁰. This observation indicates that the hydroxyl group from the resorcinol moiety does not involve in coordination to the metal ions. The spectra of the metal complexes show some new bands in the region 507-591 and 428-497 cm⁻¹ region, which indicate the formation of M-N and M-O bonds respectively¹¹ showed in **table-2**. The typical Infrared spectra of Cu(II) L¹ complex is shown in **fig.2**.

ELECTRONIC SPECTRA:

The electronic spectra of the metal complexes were recorded in DMF. The absorption regions, assignments and proposed geometry of the complexes are given in **table-3**. The band between 259 and 320 nm is due to LMCT. The spectra of Ni(II)

complexes show bands in the 420-450 nm region due to $^1A_{1g} \rightarrow ^1B_{1g}$ transition for square planar geometry. The electronic spectra of Cu(II) complexes (535-550 nm) can be assigned to the $^2B_{1g} \rightarrow ^2A_{1g}$ transition of square planar geometry. The electronic spectra of the complexes show a red shift in the d-d absorption band upon introducing an electron-withdrawing group in para position. The typical electronic spectra of Schiff base L_1 copper complex are shown in **fig.3**.

MOLAR CONDUCTANCE:

The molar conductance of the metal perchlorate complexes were measured in DMF as solvent (**table -1**). The molar conductance value of the complexes indicates that under study was non electrolytic nature¹². Co(III), Cu(II), Ni(II) and Zn(II) metal complexes are neutral electrolyte as shown by their molar conductivity measurements in DMF, which are in the range 12-16 $\text{ohm}^{-1}\text{cm}^2\text{mol}^{-1}$.

MAGNETIC SUSCEPTIBILITY:

The magnetic susceptibility measurements provide information regarding the structure of the metal complexes. The Cu(II) complex is paramagnetic and their effective magnetic moment value (1.90 B.M) indicative for a predominantly dx_{2-y_2} ground state occupied with one unpaired electron¹³. Although Zn(II), Ni(II), Co(III) complexes are diamagnetic. Therefore the Schiff base ligand coordinates to Ni(II), Zn(II) ion as a four-dentate with square planar environment. The magnetic values were recorded and discussed in **table-1**.

ANTIMICROBIAL ACTIVITY:

An antimicrobial activity of the ligands (L^1, L^2) and a series of its metal complexes [Ni(II),Cu(II)] were investigated against bacterial pathogens viz, *B. cereus*, *S. marcescens* and *K. pneumoniae* and fungal pathogens *Candida albicans* and *Cryptococcus neoformans* by using disc-agar diffusion method results were showed in **table-4 and table-5**. Generally electron withdrawing group present in para position give higher antimicrobial activity. In the present study the order of antimicrobial activity of the synthesized compounds $\text{NO}_2 > \text{H}$. All the complexes show antimicrobial activity and the presence of an electron withdrawing group enhances the antimicrobial activity. The variation in the effectiveness of different compounds against different organisms depends either on the impermeability of the cells of the microbes or on differences in ribosome of microbial cells¹⁴.

CONCLUSIONS:

The two Schiff base ligands L^1 and L^2 behave as dianionic tetradentate ligands with an ONNO donor sequence coordinating through the nitrogen of the azomethine and oxygen of phenol groups. On the basis of magnetic and electronic spectra of Ni(II) and Cu(II) complexes indicate square planar geometry. The ligands and their metal complexes reveal that the antimicrobial activities of the chelated ligands are enhanced as compared to the free ligands. The presence of an electron-withdrawing group enhances the antimicrobial activities.

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Compound	Mol. Formula	Mol. Weight	Yield %	Calculated / (Founded)				Colour	μ_{eff} (BM)	Molar cond.
				C	H	N	M			
L^1	$\text{C}_{22}\text{H}_{20}\text{N}_2\text{O}_4$	376	75	70.20 (69.90)	5.36 (5.23)	7.44 (7.28)	-	Yellow	-	-
Ni(II) L^1	$\text{C}_{22}\text{H}_{18}\text{N}_2\text{NiO}_4$	433	74	61.01 (60.12)	4.19 (4.02)	6.47 (6.33)	11.90 (11.74)	Pale brown	Dia	12
Cu(II) L^1	$\text{C}_{22}\text{H}_{18}\text{CuN}_2\text{O}_4$	438	78	60.34 (59.67)	4.14 (4.04)	14.51 (14.37)	6.40 (6.31)	Brown	1.73	16
L^2	$\text{C}_{22}\text{H}_{18}\text{N}_4\text{O}_8$	466	67	56.65 (56.25)	3.89 (3.76)	12.01 (11.91)	-	Brownish yellow	-	-
Ni(II) L^2	$\text{C}_{22}\text{H}_{16}\text{N}_4\text{NiO}_8$	523	71	50.52 (50.39)	3.08 (2.92)	10.71 (10.58)	11.22 (11.11)	Reddish brown	Dia	13

