Synthesis, Characterization and Antibacterial Activities of Schiff Base derived from quinoline derivative: (E)-2-{[(7-chloro-2-hydroxyquinolin-3-yl) methylene] amino}-3-phenylpropanoic Acid and its Co(II) and Fe(III) Complexes

Ayantu Shimelis Gurmessa

A Thesis Submitted to the Department of Chemistry
School of Applied Natural Science

In partial fulfillment of the requirements for the Master of Degree in Inorganic Chemistry

Office of Graduate Studies
Adama Science and Technology University

January 2024

Adama, Ethiopia

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DECLARATION

I hereby declare that this Master Thesis entitled "**Synthesis, Characterization and Antibacterial Activities of Schiff Base derived from quinoline derivative: (E)-2-{[(7-chloro-2-hydroxyquinolin-3-yl) methylene] amino}-3-phenylpropanoic Acid and its Co(II) and Fe(III) Complexes**" is my original work. That is, it has not been submitted for the award of any academic degree, diploma or certificate in any other university. All sources of materials that are used for this thesis have been duly acknowledged through citation

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We, the advisors of the thesis entitled "**Synthesis, Characterization and Antibacterial Activities of Schiff Base derived from quinoline derivative: (E)-2-{[(7-chloro-2-hydroxyquinolin-3-yl) methylene] amino}-3-phenylpropanoic Acid and its Co(II) and Fe(III) Complexes**" developed by **Ayantu Shimelis Gurmessa,** hereby certify that the recommendation and suggestions made by the board of examiners are appropriately incorporated into the final version of the thesis.

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Co-advisor/Co-supervisor	Signature	Date

APPROVAL OF BOARD OF REVIEWERS

We, the undersigned, members of the Board of Examiners of the thesis entitled "**Synthesis, Characterization and Antibacterial Activities of Schiff Base derived from quinoline derivative:(E)-2-{[(7-chloro-2-hydroxyquinolin-3-yl) methylene] amino}-3-phenylpropanoic Acid and its Co(II) and Fe(III) Complexes"** by **Ayantu Shimelis Gurmessa,** have read and evaluated the thesis and examined the candidate during open defense. This is, therefore, to certify that the thesis is accepted for partial the fulfillment of the requirement of the degree of Master of Science in Inorganic Chemistry.

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Final approval and acceptance of the thesis is contingent upon the submission of its final copy to the Office of Postgraduate Studies (OPGS) through the Department Graduate Council (DGC) and School Graduate Committee (SGC).

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Office of Postgraduate Studies Dean	Signature	Date

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LIST OF ABBREVIAIONS AND ACRONYMS

ASTU	Adama Science and Technology University
ATCC	American-type culture collection
$CDCl_3$	Deuterated chloroform
$(CD_3)_2CO$	Deuterated acetone
^{13}C-NMR	Carbon13-Nuclear Magnetic Resonance
DEPT	Distortion less enhancement by polarization transfer
DMSO	Dimethyl sulfoxide
DEPT	Distortionless Enhancement by Polarization Transfer
FT-IR	Fourier Transform-Infra-Red
^{1}H-NMR	Proton-Nuclear Magnetic Resonance
MHA	Muller Hinton Agar
NMR	Nuclear Magnetic Resonance
S. aureus	*Staphylococcus aureus*
E. coli	*Escherichia coli*
P. aeruginosa	*Pseudomonas aeruginosa*
S. pyogenes	*Streptococcus pyogenes*
UV-Vis	Ultraviolet Visible spectrophotometer
XRD	X-ray diffracction

ABSTRACT

In this study a Schiff base ligand (SBL) and its cobalt (II) and iron(III) complexes have been synthesized. SBL was obtained in high yield as a deep yellow powder, and its elemental composition matched the theoretical value. The cobalt (II) and iron (III) complexes of SBL were prepared in good yields as stable solids and showed experimental elemental compositions matching their proposed formulas. FT-IR and UV-Vis spectra showed shifts indicative of ligand coordination. Thermogravimetric analysis revealed that the complexes decomposed in multiple steps above 100°C, indicating reasonable stability. X-ray diffraction showed that the cobalt (II) complex had an amorphous structure while the iron (III) complex was crystalline.

The complexes exhibited moderate to high antibacterial activity against both gram-positive and gram-negative bacteria. The cobalt (II) complex demonstrated inhibition zones of 6.67 - 10.33 mm while the iron (III) complex showed zones of 6.65 - 7.67 mm. The cobalt (II) complex displayed the higher antibacterial activities than that of iron (III) complex.

Keywords: *Schiff base ligand, quinoline derivatives, cobalt(II) and iron(III) complexes., antibacterial activities*

1. INTRODUCTION

1.1 Background

Coordination chemistry of transition metal complexes is gaining much popularity in the recent years due to their versatile applications in the various fields of chemical and medical sciences and comprises a large body of bio-inorganic chemistry research. It has inspired the chemical researchers to design and fabricate novel metal complexes, all over the world. Metal ions make bridge between the drug substances and pathogenic organisms and thus the field of metal drug interaction chemistry is growing rapidly in the medical and chemical sciences. Microbial interaction with a variety of metal ions at various oxidation states is sometimes beneficial or detrimental that depends on the physical and chemical nature of the metal ions (Abdallah, Mohamed, Zayed, & Abou El-Ela, 2009). Treatment of diseases by pure herbal medicines from nature's chest has been a quest of mankind since ancient times. Currently, there is a substantial decline in the use of pure herbal medicines because of complexity in their chemical extraction and slow interaction with diseases (Dias, Urban, & Roessner, 2012). Pharmaceutical research has expanded after the Second World War to include a massive screening of microorganisms for new antibiotics because of the discovery of penicillin. With the successful record of synthetic medicinal chemistry, the identification of new metabolite from living organisms would be the core pharmaceutical discovery efforts. However, the menace of drug resistance is haunting the medical science and the discovery of synthetic drugs is today's therapeutic desire of pharmaceutical research. Still, many natural product-based drugs are in the clinical practices that need extensive research (Bérdy, 2012).

The first metal-based drug that emerged in the late 19th century was cisplatin whose serendipitous discovery as a potent anticancer drug opened the gate of unexplored world of metal-based chemotherapeutic agents. It was the most effective anticancer drug in the market (Chakraborty, Kumar, Ghosh, & Roy, 2010; Gibson, 2016). The resounding therapeutic success of cisplatin and its analogs has triggered tremendous effort in search of alternative metal-based chemotherapeutic agents in the past few decades. Since then, the metal-drug interaction in the field of coordination chemistry has been focused well and considered as an active field of research (Romero-Canelon & Sadler, 2013). There is a great battle between antibiotic research and increased antibacterial resistance in the medical science which provides ample scope for the generation of a new class of antibiotics with high-grade biological activities. There is an urgency to discover and characterize

new drugs with enhanced activity, selectivity, bioavailability and fewer side effects than conventional drugs to treat current diseases.

The coordination chemistry of transition metals and their derivatives has got much attention in recent years because many of the biological processes which are fundamental to life are controlled by transition metals (Joseyphus & Nair, 2010). Many of these coordination compounds possess remarkable biological properties such as antibacterial, analgesic (Nair, Arish, & Joseyphus, 2012), antifungal, antimalarial (Gemma et al., 2006), antiviral (K. S. Kumar, Ganguly, Veerasamy, & De Clercq, 2010), anticancer (Gwaram & Hassandarvish, 2014), antidiabetic (Sakurai, Kojima, Yoshikawa, Kawabe, & Yasui, 2002), anti-HIV (Patel et al., 2012) activities and plant growth regulating activity (S. Kumar, Dhar, & Saxena, 2009). The O- or N- terminals of proteins can be coordinated to metals in numerous ways and thus can play a vital role in the function of biological macromolecules (Nair et al., 2012). Nitrogen, oxygen and sulphur donor ligands possess a range of biological applications like antitumor, antibacterial, antifungal, antimalarial and antiviral activities (Saadeh, 2013) and they can bind the biomolecules at their active sites (Gull & Hashmi, 2015). Macrocycles which contain nitrogen have a strong tendency to form stable transition metal complexes (Singh, Grover, Kumar, & Jain, 2011). Coordination of bi, tri and tetradentate ligands containing nitrogen, oxygen or sulphur donor atoms with various transition and inner transition metal play an important role in biological systems (Alias, Kassum, & Shakir, 2014).

Dealing with infectious diseases remain an important and challenging problem due to various factors like emerging infectious diseases and the increasing number of multidrug resistant microbial pathogens (Yamgar et al., 2014). Schiff base continue over decades attracts antibiotic designer's attention because of distinctive chelating features. Schiff bases were first discovered by a German chemist, Nobel Prize winner, called Hugo Schiff in the year 1864**.** This has revolutionized the chemical research in the field of coordination chemistry in the late 19th century (Brodowska, Catthoor, Brodowska, Symonowicz, & Lodyga-Chruscinska, 2014). In doing research in aniline chemistry, he studied the reactions of aniline with many other aldehydes and finally reached to the discovery of the imine-based organic compound called Schiff base. They are also called anils, imines or azomethines. This class of compounds is mainly recognized by the presence of an active imine (-CH=N-) group that carry potential binding site for the metal ions through nonbonding electrons of the nitrogen atom (Da Silva et al., 2011). The structural unit of

Schiff bases also possesses many other hetero-elements like oxygen and sulphur as main component elements for chelate formation with metals. The nature of donor atoms that act as coordination site, their electronegativity and steric factors largely determine the bonding ability of the ligands. By virtue of the presence of lone pair electrons on N-atom, electron donating character of the double bond and low electronegativity of nitrogen, N-atom of the azomethine group (>C=N) acts as a very good donor site and Schiff bases are considered as active ligands (Kostova & Saso, 2013).

Schiff bases occupy a leading position in metal coordination chemistry and provide a significant attraction due to their simplicity in preparation, variation in properties, biomedical, biochemical and industrial applications (Jayaseelan, Prasad, Vedanayaki, & Rajavel, 2016). There are several amines and carbonyl compounds in the library of organic chemistry that enable the synthesis of Schiff bases with diverse structural features. For the synthesis of Schiff bases, the basic carbonyl group may be aldehydes (aromatic or aliphatic) or a ketone. The stability of imine group is controlled by the presence of substituent groups attached to (>C=N) linkage.

Schiff bases are very important structures for synthetic organic chemistry. Schiff bases are studied widely due to their synthetic flexibility, selectivity and sensitivity towards the central metal atom; structural similarities with natural biological compounds and also due to presence of azomethine group (-N=CH-) which imports in elucidating the mechanism of transformation and racemization reaction biologically (Abu-Dief & Mohamed, 2015). Recently, many research papers have been published during the last few decades on the synthesis and pharmacology of Schiff base metal complexes.

Thus, the present research work synthesize and characterize a Schiff base ligand (E)-2-{[(7-chloro-2-hydroxyquinolin-3-yl) methylene] amino}-3-phenylpropanoic acid and its Co(II)and Fe(III) complexes. In addition, antibacterial activities of SBL and its Co(II) and Fe(III)complexes were studied using disk diffusion methods (Damena et al., 2022).

1.2. Statement of the Problem

In recent years, ailments caused by bacterial infections have increased significantly and are becoming a serious global health concern. For instance, Gram negative bacteria (Escherichia coli and Pseudomonas aeruginosa) and Gram-positive bacteria (Bacillus subtilis and Staphylococcus

typhi) that infect humans and animals cause various illnesses such as fever, diarrhea and related complications. So, growing interest in metal drug complexes has become a potential field of research in coordination chemistry and medical science. The search for more efficient and safer antibiotics generates the ideas to design and modify the existing drug libraries. Eradication of these diseases and associated complications continues to be hampered by drug resistance developed by these disease-causing organisms. The current research publications of drug substances reveal that the drug resistance has become a great problem in the recent years (Raman, Sakthivel, & Rajasekaran, 2007), for the treatment of many infectious diseases caused by bacterial pathogens and other causative agents. Schiff base complexes are found to have immense application in various fields of sciences. Although a number of chemotherapeutic agents are available in the market there is a global threat in the medical science because the pathogenic organisms are developing resistance to these agents. Therefore, it is important to search more effective and safer chemotherapeutic agents.

No research works related to Schiff base derived from 2,7-dichloroquinoline-3-carbaldehyde and phenylalanine are in the literature search. With this expectation, metal complexes of Schiff bases derived from 2,7-dichloroquinoline-3-carbaldehyde and phenylalanine will be the new hope for better drug substances in the clinical practices.

