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SYNTHESIS, CHARACTERIZATION AND APPLICATIONS OF NI (II) BASED METAL COMPLEXES OF COUMARIN DERIVATIVES

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ABSTRACT

Heterocyclic compounds are cyclic ring structures with at least one atom other than carbon, such as nitrogen, oxygen, or sulfur. Heterocycles can be utilized as starting materials to manufacture a variety of chemical molecules. A. Vogel of Munich isolated coumarin from tonka beans for the first time in 1820. Coumarin analogues can be produced using methods such as the Claisen rearrangement, the Perkin reaction, the Pechmann reaction, the Witting reaction, and the Knoevnagel condensation. But Pechmann Condensation process is simple, inexpensive, has a rapid response time, and eliminates the formation of acidic waste streams caused by traditional methods. Many experts and scientists have reported on this. Resorcinol and β-keto ester are condensed with H_2SO_4 in the Pechmann condensation reaction to produce coumarin. Coumarin is a natural substance extracted from plants that has a variety of biological actions. Coumarin, also known as 1,2-benzopyrone, 2*H*-1-benzopyran-2-one, phenylpropanoids, cis-o-coumarinic acid lactone, or coumarinic anhydride; tonka bean camphor, is a broad class of chemicals found in plants, fungi, and bacteria. Coumarin and its derivatives are physiologically active and highly potent chemicals with antibacterial, anticancer, anti-HIV, anti-inflammatory, anticoagulant, and antioxidant effects. Coumarins were formerly believed to be benzoic acid derivatives, but Perkin, Sr.'s methodology categorized them as oxygenated heterocycles. Schiff bases are the most often utilized flexible ligands, and they are made via condensation of primary amines with carbonyl compounds. In a wide variety of fields, including agrochemicals, reagents, catalysis, medicine, and the creation of numerous industrial products, metal complexes of Schiff base ligands are used. Schiff base complexes are valuable in pharmaceutical applications due to their vast range of biological activity.

Keywords: Coumarin Synthesis, Co-ordination Chemistry, Metal Complexes, Heterocyclic compounds, Antimicrobial Activity, Coumarin derivatives

1. INTRODUCTION:

Coordination chemistry is a branch of chemistry that studies complicated compounds. Complex molecules are compounds that have a centre atom or ion, usually a metal, surrounding by a cluster of ions or molecules that keep their identity both solid and dissolved. Ligands are ions and molecules that are bonded to metal ions. The chemistry of coordination compounds, a fundamental issue of inorganic chemistry, has advanced so rapidly that these molecules now encompass a large amount of organic chemistry and even some areas of biochemistry. In addition to their significant functions in catalytic reactions and organic synthesis, metal complexes have a wide range of uses including biological, therapeutic, analytical, and industrial. The significance of coordination compounds becomes apparent when one recognises that chlorophyll, which is essential for photosynthesis in plants, is a magnesium complex and that haemoglobin, which transports oxygen to animal cells, is a ferrous metal complex **[1]**. The chemistry of coordination compounds has taken on new dimensions in recent years, owing mostly to the advancement of co-ordination bond theory and the synthesis of novel complexes. These studies are given further significance due to the relevance of metal complexes in biological systems and the usage of co-ordination compounds as catalysts in a variety of industrially important activities **[2]**. After making an important contribution in coordination chemistry over the last several years, the ligands of Schiff bases and their metal complexes had also gained widespread interest. They can be used in an extensive range of industries. All of those are model systems for biochemistry **[3]**. Hugo Schiff initially described a Schiff base ligand back in 1864. Azeotropic distillation is implemented in Schiff's conventional method to combine a carbonyl compound with an amine **[4]**.

Coumarins are the least complicated hetero cyclic compounds with the lowest toxicities that can be found in nature on a regular basis. Many studies have focused on several coumarin analogues that have been produced and tested for biological activity by well-known researchers. The ring structure of coumarin, which consists of benzene and pyrone rings, encourages biological research to identify its potential medicinal benefit. Based on changes to the basic moiety, it offers a strong anticancer potential with fewer side effects **[5]**. Many studies have been undertaken to create chemicals with minimal or no adverse effects because cancer is the second-leading cause of death globally; coumarins have been reported to have slight mild negative effects **[6]**. Due to their tendency for forming stable complexes with the majority of transition metal elements, schiff bases have played an integral part in the growth of coordination chemistry. The ability of Schiff base complexes to serve as chemically produced models for metal-containing spots in metallo-proteins and enzymes has drawn attention to them in the field of bioinorganic chemistry. Many metal ions possess the ability to establish coordination bonds with Schiff bases via either/both azomethane nitrogen and phenolic oxygen **[7]**. In biological systems, the vast majority of the 3D transition metal ions that exist play crucial functions. We refer to them as metalloproteins. Enzymatic function is centered on metal ions, which also influence the shape of the active sites and facilitate biological redox **[8]**. Some of the most significant studies on coumarins and their derivatives focused on whether they would be poisonous to both plants and animals in addition to being utilised as fragrances in food and personal care items **[9]**.

