Synthesis, characterization and biological evaluation of new mixed ligand complex (derived from Schiff base)

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Abstract

Mixed ligand complex included Schiff base derivative cobalt Co(II)complex(M(L1)(L2)) where L1 is the Schiff base derived from condensation between Vanillin (3-hydroxy-4-methoxy benzaldehyde) and 4-Amino antipyrene(4-amino-1,5-dimethyl-2-phenyl-1-H-pyrazol-2-H-one(VAAP) synthesized and characterized using conventional and spectral techniques.(VAAP) as a primary ligand (L1)and the secondary ligand an amino acid L-tryptophan (L2)is added through refluxation to form mixed ligand with Co(II) complex.

The mixed ligand complex Co(VAAPT) was characterized using 1HNMR, C13NMR, UV-visible, FTIR, SEM techniques. The structural elucidation assessed with respect to the metal complex obtained was square planar based on the analytical studies. The stable antibacterial and antifungal assay of mixed ligand was evaluated.

Keywords: Schiff base, Mixed Ligand, Tryptophan, anti-bacterial, anti-fungal assay.

Introduction

Mixed ligands of Schiff base are of captivating grade of ligands which have been subject of intensive exploration. Co-ordination compounds of various Schiff bases have found enormous applications in exemplified fields[1]. Mixed ligand complexes have been found to act as active catalyst in reactions of industrial importance i.e. hydrogenation, hydrolysis of olefins and oxidation. These complexes are known to be of great importance in environmental and biological applications and finds significant pronounced biological activities. Their myriad efficacy has contributed greatly to their popularity and the study of many biological systems. Schiff bases find exceptional pronounced biological activities. The myriad potency has contributed greatly to their popularity and the study of numerous biological enforcement[3].

Literature survey revealed that Schiff bases derived from vanillin have exhibited significant fungicidal, anti-clastagen, anti-cancer, anti-bacterial, anti-viral in pharmaceutical fields and also as corrosion inhibitors, catalyst in industries. Cobalt is an essential bio-element and its complexes have been widely studied for their broad spectrum of biological activities[4]. Azo dyes of 4-Amino antipyrene are familiar as polydentate ligands co-coordinating in neutral and ionic forms. 4-amino antipyrene plays a vital role in copious domains[9]. L-tryptophan is an unusual amino acid because of its complexity of its metabolism.

The mixed ligand derived from Cu(II) o-vanillin-l-tryptophan and heterocyclic nitrogen bases was taken as reference.[15] The metal was replaced with cobalt Co(II) and primary amine added was 1,5-dimethyl-2-phenyl-1-H-Pyrazol-3(2H)-one and secondary ligand was tryptophan as in literature. Therefore the present study is devoted on development of mixed ligand complex 4-N-(4-hydroxy-3-methoxy-benzalidine-1,5-dimethyl-2-phenyl-1-H-pyrazol-3(2H)one(VAAP) with metal cobalt and L-tryptophan an amino acid as a secondary ligand. The *in vitro* antibacterial and antifungal assay of derived complex was evaluated.

Material and Methods

All chemicals were obtained from commercial sources and were used without purification. Elemental analysis (EA) of C,H,N,O was performed using EDAX. IR spectra were recorded on Bruker -FT-IR spectrometer on KBr pellet in the wave number range of 4000-400 cm^{-1}. Electronic spectral studies were conducted on a UV-Visible 1800 series, with wavelength of 200-400 nm. NMR analysis was recorded on a 800MHZ-NMR spectrometer with TMS and DMSO solvent. SEM images are acquired from Scanning electron microscope. FLEX- SEM 1000 instrument.

Experimental procedure for synthesis of primary ligand [VAAP]: 4-Hydroxy-3-methoxy benzaldehyde (0.05 moles) was taken in 50 ml of methanol. The 4-amino-1,5-dimethyl-2-phenyl-1-H-pyrazol-3(2H)-one (0.05 moles) was dissolved in 50 ml of distilled water. These two solutions were mixed in a clean 250 ml round bottom flask and stirred with a magnetic stirrer. The reaction mixture was excited in water bath by refluxing for 30 minutes. The solution color was altered from yellow to orange. On cooling and slow evaporation at room temperature, orange red colored product was formed. The solid outcome was constituted as a result of filtration, cleaned and washed several times with hot water and with 50% methanol. Then it was dried in vaccum. This compound was recrystallized from methanol. The percentage of yield was 84%.

