

Synthesis, Characterization and Biological Activity of a Schiff Base Derived from 3-Ethoxysalicylaldehyde and Phenylhydrazine and its Metal Complexes

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Abstract

A new novel Schiff base of 2-Ethoxy-6-(phenyl-hydrazone-methyl)-phenol has been synthesized from 3-ethoxysalicylaldehyde and phenylhydrazine. Transition metal complexes of the Schiff base were prepared from metal chloride salts like Co(II), Ni(II), Cu(II) and Zn(II) in alcoholic medium. The chemical structure of free ligand and metal complexes were confirmed using the physical and spectral techniques like, FTIR, UV, ¹H NMR, TGA, magnetic moment, conductance. On the basis of spectral studies the geometry of the complexes were proposed. The FTIR spectrum shows that bidentate coordination of metal ions with ligand where O,N are the electron donating sites of azomethine group. The free Schiff base ligand and its metal complexes have been tested for their antibacterial and antifungal potential by using well diffusion method and the results were discussed.

Key Words: Schiff base, 3-ethoxysalicylaldehyde, phenylhydrazine, metal complexes, antibacterial and antifungal activities.

1. Introduction

Metal Complexes of Schiff bases have played a fundamental role in the development of coordination chemistry [1-4]. This field has a rapid development with wide variety of possible structures. The formation of carbon-nitrogen double bond plays important role in organic synthesis. This can be prepared by the reaction of aldehydes and amine which leads to the formation of Schiff base [5-7]. The transition metal complexes of Schiff bases are one of the most adaptable with thoroughly studied system and also having more applications in clinical, analytical and industrial [8-10]. The biological screening of free ligand and its metal complexes against different bacteria and fungi are reported [11]. The present work reports the synthesis, characterization and antimicrobial potential of metal complexes of 2-Ethoxy-6-(phenyl-hydrazone-methyl)-phenol (ESPH).

2. Experimental

2.1 Materials and Methods

All chemicals like 3-ethoxysalicylaldehyde, phenylhydrazine, and suitable metal salts, solvents were used in analytical grade (AR) without further purification. The FTIR spectra of ligand and its metal complexes were recorded in KBr pellets with Perkin Elmer FT-IR Spectrometer. The Electronic Spectra were recorded on Perkin Elmer Lambda 365 Spectrometer and DMSO was used as solvent. The ¹H NMR Spectra were recorded on Bruker 400 MHz Spectrometer (DMSO-d₆). Elemental analysis, Magnetic Susceptibilities and Conductivity measurements were used with suitable instruments.

2.2 Synthesis of Schiff base ligand (ESPH)

The Schiff base ligand was prepared by the condensation of 3-ethoxysalicylaldehyde and phenyl hydrazine with equal molar ratio and ethanol was used as solvent. The mixture was refluxed for 3 hours. When the resulting product was obtained it was filtered and dried over anhydrous CaCl_2 in a desiccator. The yield of the compound was found to be 82%.

2.3 Synthesis of Metal Complexes

A mixture of ligand (ESPH) and corresponding metal chlorides with (1:1) ratio in a hot ethanolic solution. A reaction mixture was refluxed about 6 hours. The obtained products were collected, filtered and washed with ethanol several times to remove any excess of the ligand. Finally the complexes were washed with diethyl ether and dried in a desiccator.