Numerous plants are naturally rich in coumarins, but tonka bean, woodruff, lavender, licorice, strawberries, apricots, cherries, cinnamon, sweet clover, and bison grass have particularly high concentrations **[10]**. The Knoevenagel reaction became a crucial synthetic technique to create coumarin derivates containing carboxylic acids in three locations in the early 1900s. Afterwards, scientists created 4-methylcoumarine compounds by condensing etylcyanoacetate and other o-hydroxyaceto-phenones **[11]**. The ability to employ various substituted phenols and p-ketonic esters allows for the synthesis of coumarins with substituents either in the benzene nucleus, the heterocyclic ring, or both. Biochemically prominent metal complexes of coumarin-based ligands are a recent topic of coumarin chemistry that is growing in prominence. The effectiveness and bioactivity of medicinal medicines are often enhanced by the interaction of metal ions with them **[12]**.

In addition to being a component of enzymes and proteins, nickel is regarded as a necessary element in mammals, microbes, and plants. In numerous species of higher plants, it is necessary for the efficient production of urease and the metabolism of urea. Leguminous plants that depend on mutually beneficial fixed nitrogen need nickel at low quantities either for the development of bacteria or for the utilisation of fixed nitrogen, or both **[13]**. In accordance with analytical, spectral (IR, UV-vis, ESR, FAB-mass and fluorescence), magnetic, and thermal studies, all metal complexes have an octahedral geometry in which the ligand is coordinated to the metal ion through deprotonation of azomethine nitrogen, thion sulphur, and phenolic oxygen atoms **[14]**.

2. MATERIALS AND METHODS

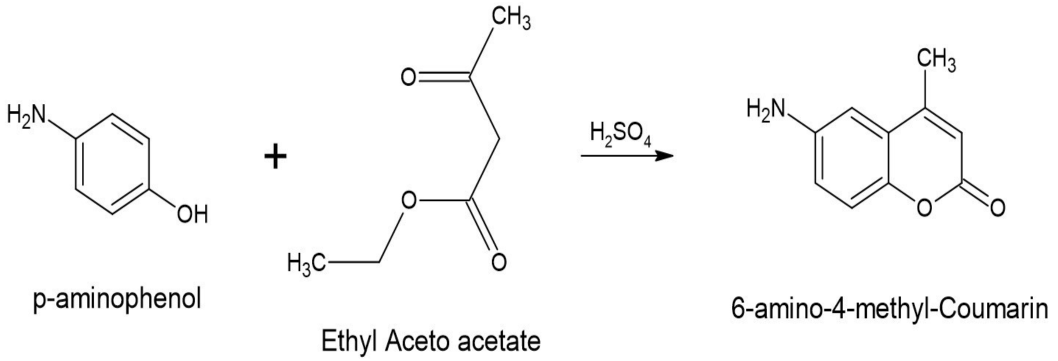
This section discusses the reagents used, as well as the various analytical and physicochemical techniques used in the characterization experiments. It also includes the production and spectral characterization of Schiff base ligands and metal complexes used in the latest research.

Materials:

Methanol Lr. was purchased from Gandhi Enterprises Pvt. Ltd., Vadodara, India. Cefdinir was received as a gift sample from Covalent Laboratories Pvt. Ltd, India. All chemical reagents were obtained from commercial suppliers and were purified before use.