Cu(II)L ²	C ₂₂ H ₁₆ CuN ₄ O ₈	528	79	50.05 (49.89)	3.05 (2.85)	10.61 (10.48)	12.01 (11.88)	Brown	1.78	19
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Tables -1. Elemental analysis, colour, molar conductance electronic spectra and magnetic susceptibility of the ligand and their complexes:

Tables - 2. IR spectral data of ligand and metal complexes:

Compound	ν OH (cm ⁻¹)	ν (C=N) (cm ⁻¹)	ν (M-N) (cm ⁻¹)	ν (M-O) (cm ⁻¹)
L ¹	3404, 3331	1635	-	-
Ni(II)L ¹	3394	1606	591	472
Cu(II)L ¹	3433	1620	536	457
L ²	3448, 3343	1621	-	-
Ni(II)L ²	3393	1582	578	497
Cu(II)L ²	3431	1604	507	428

Tables-3. Electronic spectral data of the compounds:

Compound	Solvent	Absorption (nm)	Band Assignment	Geometry
Ni(II)L ¹	DMF	259	INCT	Square planar
		319	INCT	
		426	¹ A _{1g} → ¹ B _{1g}	
Cu(II)L ¹	DMF	254	INCT	Square planar
		320	INCT	
		535	² B _{1g} → ² A _{1g}	
Ni(II)L ²	DMF	263	INCT	Square planar
		320	INCT	
		445	¹ A _{1g} → ¹ B _{1g}	
Cu(II)L ²	DMF	258	INCT	Square planar
		318	INCT	
		546	² B _{1g} → ² A _{1g}	

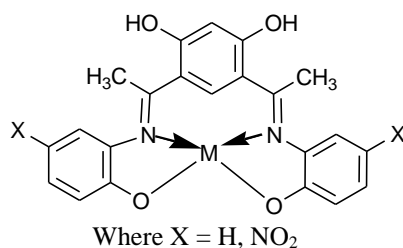
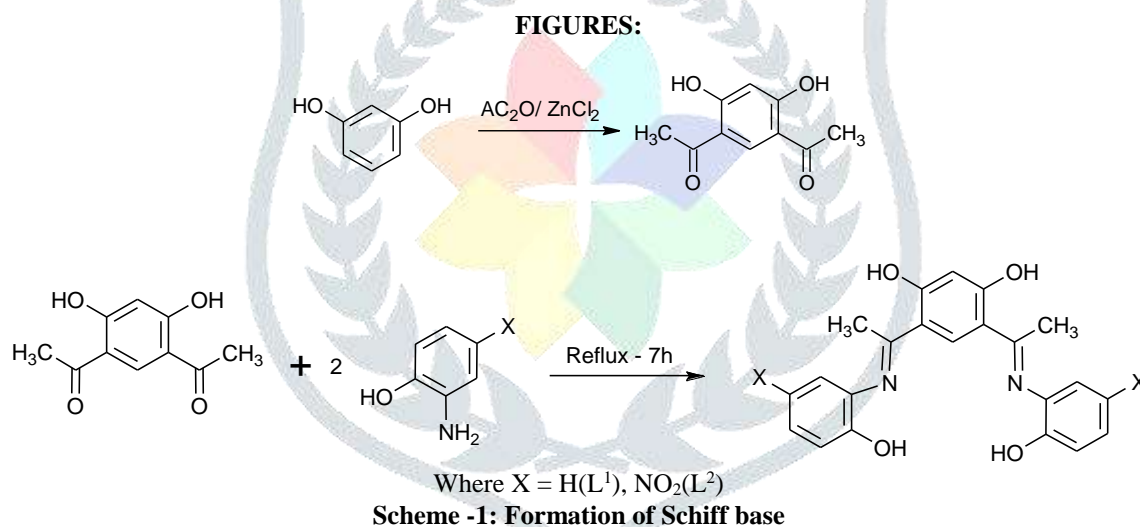
Tables -4. Antibacterial activities of ligand and its metal complexes:

