

SYNTHESIS, SPECTRAL CHARACTERIZATION AND ANTIMICROBIAL STUDIES OF Co(III), Ni(II), Cu(II) AND Zn(II) METAL COMPLEXES OF SCHIFF BASE DERIVED FROM 4,6-DIACETYL RESORCINOL AND 4-CHLORO-2-AMINO PHENOL

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ABSTRACT: A formerly new resorcinol based acyclic ligand (L) was synthesized by Schiff base condensation reaction. The ligand was synthesized by microwave assisted method at enhanced yield and hugely reduced reaction time. The new ligand was completely characterized. A series of cobalt (III), nickel (II) and copper (II) and zinc (II) complexes of the unreported ligand (L) has been synthesized by the direct reaction of the preformed ligand (L) with cobalt(III), nickel (II) and copper (II) and zinc (II) salts in 1:1 mole ratio in ethanol. The free ligand is neutral, but on complexation with metal ions, it tends to lose both the phenolic hydrogen and coordinates with cobalt (III), nickel (II), copper (II) and zinc (II) metal ions as dianionic moiety. The ligand (L) being tetradentate in nature coordinates through its two nitrogen donors and two oxygen donors in the equatorial positions, the ligand serves as dianionic tetradentate dioxadiaza moiety. The perchlorate complexes of the ligand were isolated and characterized thoroughly, using elemental analysis, electronic spectroscopy, infrared, molar conductivity measurements, magnetic susceptibility, ¹H NMR and ¹³C NMR studies. The complexes formed were of mononuclear in nature. The effective antimicrobial activity on both ligand and complexes were screened against gram positive, gram negative bacterial pathogens and fungal pathogens.

KEY WORDS: Resorcinol based ligand, tetradentate ligand, dioxadiaza ligand, resorcinol, Schiff base condensation, dianionic ligand, transition metal complexes and antimicrobial activity.

INTRODUCTION

Schiff bases are mostly widely used organic compounds. They are used as catalyst^{1,2}, photochromic properties³ and biological activity^{4,5}. The chemical compound, 2-alkyl resorcinol (where the alkyl group is linear) has been reported to have skin de pigmentation properties (Gadgil et al., 2004; Bollinger et al., 1990). Alkyl resorcinol and aromatic resorcinol are reported to possess valuable therapeutic and antiseptic properties. These useful properties present in the precursors tend to get enhanced when they are coupled with other moieties to form ligand. Schiff bases are capable of forming coordinate bonds with metal ions through both azomethine group and phenolic group⁶. Further the complexation of the ligand with the metal ion have enormous enhancement of the built in properties. In order to enhance these properties an attempt has been made. In this article we have reported the synthesis, characterization of Co (III), Ni (II), Cu (II) and Zn (II) complexes derived from the acyclic ligand (L) obtained as a Schiff base condensation of synthesized 4,6-diacetyl resorcinol with 4-chloro-2-amino phenol.

EXPERIMENTAL

MATERIALS AND METHODS

All the chemicals used in this study were of Analar grade. Metal salts were purchased from Merck and were used as such as received. Elemental analysis carried out on Elementarvario EL III-Germany. ¹H NMR spectrum was recorded used to Bruker model 4276. FT-IR spectra recorded on Perkin Elmer on KBr pellets in the range of 4000 to 400cm⁻¹. The electronic spectrum recorded on Lambda 35 in the range of 200 to 800 nm using 10⁻³M concentration solution in DMF. The new ligand (L) was synthesis from 4,6-diacetyl resorcinol and 4-chloro-2-amino phenol⁷.

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, 100 μ l 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 BASE LIGAND (L):

To a solution of 4,6-diacetyl resorcinol (9.7g 50 mmol) and 4-chloro-2-aminophenol 14.3g (100 mmol) dissolved separately in absolute ethanol with molar ratio (1:2) were mixed together and the solution mixture was left under reflux for three hours. The reaction mixture was then cooled and yellowish brown precipitate which separated out was collected by filtration and washed several times with a small amount of ethanol. The ligand was recrystallized, in absolute alcohol. The crystals were dried over anhydrous calcium chloride under vacuo. Yield was 75% m.pt 293°C.

Anal. Cal.(C₂₂H₁₆Cl₂N₂O₄): C (59.34), H (4.09), Cl (15.92), N (6.29), O (14.37).

Found: C (59.30), H (4.07), Cl (15.88), N (6.26), Cl (14.34).

IR (KBr Pellets) (C=N) 1664cm⁻¹, (C=C)_{aro} 1510cm⁻¹, (C-O) 1239cm⁻¹, (OH) 3455cm⁻¹, (OH) 3239cm⁻¹.

¹H NMR: 12.81(s, 2H, OH), 9.75 (s, 2H, OH), 8.31, 8.40 (d, 2H, Ph), 6.3-7.0 (m, 6H, Ph), 2.39 (s), 2.25 (s), 6H, CH₃.