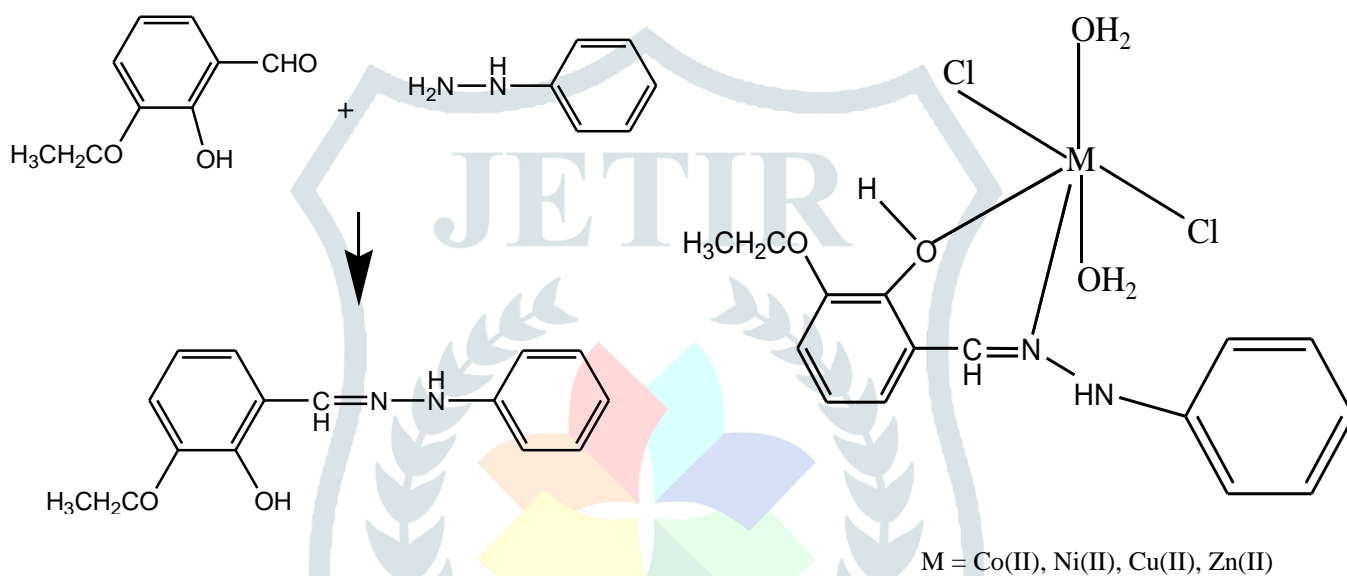


Fig.1 Proposed structure of ligand and metal complexes

3. Results and Discussion

3.1 FTIR Spectral Study

The FTIR spectral data Table[1] indicates the coordination sites of the aldimine moiety. The bands at 1615 cm^{-1} obtained for free ligand was assigned at $\nu(\text{-C=N})$ vibration. The shifting of this group to lower frequency as compared with free ligand suggesting that a coordination of metal ions through nitrogen atom of azomethine group in all metal complexes^[12]. The new bands appeared at $500\text{-}550$ and $600\text{-}650\text{ cm}^{-1}$ in the complexes is attributed to $\nu(\text{M-N})$ and $\nu(\text{M-O})$ respectively which not present in the free ligand. The broad band at 3416 cm^{-1} which attributed to phenol OH moiety for free Schiff base ligand and it was compared with metal complexes, the frequency values decreases due to the coordination on complexation.

Table 1 FTIR Spectral Data of Ligand and Metal Complexes

Compound	ν (O-H)	ν (N-H)	ν (C=N)	ν (M-N)	ν (M-O)
ESPH	3416	3303	1615	-	-
ESPH-CoCl ₂	3396	3302	1607	505	646
ESPH-NiCl ₂	3376	3303	1604	504	645
ESPH-CuCl ₂	3386	3303	1605	507	653
ESPH-ZnCl ₂	3375	3302	1603	504	645

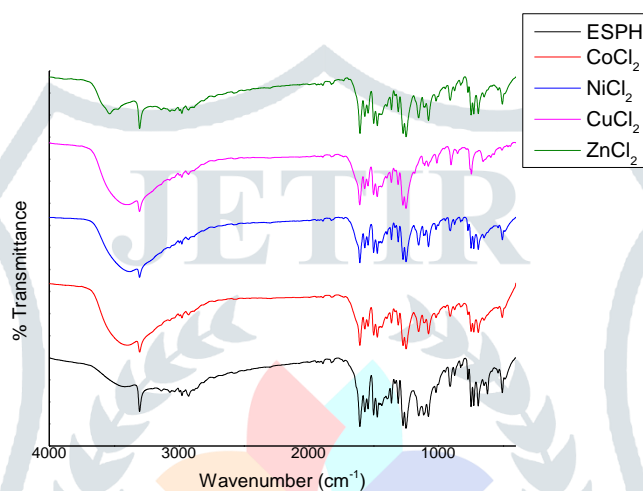


Fig.2 FTIR Correlation Spectrum of Ligand and Metal Complexes

3.2 Electronic Spectral Study

The electronic spectrum of Co (II) complex shows a band at 474 nm is attributed to $^4T_{1g} \rightarrow ^4A_{2g}$ (F) transition. This transition suggests octahedral geometry of the complex. The Ni (II) complex exhibits a band at 434 nm which is assigned to $^3A_{2g} \rightarrow ^3T_{1g}$ (F) transition. This transition confirms the octahedral geometry. The Cu (II) a complex display at 431 nm is due to $^2E_g \rightarrow ^2T_{2g}$ transition also suggests octahedral geometry of the complex.