Compound	<i>Bacillus cereus</i>	<i>Serratiamarcescens</i>	<i>Klebsiellapneumoniae</i>
L ¹	7.3 ± 0.5	7.3 ± 0.5	-
Ni(II)L ¹	9.3 ± 0.5	9.6 ± 1.5	10.3 ± 1
Cu(II)L ¹	10.3 ± 0.5	10.6 ± 0.5	9.3 ± 0.5
L ²	10.6 ± 0.5	9 ± 1	9.3 ± 0.5
Ni(II)L ²	12.3 ± 0.5	11.2 ± 1	13 ± 0.5

Cu(II)L ²	13 ± 1	14.2 ± 0.5	12.3 ± 0.5
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Tables -5. Antifungal activities of ligand and its metal complexes:

Compound	<i>Candida albicans</i>	<i>Cryptococcus neoformans</i>
L ¹	-	7 ± 1
Ni(II)L ¹	8 ± 2	9.3 ± 2.0
Cu(II)L ¹	10 ± 1	10 ± 0
L ²	12 ± 1	13 ± 3.4
Ni(II)L ²	14 ± 2	15 ± 0.5
Cu(II)L ²	13 ± 1.0	14.0 ± 1.0



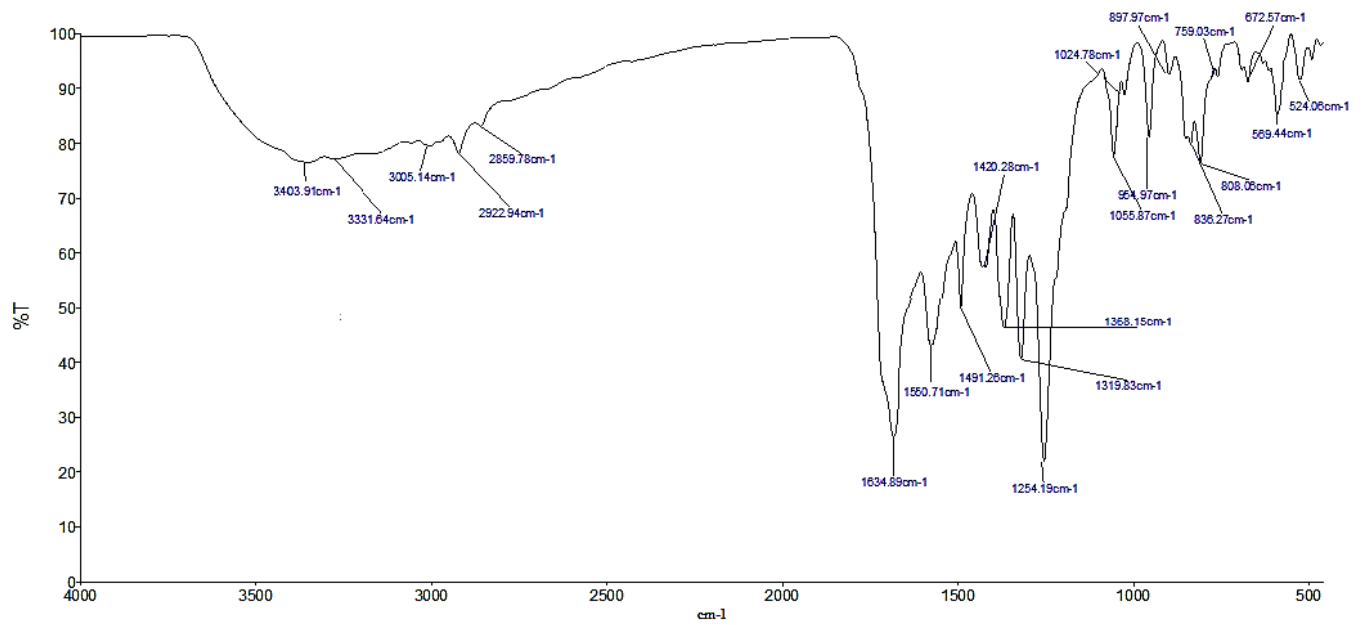