1.3. Objective of the Study

1.3.1 General objective

The main objective of this research was to synthesize and characterize the Schiff base ligands and their metal complexes and, investigate their antibacterial activities.

1.3.2 Specific objectives

The present research work has been undertaken with the following specific objectives:

- To synthesize Schiff base ligand derived from 2,7-dichloroquinoline-3-carbaldehyde and phenylalanine and characterize its structure by spectroscopic techniques
- To synthesize metal complexes of prepared Schiff base ligand taking Co(II) and Fe(III) salts and analyze their structures by spectroscopic techniques.

- To evaluate antibacterial activities of the Schiff base ligand and its Co(II) and Fe(III) complexes against Gram negative bacteria (Escherichia coli and Pseudomonas aeruginosa) and Gram positive bacteria (*Staphylococcus aureus* and *Streptococcus pyogenes*).

1.4 Significance of the Study

The development in the field of bio-inorganic chemistry has increased the interest in Schiff base complexes, since it has been recognized that many of these complexes may serve as models for biologically important species. These days, the require for more compelling antibacterial and antifungal treatments is squeezing due to the tall mortality rates that are related with bacterial and parasitic maladies as well as the developing number of multidrug-resistant strains. Microbes can quickly develop new features that make them resistant to the drugs. Therefore, there is need to develop novel drug analogues or active agents for the treatment of diseases with better mechanisms of action and structural-activity compared to the classical antibacterial organic molecules. Hence, efforts are being intensified towards the synthesis of metal based active agents with higher efficacy, increased selectivity for disease-causing organisms, lowered toxicity and wider spectrum of activity. Schiff base ligands and their metal ion complexes have been established as potential biochemically active agents.

Even though advanced modern science and technology hails for its invention and innovation to control the infectious diseases, microbial resistance to antibiotics is a severe issue to be confronted and solved. Thus, bioinorganic chemistry opens a new way for new research and development.

No research work related to Schiff base of (E)-2-{[(7-chloro-2-hydroxyquinolin-3-yl) methylene] amino}-3-phenylpropanoic acid is in the literature search. With this expectation, metal complexes of Schiff base derived from 7-dichloroquinoline-3-carbaldehyde and phenylalanine will be a new hope for better drug substances in the clinical practices.

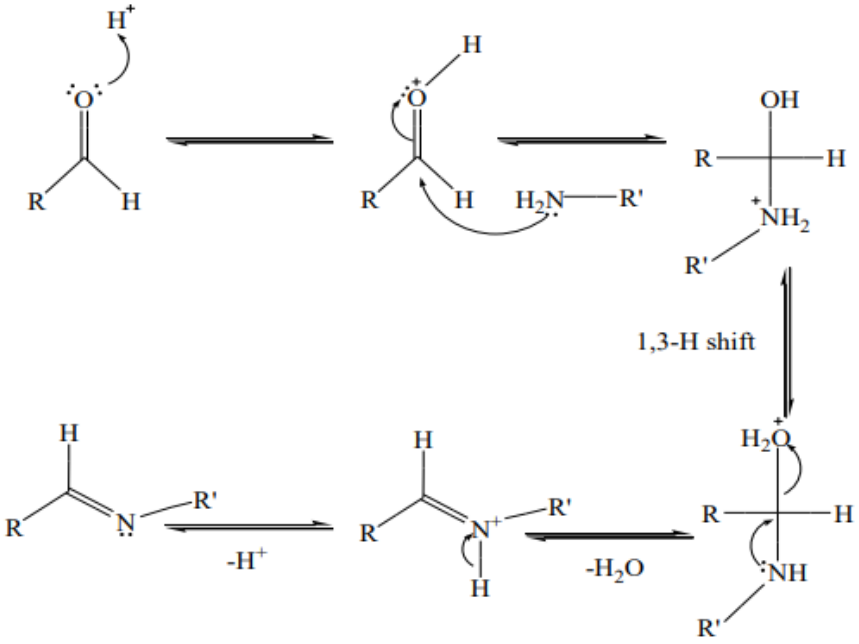
2. LITERATURE REVIEW

2.1 Schiff Base Ligands

The chemistry of the Schiff base ligands and their metal complexes brings much current intrigued and includes a wide region of organometallic compounds and different viewpoints of bioinorganic Chemistry. Schiff bases are considered as advantaged ligands, since they are effectively arranged by condensation of aldehydes or ketones with amines and are able to stabilize distinctive metals in different oxidation states (Levasseur et al., 2023). Schiff base continue over decades attracts antibiotic designer's attention because of distinctive chelating features. Schiff bases were first discovered by a German chemist, Nobel Prize winner, called Hugo Schiff in the year 1864**.** This has revolutionized the chemical research in the field of coordination chemistry in the late 19th century (Brodowska, Sykuła, Garribba, Łodyga-Chruścińska, & Sójka, 2016). In doing research in aniline chemistry, he studied the reactions of aniline with many other aldehydes and finally reached to the discovery of the imine-based organic compound called Schiff base. They are also called anils, imines or azomethines. This class of compounds is mainly recognized by the presence of an active imine (-CH=N-) group that carry potential binding site for the metal ions through nonbonding electrons of the nitrogen atom (Da Silva et al., 2011). The structural unit of Schiff bases also possesses many other hetero-elements like oxygen and sulphur as main component elements for chelate formation with metals. The nature of donor atoms that act as coordination site, their electronegativity and steric factors largely determine the bonding ability of the ligands. By virtue of the presence of lone pair electrons on N-atom, electron donating character of the double bond and low electronegativity of nitrogen, N-atom of the azomethine group (>C=N) acts as a very good donor site and Schiff bases are considered as active ligands (Kostova & Saso, 2013). According to Kejal and coworkers, these compounds form an important class of widely used organic compounds with a wide variety of applications in many fields including analytical, biological, and inorganic chemistry (Kajal, Bala, Kamboj, Sharma, & Saini, 2013). Schiff bases occupy a leading position in metal coordination chemistry and provide a significant attraction in creating novel lead due to their simplicity in preparation, variation in properties, biomedical, biochemical and industrial applications (Jayaseelan et al., 2016).

2.1.1 Synthesis of Schiff base

There are several amines and carbonyl compounds in the library of organic chemistry that enable the synthesis of Schiff bases with diverse structural features. For the synthesis of Schiff bases, the basic carbonyl group may be aldehydes (aromatic or aliphatic) or a ketone. The mechanism of Schiff base synthetic reaction involves a nucleophilic attack of the primary amine through its lone pair of electrons on the electrophilic carbonyl carbon. A 1,3-H shift follows, which facilitates the removal of water to give the protonated imine, with subsequent disassociation of this species to give the Schiff base product as shown in the Scheme 1 (Aljamali, Hadi, Mohamad, Salih, & Aljamali, 2019).



Scheme 1: Mechanism of imine formation (Aljamali et al., 2019)

Where R and R^1 represents an alkyl, aryl, cycloalkyl or heterocyclic groups which may be variably substituted. The formation of Schiff base is a reversible process and generally takes place by refluxing the mixture under the neutral condition or in the presence of acid or base catalysts.

Scheme 1: Mechanism of imine formation 0-1According to Kailas and co-workers, four common methods, namely microwave, room temperature, grindstone and reflux, for synthesizing Schiff bases have been advanced and vary in reaction time, product and percentage yield (Kailas, Sheetal, Anita, & Apoorva, 2016). The microwave method of synthesis is temperature controlled and takes a shorter time to proceed to completion. The use of microwave irradiation can generate localized heating within the reaction mixture, which can accelerate the reaction rates and reduce the reaction

times. This can lead to significantly faster reaction times compared to traditional thermal heating methods. Additionally, it can lead to higher yields of the desired product (Vass, Dudás, & Varma, 1999).

Grindstone method is a newly developed and green way of synthesizing Schiff bases. The pH of an ethanol solution of the aldehyde and the primary amine in a mortar is adjusted by addition of a few drops of citric acid. The solution is then ground using a pestle for five to ten minutes. After the reaction is complete, cold water is added to precipitate out the product. The precipitate obtained is collected by filtration, dried, recrystallized from ethanol and dried at room temperature (Garay, Pichon, & James, 2007; Kailas et al., 2016).

Solvent-based (reflux method) synthesis of Schiff bases typically involves the use of appropriate solvents, such as ethanol or methanol, in which a mixture of an amine and an aldehyde or ketone is refluxed in an acidic, basic, or neutral medium. The solvent helps to promote the reaction between reactants and control the reaction conditions, such as temperature and concentration. The reaction mixture is then refluxed with controlled heating for two to three hours and then cold water added to precipitate out the product. The precipitate is collected by filtration, dried, recrystallized from ethanol and dried at room temperature. This is an important and widely used method, particularly when high-quality products are required and solvent choice is carefully considered (Cao, Crawford, Shi, & James, 2020).

Room temperature method entails the addition of a solution of an aldehyde to a primary amine in ethanolic solution in a reaction vessel. The pH of the resulting mixture is adjusted by addition of two to three drops of sodium hydroxide. The reaction mixture is then magnetically stirred for one to two hours at room temperature and cold water added to precipitate out the product. The precipitate obtained is collected by filtration, dried, recrystallized from ethanol and dried at room temperature. This method gives the best yield and easily forms the product (Garay et al., 2007).

In this study, the solvent method was used to prepare the SBL because the method is an important and widely used method, particularly when high-quality products are required and solvent choice is carefully considered. The complexes on the other hand were prepared using the aqueous based reflux method. This is because the method is simple, low cost and gives the desired product with precise control over reaction parameters.

2.1.2 Application of Schiff bases

The compounds containing azomethine group known as Schiff bases, are an excellent class of ligands that show a lot of biological importance as well as wide range of applications (Althobiti & Zabin, 2020). These include application in coordination chemistry, agriculture, in synthesis and chemical analysis, and in medicine and pharmacy. Schiff base had recognized as a significant class of biologically active molecules, which has gained key attention of medicinal chemists attributable to their broad range of pharmacological properties. Many researchers have synthesized these compounds to battle various diseases with the minimum toxicity and maximum effects (Patil & Vibhute, 2021).

2.1.2.1 Application of Schiff bases in coordination chemistry

Schiff bases are very important structures for synthetic coordination chemistry. Transition metal complexes of Schiff bases are generally formed by the chelation of Schiff base ligands with metal ions at variable oxidation states. The vacant d-orbitals of metal ions make available space for the easy coordination of nonbonding electrons of donor atoms of ligand and even sometimes this ligation takes place by deprotonation process. There is a general rule of coordination chemistry that chelation makes the complex compounds more stable due to electron circulation inside the ring and changes the physiological profile of the complexes (Sumrra et al., 2014). In fact, their stability increases when the chelate ring is five or six member. The aryl group bonded to the nitrogen or to the carbon of the azomethine group prevents them from rapid decomposition and polymerization. A lone pair electron in sp^2 hybrid orbital of azomethine nitrogen is of considerable chemical and biological importance since it makes easy coordination with metals. Variation in the denticity of Schiff bases makes control over the stereochemistry of metal complexes which affects in their physiological profiles. These complexes carry a wide range of applications in catalytic chemistry, analytical, clinical and biochemical fields and in addition, they also possess considerable physiological activities. Multifunctional activities of such metal complexes are the prime sources of metal-based research in the chemical science (Abou-Hussein & Linert, 2014; Cozzi, 2004; Shebl, 2014).

2.1.2.2 Application of Schiff bases in medicine and pharmacy

Schiff bases are studied widely due to their synthetic flexibility, selectivity and sensitivity towards the central metal atom; structural similarities with natural biological compounds have a broad

range of biological properties which include: antitumor, antiviral, antifungal, antibacterial activities. This is mainly due to presence of azomethine group (-N=CH-) which imports in elucidating the mechanism of transformation and racemization reaction biologically (Abu-Dief & Mohamed, 2015). Schiff base had recognized as a significant class of biologically active drug molecules, which has gained key attention of medicinal chemists attributable to their broad range of pharmacological properties. Many researchers have synthesized these compounds to battle various diseases with the minimum toxicity and maximum effects (Patil & Vibhute, 2021).