Table.2 Electronic Spectral Data of Metal Complexes

Compound	UV-Visible (nm)	UV-Visible (cm ⁻¹)	Geometry
Co(II) complex	474	21,097	Octahedral
Ni(II) complex	434	23,041	Octahedral
Cu(II) complex	431	23,201	Octahedral

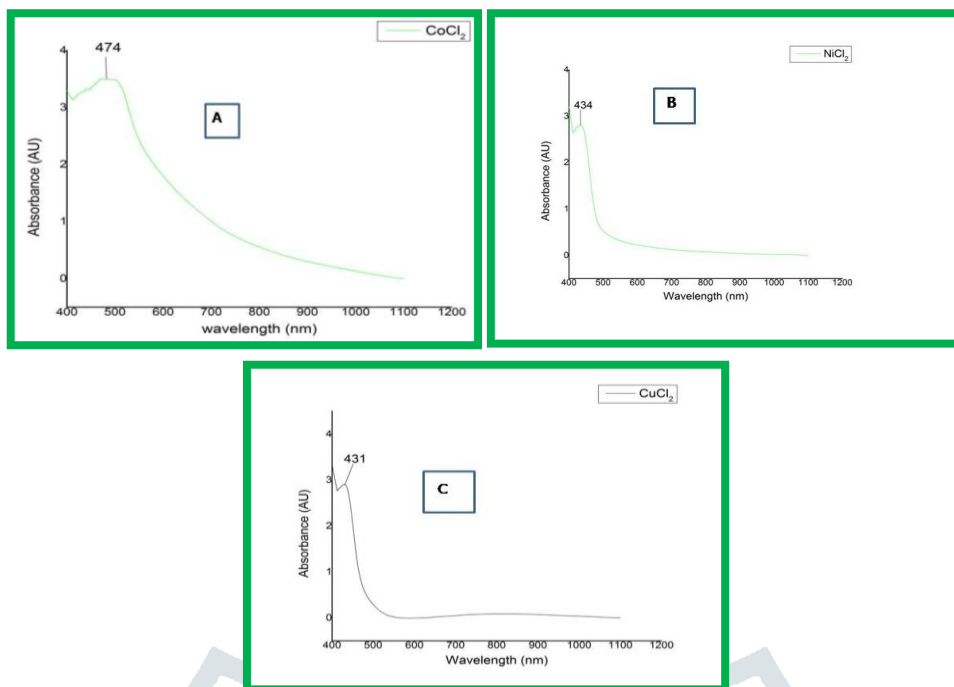


Fig.3 UV-Visible spectrum of metal complexes of [A] ESPH-CoCl₂, [B] ESPH-NiCl₂, [C] ESPH-CuCl₂

3.3 ¹H NMR Spectra

The ¹H NMR spectra of ligand was recorded in DMSO-d₆ support the proposed structure of the free ligand. The signals appeared at 8.14 ppm due to the azomethine proton. The signals at 10.21 and 10.42 ppm attributed to the N-H of hydrazine and O-H proton of phenolic hydroxyl group^[13]. The aromatic protons appear between 6.7-7.2 ppm respectively. The peak at 1.3 ppm which is a triplet, is assigned to -CH₃ group of ethoxy substituent on the benzene ring while peak at 4.0 ppm which is quartet, is attributed to -CH₂ protons of the ethoxy substituent.

Table.3 ¹H NMR Spectral Data

-OH (δ, ppm)	-NH (δ, ppm)	Aromatic Protons (δ, ppm)	-HC=N (δ, ppm)	-CH ₃ (δ, ppm)	-CH ₂ (δ, ppm)
10.42	10.21	6.7-7.2	8.14	1.3	4.0