The synthesis of the ligand (L) is depicted in **Scheme-1**

SYNTHESIS OF METAL COMPLEXES:

To a refluxing solution of the ligand (L) (10mmol) in 30 mL of the ethanol was added an equivalent mole ratio of the corresponding perchlorate salts M(ClO₄)₆H₂O (M = Co(III), Ni(II), Cu(II) and Zn(II)) dissolved in 20 mL of ethanol. The resulting mixture was refluxed for 6hrs. The colored precipitate which separated due to low solubility was filtered, washed repeatedly with absolute ethanol and diethyl ether and dried over anhydrous CaCl₂ in vacuo.

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 dioxadiaz tetradentate acyclic ligand (L) was synthesized by the reaction of 4,6-diacetyl resorcinol and 4-chloro-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 dioxadiaz 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**.

Infrared spectra of ligand:

The infrared spectra provide valuable information regarding the formation the dioxadiaz tetradentate acyclic ligand (L) and the coordination behavior of the ligand to the metal ions. The infrared spectrum of the ligand (L), show two broadened bands in the region 3239 cm⁻¹ and 3455 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 4-chloro-2-amino phenol moiety. 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 1664cm⁻¹ corresponds to the ν (C=N) stretching of newly formed azomethine groups. The infrared spectrum of the ligand is depicted in **Fig.1**.

The proton NMR spectrum of the ligand exhibits a sharp peak at 12.81 ppm assignable to the phenolic protons of 4,6-diacetyl resorcinol and another single sharp signal at 9.75 ppm assignable to the phenolic protons of 4-chloro-2-aminophenol. A broad band centered around 8.40 and 6.3 ppm has been assigned to the aromatic protons. The quartet centered around 2.39 -2.25 ppm is due to the 6 methyl protons.

¹³C NMR Spectral Study:

The ¹³C NMR spectrum of the compound DARCAP was recorded in DMSO-d₆ solvent and the spectrum is given in Fig.7.

The spectrum shows absorption at δ 165 ppm due to imine carbon. The absorption peaks at δ 110-146 ppm are due to aromatic carbons. The absorption peaks at δ 16-20 are due to aliphatic carbon. The chemical shift due to the carbonyl carbon connecting the nitrogen atom of 4-chloro-2-amino phenol moiety is observed at δ 165 ppm. The ¹³C NMR signals of the compound DARCAP and the assignments of different

carbon atoms are in good agreement with the ^1H NMR data and hence confirm the structure of DARCAP. The ^1H NMR spectrum and the ^{13}C NMR spectrum of the ligand are depicted in **Fig.2** and **Fig.3**, respectively.

Synthesis and Characterization of the metal complexes of the ligand (L):

IR-Spectral Study:

The broad hydroxyl band present in the ligand corresponding to the 4-methyl-2-amino phenol moiety disappears in the spectra of the complexes indicating that the hydroxyl groups are coordinated to metal through the deprotonated form^{9,10}. The other band at 3455-3403 cm^{-1} indicates the presence of -OH group from the resorcinol phenolic group are present in the ligand as well as metal complexes. This observation indicates that the hydroxyl group from the resorcinol moiety does not involve in coordination to the metal ions. The azomethine band around 1664 cm^{-1} present in the free ligand, has been shifted to lower frequencies in the metal complexes, suggested that coordination took place through the C=N moiety. In the spectra of Co (III) complex the broad band at 3423 cm^{-1} together with new band at 627 cm^{-1} indicating the presence of coordinated water¹¹. The infrared show stretching frequencies in the region 550-592 cm^{-1} corresponding to $\nu(\text{M-O})$ vibration and also the presence of bands at 431-533 cm^{-1} assigned to $\nu(\text{M-N})$ band respectively, supporting that the bonding of the ligand to the metal ions is achieved by the phenolic oxygen, and azomethine nitrogen atoms of the ligand¹². IR spectrums of the complexes are depicted in **Fig.4** and **Fig.5** respectively.

Electronic Spectral data:

Electronic absorption spectra of the Schiff base metal complexes were recorded in DMSO at room temperature. The electronic spectra of the Co(III) complex display absorption bands in the region of 426 and 473 nm which may be assigned to $^4\text{T}_{1g}(\text{F}) \rightarrow ^4\text{T}_{1g}(\text{P})$ and $^4\text{T}_{1g}(\text{F}) \rightarrow ^4\text{A}_{2g}(\text{F})$ transition respectively which indicates an Octahedral geometry¹³. The appearance of a band at 484 nm due to $^1\text{A}_{1g} \rightarrow ^1\text{B}_{1g}$ favours a square planar geometry for Ni(II) complex¹⁴. The electronic spectra of the Cu(II) complex display absorption band in the region of 599 nm assigned to $^2\text{B}_{1g} \rightarrow ^2\text{A}_{1g}$ which is in conformity to a square planar geometry. UV spectrums of the complexes are depicted in **Fig.6** and **Fig.7** respectively.