Quinoline is classified under the alkaloid class of natural products and is present in various plants, pharmaceuticals, agrochemicals, and dyes. It had used as a chelating agent due to its N-donor ligands in coordination chemistry to form complexes. Quinoline and its derivatives have numerous applications in the biological field with diverse pharmacological properties. Interesting pharmacological properties have been associated with quinoline derivatives like 2-oxo-quinoline, 2-chloro-quinoline, and 2-chloroquinoline-3-carbaldehyde shows antimicrobial, antimalarial, anti-inflammatory, antitumor, anti-parasitic, antiproliferative, antineoplastic, antidiabetic, antifungal, anticonvulsant, antiviral and anticancer activities (Patil & Vibhute, 2021; Rajewar, Dharmale, & Pingalkar, 2015).

Schiff bases continue to be of great interest, owing to their inherent biological activities, versatile metal binding properties, and flexibility to modify the structure to fine-tune it for a particular biological application (Malik, Dar, Gull, Wani, & Hashmi, 2018). Imines derived from chloroaniline and salicyladehyde, specifically, have been considered as potential pharmaceutically interesting compounds. This is because; several of the members of this family have shown antiviral, antitumor or antimicrobial activities (Ma et al., 2002; Siddiqui, Iqbal, Ahmad, & Weaver, 2006). These biological activities are attributed to the imine group, the C=N linkage. As biological models, they help in understanding the structure of biomolecules and biological processes occurring in living organisms. The bases have also been identified as promising antibacterial, antiviral, anticancer agents and often tested as antimalarial (Malik et al., 2018). For example, N-(Salicyldene)-2-hydroxyaniline is active against M. tuberculosis (Ommenya, 2021). Imine derivatives of N-hydroxy-N'-aminoguanidine exhibited a high antitumor activity. The imine blocks ribonucleotide reductase in tumor cells, and is used in the treatment of leukemia (Ommenya, 2021). Thus, Schiff bases are being researched upon deeply owing to their unique and important role in coordination chemistry and medicine.

2.1.2.3 Application of Schiff bases in some more areas

Schiff bases and their complexes have been extensively studied for their interesting and significant properties. These compounds exhibit a wide range of chemical and biological activities, making them useful in a variety of applications. One of the most notable properties of Schiff bases and their complexes is their ability to reversibly bind oxygen. This property has made them useful in the development of oxygen carriers for biomedical applications. Schiff bases have also been found to exhibit catalytic activity in the hydrogenation of olefins, making them useful in the production of fine chemicals (Igota et al., 2013).

Another important property of Schiff bases is their photochromic properties. These compounds can undergo reversible color changes upon exposure to light, making them useful in the development of photochromic materials. Schiff bases have also been found to exhibit complexing ability towards some toxic metals, making them useful in the development of chelating agents for metal detoxification. Additionally, Schiff bases have played a special role as chelating ligands in main group and transition metal coordination chemistry, due to their stability under a variety of oxidative and reductive conditions. The imine ligands in Schiff bases are borderline between hard and soft Lewis bases, making them useful in a variety of applications where ligand selectivity is important. This unique property has made Schiff bases and their complexes valuable tools in the development of new catalysts, sensors, and materials. The diverse and interesting properties of Schiff bases and their complexes make them important compounds in a wide range of fields, including chemistry, biology, and materials science (Igota et al., 2013).

The high affinity of Schiff bases towards transition metal ions is often utilized in the preparation of their solid complexes. The chelating ability of Schiff bases arises from their ability to coordinate with metal ions through the nitrogen and oxygen atoms in the imine and/or amine functional groups. This coordination can lead to the formation of stable complexes, which can be useful in a variety of applications. Solid complexes of Schiff bases and transition metals are of particular interest due to their potential applications in catalysis, sensing, and materials science. These complexes can exhibit unique and tunable properties, depending on the choice of metal ion and Schiff base ligand. For example, the electronic properties of the metal ion can influence the catalytic activity of the complex, while the structure of the Schiff base ligand can affect the stability and selectivity of the complex (Sobola, Watkins, & Van Brecht, 2014).

In addition to their chelating ability, Schiff bases and their metal complexes can exhibit a range of other interesting properties, such as the ability to reversibly bind oxygen, catalytic activity in hydrogenation of olefins, transfer of an amino group, and photochromic properties. These properties have made Schiff bases and their complexes important compounds in a wide range of fields, including chemistry, biology, and materials science. The chelating properties of Schiff bases and their ability to form stable complexes with transition metal ions make them valuable compounds for a variety of applications. The ability to tailor the properties of these compounds through choice of metal ion and Schiff base ligand make them particularly useful in the development of new materials and catalysts (Sobola et al., 2014).

2.2. The Chemistry of Transition Metal Complexes of Schiff Bases

Schiff bases are versatile pharmacophores that cave in metal ions within their structural unit due to the presence of various donor atoms (Kostova & Saso, 2013). Transition metal complexes of Schiff bases are generally formed by the chelation of Schiff base ligands with metal ions at variable oxidation states. The vacant d-orbitals of metal ions make available space for the easy coordination of nonbonding electrons of donor atoms of ligand and even sometimes this ligation takes place by deprotonation process. There is a general rule of coordination chemistry that chelation makes the complex compounds more stable due to electron circulation inside the ring and changes the physiological profile of the complexes (Sumrra et al., 2014). In fact, their stability increases when the chelate ring is five or six members. The aryl group bonded to the nitrogen or to the carbon of the azomethine group prevents them from rapid decomposition and polymerization. A lone pair electron in sp^2 hybrid orbital of azomethine nitrogen is of considerable chemical and biological importance since it makes easy coordination with metals. Variation in the denticity of Schiff bases makes control over the stereochemistry of metal complexes which affects in their physiological profiles. These complexes carry a wide range of applications in catalytic chemistry, analytical, clinical and biochemical fields and in addition, they also possess considerable physiological activities (Abou-Hussein & Linert, 2014; Cozzi, 2004; Shebl, 2014). Multifunctional activities of such metal complexes are the prime sources of metal-based research in the chemical science. Many drug substances have the metal ion that plays a key for the better success of biological activities (Barnham & Bush, 2014). Several research papers describe the enhanced activities of metal complexes compared to the free ligand. Recently a large volume of research reports on Schiff bases

highlights them as a type of potential antibiotic which by chelation with metals further enhance their potency. Chelation causes a drastic change in the biological properties of the ligands and the metal moiety (Majumder, Panda, & Choudhuri, 2003). It has been reported that chelation is the cause and cure of many diseases including cancer. The present study of the research focuses the formation of several Schiff base ligands from different precursor compounds and their metal complexes with 3d-metal ions.

Metal complexes have received overwhelming attention due to the ease of their preparation and structural variability. Metal complexes play critical part in numerous natural system. It has been observed that metal particles have significant impact on the antimicrobial movement of antibiotics. Similarly metal particles are known for their antitumor movement (Liang et al., 2017). Transition metal complexes derived from Schiff base ligands with promising biological activity are the focal point of extensive investigations in coordination chemistry due to their improvement in biological activities as compared to non-Schiff base complexes (Gul et al., 2024).

Transition metal complexes with Schiff base ligands have been extensively synthesized and studied due to their various advantages and applications. Schiff bases offer flexible chemistry by allowing modifications to their structure, yielding complexes with different properties. This has made Schiff base complexes useful for a wide range of biological, photochemical and catalytic applications.

Biologically, Schiff base metal complexes have shown antimicrobial, anticancer, anti-inflammatory and enzyme inhibitory activities. This is attributed to their ability to interact with biomolecules like proteins and DNA via chelation. Schiff base complexes have also been found to exhibit photochromic effects, changing color reversibly when exposed to certain wavelengths of light.

Schiff base complexes play an important role as catalysts in homogenous and heterogeneous reactions. The presence of donors like nitrogen and oxygen atoms in the ligand allows efficient binding of substrates and activation of reactants. This catalytic activity has enabled the use of Schiff base complexes as agrochemicals for crop protection. The ease of synthesis, structural versatility and coordination flexibility of Schiff bases make them ideal ligands for forming stable complexes with transition metals. By modifying the aryl groups and substituents on the Schiff base

ligand, complexes with tailored properties and reactivity can be obtained. In summary, the diverse applications of transition metal Schiff base complexes arise from their ability to form stable structural motifs with variable characteristics. This tunability, stemming from the modifiable Schiff base ligands, has fueled the extensive synthesis and study of these complexes for biological, photochemical and catalytic purposes (Tan, Yang, Zheng, Sarwar, & Yang, 2023).

2.2.1 Biological Applications of Schiff Bases and Their Metal Complexes

Recent advances in coordination chemistry reveal Schiff base as a privileged ligand since most of the bio-molecules in the living system are structurally similar to this class of compound. The biofunctional activity of metal-based complexes in medicine and chemotherapy has spurred the growth of interest in the scientific world in the past few decades, after the successful clinical application of Cisplatin as a potential anticancer drug. So, metal drug interaction in medical science is becoming a subject of great research interest (Hannon, 2007; Reedijk, 2008). Transition metal chemistry of Schiff bases has gained momentum in the late 19th century and since then metal-based drugs of Schiff bases drew the significant interest of researchers in the medical science for their immense biological activities. Most of the metals being unnatural to the human body, because of having no effective mechanism for their rejection and toxic behavior (Murtaza et al., 2012), there has been a rapid expansion in research and development of novel metal-based drugs with improved pharmacological properties. Several medical problems that arise due to free metal ions toxicity may be ameliorated by their chelation with ligands.

Schiff base metal complexes have important biological applications as antibacterial, antifungal, antitumor, analgesic, anti-inflammatory and antimicrobial agents. It has found, that some drugs have greater activity when administered as metal complexes than as free organic compound (Shoaib, Rahman, Shah, & Umar, 2015).

Antibacterial activity of such ligand containing donor atoms can be enhanced significantly by coordination to a metal ion (Al-Redha, Ali, & Mohammed, 2022). The compounds containing azomethine group known as Schiff bases, are an excellent class of ligands and widely used in coordination chemistry (Althobiti & Zabin, 2020). Schiff base had recognized as a significant class of biologically active drug molecules, which has gained key attention of medicinal chemists attributable to their broad range of pharmacological properties. Many researchers have synthesized

these compounds to battle various diseases with the minimum toxicity and maximum effects (Patil & Vibhute, 2021).

The enlargement in the branch of bio-inorganic chemistry has expand the interest in Schiff base metal complexes, since many of the Schiff base metal complexes may distribute as modal for important biological applications (Yadav, Sarkar, & Kumar, 2019). Schiff base metal complexes with nitrogen, sulfur and oxygen donors have been exhibited wide range of biological activities. Schiff base compound have been taken considerable attention by many researchers for many reasons like ease of preparation, stability, in addition to its wide applications in various fields. Schiff base transition-metal complexes used in pharmaceutical and medicinal chemistry since the discovery of cisplatin. Several coordination compounds of metal ions (chromium, cobalt, copper, manganese, molybdenum, palladium, ruthenium, tungsten, vanadium, and zinc) have been applied in the treatment of various diseases owing to their antimicrobial and antioxidant, anticancer, antiproliferative, anti-inflammatory, antitumor and antidiabetic activities.

2.2.2 Other Applications of Schiff Bases and Their Metal Complexes

Schiff base metal complexes also bear various important applications in chemical, industrial and electronic fields. In the material science, they are found to have good corrosion inhibitory activity (Madkour & Elroby, 2015). This phenomenon is the spontaneous formation of a monolayer on the surface to be protected. A large number of Schiff base metal complexes are identified by an excellent catalytic activity in a variety of synthetic chemical reactions at high temperature (> 100 °C) and in the presence of moisture. Many research reports display their use in homogeneous and heterogeneous catalysis. In many biological systems, Schiff bases and metal complexes show active participation in the synthesis of some life molecules like enzymes and biopolymers (Hameed, Al-Rashida, Uroos, Abid Ali, & Khan, 2017). Numerous scientific publication reports, appearing annually in the recent years, highlight the keen interest of researchers in metal complexes in which Schiff bases play a critical role as ligands. Due to excellent selectivity, sensitivity and stability of Schiff bases for specific metal ions, a large number of Schiff base ligands have been used as cation carriers in potentiometric sensors.

Schiff bases and metal complexes deliver important applications because of their photo- and thermochromic properties (Rawat, Mal, & Singh, 2015). They have applications in optical computers, to measure and control the intensity of radiation, in imaging systems, as well as in the molecular memory storage devices. Due to photochromic properties, they function as photo stabilizer, dyes for solar collectors and solar filters. Schiff bases can also be used as stationary phase in gas chromatography, due to their thermal stability (Lodyga-Chruscinska et al., 2015).