Method of Synthesis of 6-Amino Coumarin:

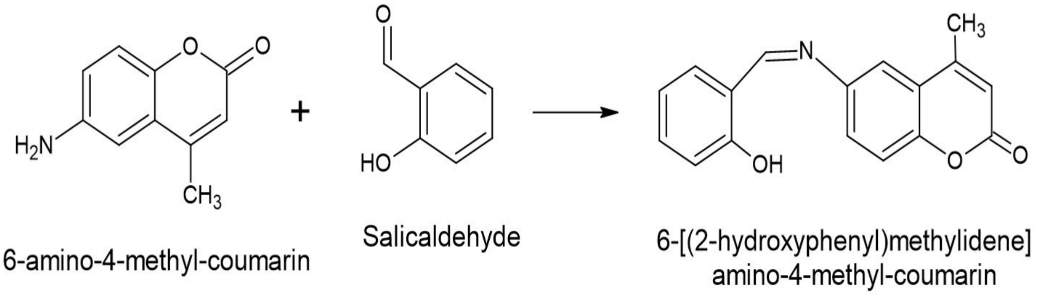
Initially, Start the procedure by taking 40 ml H_2SO_4 in a beaker and 23 ml Ethyl acetoacetate in another clean beaker. Pour H_2SO_4 in the beaker containing Ethyl acetoacetate. Now the mixture will start evaluating heat from the system, so to avoid the heat place the beaker of mixture on an ice bath for approximately 5-10 minutes. While the mixture still in ice bath, start the addition of total 20 grams of *p*-amino phenol with 2 grams addition in time duration every 5 minutes. Avoid the disturbance of the mixture containing beaker for 24 hours. Take a beaker with an amount of fully crushed ice. After 24 hours of time span, transfer the obtained mixture into the beaker containing crushed ice. Let the mixture dissolve properly into the ice solution. After dissolution, filter the derived product with the help of Whatman filter paper. Now, collect the filtrate which is onto the filter paper and leave it for 6 days straight. Observe the product after 6 days, the crystals of 6-amino coumarin are been obtained as displayed in **(Scheme 1)**. TLC of the formed compound was noted to confirm the proceeding of the reaction. Presence of the compound 6-amino coumarin was also detected by various spectroscopic techniques.



Scheme 1

Method of synthesis of 6-[(2-hydroxyphenyl) methylidene] amino-4-methyl-coumarin (L1):

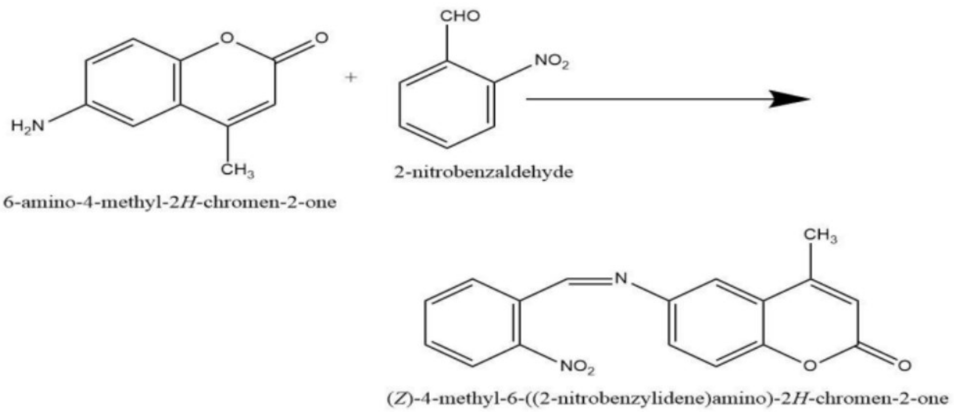
Once 6-amino coumarin has been successfully synthesised, add 2 grammes of salicylaldehyde to a beaker. The Round Bottom Flask holding 2.5 grammes of synthetic 6-amino coumarin received the salicylaldehyde right away. Only five minutes later, 20 ml of methanol were added to the mixture. The product was kept for reflux into a water bath by heating the mixture and using a condenser to control the temperature of the reflux system. Glacial Acetic Acid is added in a few droplets to the Round Bottom Flask containing the reaction mixture over the course of 10 minutes. The mixture was kept in reflux on a magnetic stirrer with continuous agitation and heating for at least six hours. After the product's six-hour reflux, precipitate **(Scheme 2)** was generated. After that, the precipitate was collected using filter paper (Whatman paper). Prior to recrystallization with acetic acid, the product was cleaned with ice-cold methanol.