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 nature¹⁵. 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 2-6 $\text{ohm}^{-1}\text{cm}^2\text{mol}^{-1}$

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 $\text{d}_{x^2-y^2}$ ground state occupied with one unpaired electron¹⁶. 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

Table-1.

Antimicrobial activity:

An antimicrobial activity of the ligand and a series of its metal complexes [Cu (II), Ni (II), Co(III) and Zn(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, where it has highest activity was observed on Ni and Co complexes against *Bacillus cereus*. High zones of inhibition were observed on Co and Zn complexes against *Klebsiella pneumoniae*. The ligand and Co complex has highest activity against *Serratia marcescens*. The results showed in table-4. In present study antimicrobial activity results were observed against tested fungal pathogens. The highest zones of inhibition were observed on Co and Zn complex against *Cryptococcus neoformans* and *Candida albicans*. Moderated zone was observed on Cu complex against tested fungal pathogens. Lowest activity observed on ligand against tested fungi. The result was showed in table-5. 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 cells¹⁷. An antimicrobial activity images are depicted in **Fig.8**.

Conclusion:

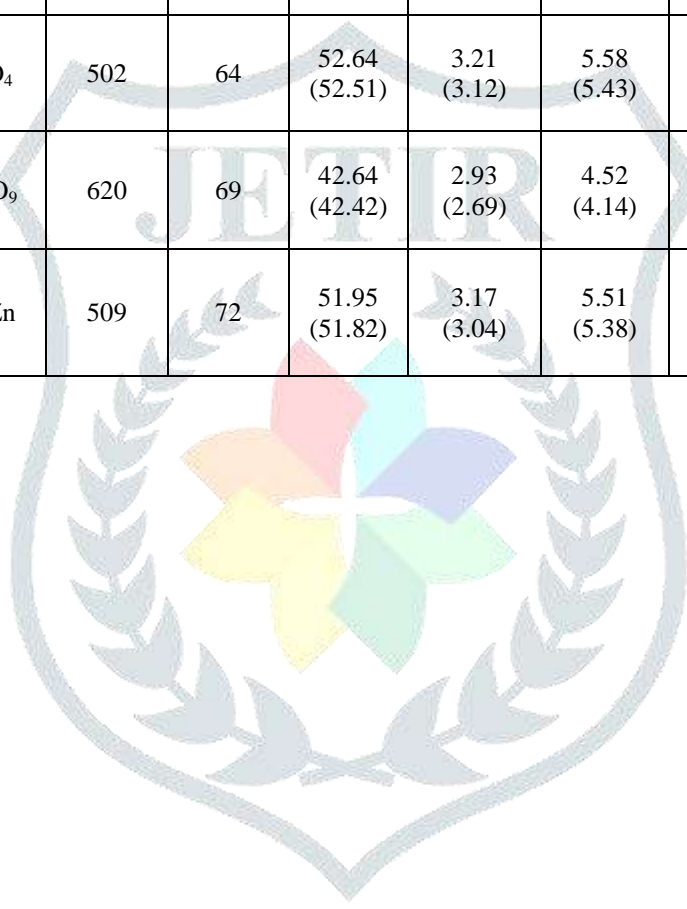
The design and synthesis of Schiff base ligand obtained from the reaction of 4-chloro-2-amino phenol and 4,6-diacetyl resorcinol is described. The synthesized compound and its complexes of Co(III), Ni(II), Cu(II) and Zn(II) metal ions were characterized. The structural data established on the basis of ^1H ^{13}C NMR, elemental analysis (C,H,N,O) infrared, ultra violet and magnetic susceptibility analysis of complexes were recorded and discussed. In the light of the above discussion the ligand behaves as a dianionic tetradentate ligand with N₂O₂ donor sequence coordinating through the nitrogen of the azomethine and oxygen of phenolic group of amino phenol. All the complexes have a square planar complexes except Co(III) complex are proposed. The complex screen for antibacterial and antifungal activity and result show moderate in comparison with standard drugs.