Transition metal complexes are powerful catalysts for various organic transformations. They play important roles in oxidative processes employed in laboratory synthesis and chemical industries. In the recent years, Schiff bases and their metal complexes have been extensively investigated due to their wide range of applications as valuable catalysts. The Schiff base compounds have the ability to stabilize many metals in various oxidation states and control the performance of metals in several catalytic transformations. The Schiff bases and their transition metal derivatives are known to possess catalytic activity for the oxidation of alcohols and alkenes in several synthetic organic reactions because of their cheap, easy synthesis, their thermal and chemical stability. (Abdel-Rahman, Abu-Dief, Ismael, Mohamed, & Hashem, 2016)(AbdelRahman et al. 2016) have synthesized a new series of hexa-coordinated Cu(II) complexes of tri and tetradentate Schiff base ligands. The ligands were prepared by the condensation of 2-hydroxy-1-naphthaldehyde with 2-aminopyridine for npap ligand, 4-nitro-o-phenylenediamine with isatin and 5-bromosalicylaldehyde for bsisnph and 4-nitro-o-phenylenediamine with isatin and 2-hydroxy-1-naphthaldehyde for npisnph ligands. These ligands were derivatized for copper (II) complexes. The resulted compounds were tested for catalytic oxidation of benzyl alcohols to corresponding aldehydes and ketones. The detailed investigation showed that copper complex of bsisnph Schiff base ligand possesses excellent catalytic activity than other compounds.

Various lanthanide and ruthenium compounds are also known to possess excellent catalytic activity in several organic synthetic chemical reactions and deserve themselves as a very good catalyst. In the similar work of (Bhowon et al. 2004), some ruthenium and lanthanide Schiff base complexes derived from pyrrole-2- carboxaldehyde and 3,4-diaminotoluene, 1,2-diaminocyclohexane, 1,8- diaminonaphthalin, 1,3-diaminopropane, 1,2-phenylenediamine, 1,2-diaminoethane and aminophenol were prepared and characterized. They have been investigated as catalysts for the oxidation of primary alcohols in the presence of Nmethylmorpholine-N-oxide as

an oxidant. The catalytic activity results revealed that the synthesized metal complexes of Schiff bases were found to be better catalysts than other ruthenium and lanthanide catalysts.

2.3 Choice of Ligand and Metallo-Elements under Investigation

2.3.1 Quinoline derivative Ligands

Quinoline is classified under the alkaloid class of natural products and is present in various plants, pharmaceuticals, agrochemicals, and dyes. It had used as a chelating agent due to its N-donor ligands in coordination chemistry to form complexes. Quinoline and its derivatives have numerous applications in the biological field with diverse pharmacological properties. Interesting pharmacological properties have been associated with quinoline derivatives like 2-oxo-quinoline, 2-chloro-quinoline, and 2-chloroquinoline-3-carbaldehyde shows antimicrobial, antimalarial, anti-inflammatory, antitumor, anti-parasitic, antineoplastic, antidiabetic, antifungal, anticonvulsant, antiviral and anticancer activities (Hegazy, Hasan, Emara, Bakr, & Youssef, 2012; Patil & Vibhute, 2021).

2.3.2.1 Cobalt

Cobalt belongs to first-row transition metal series and displays three oxidation states, +1, +2 and +3. Its +3 oxidation state is extremely unstable but nevertheless is important in biology. +2 oxidation state of the cobalt is the most stable and bears significant importance in the biological system. It is an essential element for life in a very trace amount and constitutes a central component of the vitamin B12 (cyanocobalamin), which is essential in protein formation and DNA regulation. Cobalt is used to treat anemia in pregnant women because it stimulates the production of red blood cells (RBC). However, its high concentration may damage human health (Sinha, 2014)(Sinha, 2014). Several literatures reveal important bio-functions of cobalt complexes as having antibacterial, anti-tumor and others.

2.3.2.2 Iron

Iron belongs to first-row transition metal series and displays two oxidation states, +2 and +3. Its Both oxidation state is stable and is important in biology. It is an essential element for life and constitutes a central component of the hemoglobin, which is essential in oxygen transport. Iron is used to treat anemia in pregnant women because it stimulates the production of red blood cells

(RBC). Several literatures reveal important bio-functions of iron complexes as having antibacterial, anti-tumor antiulcer and others.

2.4 The Chemistry of Co(II), and Schiff base Complexes

Metal complexes of Schiff bases derived from substituted salicylaldehyde and various amines have been widely investigated because of their wide applications such as: pigments, dyes, catalysts, intermediates in organic synthesis and as polymer stabilizers (Sakhare, 2020).

Cobalt (II) complex of a tridentate Schiff base from a salicylaldehyde derivative on Cesium matrix was also prepared and structurally characterized regarding its supra molecular structure on the basis of XRD data revealing a distorted octahedral character for the complex. The syntheses and crystal structures of the mononuclear nickel (II) complexes with Schiff-base ligands derived from the epimeric sugars glucosamine (2-Amino-2-deoxy-D-glucopyranos,$C_6H_{13}NO_5$) and mannosamine (2-amino-2-deoxymannose, $C_6H_{13}NO_5$) are reported (Wen, Liu, & Huang, 2019).

2.5 The Chemistry of Fe(III) and Schiff base Complexes

A novel Fe(III) complex of Schiff's base derived from phenylacetylurea condensed with salicylaldehyde (SBPS) and thiocyanate(SCN-) ion synthesized by using microwave irradiation tested against *E.coli, Klebsiella Pneumonia, P.aeurginosa, S. aureus, Bacillus cereus. Aspergillusflavus, Aspergillusniger, Aspergillusoryzae, Aspergillussojae* using agar-well diffusion method and the complex did not show activity against the tested. Whereas, the antifungal activity of the complex showed enhanced activity against *Aspergillus sojae* (30mm), moderate activities against *Aspergillus flavus* (23mm) and *Aspergillus niger* (24mm), and low activity against *Candida albicans* (21mm) using the same technique (Govindharaju et al., 2019). On the other hand, a synthesis of series of metal ions, such as Cr(III), Fe(III) and Co(III) complexes of tetradentate (ONNO) Schiff base ligands showed antibacterial activity against the bacteria: *Escherichia coli* (ATCC 11230), *Yersinia enterocolitica* (ATCC 1501), *Bacillus magaterium* (RSKK 5117), *Bacillus subtilis* (RSKK 244), *Bacillus cereus* (RSKK 863) and the fungi: *Candida albicans* (ATCC 10239) (Keskioğlu, Gündüzalp, Cete, Hamurcu, & Erk, 2008)

2.6 Synthesis of Transition Metal Complexes of Schiff Bases

2.6.1.1 Conventional or Wet Chemical Method of synthesis of Metal Complexes of Schiff Bases

The conventional or wet chemical method for the preparation of metal complexes typically involves stirring and refluxing a mixture of metal salts and Schiff bases in a suitable solvent, such as ethanol. This method allows for the controlled formation of metal complexes through the coordination of the metal ion with the functional groups in the Schiff base ligand. The reaction is typically carried out under controlled conditions of temperature and time, to ensure production of the desired product. After the reaction is complete, the metal complex is washed with alcohol to remove any unreacted starting materials or impurities. The complex is then dried and purified for further characterization and use (Siddappa & Reddy, 2012).

The wet chemical method is a versatile and widely used approach for the preparation of metal complexes. It allows for the synthesis of a wide range of metal complexes with different metal ions and Schiff base ligands. The method is relatively simple and straightforward, making it suitable for large-scale production. In the specific example mentioned, a metal complex with a carbonyl releasing Schiff base chelate was synthesized using the wet chemical method.

2.6.1.2 Template synthesis Method of synthesis of Metal Complexes of Schiff Bases

Template synthesis is a single step synthesis of metal complexes, i.e., without the isolation and purification of the ligand, the complex is synthesized. It is an in situ reaction (Kumbalpuri, Kachare, Shankarwar, & Chondhekar, 2015). The condensation of carbonyl compound and amine, and the coordination of metal takes place in a single step reaction (Mukherjee, Sengupta, Drew, & Ghosh, 2009). Template can be defined as “any species that organizes an assembly of molecular building blocks by non-covalent interaction favoring of a specific product” (Busch, 1992) Template synthesis is a useful technique to achieve the synthesis of assemblies that have unusual topologies such as macro cycles, rotaxanes, helicates and catananes (Neelakantan et al., 2008).

Template synthesis can be carried out in several ways, thermodynamic, microwave irradiation and ultra-sonication method. In thermodynamic processes, one of the reactants binds the template and equilibrium is formed. This equilibrium is shifted towards the formation of a specific product. Microwave irradiation is an irreversible process leading to the formation of wanted product. In this case the reaction is very fast and shorter time with high yield. In recent years, microwave-assisted

synthesis has gained much attention because is pollution free, eco-friendly, low cost and offers high yields, simple process and handling (Busch, 1992).

2.6.2 Synthesis of Transition Metal Complexes with Schiff Base Ligands

Schiff bases are compounds that contain azomethine or imine (-C=N-) functional groups. The imine functional group in Schiff bases acts as a donor atom and provides binding sites for transition metal ions through coordination. Transition metals can form stable complexes by binding to the donor nitrogen atom, as well as other heteroatoms like oxygen and sulfur present in the Schiff base ligand (Wen et al., 2019).

The synthesis of transition metal complexes with Schiff base ligands typically requires a few key components. An aromatic aldehyde is reacted with an amine to form the Schiff base ligand. A transition metal salt like a chloride or acetate salt is then added along with a base to deprotonate the ligand and facilitate its coordination to the metal ion. Triethylamine is often used as the base to make the reaction medium more basic. This helps deprotonate the ligand and generates the nucleophilic anion that can then coordinate to the metal ion. A weak acid like acetic acid is sometimes added to the reaction to prevent precipitation of the metal hydroxide (Wen et al., 2019). Upon ligand coordination and complex formation, several physical changes can be observed. The solution color typically changes, indicative of metal-ligand charge transfer transitions. Precipitation of the complex from the reaction mixture may also occur. The complex product can then be isolated by filtration, washed and dried for further characterization. The imine group in Schiff bases provides a donor atom for binding transition metal ions (Halabi & Strumia, 2000).

2.7 Antimicrobial Activities of transition metal complexes of Schiff Base Ligands

Antibacterial activity of such ligand containing donor atoms can be enhanced significantly by coordination to a metal ion(Al-redha, Ali, and Mohammed 2022). The compounds containing azomethine group known as Schiff bases, are an excellent class of ligands and widely used in coordination chemistry(Hanan A. Althobiti 2020). Schiff base had recognized as a significant class of biologically active drug molecules, which has gained key attention of medicinal chemists attributable to their broad range of pharmacological properties. Many researchers have synthesized these compounds to battle various diseases with the minimum toxicity and maximum effects(Patil and Vibhute 2021).

The enlargement in the branch of bio-inorganic chemistry has expand the interest in Schiff base metal complexes, since many of the Schiff base metal complexes may distribute as modal for important biological applications(Yadav, Sarkar, and Kumar 2019). Schiff base metal complexes with nitrogen, sulfur and oxygen donors have been exhibited wide range of biological activities. Schiff base compound have been taken considerable attention by many researchers for many reasons like ease of preparation, stability, in addition to its wide applications in various fields (Acid et al. n.d.). Schiff base transition-metal complexes used in pharmaceutical and medicinal chemistry since the discovery of cisplatin. Several coordination compounds of metal ions (chromium, cobalt, copper, manganese, molybdenum, palladium, ruthenium, tungsten, vanadium, and zinc) have been applied in the treatment of various diseases owing to their antimicrobial and antioxidant, anticancer, antiproliferative, anti-inflammatory, antitumor and antidiabetic activities.

2.8 Characterization Techniques

Ligands and their complexes are characterized by their physical (melting point, color, solubility), elemental analysis, thermal analysis, magnetic susceptibility, electro-chemical (conductance measurements and cyclic voltammetry) and spectral (UV–Visible, FTIR, 1HNMR, ^{13}C NMR, and mass analysis) analytical techniques. FT-IR spectral studies revealed coordination of different functional groups of Schiff bases including OH, NH, CO, HC=N and azomethine, nitrogen. Electronic absorption spectra and magnetic susceptibility measurements indicate the electronic structure of the metal ion in the complexes. The electrochemical behavior (redox behavior) of the metal complexes is studied by cyclic voltammetry. Conductance data indicate electrolytic nature of metal complexes. Based on all the experimental results coordination behavior of ligands and geometry of metal complexes are proposed. Thermal stability as well as decomposition mechanisms of Schiff base and its complexes are analyzed by thermogravimetric measurements under an inert atmosphere. X-ray crystallography analysis revealed complexes of Schiff bases to have similar molecular structures providing bond lengths and angles. The structure of the complexes proposed from experimental analysis is validated using quantum mechanics calculations based on density functional theory (DFT) methods. Frontier molecular orbital's (FMOs) and natural bonding orbital's (NBOs) analysis performed by computational analysis (Fu, Uddin, & Zhang, 2020).