Experimental procedure for synthesis of mixed ligand Co[VAAPT]: To the warm methanolic solution of (10 ml) of 4-N (4-Hydroxy-3-methoxy benzalidine)-1,5-dimethyl-2-phenyl-1-H-pyrazol-3(2H)-one (0.05 moles) as a primary ligand is added to 10 ml of warm methanolic solution of cobalt nitrate . After 30 min, 5ml of methanolic solution of L-tryptophan (0.05 moles) amino acid was added as secondary ligand. The mixture was stirred vigorously. Further, the mixture was refluxed for about 3-4 hours. The product obtained turned to brown from orange red color. The obtained precipitate was brown and it was filtered and washed with warm water and dried in vacuum.

FT-IR spectral studies: Valuable evidence concerning the environment of the functional group attached to the metal has been obtained from spectra. The IR spectrum of primary ligand (L1) exhibited characteristic band at 1648cm and 1579cm assigned to √(C=O) and√(C=N) respectively. The band at 1648 is attributable to the√(C=O) stretching vibration of Schiff base ligand is shifted to another region 1580cm to 1623cm indicating co-ordination of carbonyl oxygen to the metal ion. The presence of band at 699cm in the IR spectra is due to metal to oxygen stretching vibration.

The azomethine band at 1580 of Schiff base was shifted to lower frequency ranging 1513-1486cm in the spectra of complexes confirming the participation of the azomethine nitrogen atom in co-ordination with metal. The spectrum shows well-defined peaks (3418-3109) attributed to √(O-H) of carboxyl moiety and √(N-OH) indole moiety.

There was change in frequency with change in shape and intensity on co-ordination with metal ion at(1623-1734cm) indicating that the carbonyl oxygen of antipyrene has been involved in chelation. The band at 767 cm is related to √(C=N) of tryptophan for secondary ligand. This band is shifted to 699 cm binding of mixed ligand, therefore the IR data confirms that ligand co-ordinate with metal complex through O and N respectively.

UV visible spectra: The electronic spectral bands of ligand and its metal complexes with tentative assignments are represented in the table 1. The electronic spectra of mixed ligand shows two bands maxima at 26,790 and 39,528 cm corresponding to n-π* and π-π* transitions respectively. In Co (II) complex, both n-π* and π-π* bands at 328 nm and 238 nm are found to be shifted and appeared in the region 26,158-27,189cm and 39,610-45,158cm compared to that of ligand. The electronic spectra of ligand (VAAPT) with Co (II) were performed in methanol as reference. π-π* transition is resemblance of heterocyclic moiety and this transition owing to the inter-molecular charge transfer takes place through azoic moiety. The maximum absorption λ(nm) and Max(cm) is shown in the table 1.

The 1H-NMR and C13-NMR spectral studies: The 1HNMR spectra data of ligand is recorded in DMSO solution with TMS as internal standard. The spectrum of ligand (TMBAAP) exhibited a signal related to one proton appeared at (9.81 ppm) which is assigned to NH proton of indole ring. The signals obtained in the range (6.94-7.49 a ppm) were assigned to a doublet due to presence of one proton of aromatic ring of phenyl and chemical shifts of aromatic protons of naphtyl and indole ring. The signals at 8.25ppm were assigned for singlet to (CH-NH_2) azo-methine moiety. This observation was also supported by the FTIR data of the ligand confirming the formation of Schiff base. For the following compounds, characteristic C13-NMR signal of the azomethine group(C=NH) was observed at 136.21ppm. This characteristic peak has been seen at 159.48, 136.21, 127.14, 127.09, 127.09, 127.07, 126.65, 125.8 ppm contributed to aromatic carbon atoms.