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Tables -1. Elemental analysis, colour, molar conductance electronic spectra and magnetic susceptibility of the ligand and their complexes

Compound	Mol. Formula	Mol. Weight	Yield %	Calculated / (Founded)				Colour	μ eff (BM)	Molar cond.
				C	H	N	M			
L	$C_{22}H_{18}Cl_2N_2O_4$	445	70	59.34 (59.30)	4.09 (4.07)	6.29 (6.26)	-	Yellowish brown	-	-
[Cu (L)]	$C_{22}H_{16}Cl_2CuN_2O_4$	507	68	52.14 (52.10)	3.18 (3.15)	5.53 (5.47)	12.54 (12.41)	Greenish Brown	1.90	2.5
[Ni (L)]	$C_{22}H_{16}Cl_2N_2NiO_4$	502	64	52.64 (52.51)	3.21 (3.12)	5.58 (5.43)	11.69 (11.54)	Pale Brown	Dia	4.3
[Co (L)ClO ₄ (H ₂ O)]	$C_{22}H_{18}Cl_3CoN_2O_9$	620	69	42.64 (42.42)	2.93 (2.69)	4.52 (4.14)	9.51 (9.21)	Violet	Dia	3.2
[Zn (L)]	$C_{22}H_{16}Cl_2N_2O_4Zn$	509	72	51.95 (51.82)	3.17 (3.04)	5.51 (5.38)	12.86 (12.71)	Yellow	Dia	5.6



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

Compound	ν OH (cm ⁻¹)	ν (C=N) (cm ⁻¹)	ν (M-O) (cm ⁻¹)	ν (M-N) (cm ⁻¹)
L	3455, 3239	1664	-	-
[Cu (L)]	3403	1652	570	533
[Ni (L)]	3458	1624	579	494
[Co (L)ClO ₄ (H ₂ O)]	3423	1635	592	518
[Zn (L)]	3457	1634	550	431

Tables -3. Electronic spectral data of the compounds

Compound	Solvent	Absorption (nm)	Band assignment	Geometry
[Cu (L)]	DMF	254 319 599	INCT INCT ² B _{1g} → ² A _{1g}	Square planar
[Ni (L)]	DMF	256 327 484	INCT INCT ¹ A _{1g} → ¹ B _{1g}	Square planar
[Co (L)ClO ₄ (H ₂ O)]	DMF	259 330 426 473	INCT INCT ⁴ T _{1g} (F) → ⁴ T _{1g} (P) ⁴ T _{1g} (F) → ⁴ A _{2g} (F)	Octahedral
[Zn (L)]	DMF	265 323	-	Square planar

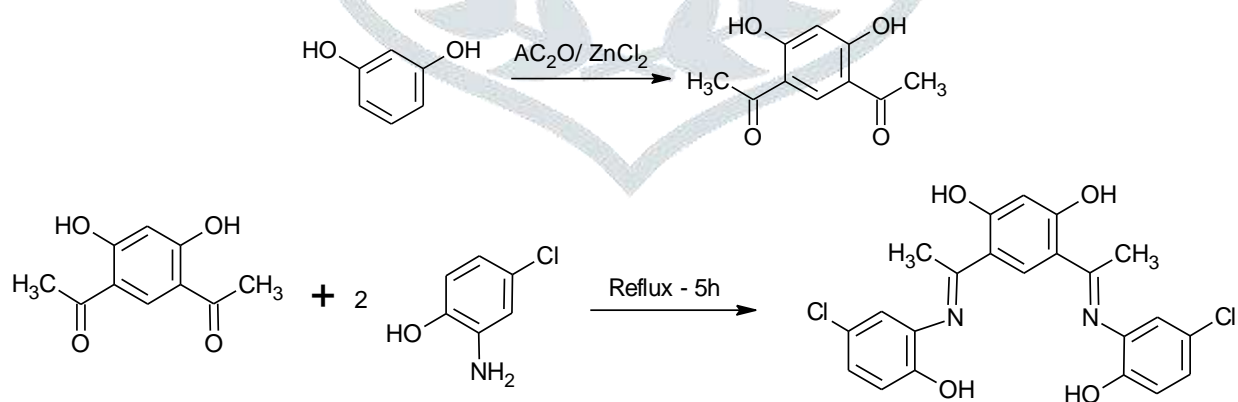
Tables -4. Antibacterial activities of ligand and its metal complexes

Compound	<i>Bacillus cereus</i>	<i>Serratia marcescens</i>	<i>Klebsiella pneumoniae</i>
Ligand	-	8.3 ± 0.5	8.6 ± 1.5
[Cu (L)]	-	9.6 ± 1.5	9.3 ± 0.5
[Ni (L)]	8.3 ± 0.5	-	9.3 ± 0.5
[Co (L)ClO ₄ (H ₂ O)]	7.3 ± 0.5	-	10.3 ± 0.5
[Zn (L)]	-	9 ± 1	10.3 ± 0.5
Chloramphenicol (30mcg/disc)	18.6 ± 0.5	28 ± 0	12.3 ± 0.5

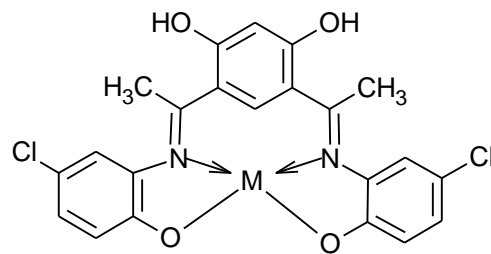
Tables -5. Antifungal activities of ligand and its metal complexes