3. MATERIALS AND METHODS

3.1 Chemical and Reagents

All chemicals and reagents have been obtained from commercial sources with high quality and were directly used as purchased without any further treatment.

The following chemical and reagents were used: 2,7-dichloroquinoline-3- carbaldehyde, (E)-2-{[(7-chloro-2-hydroxyquinolin-3-yl) methylene] amino}-3- phenylpropanoic acid, cobalt (II) chloride ($CoCl_2$) and Iron (III) chloride ($FeCl_3$), hydrochloric acid, methanol, distilled water, ethanol, and DMSO. The Schiff base and metal complexes were prepared by standard methods.

To perform this thesis, the following chemical and reagents were used. 2,7-dichloroquinoline-3-carbaldehyde, HCl (E)-2-(((7-chloro-2-hydroxyquinolin-3-yl) methylene) amino)-3-phenylpropanoic acid, metal salt (MX2, where M= Co (II) and Fe(III) where X= Chloride Cl_2), methanol, distilled water, ethanol, and DMSO. All the chemicals such as 2-hydroxybenzaldehyde, aromatic amine, metal salts, and other solvents used would be of analytical graded. The Schiff bases and metal complexes was prepared by standard methods.

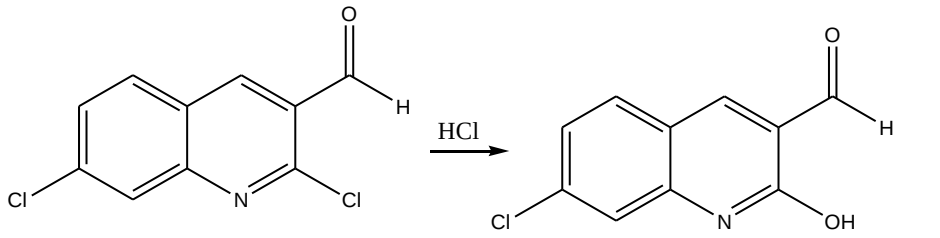
3.2 Instruments and Apparatus

In this study the following apparatus were used to achieve the expected results. The ^{1}H- and ^{13}C-NMR spectra of the Schiff base ligands were recorded on NMR gear working at 400 MHz utilizing deuterated chloroform with TMS as internal standard. The FT-IR assimilation spectra and of the compounds were recorded in the wavelength range of 4000 - 400 cm using Perkin Elmer Range 100 FT-IR and Perkin Elmer Lambda 25 spectrophotometer, respectively. The FT-IR spectrometer were prepared with all-inclusive constricted add up to reflectance (ATR) adornment. The Elemental analyses examination, CHN, were done on Vario Smaller scale V1.6.2 natural analyzer framework GmbH, whereas the softening focuses (uncorrected) of the compounds were decided utilizing the Galenkemp softening point device. Electronic spectra, ultraviolet-Visible spectra were recorded employing Perkin Elmer Lamda Spectrophotometer within the range of 200–800 nm.

3.3 Synthesis of SBL:(E)-2-{[(7-chloro-2-hydroxyquinolin-3-yl) methylene] amino}-3-phenylpropanoic Acid

An equimolar 0.016 mol of HCl and 2,7-dichloroquinoline-3-carbaldehyde was mixed in 30 mL of ethanol in a beaker. And this solution was slowly poured to a solution of equimolar 0.016 mol

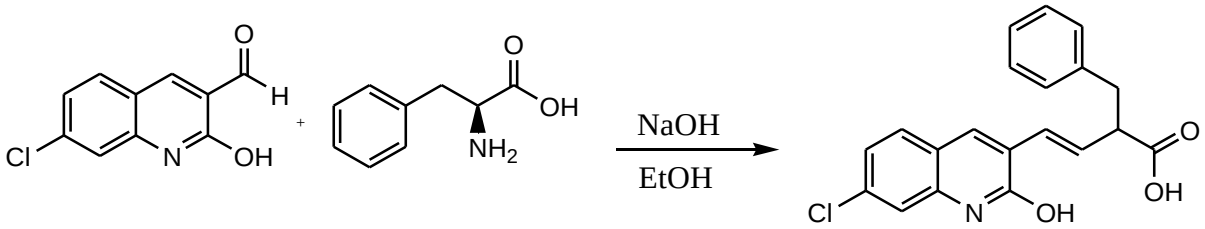
of a mixture prepared in another beaker by dissolving NaOH and Phenylalanine at room temperature under continuous stirring. After the solution was mixed in the two beakers the reaction was allowed to stand for one hour and the reaction completion was followed using TLC. Then, acetic acid (0.016 mol) was added and the mixture kept overnight at room temperature. The resulting pale-yellow solid was filtered using Whatman filter paper and dried at room temperature.



2,7 dichloroquinoline-3-carbaldehyde — 7 chloro-2-hydroxyquinoline-3-carbaldehyde

Scheme 2. 7-chloro-2-hydroxyquinoiline-3-carbaldehyde formation

ligand was prepared by adding a solution of 4-chloro-o-phynelendiamine 0.71 g; 5 mmol in 20 mL of hot ethanol drop wise with continuous stirring to a solution of 5-bromo-salicyaldehyde (2.01 g; 10 mmol) in 20 mL hot ethanol too. The reaction mixture was refluxed for 2hrs at 70 ^{0}C. The resulting deep orange solid was filtered off, purified by washing several times with diethyl ether and recrystallized from ethanol (Abdel-Rahman et al., 2022).

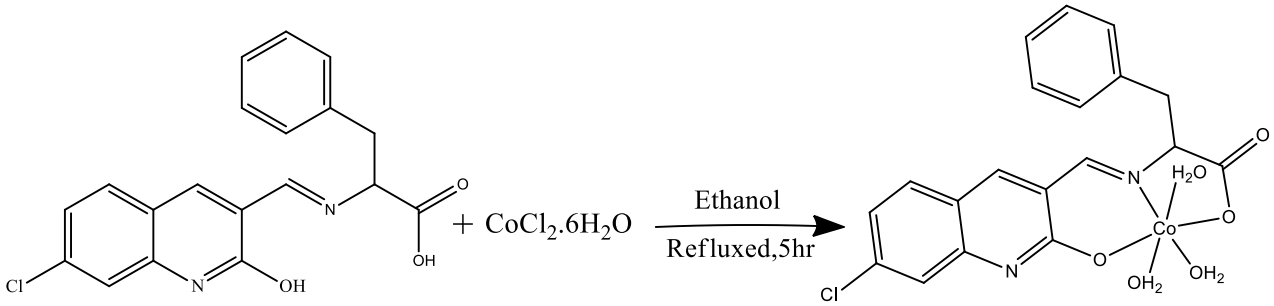


Scheme 3. (E)-2-{[(7-chloro-2-hydroxyquinolin-3-yl) methylene] amino}-3-phenylpropanoic acid formation

3.4 Synthesis of Cobalt(II) Complex of the Schiff Base

Cobalt(II) complex of the quinoline derivative was prepared by mixing a 2g $CoCl_2 6H_2O$ salt into 40 mL of ethanol and continuous stirring at room temperature. To the other reaction vessel, SBL was added to 50 mL of ethanol. Then after the two solutions were mixed into 250 mL round bottom flask, the pH of solution was adjusted to 6-8 using 25% ammonia solution at room temperature. The reaction mixture was then refluxed on an oil bath for 5 h at 75 – 80 ^{o}C while continuous stirring and the progress of the reaction was monitored using TLC. After completion

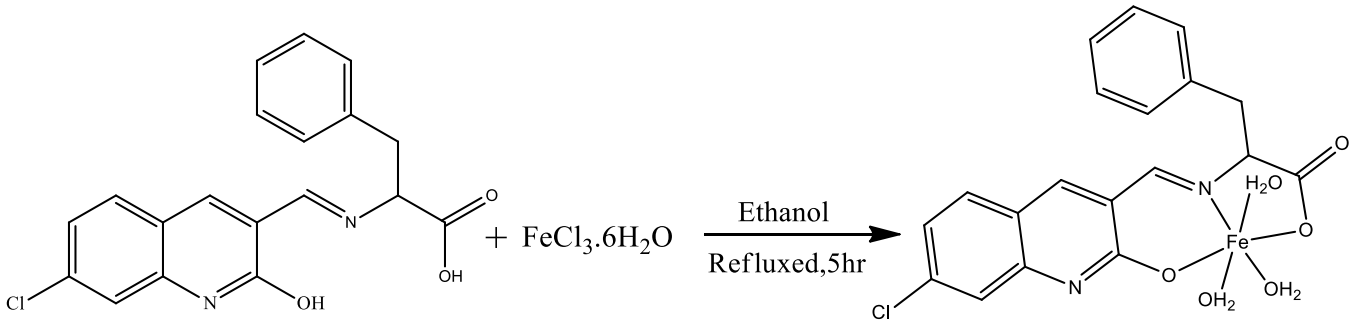
of the reaction, the mixture was cooled down to room temperature and filtered using Whatman paper and washed repeatedly using ethanol and then dried in a desiccator over anhydrous calcium chloride (Damena et al., 2022; Yamgar et al., 2014).



Scheme 4. Synthesis of Cobalt(II) complex of SBL

3.5 Synthesis of Iron (III) Complex of the Schiff Base

Iron (III) complex of the quinoline derivative was prepared by mixing a 2g $FeCl_36H_2O$ salt into 40 mL of ethanol and continuous stirring at room temperature. To the other reaction vessel, SBL was added to 50 mL of ethanol. Then after the two solutions were mixed into 250 mL round bottom flask, the pH of solution was adjusted to 6-8 using 25% ammonia solution at room temperature. The reaction mixture was then refluxed on an oil bath for 5 h at 75 - 80 ^oC while continuous stirring and the progress of the reaction was monitored using TLC. After completion of the reaction, the mixture was cooled down to room temperature and filtered using Whatman paper and washed repeatedly using ethanol and then dried in a desiccator over anhydrous calcium chloride (Yamgar et al., 2014).



Scheme 5. Synthesis of Iron (III) complex

3.6 Antimicrobial Study of SBL and its Co(II) and Fe(III) Complexes

The free organic ligand and its Co(II) and Fe(III) metal complexes were assessed for their antimicrobial capacity against different pathogenic Gram-negative and Gram-positive bacterial strains and fungal strains. The two Gram-negative bacterial strains used in the experiments were P. aeruginosa (ATCC 27853) and E. coli (ATCC25922), and the two Gram-positive bacterial strains used in the experiments were S. aureus (ATCC 25923) and E. faecalis (ATCC 29212). For antifungal activity, the common pathogenic yeast C. albicans (ATCC10231) was used. The method followed was agar disk- diffusion assessment method according to the Clinical and Laboratory Standards Institute (Cockerill et al., 2012). Muller Hinton Agar was used as a growth medium for bacterial strains, while Sabouraud dextrose agar nutrient was used as a microbiological growth medium for fungal strains. Stock solutions of the examined compounds were prepared by dissolving 0.02 g of each compound in 5.0 mL DMSO solvent and used for experimental tests. DMSO solvent was used as the negative control. The common antibacterial amoxicillin and the antifungal fluconazole drugs were used as references for comparison. The zones of complete inhibition (in millimeters) after the incubation period were measured around every compound, which indicates the lethality of the tested compound on the microbial microorganisms in question (Althobiti & Zabin, 2020)

3.7 Statistical Analysis of Biological Activities

Data was presented as mean ± standard deviation (SD). All variables were measured with triplicate. Graph Pad prism version 6 were used to analyze data. Students t- test were used to compare differences between groups and one-way analysis of variance (ANOVA) followed by Tukey‟s multiple comparison test to compare differences among groups. A value of $P < 0.05$ was considered to be statistically significant.

4. RESULTS AND DISCUSSION

The Schiff base ligand (E)-2-{[(7-chloro-2-hydroxyquinolin-3-yl) methylene] amino)-3-phenylpropanoic acid} was successfully synthesized. The synthesis involved reacting 7-chloro-8-hydroxyquinoline-2-carbaldehyde with L-phenylalanine in an ethanol solution. The ligand was reacted with cobalt chloride hexahydrate and ferric chloride hexahydrate in the presence of ethanol in molar ratios (1:2) $CoCl_3.6H_2O$ and $FeCl_3.6H_2O$. The complexes precipitated out of solutions were isolated by filtration, washed and recrystallized for further studies.