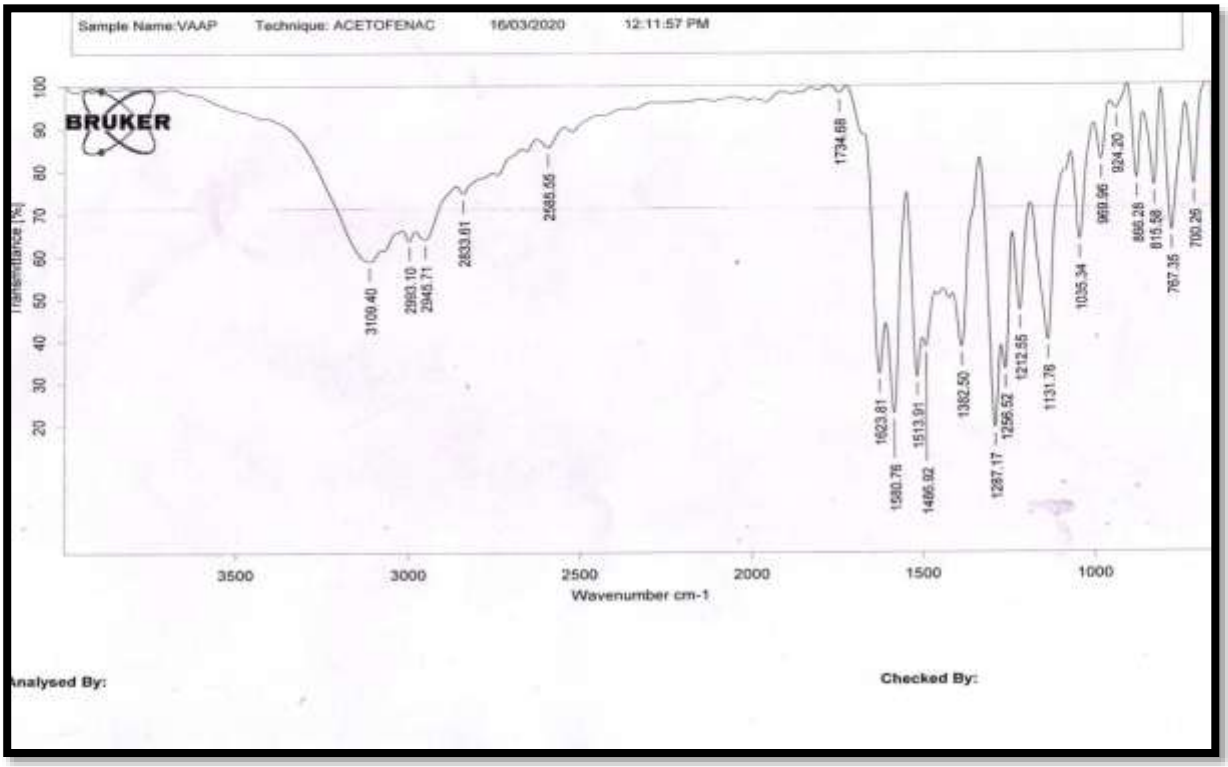

Fig. 1: FTIR data of primary ligand (VAAP)