Scheme 2

Method of synthesis of 6-[(2-nitrophenyl) methylidene] amino-4-methyl-coumarin (L2):

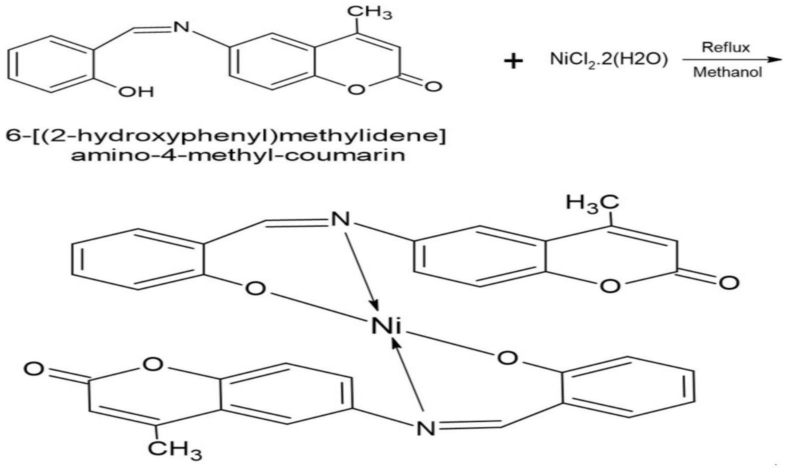
Once 6-amino coumarin has been successfully synthesised, add 2 grammes of 2-nitro benzaldehyde to a beaker. The Round Bottom Flask holding 2.5 grammes of synthetic 6-amino coumarin received the 2-amino benzaldehyde right away. Only five minutes later, 20 ml of methanol were added to the mixture. The product was kept for reflux into a water bath by heating the mixture and using a condenser to control the temperature of the reflux system. Glacial Acetic Acid is added in a few droplets to the Round Bottom Flask containing the reaction mixture over the course of 10 minutes. The mixture was kept in reflux on a magnetic stirrer with continuous agitation and heating for at least six hours. After the product's six-hour reflux, precipitate **(Scheme 3)** was generated. After that, the precipitate was collected using filter paper (Whatman paper). Prior to recrystallization with acetic acid, the product was cleaned with ice-cold methanol.



Scheme 3

Method of Ni (II) Metal binding with L1 & L2:

Following the synthesis of the ligand, a methanolic solution of the ligand is made in an RBF by mixing 10 ml of methanol with 1 g of the ligand. There is 0.25 grammes of nickel metal added to a certain Round Bottom flask. That resulting mixture was then allowed to reflux in a water bath for an hour. 0.14 grammes of sodium acetate then were slowly added to the mixture after an hour was passed. The reflux then maintained for yet another three hours. The solution was subsequently filtered and washed-out using water and methanol. Vacuumed after drying. The resulting product was subsequently verified by several spectroscopic methods to be a ligand-metal complex as shown in **Scheme 4**.



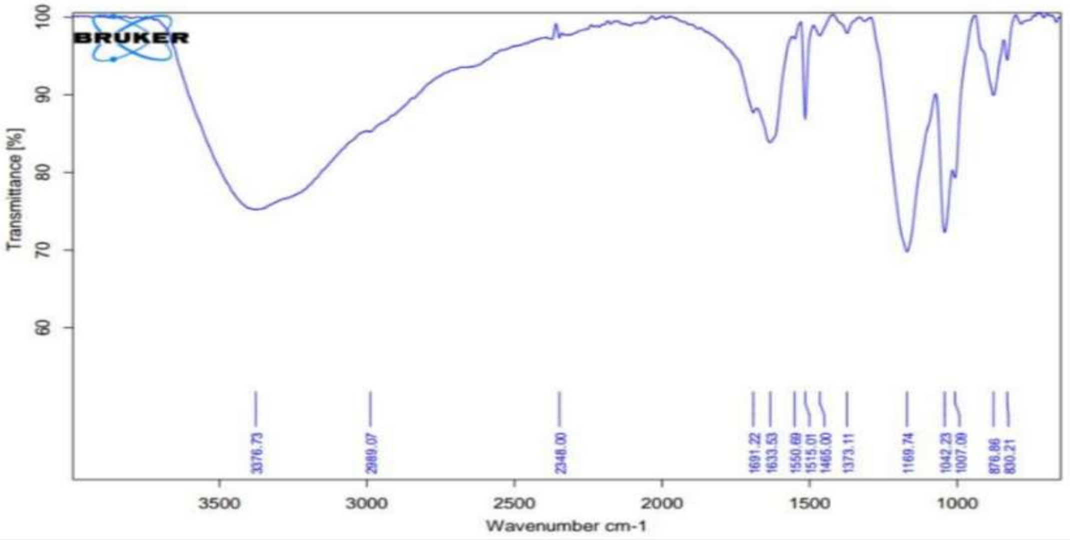
Scheme 4

Characterization of Ligands (L1&L2) and Metal Complex:

Both (mass and IR spectroscopy) studied were conducted as per regular standard procedures. Mass spectrometry (MS) is a method for the mass-to-charge ratio measurement of ions. IR spectra of Ligands and Ni (II) metal complex were noted from 4,000 to 500 cm^{-1}; Parul Institute of Pharmacy, Parul University, Vadodara, India. Around 30-40 mg of test samples were taken for IR Spectroscopy.