4.1 Physical Properties of the SBL and its Co(II) and Fe (III) Complexes

The Schiff base and its Co(II) and Fe(III) complexes were obtained in good yields. The physical properties of the synthesized Schiff base and its metal complexes were analyzed and presented in table 1.

Table 1: Physical Properties of the Schiff base and its Co(II) and Fe(III) Complexes

Compound	Color	%yield	M.P(^{0}C)	D. Temp (^{0}C)	μ (B.M)	M.L($\Omega^{-1}cm^2$ mol^{-1})
SBL	Deep yellow	89.75	above 170	-----	----	----
Co(II) complex	Light purple	78.05	210-215	210	17.31	17.31
Fe(III) complex	Dark yellow	78.05	215-220	215	20.17	20.17

The percentage yield of the Schiff base was 89.75%, while that of the complexes were 78.05%, and 78.05%. The Schiff base (Figure 4.1) was deep yellow in color, non-hygroscopic, and an amorphous powder while the Co(II) and Fe(III) complexes were light purple and dark yellow respectively. It was found that the melting point of the Schiff base is above 170 ^{O}C and the decomposition temperature of the Co(II) and Fe(III) complexes are 210 and 215 ^{O}C, this is an indication of thermal stability of the ligand and its metal complexes.

The molar conductance of the metal complexes is 17.31 and 20.17 Ω^{-1} cm^2mol^{-1} for Co(II) and Fe(III) complexes, respectively. These high values of their molar conductance are due to their electrolytic nature as reported by (Misra, Das, & Sinha, 1999). The calculated effective magnetic moment of metal complexes is 17.1 B.M. and 20.17 B.M. for Co(II) and Fe(III) complexes, respectively, indicate that these complexes are paramagnetic in nature.

Figure 1. Synthesized Schiff Base Ligand (SBL), Deep-yellow

4.2 Solubility Test of SBL and its Co(II) and Fe(III) Complexes

Water and some common organic solvents were used to determine the solubility of the Schiff base and its Co(II) and Fe(III) complexes. From the result of solubility test presented in Table 4.2, it can be seen that the Schiff base and its metal complexes were Soluble in dimethylsulfoxide (DMSO) and dimethylformamide (DMF), slightly soluble in ethanol and insoluble in n-hexane and water.

Table 2. Solubility test of the Schiff base and its Co (II) and Fe (III) complexes

Compound	Solvent				
	H_2O	n-hexane	Ethanol	DMSO	DMF
SBL	*Insoluble*	*Insoluble*	*Slightly soluble*	*Soluble*	*Soluble*
Co(II) complex	*Insoluble*	*Insoluble*	*Slightly soluble*	*Soluble*	*Soluble*
Fe(III) complex	*Insoluble*	*Insoluble*	*Slightly soluble*	*Soluble*	*Soluble*

4.3 Elemental Analysis

The elemental analysis of the Schiff base and its Co(II) and Fe(III) complexes were determined and presented in table 4.3. The calculated and observed values were found to be in good agreement. The elemental analysis data of the Schiff base suggested the formation of $C_{19}H_{15}ClN_2O_3$ while that

of the complexes revealed the formation of $C_{19}H_{15}ClN_2O_4Co$ and $C_{19}H_{15}ClN_2O_4Fe$. The complexes are formed in 1:1 metal ligand ratio.

Table 3. Elemental Analysis Data of the Schiff base and its Co (II) and Fe (III) Complexes

Compound	Percentage Found (Calculated)					
	% N	% C	% H	% Cl	% O	% M
SBL	7.85(7.90)	64.27(64.32)	4.26(**4.26**)	9.91(**9.99**)	13.43(**13.53**)	
Co(II) complex	6.07 (6.01)	48.87 (48.98)	3.97(4.08)	7.49(7.63)	20.49(20.62)	12.91(12.66)
Fe(III) complex	6.08 (6.05)	49.18 (49.31)	4.01(4.11)	7.47(7.68)	20.60(20.76)	11.89(12.08)

Calculated molecular mass of SBL is 354.08, while the observed molecular mass was: 354.79 m/z: 354.08 (100.0%), 356.07 (32.0%), 355.08 (20.8%), 357.08 (6.8%), 356.08 (2.8%)

The percentage yield of the synthesized Cobalt complex was determined to be 78.05%. The composition of the complex was also determined. The theoretical composition was calculated for the molecular formula $C_{19}H_{19}ClN_2O_6Co$, and the percentages of each element was found to be C 20.62%, H 4.08%, Cl 7.63%, N 6.01%, O 20.62%, and Co 12.66%..The experimental composition of the complex was found to be very close to the theoretical composition, with the percentages of each element being C 48.87%, H 3.97%, Cl 7.49%, N 6.07%, O 20.49%, and Co 12.91%. The elemental analysis data of the cobalt complex revealed the formation of $[Co\ L(H_2O)_3].H_2O$ with high purity. The complex is formed in 1:1 metal-ligand ratio.

Figure 2. Synthesized Co(II)-SBL complex

The Fe(III) chloride hexahydrate was reacted with SBL in ethanol gave a complex of dark yellow in color, non-hygroscopic, and an amorphous powder. The percentage yield of the complex was found to be 78.05 %..The calculated elemental Composition for $C_{19}H_{19}ClN_2O_6Fe$ is C, 49.31%; H, 4.11%; Cl, 7.68%; N, 6.05%; O, 20.76%; Fe, 12.08%. The experimentally obtained value for the complex was C, 49.18%; H, 4.01%; Cl, 7.47%; N, 6.08%; O, 20.60%; Fe 11.82% (Table 4.3).

The experimental composition of the complex was found to be very close to the theoretical composition. The elemental analysis data of the Fe (III) complex revealed the formation of [Fe L $(H_2O)_3$].H_2O. The complex is formed in 1:1 metal-ligand ratio. The metal percentages of newly synthesized Schiff base metal complexes which are shown in Table 4.3, give a good agreement with the proposed formula (calculated), and confirm binding of the metal ion to ligand site. The non-hygroscopic nature of the complex also suggests it has adequate stability for further studies. The reliable synthesis and binding properties of Fe(III) complex will provide an ideal system to investigate its potential applications such as antimicrobial activity.

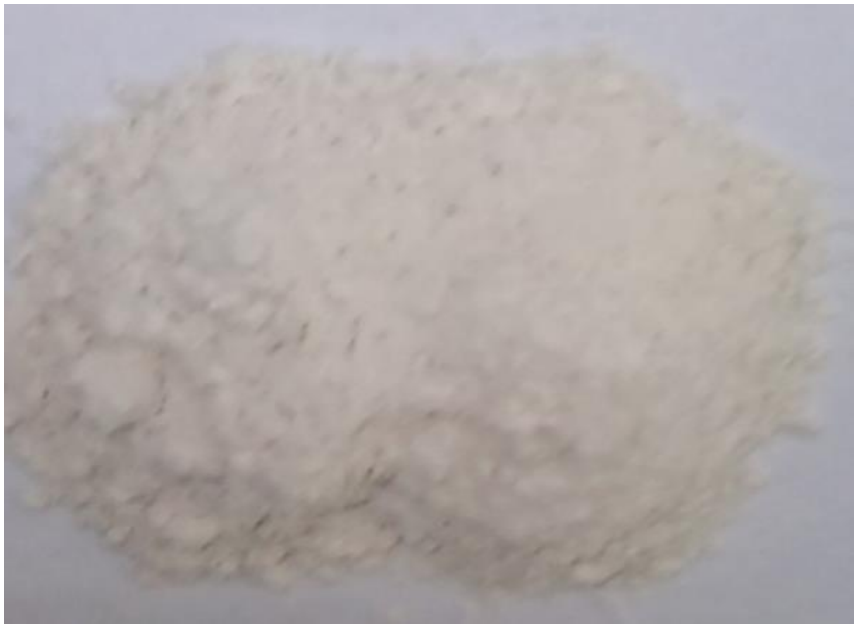


Figure 3. Synthesized Fe(III)-SBL complex

4.4 FTIR Analysis

The FTIR spectral data of the Schiff base and metal complexes are presented in Table 4.4 and Figures 4.4, 4.5 and 4.6. The FTIR spectra of the ligand and its metal complexes were recorded in KBr disc between 4000 cm^{-1} to 400 cm^{-1}.

Table 4. The characteristic IR bands (cm^{-1}) of the SBL and its Co(II) and Fe(III) complexes.

Compound	νOH	νH_2O	νC=N	νC=O	νC-O	νM-O	νM-N
SBL	3442	--	1605	1678	1330	-	-
Co(II) complex	---	3200	1565	1634	1060	425	530
Fe(III) complex	---	3210	1440	1616	1040	470	531

The FTIR spectral comparison of Schiff base ligand and metal complexes provide crucial information about the metal-ligand interaction and coordination mode of the ligand to the metal ions (Aziz, Salem, Sayed, & Aboaly, 2012) In our work, SBL displayed various IR spectral bands characteristic of the groups present in it, which have been shifted and even diminished in some cases after coordination with the metal ions.

Preliminary identification regarding the formation of Schiff base compound was obtained from the absence of characteristic IR bands for amino group of aryl amine and the carbonyl group of aldehyde. This is further confirmed by the appearance of a new band characteristic of νC=N (Agarwal, Prakash, Kumar, & Aslam Khan, 2007; Mapari, Hate, & Mangaonkar, 2011).

There is a band in the infrared spectrum of the Schiff base due to the phenolic ν (OH) stretching vibration at 3442 cm^{-1}. This band disappeared in the spectra of the complexes due to de-protonation and involvement of the oxygen atom in complexion.

The FTIR spectrum of the free Schiff base ligand has showed a strong υ(C=N) stretching vibration band at 1605 cm^{-1}. This band shifted towards lower frequencies of 1565 and 1440 cm^{-1} in the complexes, and this suggested the participation of the nitrogen atom of the azomethine in coordination (Hasan et al., 2021). The weak peak indicated at 1745 cm^{-1} confirms an aromatic ring existence while a strong band at 1605 cm^{-1} was attributed to the ν(C = N) (Muleta, Desalegn, Eswaramoorthy, & Garg, 2022).

The v(C-O) phenolic stretching of the Schiff base is observed at 1330 cm^{-1} which shifted to lower frequencies of 1060 and 1040 cm^{-1} in the complexes. This is an indication of coordination through the phenolic oxygen as reported by Mounika et al.2010 (Mounika, Pragathi, & Gyanakumari, 2010).

The Schiff base coordination with the metals is further evidenced by the appearance of weak low frequency non ligand bands at 530 and 531 cm^{-1} due to v(M-N) stretching vibration, and at 425 and 470 cm^{-1} due to v(M-O) stretching vibration. Similar result was reported by Rasha and Farah.2012.

A broad band at 3442 cm^{-1} characteristic to the stretching vibrations of phenolic O-H group and a broad band at 3147 cm^{-1} characteristic to the stretching vibrations of carboxylic O-H group, in the free ligand, the disappearance of this peak in the spectra of both complexes indicates the de-protonation of phenol proton prior to coordination (Gunasekaran & Uthra, 2008).

A sharp peak around 1678 cm^{-1} is due to C=O stretching vibrations in the free ligand. This band shifted towards lower frequencies of 1634 and 1616 cm^{-1} in the complexes, and this suggested the participation of the carbon atom of the carboxylic acid in coordination. The hydrated complexes exhibited an IR broad band at 3200 and 3210 cm^{-1} due to $\nu_{(H2O)}$, suggesting the coordination of water molecules in both complexes. The coordination of oxygen of the phenolic group (OH) and nitrogen of the azomethine group (C=N) atoms is further supported by appearance of two non-ligand bands for both complexes at 530 and 531 and 425 and 470 cm^{-1} due to υ(M—N) and υ(M—O) respectively, studies on the stretching vibrations of these bonds are important in elucidating the structure of the complex (Abdallah et al., 2009).