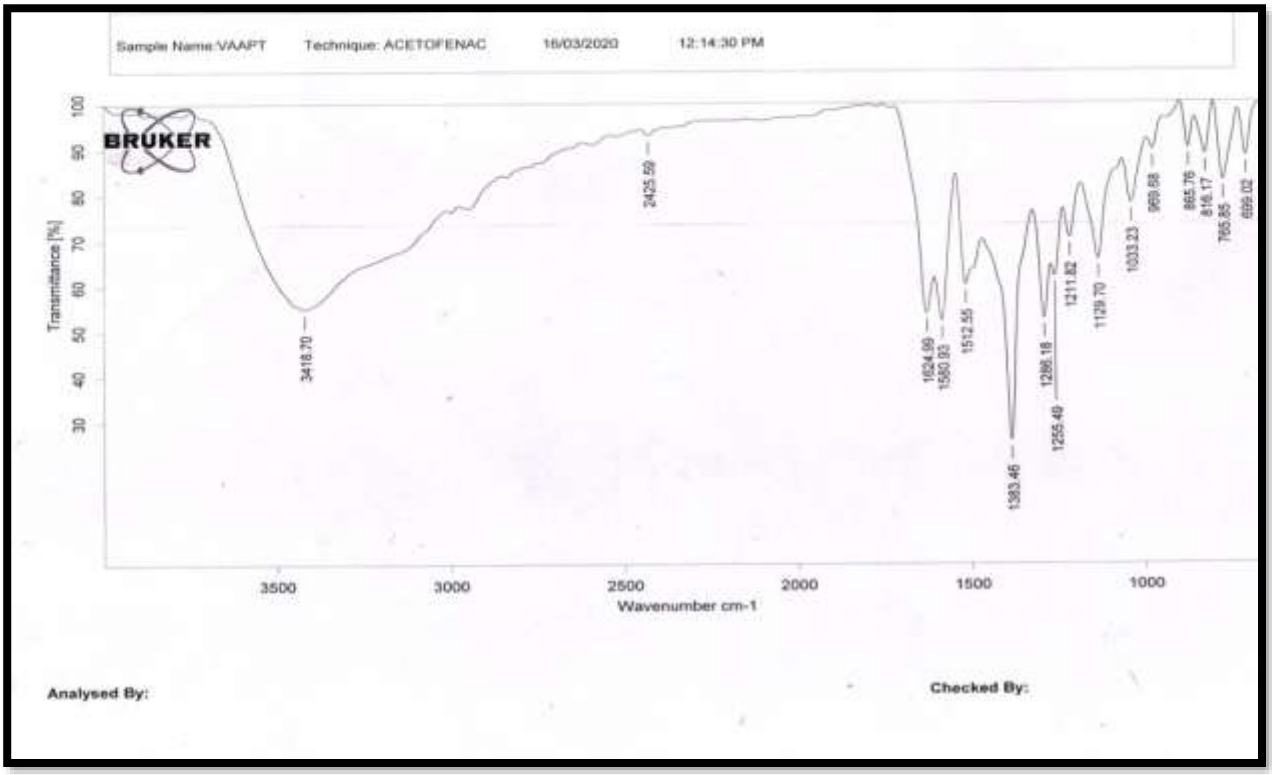

Fig. 2: FTIR data of Mixed ligand (VAAPT).