3. RESULTS AND DISCUSSION:

IR Spectroscopy:



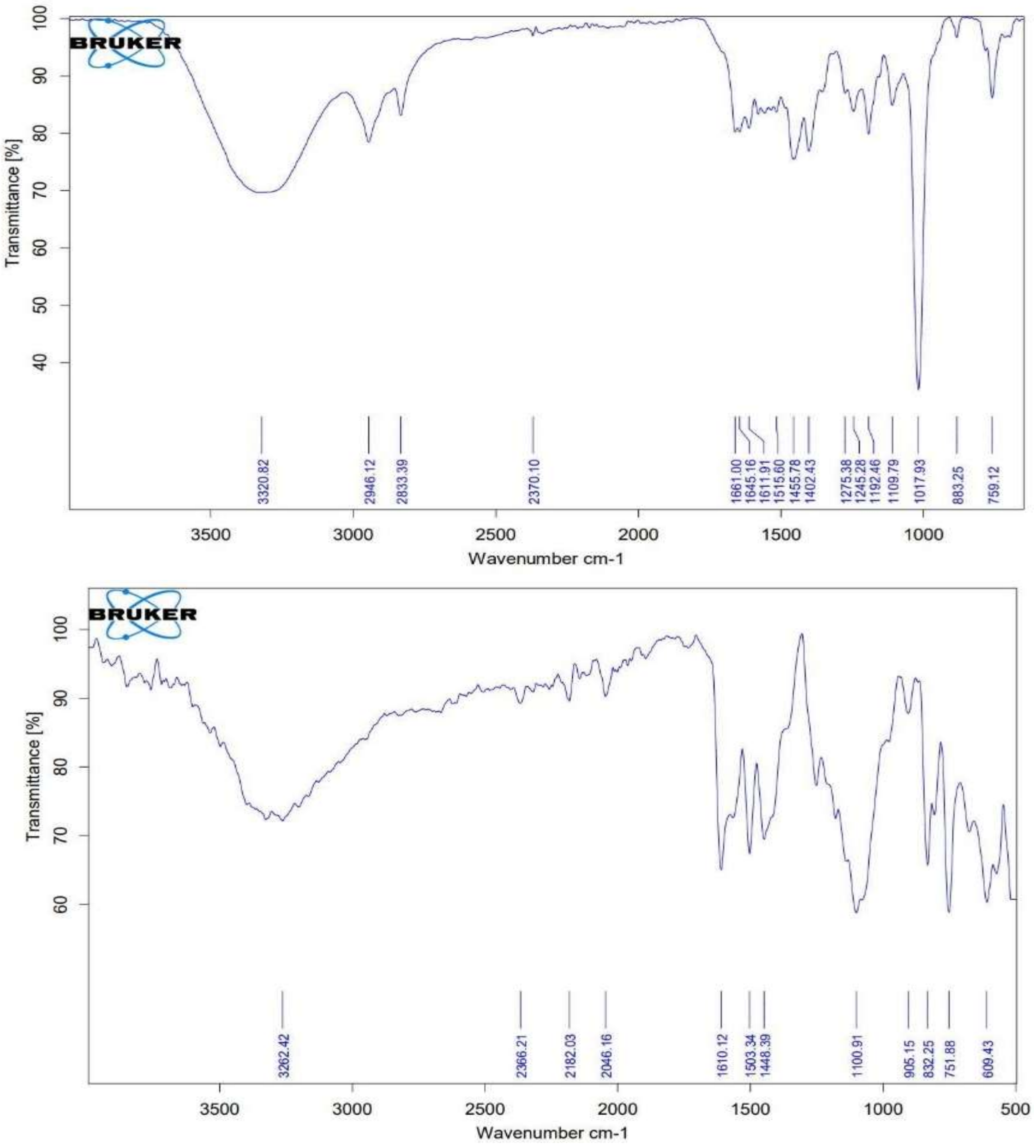