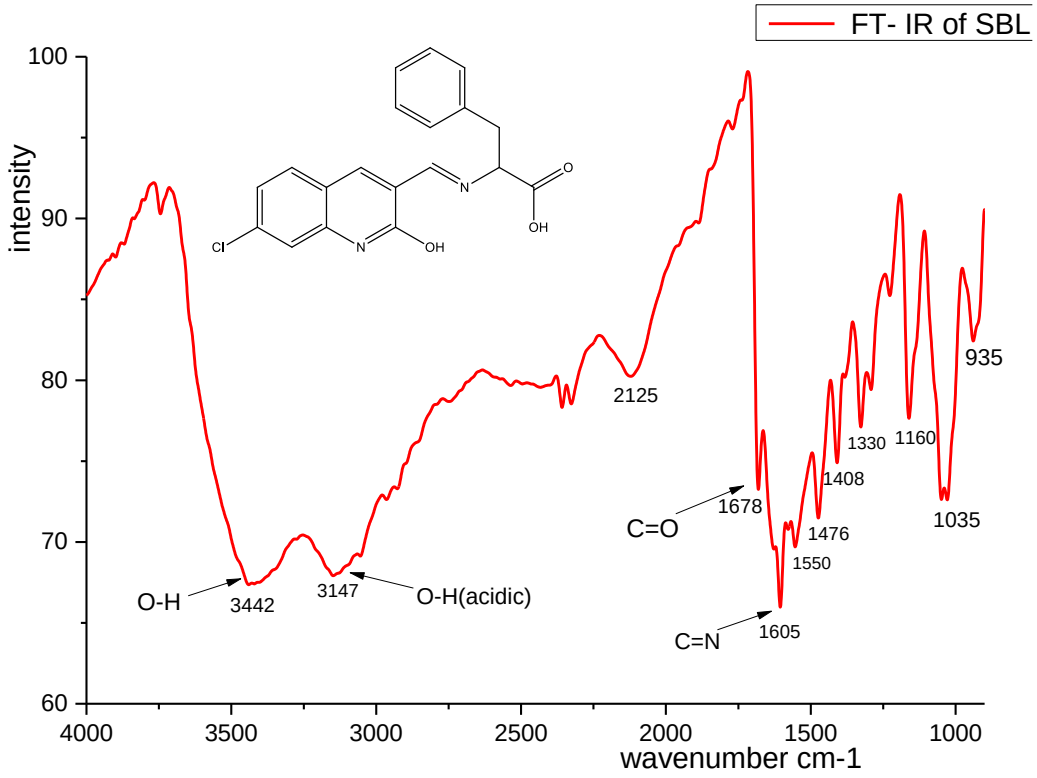


Figure 4. FT-IR spectra of SBL

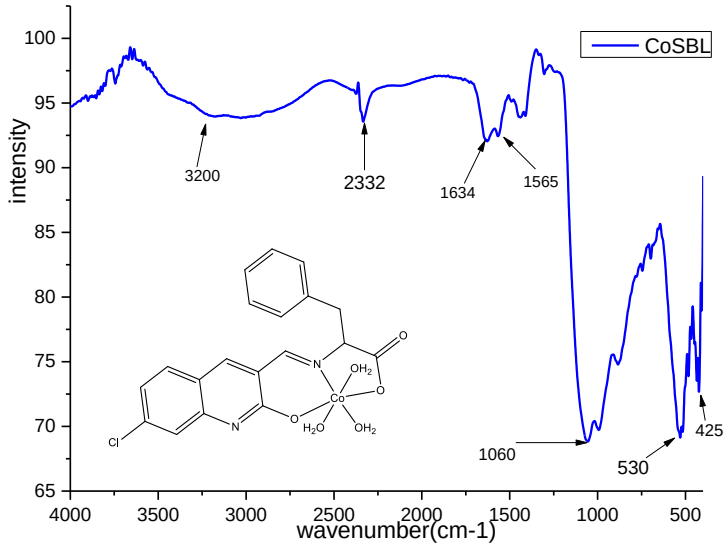


Figure 5. FT-IR spectra of Co (II) complex

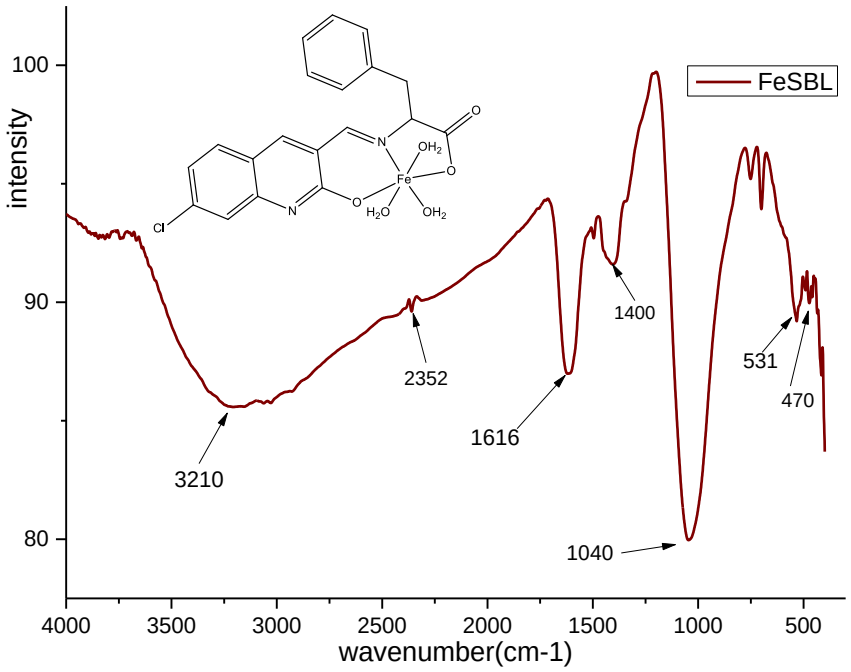


Figure 6. FT-IR spectra of Fe (III) complex

4.5. Electronic Spectral Analysis

The UV-VIS spectral data of the Schiff base and metal complexes are presented in in Table 4.5 and Figures 4.7, 4.8 and 4.9. Electronic spectra of all the compounds were recorded in DMSO.

Table 5. Electronic spectral data λ_{max} (nm) of the SBL and its Co (II) and Fe (III) complexes

Compound	λ_{max} (nm)	ε (dm mol^{-1} mm^{-1})	Transition	Assignment
SBL	239	(π-π*)	----------	
	253	(π-π*)		
	324	(n-π*)		
	311	(n-π*)		
Co(II) complex	315	π-π*	$(\nu_3)\,^4T_{1g}(F) \rightarrow {}^4T_{2g}(P)$, $(\nu_2)\,^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)$ $(\nu_1)\,^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$	Distorted octahedral
	375	n-π*		
	330.5	*π-π*		
	380	n-π		
Fe(III) complex	295	(π-π*)	$^6A_{1g} \rightarrow {}^4T_{2g}$, $^6A_{1g} \rightarrow {}^4T_1(G)$	octahedral
	284	(n-π*)		
	262	(*π-π*)		
	301	(n-π)		

The ligand structure reveals that, the azo group lone pairs of electrons are not the only interacting nonbonding electrons, since hydrazone moiety is additional source of lone pair of electrons (nitrogen and oxygen atoms). Thus, other n→π* transition is predictable to take place from these non-bonding orbitals to various molecular orbital extending over such a big molecule (Rageh, Abdel Mawgoud, & Mostafa, 1999)(Rageh, N.M.;et.al 1999). The data revealed that, the ligand comprised many peaks in the UV and visible regions. The shortest wavelength peaks observed at 239 and 253 nm could be assignable to π→π* transitions of the benzenoid and intra-ligand [Kurtoğlu, M.; et.al 2008 and Samanta, B.; et.al 2007]. Whereas the bands appeared at 324 and 335 nm could be imputed to n→π* transitions of carbonyl and azomethine groups (Gup & Kırkan, 2005)[Gup, R et.al 2005]. The bandsituated at 301 nm could be corresponded to π→π* transition including the π electron of the azo group (Rageh, N.M.;et.al 1999). The peak situated at 380 nm could be assigned to π→π* transition including the whole electronic system of the compounds with a considerable charge transfer character emerging fundamentally from the phenolic moiety (Rag eh, N.M.; et.al 1999).

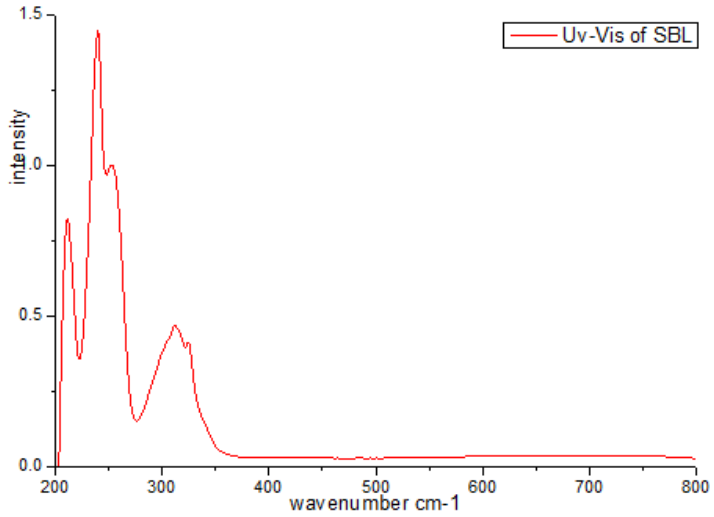


Figure 7. UV-Vis spectra of SBL

The Co(II) complex showed bands at 330, 375 and 380 nm, which could imputed to $(\nu_3)^4T_{1g}(F)\rightarrow {}^4T_{2g}(P)$, $(\nu_2)\ {}^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)$ $(\nu_1)\ {}^4T_{1g}(F)\rightarrow {}^4T_{2g}(F)$ transitions, respectively, referring to high spin Co^{2+} octahedral complex [Singh, B.; et.al 1987 and Lever, A.B.P 1984]. The Co-SBL

complex exhibits two distinct bands in the high wavelength region of the spectrum at 425-490 nm and 535 nm. The former band is assignable to $^4T_{1g}$ (F) $\rightarrow$ $^4T_{1g}$ (P) and latter band indicates $^4T_{1g}$(F)$\rightarrow$$^4T_{2g}$(F) transition, confirming its octahedral geometry (Lever, A.B.P 1984, and Tiliakos, M.; et.al 2001). The magnetic moment value (17.31BM) executes high spin state of cobalt with 3 unpaired electrons and this further supports this geometry. The high energy bands for this complex are observed at the range of 346-371 nm, assignable to n$\rightarrow\pi$ * ligand metal charge transfer (LMCT) transition. The ν_2/ν_1 ratio for the complex is 1.61 which is lower than the regular range (1.95–2.48), referring that Co(II) complex has a distorted octahedral geometry (El-Tabl, Shakdofa, El-Seidy, & Al-Hakimi, 2012).

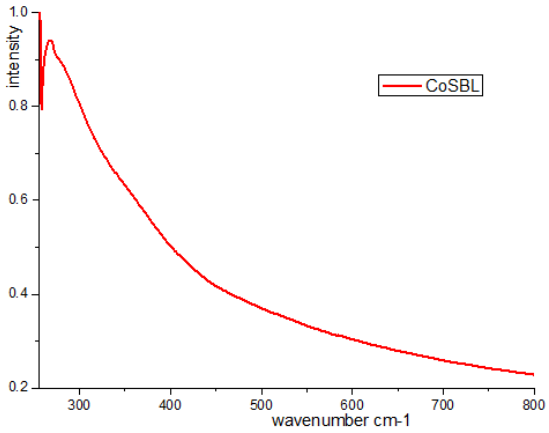


Figure 8. UV-Vis spectra of Co (II) complex

Fe (III) complex gave bands at 295, 301 nm which due to $^6A_{1g}\rightarrow^4T_{2g}$ and $^6A_{1g}\rightarrow$ $^4T_1$(G) transitions. These peaks are distinctive of octahedral Fe (III) complex (Lever, A.B.P 1984, and Tiliakos, M.; et.al 2001). The Fe-SBL complex exhibits two distinct bands in the high wavelength region of the spectrum at 425-490 nm and 535 nm. The former band is assignable to $^4T_{1g}$ (F) $\rightarrow$ $^4T_{1g}$ (P) and latter band indicates $^4T_{1g}$ (F) $\rightarrow$$^4T_{2g}$ (F) transition, confirming its octahedral geometry (Lever, A.B.P 1984, and Tiliakos, M.; et.al 2001). The magnetic moment value (20.17 BM) executes high spin state of iron with 5 unpaired electrons and this further supports this geometry.