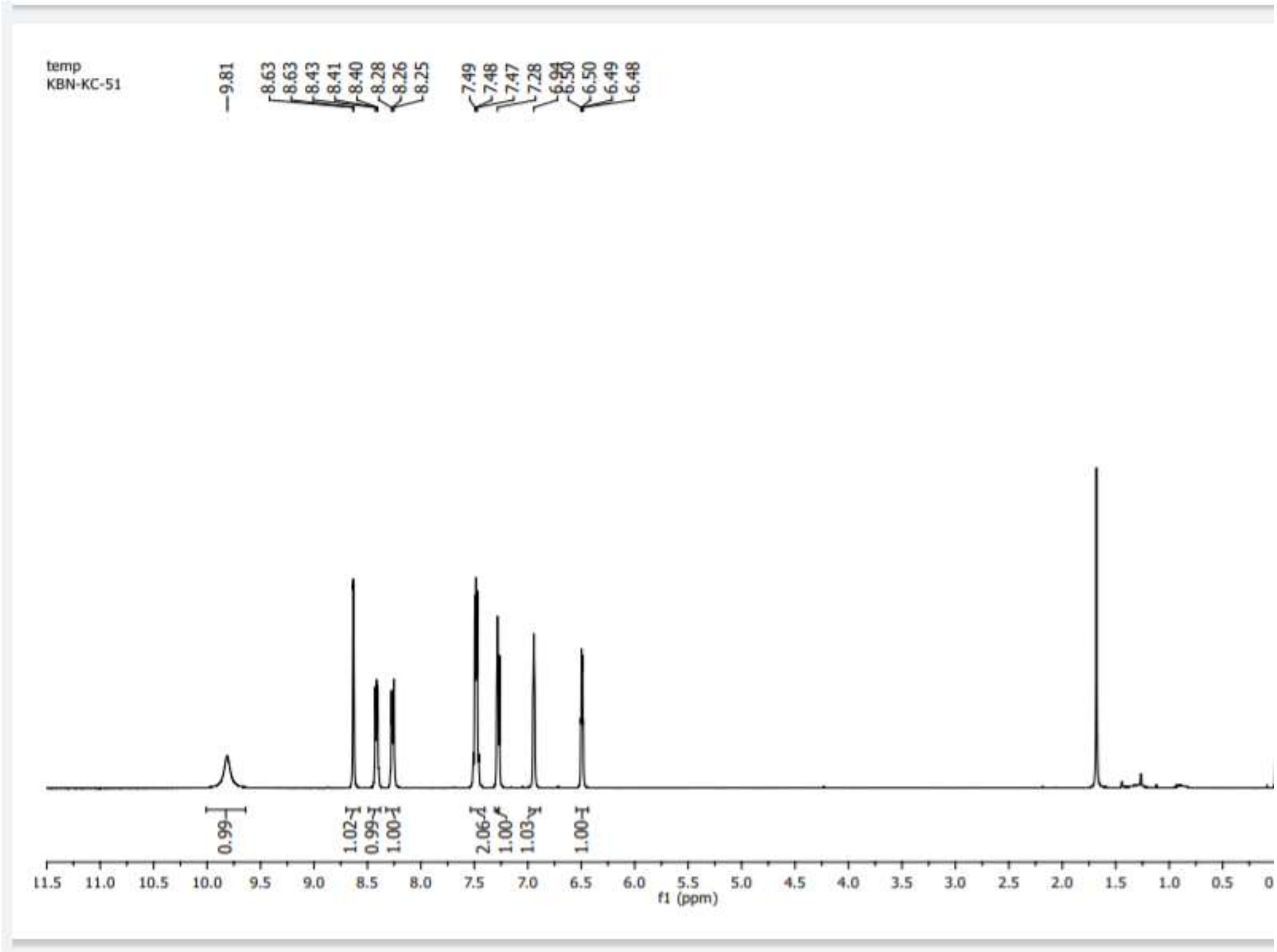

Fig. 3: H^1-NMR data of Schiff base Ligand (VAAP)