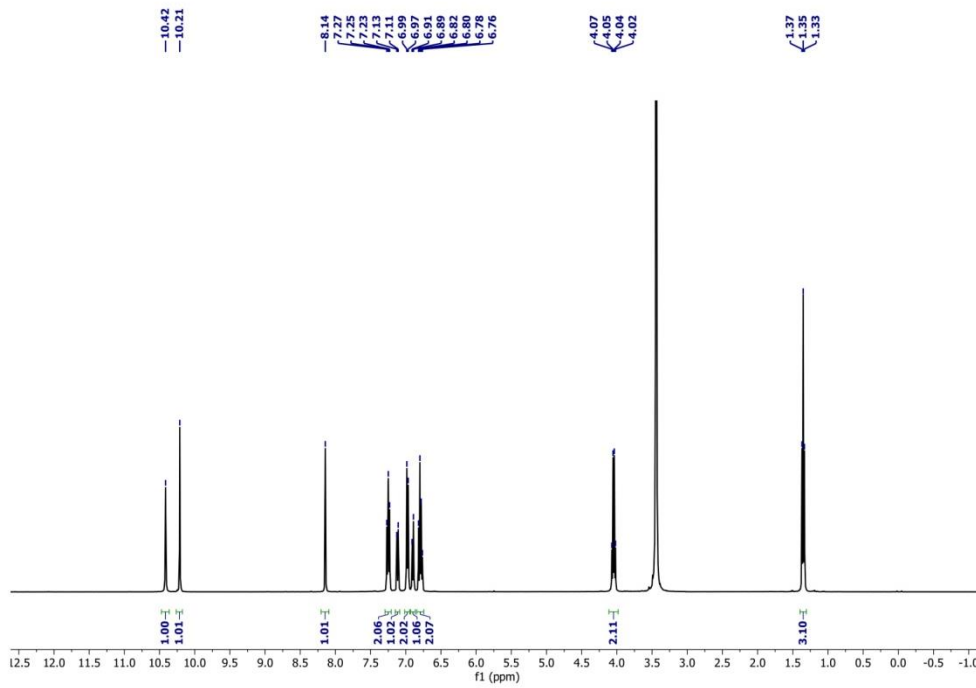
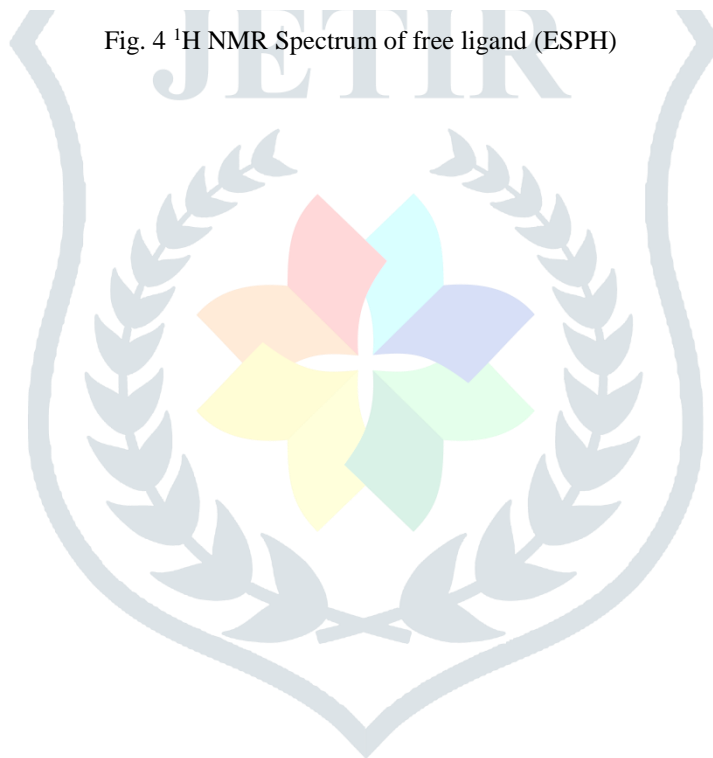


Fig. 4 ¹H NMR Spectrum of free ligand (ESPH)



3.4 Thermal Study

The thermal stability of Co(II) complex of the Schiff base ligand was studied in the temperature ranges from 0°C - 800°C. The TGA/DTA spectrum of Co(II) complex were shown in Fig 5. The coordinated water molecule eliminates up to 150°C. The weight loss between 200-550°C indicates the decomposition of organic ligand. Above 600°C the decomposition takes place and to form the final residue of metal oxide. And also it was further supported for the elimination of organic molecule and appearance of endothermic peak in DTA.