Fig. 1: Infrared spectrum of Ligand L¹

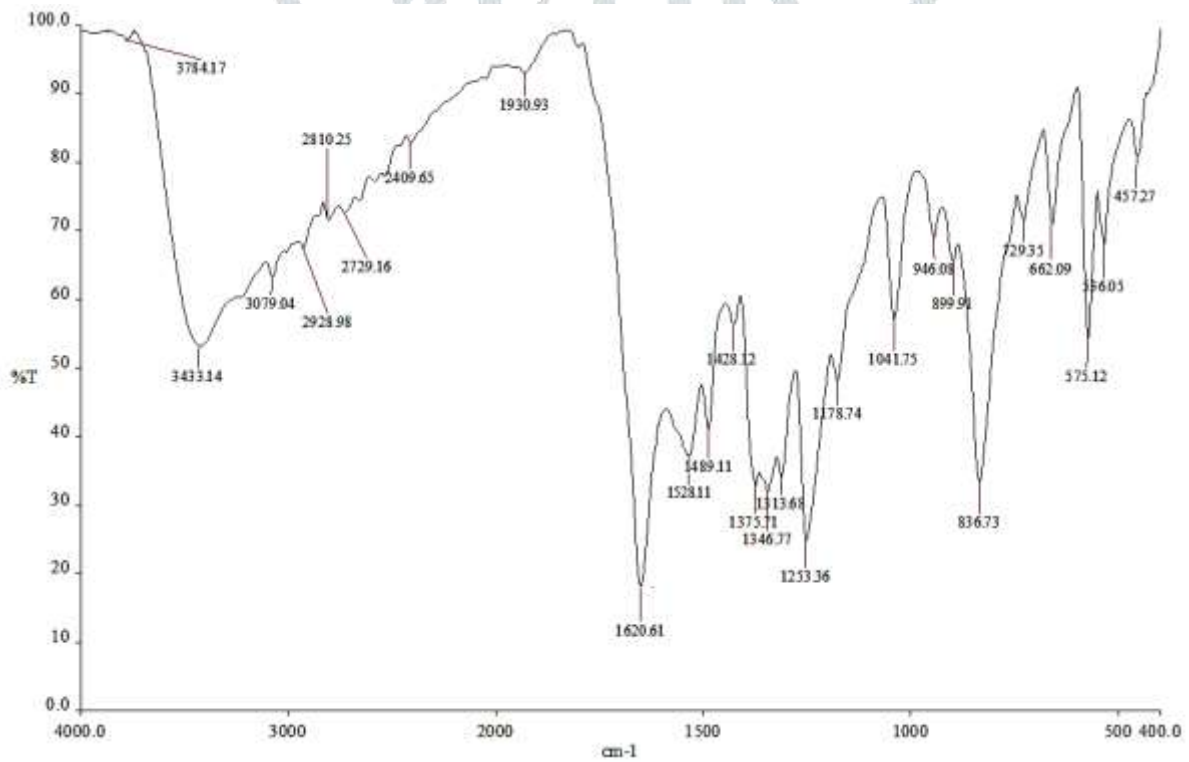
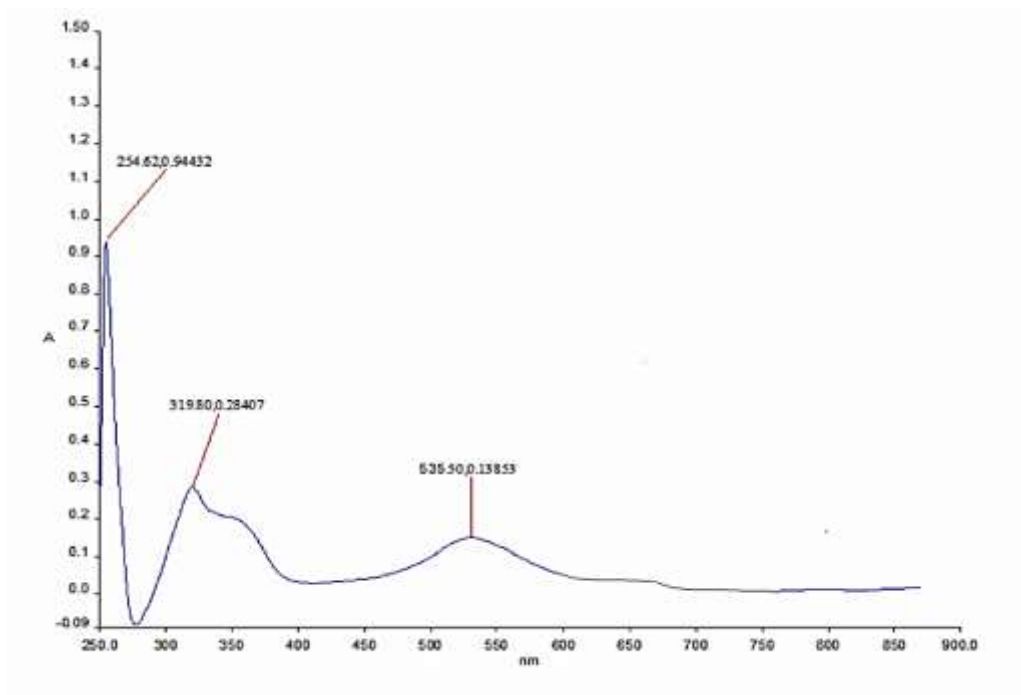
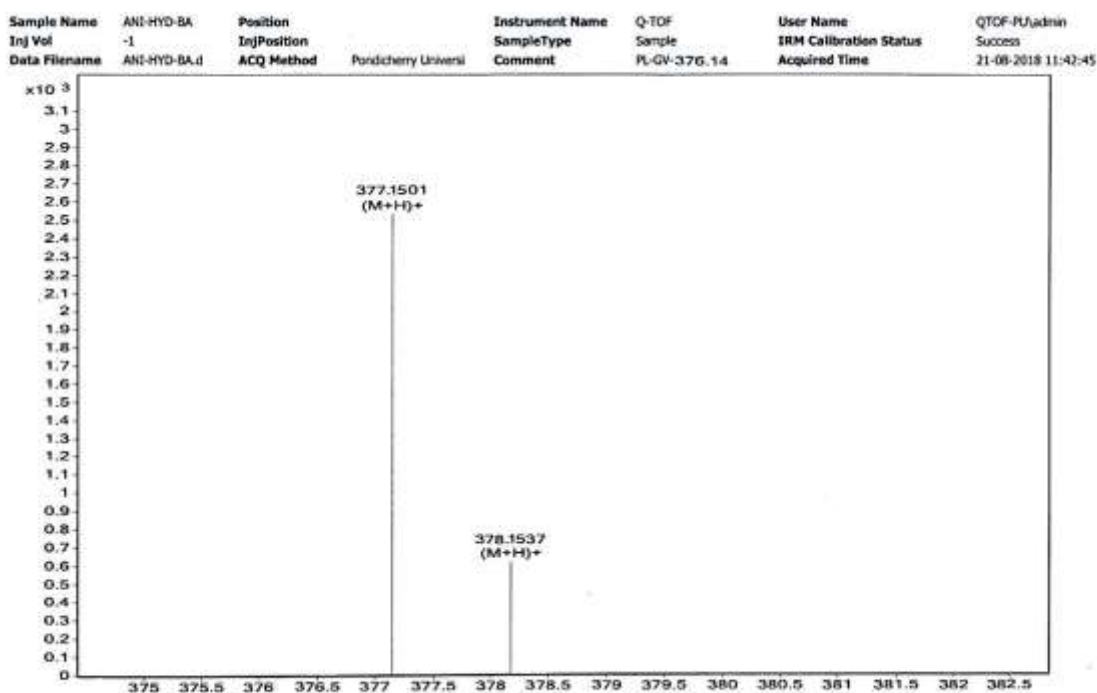


Fig. 2: Infrared spectrum of Cu(II) L¹ complex.

Fig. 3: UV- spectrum of Cu(II) L¹ complex.Fig. 4: Mass spectrum of the ligand (L¹).

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