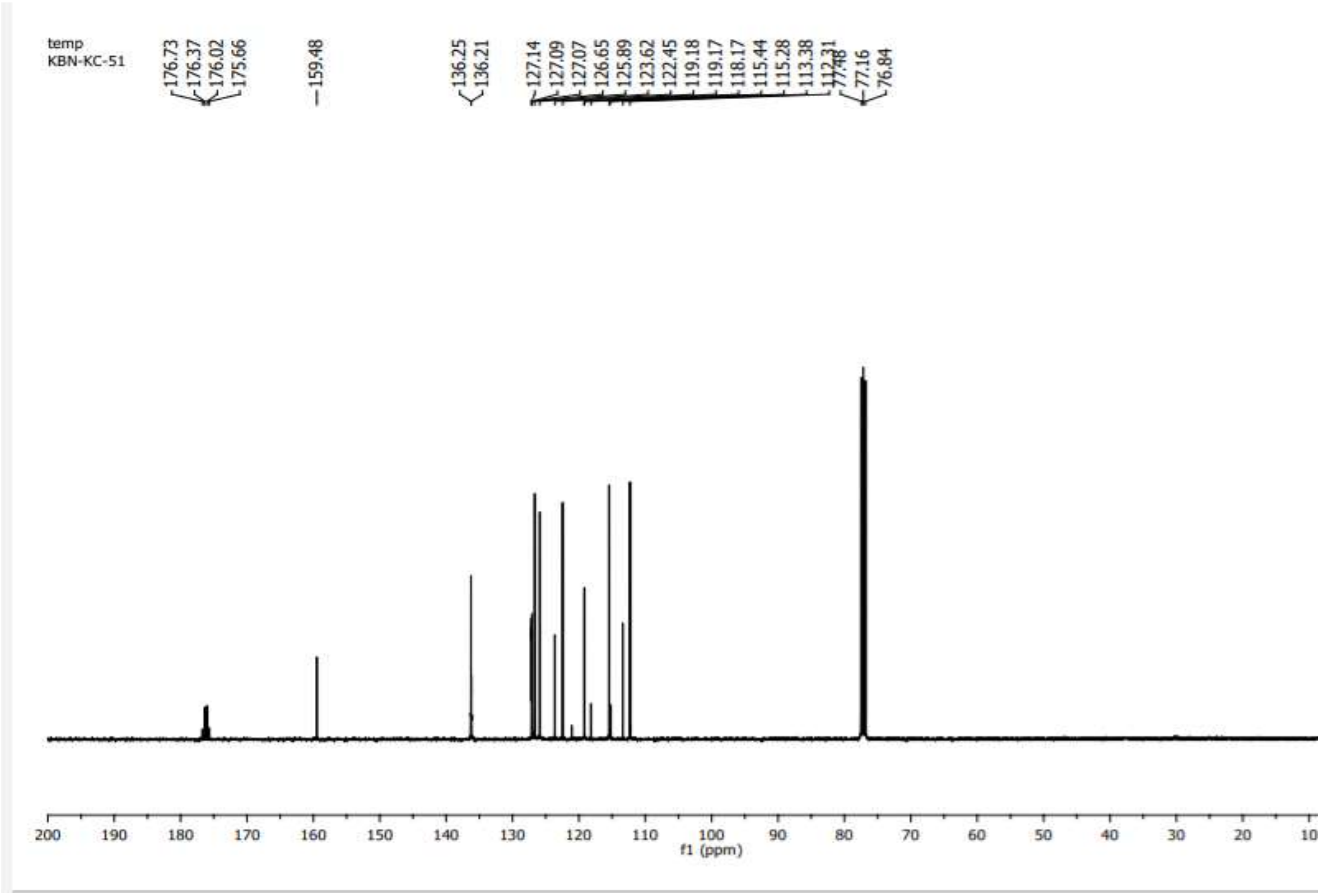

Fig. 4: C-13 NMR spectrum of Ligand (VAAP)

Table 1
Electronic spectral studies

Compounds	Absorption		Tentative assignments
	λ(nm)	Max cm	
Ligand(L_1)(TMBAAP)	327	39,528	π-π^*
	236	26,790	n-π^*
Co(L_1)(TMBAAP)	256	45,158	π-π^*
	301	39,820	π-π^*
	296	27,289	n-π^*
Co(L_1)(L_2)(TMBAAPT)	223	40,000	π-π^*
	236	26,148	n-π^*
	344	21,739	d-d transition

SEM analysis: The binding of ions and molecules is done through physical bonding, ion exchange, complexation, chelation or combination of any these interactions. In the present study the Schiff base 4-N[4-Hydroxy-3-methoxy benzalidine-4-amino-1,5-dimethyl-2-phenyl-1-H-pyrazol-2-H-one] along with secondary ligand tryptophan has the –OCH_3 and C=N functional groups as the active sites to interact with metal cobalt . At optimum p_H, the oxygen and nitrogen atoms on these active sites behave as the electron donars and can form complex with metal present confirmed through FTIR, UV and 1H-NMR and C-13 NMR spectral data attained.

The complexation of Schiff base with metal was proven based on SEM analysis carried out on Schiff base previously and after refluxation. The SEM micrographs are shown in fig. 5. The SEM image of SB obtained shows an smooth surface morphology with 2µm nano size.

The complexation of (azo-methine) SB with metal Co (II) shown tectonic structure so as a result morphology was changed drastically. The surface was with craggy facet with 10µm size. The SEM image thus reveals that Schiff base and its mixed ligand synthesized were of nano sizes with 2µm and 10µm.