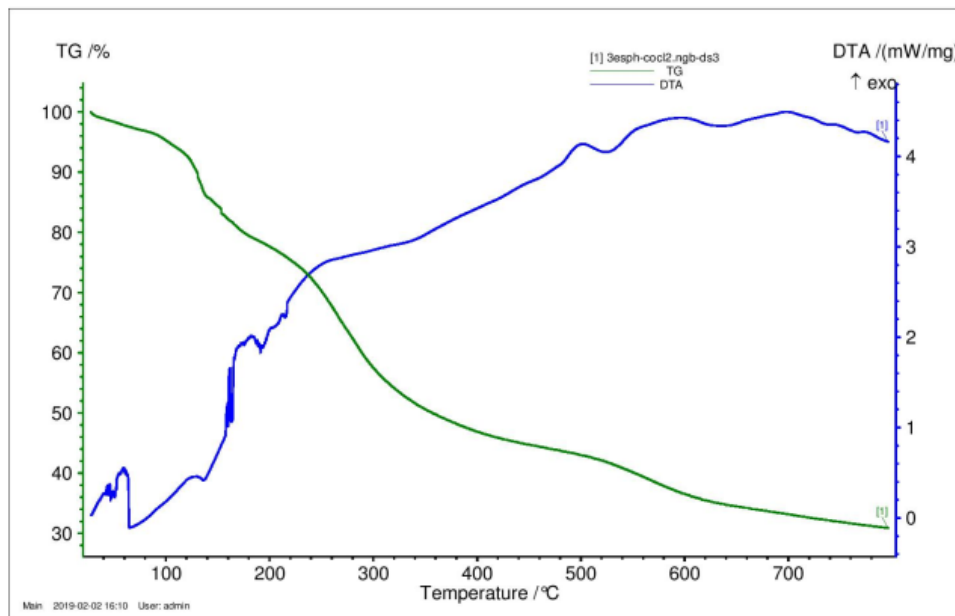


Fig. 5 Thermal Studies of ESPH.CoCl₂.2H₂O

Table. 4 Elemental Analysis, Colour, Molar Conductance, and Magnetic Susceptibility of the Ligand and Metal Complex

Compound	Mol. Formula	Mol. Weight	Yield %	Melting Point	Elemental analysis Calculated / (Founded)					Colour	μ eff (BM)	Molar Cond.
					C	H	N	M	Cl			
ESPH	C ₁₅ H ₁₆ N ₂ O ₂	256	82%	186°C	70.29 (69.71)	6.29 (5.79)	10.93 (9.84)	-	-	Red	-	-
ESPH-CoCl ₂	C ₁₅ H ₂₀ CoN ₂ O ₄	421	76%	>300	42.67 (41.88)	4.78 (4.02)	6.64 (5.90)	13.96 (12.07)	16.80 (15.94)	Light orange	4.62	41.13
ESPH-NiCl ₂	C ₁₅ H ₂₀ NiN ₂ O ₄	421	65%	>300	42.70 (41.94)	4.78 (4.18)	6.64 (5.78)	13.91 (12.11)	16.81 (15.70)	Light green	3.23	35.76
ESPH-CuCl ₂	C ₁₅ H ₂₀ CuN ₂ O ₄	425	62%	>300	42.21 (41.76)	4.72 (3.95)	6.56 (5.78)	14.89 (13.67)	16.61 (15.82)	Dark green	1.56	38.61
ESPH-ZnCl ₂	C ₁₅ H ₂₀ ZnN ₂ O ₄	426	74%	>300	42.03 (41.83)	4.70 (4.15)	6.54 (5.83)	15.26 (14.67)	16.54 (15.14)	Yellow	Dia	29.86

4. Antimicrobial Activity

4.1 Antibacterial Activity

The results of antibacterial activity of the free ligand and its subsequent metal complexes at various concentrations (100 and 200 µg/mL) for both gram positive (*S.coccus*) and gram negative (*E.coli*) bacterial species using well diffusion method is given in Table 5. It was observed that the inhibitive power of the free ligand and its metal complexes against the bacterial species was effective at higher concentration (200µg/mL). The free ligand inhibits *E.coli* (3.6 cm) and *S.coccus*(7.2 cm) respectively. The metal complexes such as CoCl₂, NiCl₂, CuCl₂ and ZnCl₂ were found to be efficient against *E.coli* (13.2, 11.5, 9.0 and 6.8 cm) and *S.coccus* (12.2, 9.0, 17.5 and 7.3) respectively.

