SYNTHESIS, CHARACTERISATION AND BIOLOGICAL EVALUATION OF NEW MIXED LIGAND COMPLEX (DERIVED FROM SCHIFF BASE)

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ABSTRACT

Mixed ligand complex included Schiff base derivative Ni(II) complexes (M(L1)(L2)) where L1 is the Schiff base derived from condensation between (3,4,5-Trimethoxy benzaldehyde) and 4 Amino antipyrine (4-amino-1,5-dimethyl-2-phenyl-1-H-pyrazol-2-H-one (3,4,5-TMBAAP) was synthesized and characterized using conventional and spectral techniques. 3,4,5(TMBAAP) is taken as a primary ligand or parent ligand (L1) and an amino acid L-tryptophan (L2) is added as the second ligand through refluxation to form mixed ligand with metal Ni(II) to form a complex. The mixed ligand complex 3, 4, 5(TMBAAPT) was characterized using ¹H-NMR, ¹³C-NMR, (EDAX) (Energy dispersive x-ray elemental analysis), UV-visible, FTIR, SEM techniques. The structural elucidation assessed with respect to the metal complex obtained was octahedral geometry based on the analytical studies. The invitro antibacterial and antifungal assay of mixed ligand were evaluated. The details of the results are well presented in the research investigation.

Keywords: Schiff Base, EDAX, Tryptophan, Anti-bacterial, Anti-fungal Assay

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INTRODUCTION

Schiff bases and their complexes are adaptable compounds made by precipitating an amino acid with a carbonyl group. The perusal of literature reveals that Schiff base complexes or azomethines and imines show virtuosic incentive activities exemplified in copious reactions. The maneuver is frequently enhanced by a result, understanding the properties of both ligands and metals requires complexation, which leads to the generation of tremendously energetic composites.¹⁻² The impact of metals on the biological exertion of Schiff bases and their peculiar chemical attentiveness has persuaded a substantial extension in the growth of their coordination behavior.³⁻⁴ The mixed ligand or assimilated complexes are an imperative category of coordination compounds and have captivated prominent attentiveness and are also known as azomethines and imines.⁴⁻⁹ It is possible to prepare a wide range of mixed ligand complexes with a single metal ion, and a colossal number of complexes can be synthesized by mixing different metal ions and could be amalgamated. This furnishes an admirable scope for the study of complex structure and concomitant correlations. A huge number of such complexes are integrated and investigated. Amid them, variegated ligands with complexes derived from tryptophan exhibit antimicrobial assay.¹⁰ Azo-methine ligands on another point of view are of the fascinating grade of ligands which have been the study of concerted examination of co-ordination amalgam of numerous variants; Schiff bases have initiated tremendous usages in extensive fields such as Biochemistry, Medical, Industries, and Laboratories. In this concern, azomethines or Schiff base ligands have revealed an influential place and are classified as monodentate, bidentate, tridentate according to their density.¹¹⁻¹³ Azo dyes of 4-Amino antipyrine are familiar as polydentate ligands co-coordinating in neutral and ionic forms.¹⁴ 4-amino antipyrine plays a vital role in numerous domains such as anti-cancer anti-inflammatory, anti-oxidant, anti-HIV have been reported earlier-tryptophan is an unusual amino acid because of the complexity of its metabolism, the variety of diseases it is involved as a pharmacological agent.¹⁵ Therefore in the present study, the author has focused on the development of mixed ligand complex 4-N-(3, 4,5-Trimethoxy benzalidine-1, 5-dimethyl-2-phenyl-1-H-pyrazole-3(2H) one, with metal Ni (II) and L-tryptophan an amino acid as a secondary ligand. The invitro antibacterial and antifungal assay of the derived complex was evaluated.

EXPERIMENTAL

Materials and Methods

All chemicals were procured from mercantile sources and were utilized without atonement. Elemental analysis (EA) of C, H, N, O was performed using EDAX (energy dispersive x-ray analysis), IR spectra were recorded on Bruker Fourier Transform Infrared (FT-IR) spectrometer on potassium bromide (KBr) pellet in the wave numeral radius of 4000-400 cm⁻¹. Electronic spectral studies were conducted on an Ultra Violet (UV-Visible) 1800 series, with a wavelength of 200-400 nm. NMR interpretation was chronicled on a 800MHZ-NMR spectroscopy through the reference of TMS and DMSO solvent. SEM images are acquired from a scanning electron microscope. FLEX- SEM 1000 instrument.

Synthesis of Primary Ligand (L₁) [TMBAAP]

3, 4, 5 Trimethoxy benzaldehyde (2g) (0.1M) was taken and dissolved in 50 ml of methanol. The 4-amino-1,5-dimethyl-2-phenyl-1-H-pyrazole-3(2H)one, (2.2g) (0.1M) Was dissolved in 50 ml of distilled water. These solutions were mixed in a sterilized 250ml round bottom flask and stirred with a magnetic rioter. This reaction mixture was excited in a water bath by refluxing for one hour. On cooling and slow evaporation at room temperature, a yellow-colored precipitate was formed. The solid outcome was isolated by clarifier and drenched many times with hot water. Then it was evaporated in a vacuum. The compound was recrystallized from methanol. The percentage of yield is 85%.