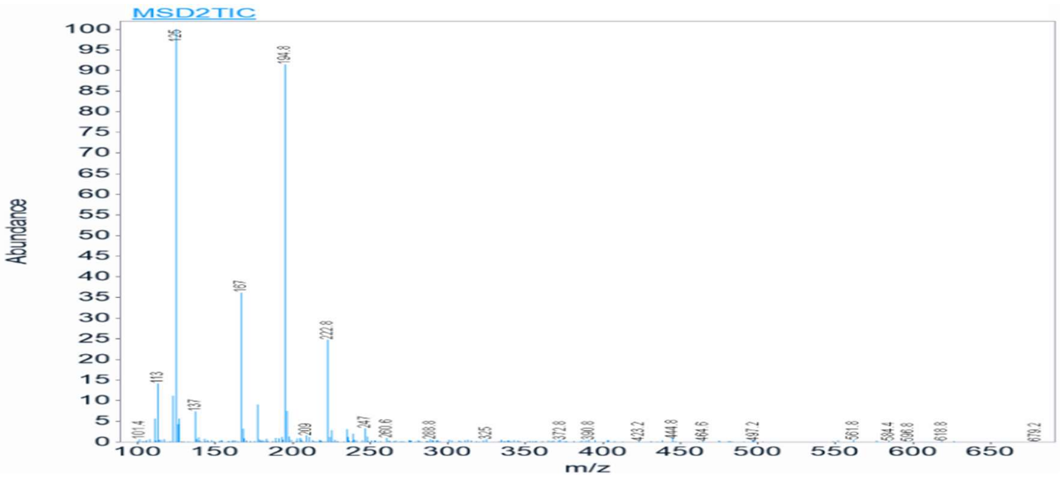
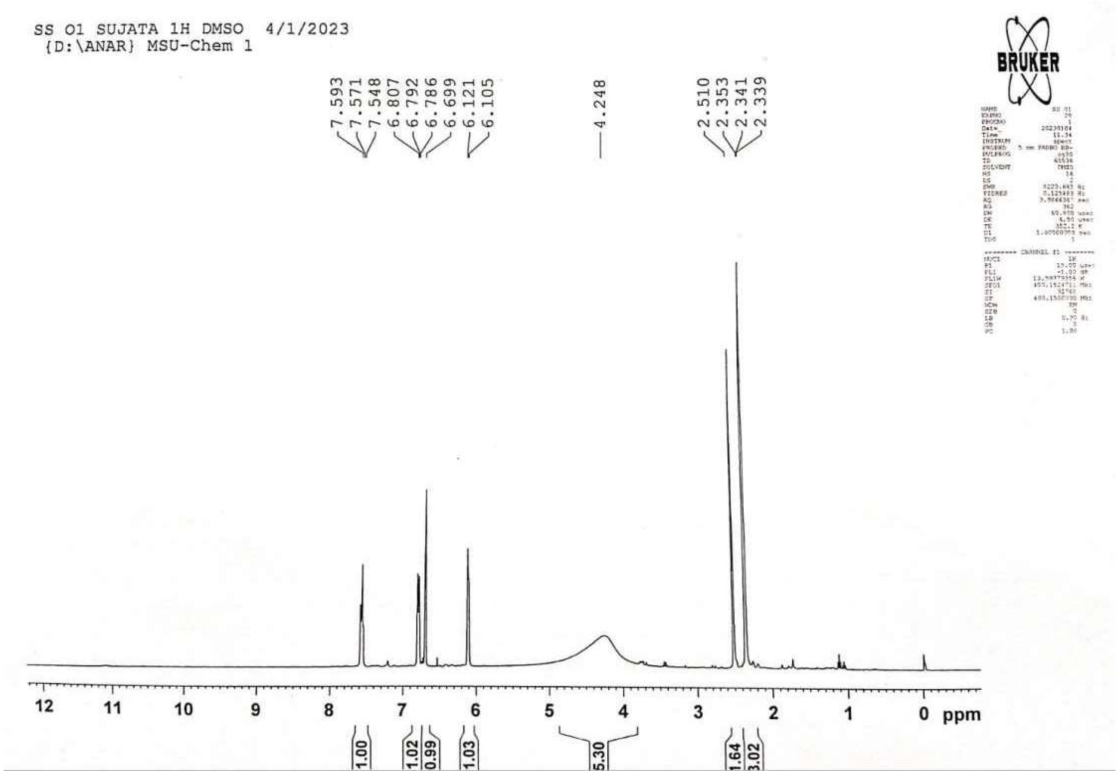