Table.5 Antibacterial Activity of Ligand and Metal Complexes

Compound	Zone length of Inhibition (mm)					
	<i>E-Coli</i>			<i>Strep. Coccus</i>		
	100 µg	200 µg	Positive control	100 µg	200 µg	Positive control
ESPH	2.0	3.6	5.8	5.8	7.2	7.5
ESPH-CoCl ₂	6.5	13.2	14	11.5	12.2	14
ESPH-NiCl ₂	11.0	11.5	19	8.0	9	5
ESPH-CuCl ₂	8.0	9.0	19	15	17.5	18
ESPH-ZnCl ₂	6.5	6.8	19	7.0	7.3	20

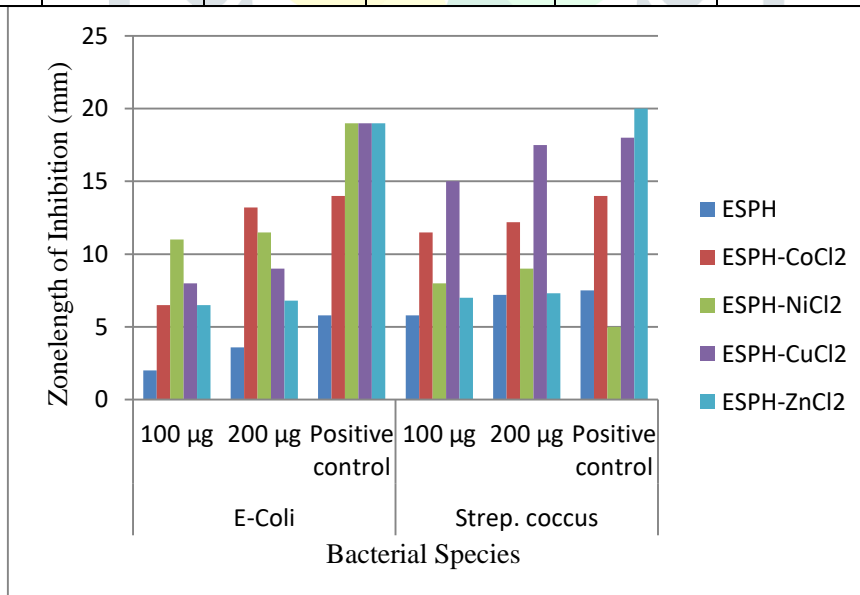


Fig. 6 Antibacterial Activity of Ligand and Metal Complex

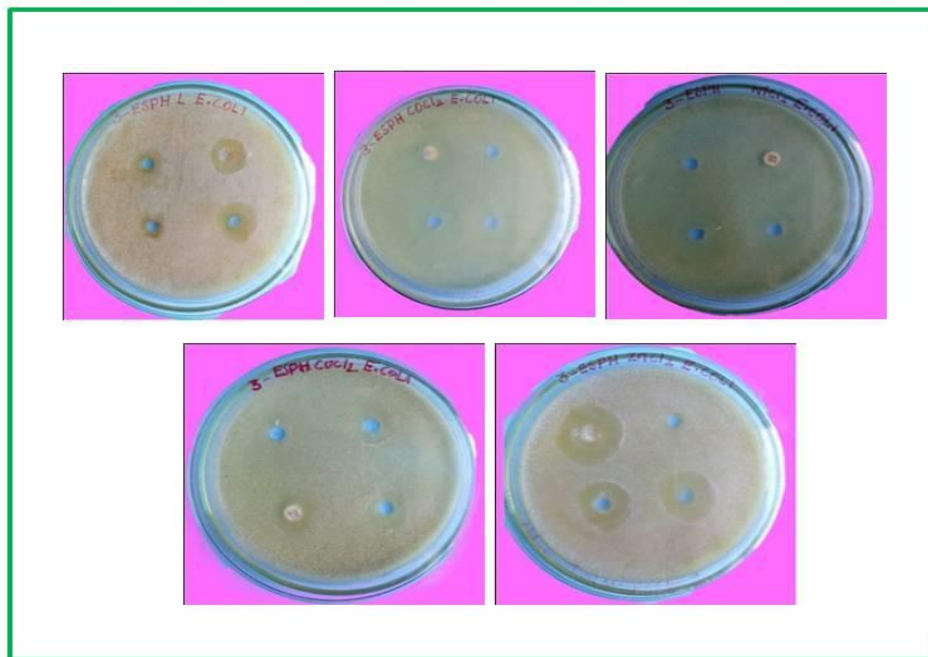


Fig.7 Antibacterial activity of E-Coli

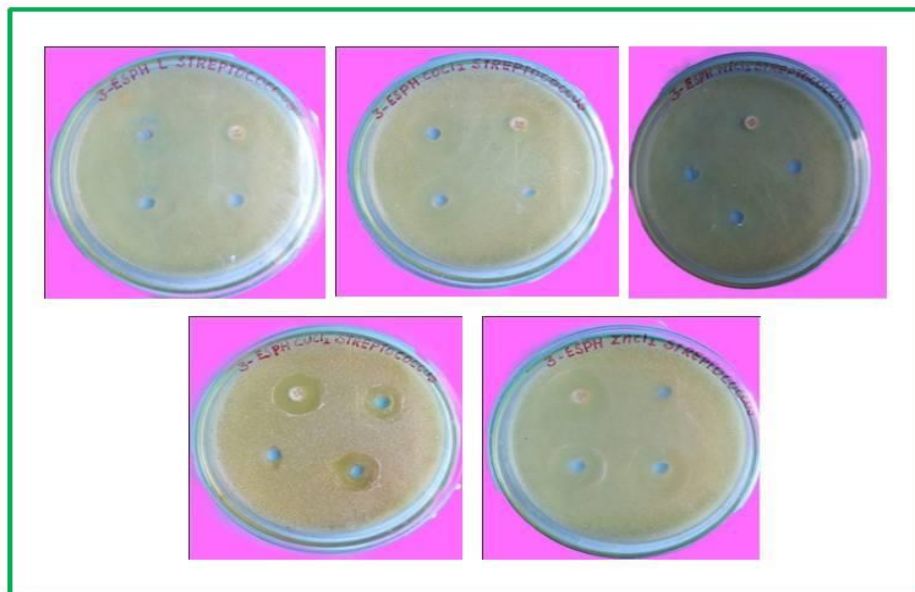


Fig.8 Antibacterial activity of Strep.coccus

4.2 Antifungal Activity

The results of antifungal activity of the free ligand and its subsequent metal complexes at various concentrations (100 and 200 $\mu\text{g/mL}$) for the two fungal species were examined using well diffusion method is tabulated in Table (6). It was observed that the inhibitive ability of the free ligand and its metal complexes against the fungal species was effective at higher concentration (200 $\mu\text{g/mL}$). The free ligand inhibits *Cryptococcus* (7.2 cm) and *Aspergillus* (8.0 cm) respectively. The metal complexes such as CoCl_2 , NiCl_2 , CuCl_2 and ZnCl_2 were found to be efficient against *Cryptococcus* (11.5, 9.0, 9.0 and 17.0 cm) and *Aspergillus* (10.0, 8.5, 15.0 and 4.5) respectively.

Table. 6 Antifungal Activity of Ligand and Metal Complexes

Compound	Zone length of Inhibition (mm)					
	<i>Cryptococcus</i>			<i>Aspergillus</i>		
	100 μg	200 μg	Positive control	100 μg	200 μg	Positive control
ESPH	6.8	7.2	20.0	7	8	9.6
ESPH- CoCl_2	10.5	11.1	12	13	22	15
ESPH- NiCl_2	18	19	22	8	15.1	14.3
ESPH- CuCl_2	2.0	3.0	4.0	9	10	11
ESPH- ZnCl_2	17	19	20	18	21	22