Compound	<i>Candida albicans</i>	<i>Cryptococcus neoformans</i>
Ligand	7±0	7±1
[Cu (L)]	8±2	9.3± 2.0
[Ni (L)]	7±1	7±0
[Co (L)ClO ₄ (H ₂ O)]	9 ±2	12 ±3.4
[Zn (L)]	8± 2	12± 2
Amphotericin (100mcg/disc)	12.6 ±1.5	13.0± 1.0

FIGURES:



Scheme -1: Formation of Schiff base



Scheme - 2: Formula of the metal complexes M= Ni(II), Cu(II) and Zn (II)

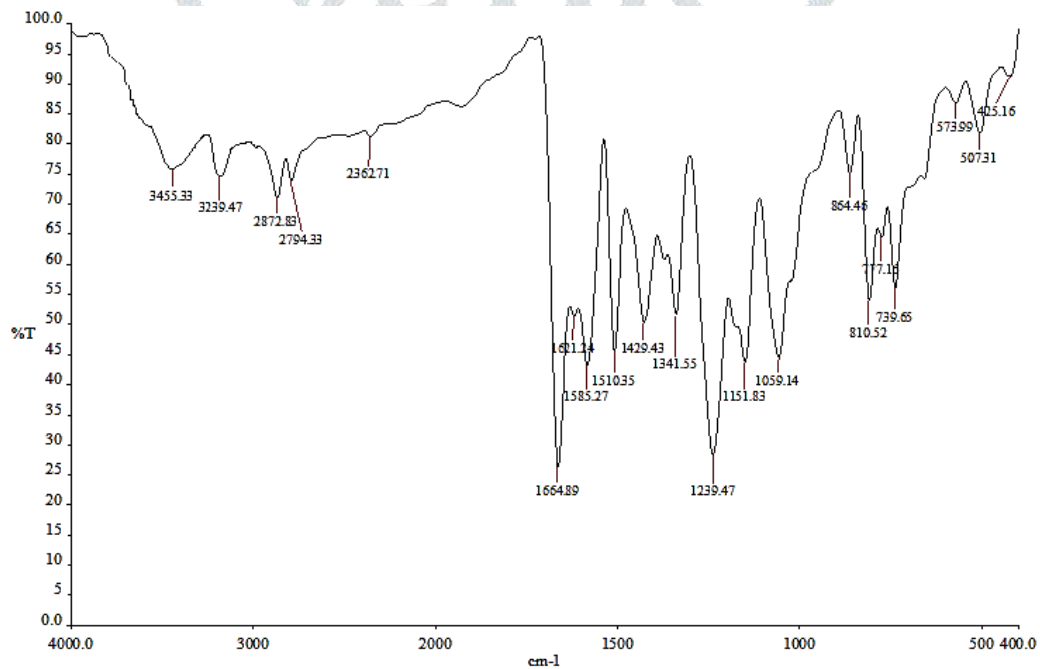
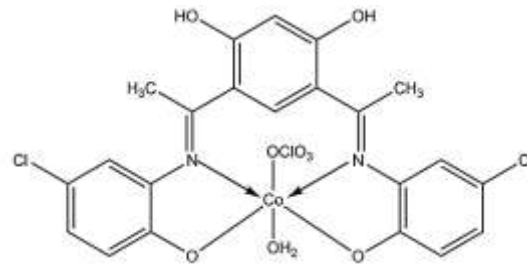


Fig-1: Infrared spectrum of Ligand (L) (DARCAP)

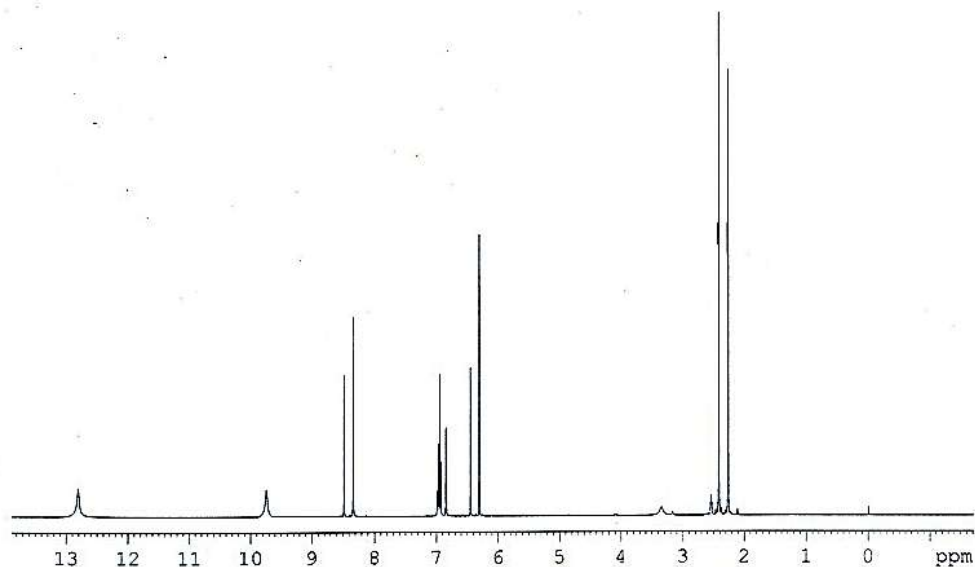


Fig-2: ¹H Spectrum of Ligand (DARCAP)