Figure 1: IR spectroscopy of L1; L2; Ni (II) Metal Complex

Mass Spectroscopy:



NMR Spectroscopy:



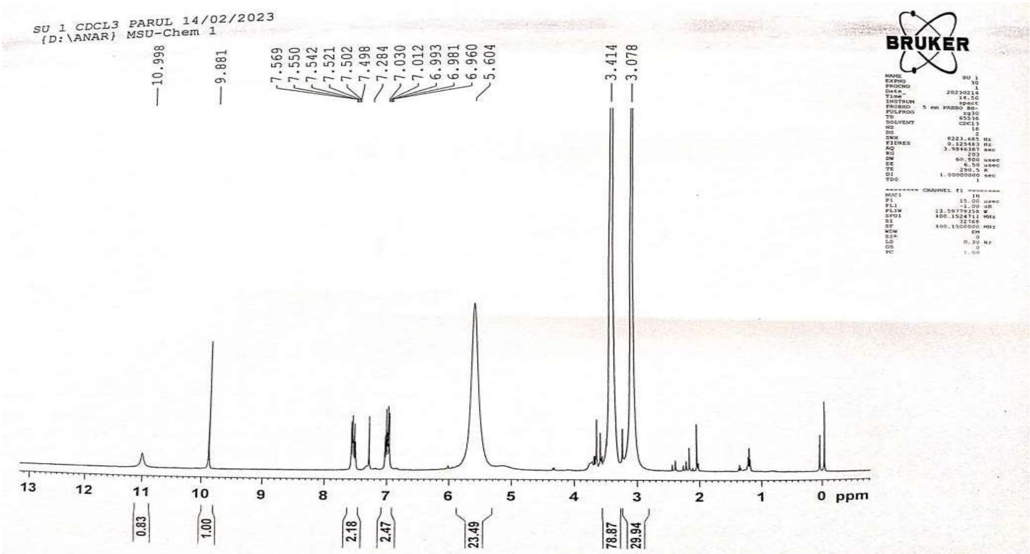
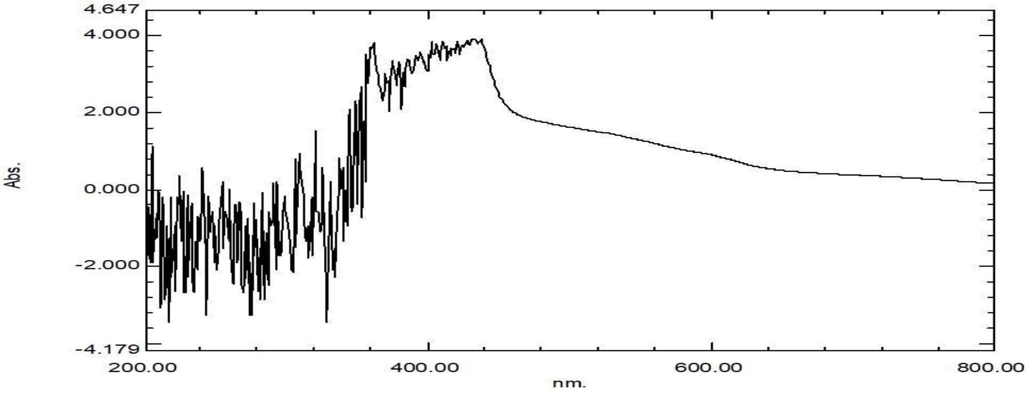
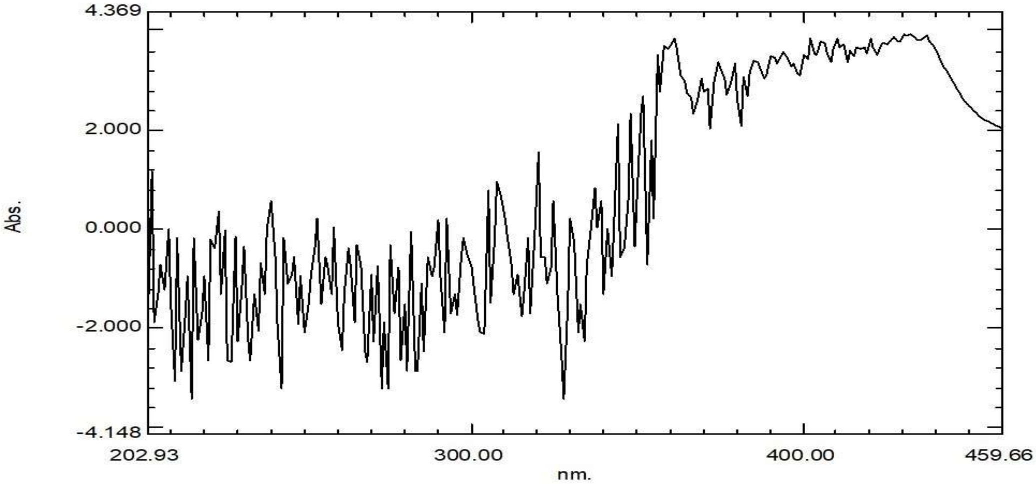