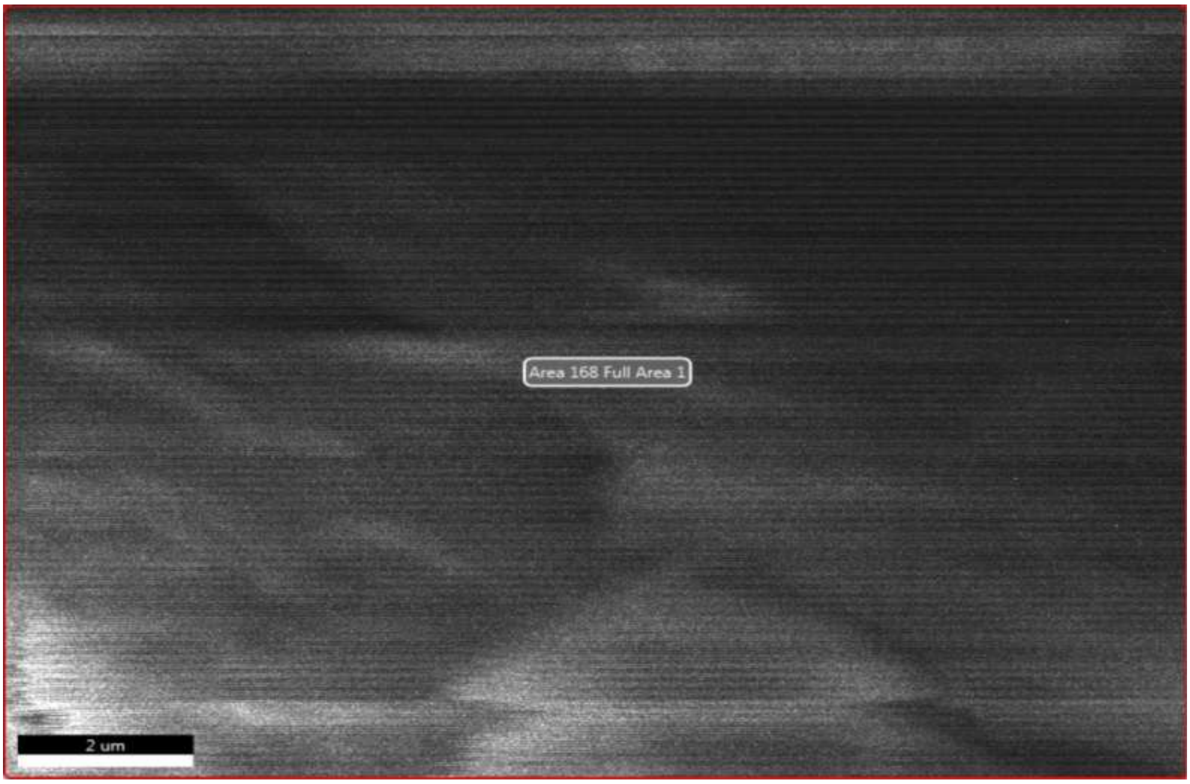

Fig. 5: SEM images of Schiff base with 2μm and mixed ligand with metal cobalt with 10μm size.

Fig. 6: SEM image of mixed ligand with metal (10μm) Co (II)[VAAPT]

Microbial Activity: Microbial activity was conducted using disc diffusion procedure. Schiff base ligand and mixed ligand with metal complex were screened separately against two bacterial cultures *Staphylococcus aureus* and *Salmonella typhi* and two fungal species Aspergillus fumigatus and Candida albicans. The results are given in the table 3. When the activity of Schiff base ligand and its metal complex were increased by increasing the antimicrobial screening concentration, the concentration plays a key role in the zone of inhibition and chelated resins deactivate the various cellular enzyme. The sterilized paper discs are soaked in 5ml of methanol and it was taken (150μg/ml).

Mixed ligand complex shows considerable antimicrobial activity even at low concentration and more toxic towards both bacterial strains and fungal strains compared with Schiff base ligand. The anti-microbial data shows cobalt complex has an excellent activity .The metal ion discourages of one or more cellular proteins causing destruction of microorganism. The images of activity of mixed ligand and metal complex and their zone of inhibition are shown in fig. 7. The results are tabulated in table 3.

Conclusion

In the present study, we described about synthesis of mixed ligand complex containing (ML) [4-hydroxy-3-methoxy-benzalidine-4-amino-1,5-dimethyl-2-phenyl-1-H-Pyrazol-2-H-One-2-amino-3-1-H-indol-3yl-propanoic acid] with Co(II) metal. The ligand and its complex are soluble in water and DMSO and exhibits square planar geometry. The anti-fungal and anti-bacterial screening assignment were tested against *Staphylococcus aureus*, *Salmonella typhi*, *Candida albicans* and *Aspergillus fumigatus*.

Table 2
The physico-chemical properties of primary ligand (VAAP) and mixed ligand Co (VAAPT)

Compound	Colour	M.P [^{0}C] (Yield %)	Elemental analysis			
			C	H	N	O
Primary ligand (VAAP)	Orange	300 (84%)	62.25	5.36	20.10	31.68
Secondary ligand Co (VAAPT)	Brown	210(79%)	56.82	4.37	15.9	43.18