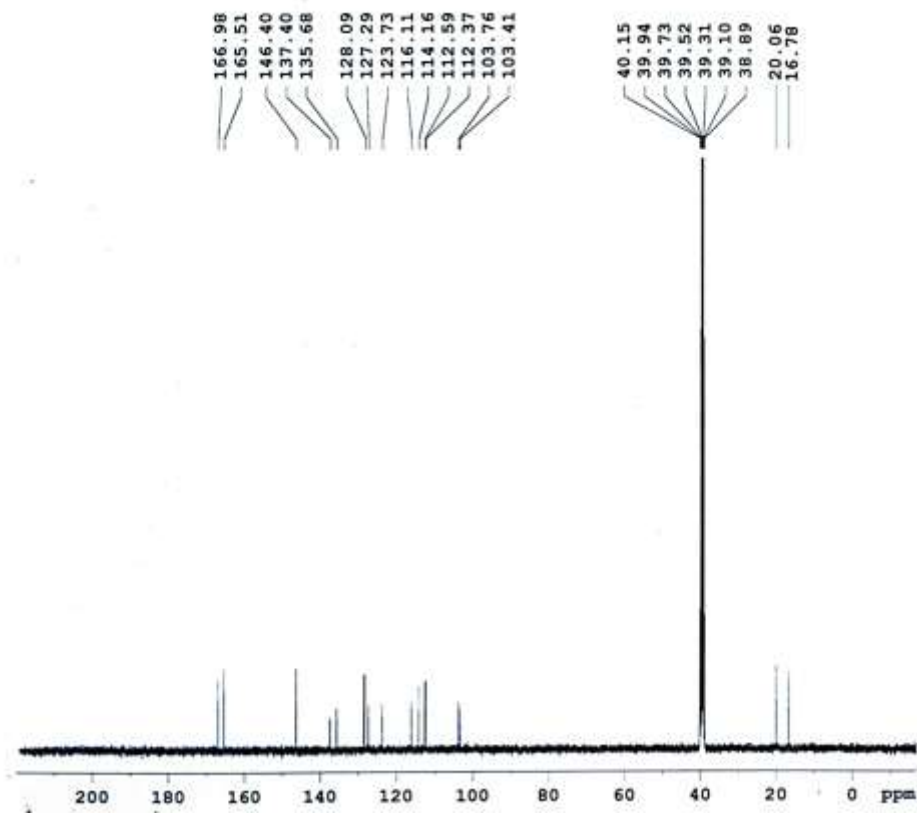


Fig - 3: ¹³C Spectrum of Ligand (L) (DARCAP)

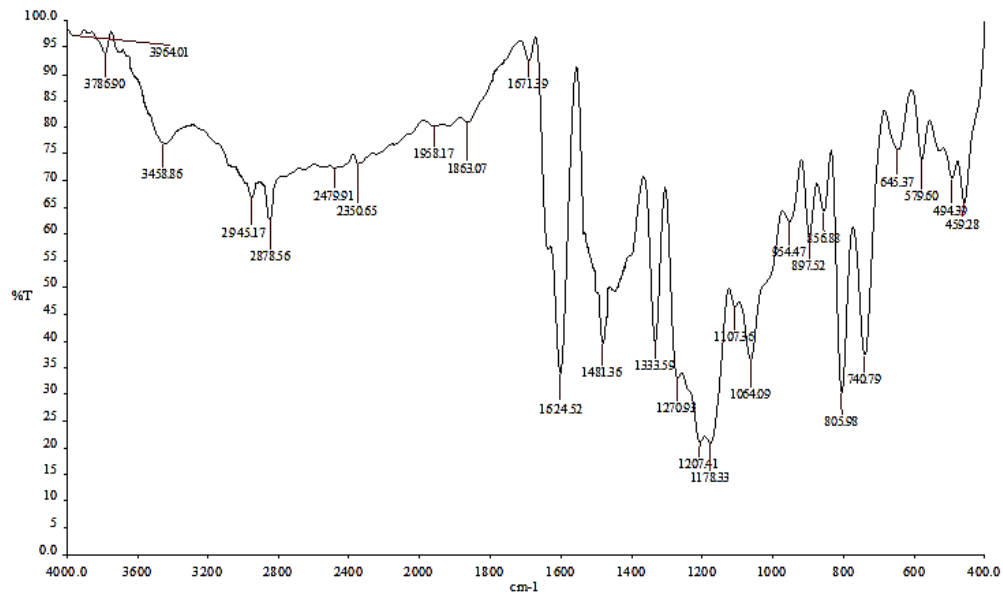


Fig -4: Infrared spectrum of complex [Ni (DARCAP)]