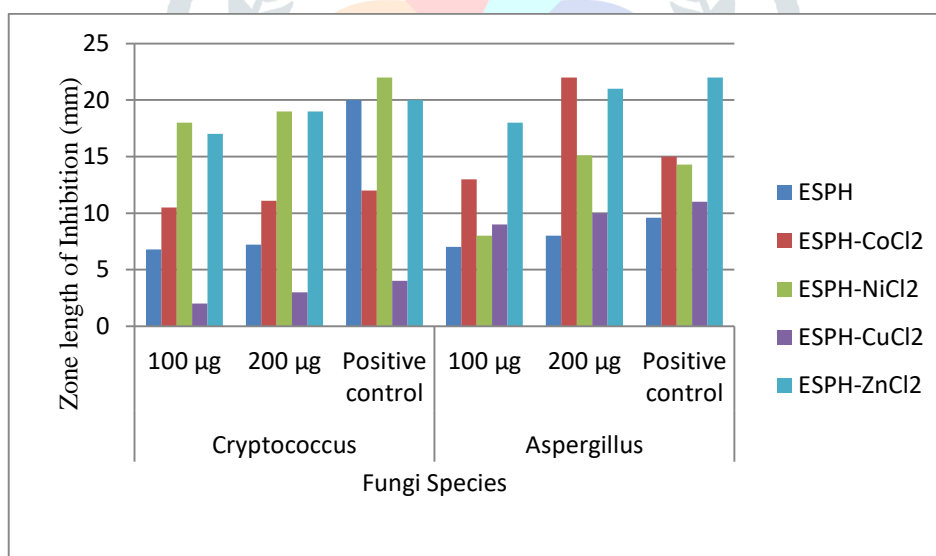


Fig. 9 Antifungal Activity of Ligand and Metal Complexes

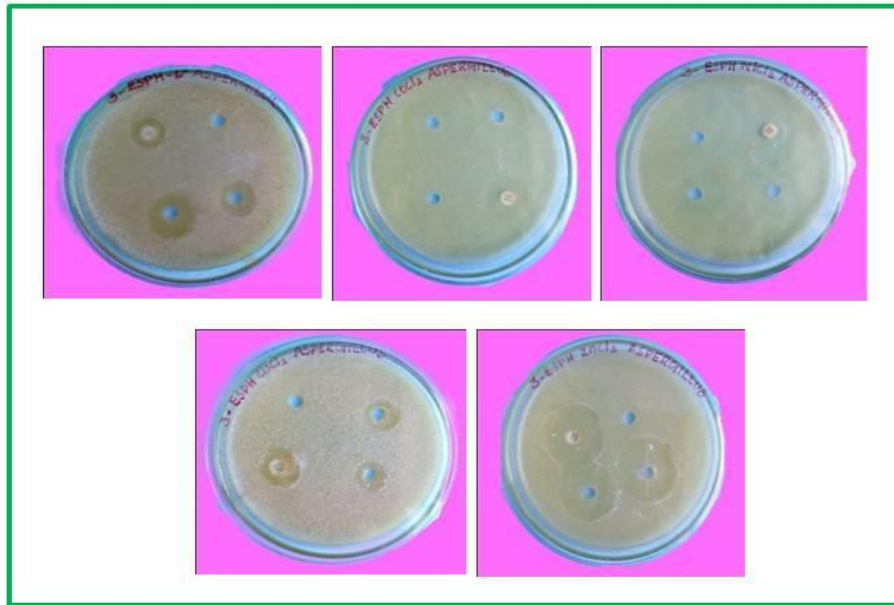


Fig. 10 Antifungal activity of Aspergillus

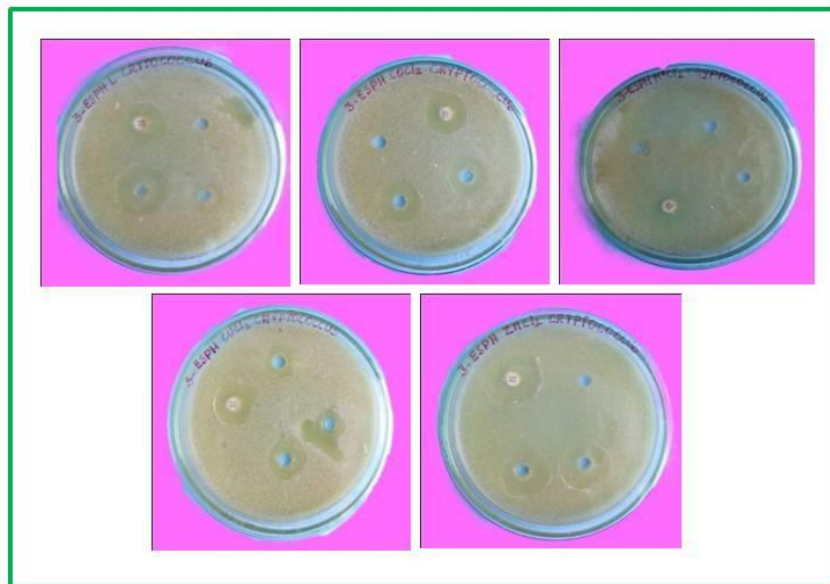


Fig. 11 Antifungal activity of Cryptococcus

5. Conclusion

Thus it is concluded that the prepared, characterized and biological study of Schiff base ligand and their Co(II), Ni(II), Cu(II) and Zn(II) metal complexes. The proposed structure of ligand and metal complexes were confirmed by using FTIR, UV-Vis, ¹H NMR, TGA and elemental analysis. In microbiological studies the metal complexes gives good results than free Schiff base ligand.

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