Synthesis of Secondary Ligand (L₂) [TMBAAPT]

To the warm methanolic solution of 10 ml of 4-N(3,4,5 Trimethoxy benzalidine -1,5-dimethyl-2-phenyl-1-Hpyrazol-3(2H)-one)(TMBAAP) (0.1M) as a primary ligand was appended to 10 ml of warm methanol suspension of Nickel sulphate (0.75g)(0.05M). After 30 min, 5ml of methanolic solution of L-tryptophan [2-amino-3-1-H-indol-3-yl-propanoic acid] (2.2g) (0.1M) amino acid was added as secondary ligand. The composition was stirred vigorously. Further, the mishmash was refluxed for about 2 hours. The resultant precipitate was altered from yellow to green-colored crystals. The obtained crystals were percolated and cleansed with warm water and dried in the void. The percentage of yield was 79%. The physicochemical properties of the primary ligand and mixed ligand were given in the following table. (Table-1).

RESULTS AND DISCUSSION

Infrared Spectral Studies

The IR spectrum of primary ligand (L₁) exhibited a characteristic band at 1648cm⁻¹ and 1579cm⁻¹ ascribed to $\nu(\text{C=O})$ and $\nu(\text{C=N})$ sequent. The band at 1648 is referable to the $\nu(\text{C=O})$ extended quivering of azomethine ligand is conveyed to flipside terrain 1594cm⁻¹ to 1579cm⁻¹ indicating co-ordination of oxygen belonging to carbonyl group towards the metal ion. The presence of a band at 698cm⁻¹ in the IR spectra is due to Metal to oxygen perpetuating vibration. The azomethine band at 1578 of Schiff base was shifted to a lower frequency ranging 1496-1452cm⁻¹ in the spectra of complexes confirming the contribution of the nitrogen atom belonging to the azo-methine group in co-ordination with metal. The spectrum shows well-defined peaks at (3431-3080) are attributed to $\nu(\text{O-H})$ of carboxyl moiety and $\nu(\text{N-OH})$ indole moiety. There was a change in frequency with a change in shape and intensity on coordination with the metal ion at (1648-1899cm⁻¹) indicating that the carbonyl oxygen of antipyrine has been involved in chelation. The band at 776 cm⁻¹ is related to $\nu(\text{C=N})$ of tryptophan for secondary ligand. This band is shifted to 698 cm⁻¹ binding of mixed ligand therefore the IR data confirms ligands coordinate with metal complex through O and N respectively. The FTIR spectra of primary ligand (TMBAAP) and mixed ligand with the metal Ni (II) were represented in Fig.-1 and 2 respectively.

The ¹H-NMR and ¹³C-NMR Spectral Studies

The ¹H-NMR spectra data of ligand is recorded in Dimethyl sulfoxide (DMSO) solution with Tetramethylsilane (TMS) as in most criterion. The spectrum referring to ligand (TMBAAP) exhibited a signal related to one proton that appeared at (9.69 ppm) which is assigned to NH proton of indole ring. The multiple signals that appeared in the region (7.50-7.26ppm) were assigned to chemical shifts of aromatic protons of naphthyl and indole ring. The signals at 3.91 are attributed to (CH-NH₂) azo-methine

moiety. For the following compound characteristic ^{13}C -NMR signal of the azomethine group($\text{C}=\text{NH}$) was observed at 134.97ppm.

Fig.-1: FTIR Spectrum of the Ligand TMBAAP

Fig.-2: FTIR Spectrum of the Mixed Ligand with Metal Complex Ni (TMBAAPT)

This characteristic peak has been seen for others at 138.4, 134.5, 135.5, 132.0, 131.5ppm respectively. Furthermore, signals attributed at 151.93, 134.97, 133.57, 129.31, 127.01, 124.46 ppm are contributed to aromatic carbon atoms reciprocally. The ^1H -NMR spectrum and ^{13}C - NMR spectrum of mixed ligand are shown in Fig.-3 and Fig.-4 respectively.

Fig-3. ^1H -NMR Data of Ligand

Fig.-4: ^{13}C - NMR Data of Ligand

Ultraviolet (UV) Spectral Inquest

The voltaic spectral bands of ligand and its metal complexes with preliminary values are represented in Table-2 given below. To attain a wider insight into the properties of the transitions in the coordination field of prepared complexes. The UV spectrum of mixed ligand displays both band maxima at 26,798 and 39,525 cm corresponding to $n\text{-}\pi^*$ and $\pi\text{-}\pi^*$ conversions consequently. In Ni (II) complex, both transitions appeared at $n\text{-}\pi^*$ and $\pi\text{-}\pi^*$ bands at 328 nm and 238 nm are found to be shifted and raised in the region 26,168-27,289 cm and 39,640-45,148 cm compared to that of ligand. The electronic spectra of ligand (TMBAAPT) with Ni (II) were performed in methanol as reference. $\pi\text{-}\pi^*$ transition is a resemblance of heterocyclic moiety and this transition owing to the intermolecular charge transfer taken place through azoic moiety. The absorption maximal data in λ (nm) and Max (cm) are summarized in the Table-2 given below.