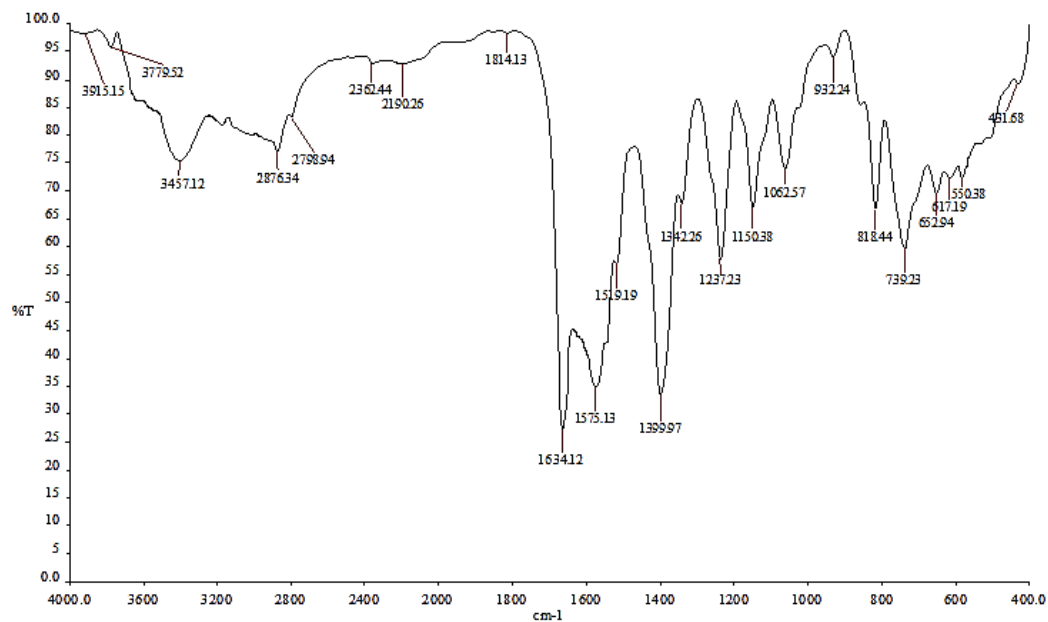


Fig -5: Infrared spectrum of complex [Zn (DARCAP)]

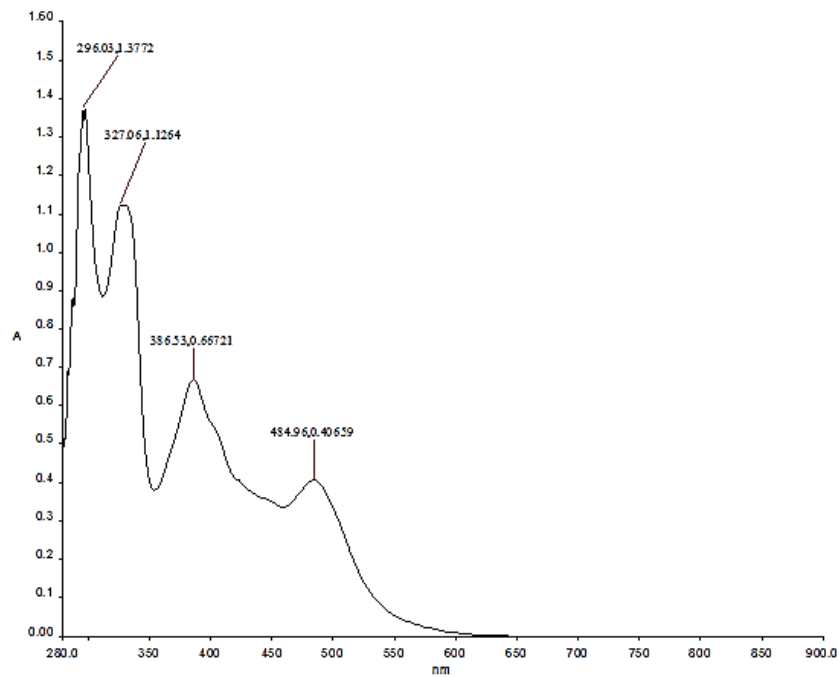


Fig - 6: UV- spectrum of complex [Ni (L) (DARCAP)]