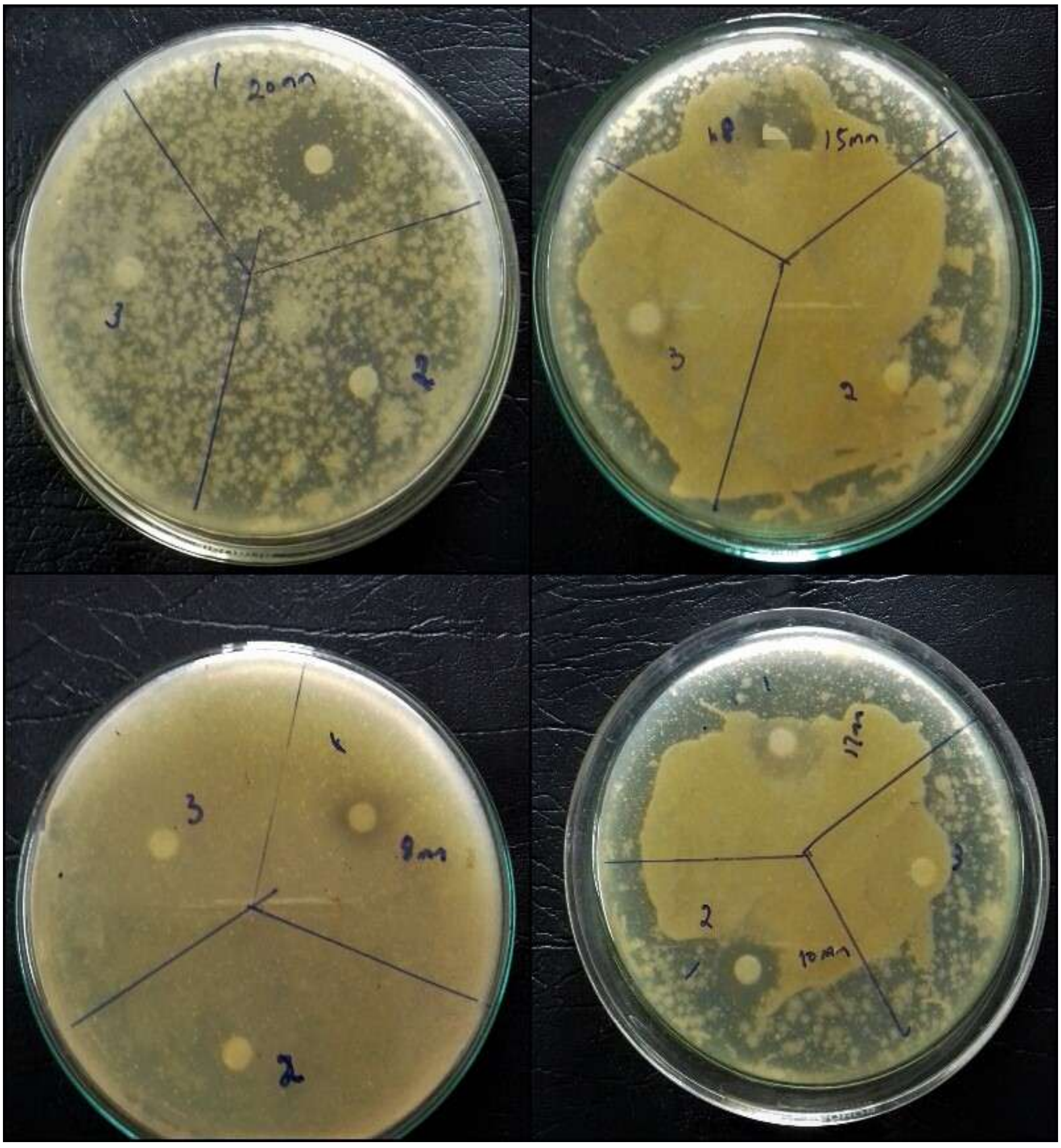

Fig. 7: Zone inhibition of microorganisms

Table 3
Activity of microorganism

Compound	**Bacteria**		**Fungi**	
	Staphylococcus aureus	**Salmonella typhi**	**Candida albicans**	**Aspergillus fumigatus**
Primary ligand (VAAP)	8mm	8mm	11mm	9mm
Mixed ligand Co (VAAPT)	15mm	8mm	17mm	20mm

Slightly active = inhibition zone(6-9mm).
moderatively active = inhibition zone(9-12mm)
Highly active = inhibition zone (more than 12mm

The resulted data displayed that the mixed ligand complex showed potential activity against microbes examined.

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