Table-1: The Physico-chemical Properties of Primary Ligand (TMBAAP) and mixed Ligand Ni(TMBAAPT)

Compound	Color	M.P [$^{\circ}\text{C}$] (Yield %)	Elemental Analysis			
			C	H	N	O
Primary Ligand(TMBAAP)	Yellow	300 (84%)	62.26	5.38	20.11	31.78
Secondary Ligand Ni(TMBAAPT)	Olive green	210(79%)	56.84	4.39	16.9	45.18

Table-2: Electronic Spectral Studies

Compounds	Absorption		Tentative Assignments
	λ (nm)	Max cm	
Ligand(L ₁)(TMBAAP)	328	39.525	$\pi\text{-}\pi^*$
	238	26.798	$n\text{-}\pi^*$
Ni(L ₁)(TMBAAP)	262	45.148	$\pi\text{-}\pi^*$
	302	39.825	$\pi\text{-}\pi^*$
	293	27.289	$n\text{-}\pi^*$
Ni(L ₁)(L ₂)(TMBAAPT)	225	40.000	$\pi\text{-}\pi^*$
	229	26.148	$n\text{-}\pi^*$
	342	21.739	d-d transition

Scanning Electronic Microscope

The scanning electron micrographs (SEM) unveil the framework of Schiff bases with Ni (II) complexes. The SEM images are taken at 15 kV stimulated potential and amplification was fixed following the need from 150 xs to 3000x. In SEM images perceptible phase separations in the dense layer were observed. The province size of $2\mu\text{m}$ in ligand, $20\mu\text{m}$ in metal complex and $50\mu\text{m}$ in mixed ligand were detected. In SEM images the surface of the ligand was soft and smoothy layer, after coordination with metal there was a large macroscopic phase separation. This phase separation was minimized after the formation of a mixed ligand. Also, the snugness and softness were reduced due to the introduction of metal. It was

evident that there was a substantial change in the morphology of Schiff base on complexation. The SEM images of primary ligand, a mixed ligand of the metal complex have shown in Fig.-5.

Antimicrobial Assay

Mixed Ligand derived from Schiff base was tested against bacteria and fungi. These ligands with a metal complex show anti-microbial activity. The prepared Ligand Ni[TMBAAPT] with (150 μ g/ml) along with metal was tested in-vitro against the following microorganisms, the two bacterial species *Staphylococcus aureus* and *salmonella typhi* and two fungal species *Aspergillus fumigatus* and *Candida albicans*. The effect of the synthesized mixed ligand towards microbes is represented in Table-3. The prepared complex exhibits high anti-microbial activity than the parent ligand [TMBAAP]. The elevated exertion of the complex may be allocated to the different properties of metal ions upon chelation, it gets adsorbed on the cell wall of microorganism, causes blockage of protein synthesis, which results in an abatement of microorganism. Thus metal ions are considered as a growth-inhibitory influencer. A computational observation of the values of parent ligand with mixed ligand complex exhibits high anti-microbial assay. Using Tweed's chelation theory as a base, chelation greatly decreases the polarity of the metal ion due to biased splitting of its positive charge with the contributor cluster, as well as –negative particle demobilization on the donor group on the entire chelate ring. Furthermore, the metal ions discourage one or more cellular proteins from destroying microorganisms. The images of activity and clime of restraint are shown in Fig-5.

Fig.-5: SEM Images of (Area-168) Primary Ligand [TMBAAP] with (2 μ nm) Size, (Area-171) Image of Metal Complex Ni[TMBAAP] with (10 μ nm) Size, (Area-169) Secondary Ligand along with Metal Complex Ni[TMBAAPT] with (50 μ nm)

Table-3: Activity of Microorganism

Compound	Bacteria		Fungi	
	<i>Staphylococcus aureus</i>	<i>Salmonella Typhi</i>	<i>Candida albicans</i>	<i>Aspergillus Fumigatus</i>
Primary Ligand[TMBAAP]	8mm	8mm	11mm	9mm
Mixed Ligand [TMBAAPT]	17mm	17mm	15mm	20mm

Where,

Marginally effective = restraint clime (6-9mm)

Adequately effective = restraint clime(9-12mm)

Highly effective = restraint clime (more than 12mm)

Fig.-5: Restraint Clime of Microorganisms

CONCLUSION

In the present paper, the author described the synthesis of mixed ligand complex containing (ML) [3, 4, 5-Trimethoxy benzalidine-4-amino-1,5-dimethyl-2-phenyl-1-H-Pyrazol-2-H-One-2-amino-3-1-H-indol-3-yl-propanoic acid] with Ni(II) metal. The ligand and its complex are soluble in water and DMSO and it exhibits octahedral geometry. The anti-fungal and anti-bacterial screening assignment were inspected against *Staphylococcus aureus*, *Salmonella typhi*, *Candida albicans* and *Aspergillus fumigatus*. The resulted data displayed that the mixed ligand complex showed potential activity against microbes examined.

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