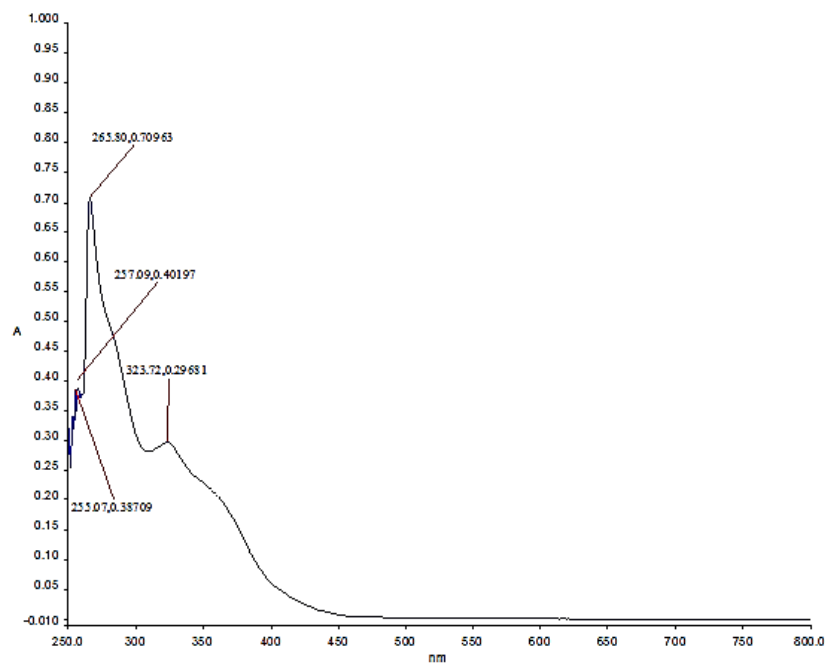


Fig - 7: UV- spectrum of complex [Zn (L) (DARCAP)]

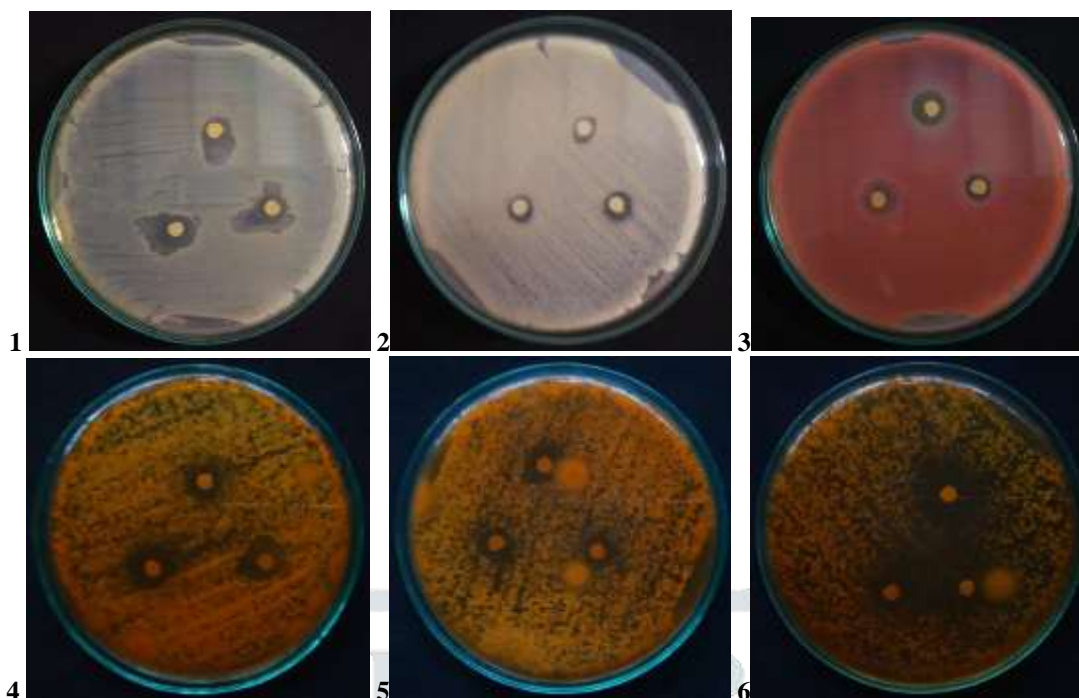


Fig-8: Zones of inhibition on ligand and complexes antimicrobial activity against selected human pathogens

1. zone of inhibition on [Zn (L)] complex against *Klebsiella pneumoniae*
2. zone of inhibition on [Co (L)ClO₄(H₂O)] complex against *Bacillus cereus*
3. zone of inhibition on [Cu (L)] complex against *Serratia marcescens*
4. zone of inhibition on [Co (L)ClO₄(H₂O)] complex against *Candida albicans*
5. zone of inhibition on [Cu (L)] complex against *Candida albicans*
6. zone of inhibition on [Zn (L)] complex against *Cryptococcus neoformans*

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