Figure 2: NMR Spectroscopy of 6-Amino Coumarin & 6-[(2-hydroxyphenyl) methylidene] amino-4-methyl-coumarin(L1)

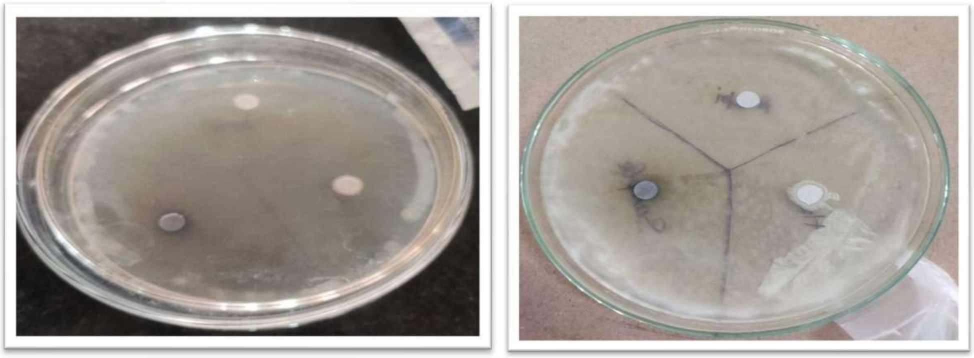
UV Visible Spectroscopy:





Biological Activity:

This synthesis of Pyrazalone-derived ligand and its co-ordination complex was evaluated with a fungus. Onto the test, the synthesized compounds had a variety of inhibitory actions. Both synthesized ligands and transition metal complexes showed several activities but on comparison, the formed complex was observed to be more fungicidal than the ligand. This observation leads on to the conclusion that the prepared ligand's biological activity enhanced as a result of the complex formation with nickel metal.



Anti-Fungal Activity of Ligand and Metal Complex

DISCUSSION:

The Mass spectroscopy results indicated that highest mass to charge ratio in mass spectrum created due to the loss of an electron from a molecule, and it is concluded that after metal complex formation molecular weight was increased compared with ligand molecule because of attachment of functional groups (OH, C=O) to the FMWCNT that confirms the functionalization. From IR results it is observed that oxygen and nitrogen containing groups (OH, C=O, C=N) in ligand is present. More absorption peaks were observed in the spectra of Metal complex because after complexation, Ni (II) metal gets bonded to the oxygen and nitrogen atoms. It means there might be successful complexation of metal to Schiff based ligand. IR spectra of Ligands and Metal complex indicated intensive IR peaks at their respective ideal wavelengths as shown in Table 1. As in the spectra of Ligands, there was no observed peak of Co-ordination Metal complex, whereas in that of metal IR spectra, distinctive peak of metal was observed at 609.43 cm^{-1}.

The Anti-Fungal Property was shown by both the molecules i.e., Ligand and Metal complex compound. On comparing both the obtained results, it was observed that the synthesized ligands L1 and L2 shows fungicidal activity less efficiently as that of displayed by metal complexes. On the agar plate, Zone of inhibition was displayed but the inhibition zone was larger in case of metal complex as compared to that of ligands.

CONCLUSION

The effective formation of a coumarin derivative chemical is described in this study's conclusion. The creation of two distinct unique compounds through the introduction of salicylaldehyde and 2-nitro benzaldehyde to the 6-amino coumarin molecule, which led to the development of a ligand with a Schiff base, was the originality of the research. The transition metal-ligand complex was created after the ligand was produced and then further complexed with nickel chloride. Data from Infrared, Nuclear

Magnetic Resonance, mass, and Ultraviolet Spectroscopic Methods were used to validate the complex formation. This nickel metal compound exhibits strong anti-fungal properties.

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