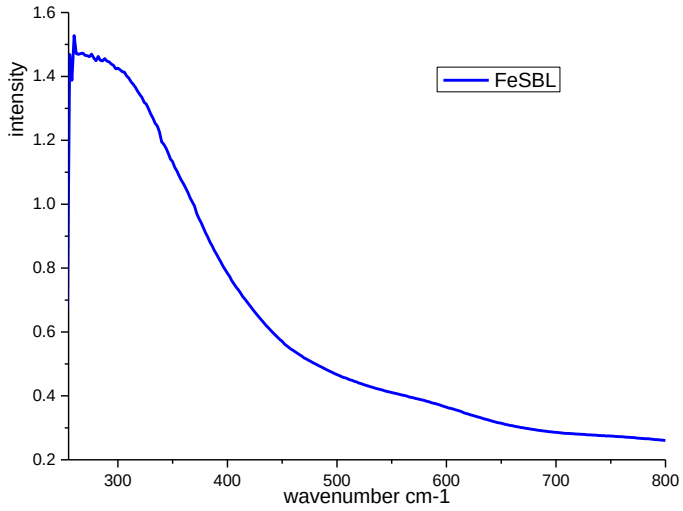


Figure 9. Uv-Vis absorption spectra Fe (III) complex

4.6 NMR spectra of SBL

NMR spectroscopy is used to identify the carbon-hydrogen framework of the organic ligand and metal complexes. Due to the different electronic environment of protons in the molecules, they show the resonance peaks at different regions of the spectrum, depending on their extent of shielding and deshielding effects. Furthermore, the splitting of signals into multiplets furnishes important information regarding the types of protons present in the molecule. Sometimes the loss of signal in the NMR spectrum of metal complexes relative to ligand also executes important information about the point of attachment of ligand with metal center (Claridge, 2009).

4.6.1 ^{1}H NMR Spectra of SBL

The ^{1}H NMR Spectra results of the SBL is presented in Figure 4.10 and Table 4.6. The formation of SBL is supported by the ^{1}H NMR spectral study. The ^{1}H NMR spectrum of the Schiff base showed a singlet peak at δ = 8.92 ppm corresponding to the azomethine proton (– N=CH–) (El-Sherif & Eldebss, 2011), an indication that the Schiff base was formed during the condensation reaction. The spectrum SBL exhibits a multiplet in 7.75 -8.02 ppm and 8.30 – 8.43 ppm regions which may be assigned to Ar-H and pyridin ring protons, respectively. Doublet peaks at 5.45 ppm is assigned to N=C-CH proton. The signal for carboxylic and phenolic proton appears at δ 10.35 ppm and 9.05 ppm, respectively (El-Sherif & Eldebss, 2011).

Table 6. ^{1}H NMR spectral data of SBL

Chemical shift (δ) (ppm)	Assignment
10.35(s)	Carboxylic proton
9.05 (s)	Phenolic OH proton
8.92(s)	Azomethine proton
8.30 – 8.43(m)	Pyridine ring protons
7.75 – 8.02 two (d)	Ar-H protons

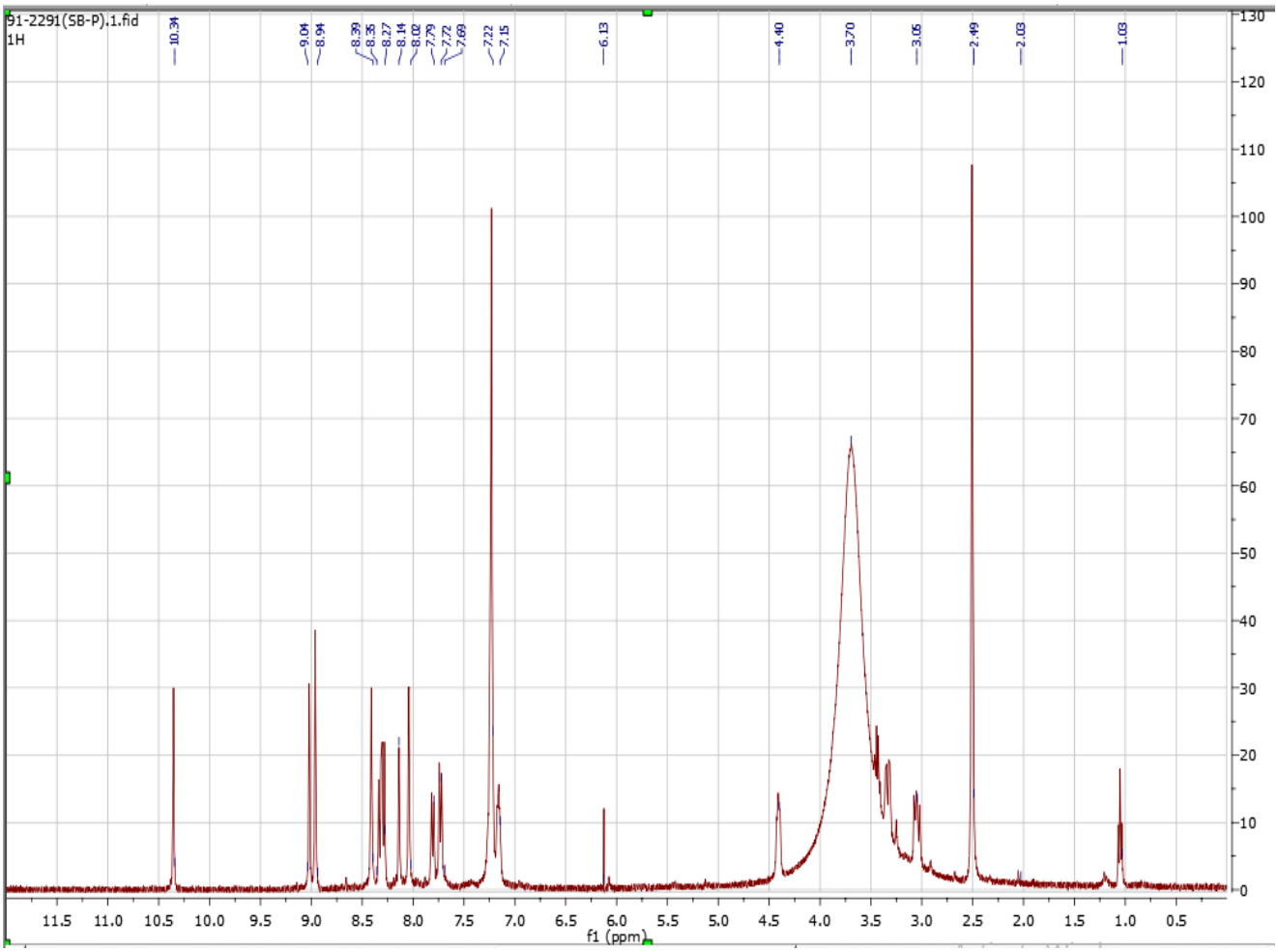


Figure 10. ^{1}H-NMR spectra of SBaL

4.6.2. ^{13}C NMR Spectra of SBL

^{13}C NMR spectral study furnishes idea about the different kinds of carbon atoms and their electronic environment in the molecules. The ^{13}C NMR spectrum of SBL delivers a signal for carboxylic carbon at 190 ppm. The signal for azomethine carbon appears at 172 ppm. The signal at 151 ppm is attributed phenolic carbon. The signal for methylene carbon appears at 39 ppm. The aromatic ring carbons deliver the signal in the range of 126 to 132 ppm and the signals in the range of 137 to 149 are attributed to pyridine ring carbons (El-Sherif & Eldebss, 2011). The recorded spectrum of SBL is given in the Figure 4.11 and the spectral data are reported in the Table 4.7.

Table 7. ^{13}C NMR spectral data of SBL

Chemical shift (δ) ppm	Assignment
190	carboxylic carbon
172	azomethine carbon
151	phenolic carbon
137 -149	Pyridine ring carbons.
126 – 132	aromatic ring carbons
39	methylene carbon

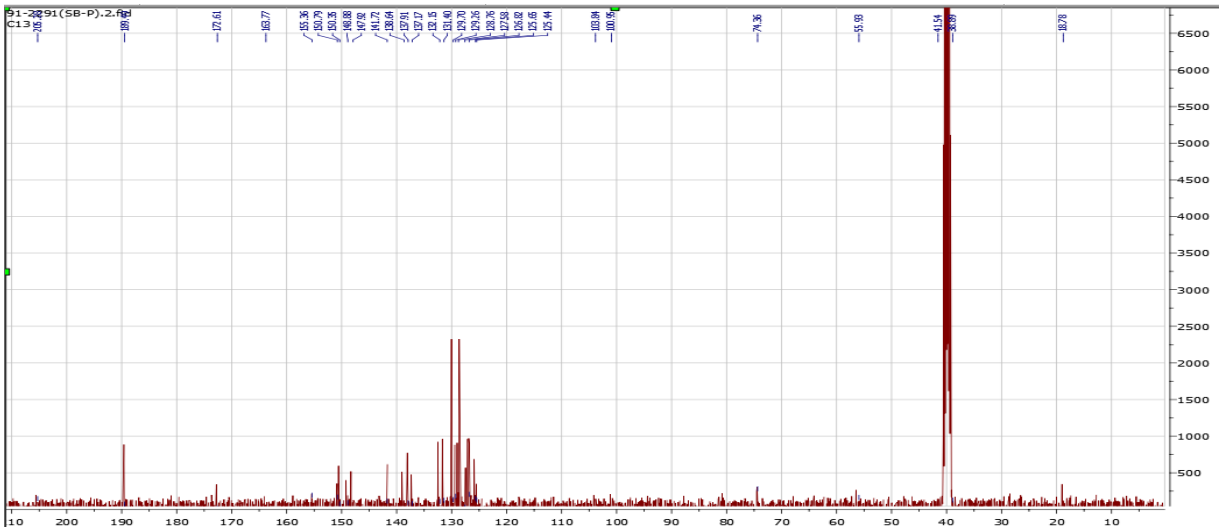


Figure 11. ^{13}C-NMR spectra of SBL

4.7 Thermogravimetric Analysis

Heat sensitive physical and chemical properties of the complexes are well studied by thermal analysis techniques and have found wide applications in the recent years in characterizing the chemicals by measuring changes of properties at elevated temperatures as a function of increasing temperature. Measurements are used primarily to determine the composition of substances and also to predict their thermal stability. The thermogravimetric analysis (TGA) measures the changes in weight of substance as a function of temperature (Al-Resayes, 2010). The sample under investigation is heated at a controlled rate in an atmosphere of nitrogen and the mass loss of the substances is recorded as a function of temperature. The results from thermogravimetric run may be presented by (i) weight versus temperature curve, referred to as thermogravimetric (TG) curve, or (ii) rate of the weight loss versus temperature curve, referred to as the differential thermogravimetric (DTG) curve. The weight of the substances in the thermogram may be scaled as true weight scale or as a percentage of total weight.

Thermogravimetric analyses (TGA) of the newly synthesized Co(II) complexes was carried out to get information about their thermal stability and to suggest a general scheme for their thermal decomposition as well as to ensure the nature of the associated water molecules. In this analysis, the heating rate was controlled at 10 °C min^{-1} under a nitrogen atmosphere and the mass loss was measured from the room temperature to 800 °C. The TGA and DTA curves for Co (II) complex is presented in Figures 4.12.

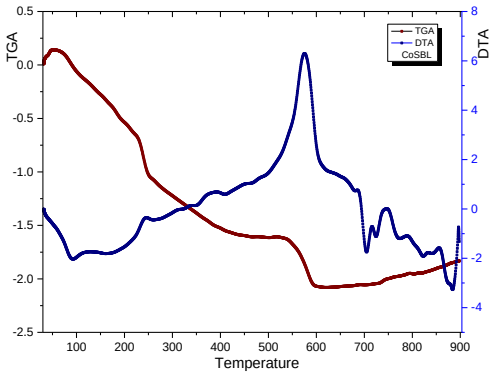


Figure 12. TGA-DTA graph of Co(II)-SBL Complex

The thermogram of the Co(II)-SBL complex showed four decomposition steps in the temperature range of 50 to 380 °C. The first decomposition step in the range of 50 to 110 °C with % mass loss

of 4.826% (0.226 g) is assignable to loss of two lattice water molecules in the outer sphere region. The DTG temperature for this step is 80.85 °C and corresponding DTA temperature is 103.68 °C and reveals endothermal effect. The second and third decomposition steps with % mass loss of 25.923% and 33.837% in the temperature range of 241 - 273 °C and 279- 300 °C respectively are considered to be due to loss of organic ligand moiety. The last decomposition step represents complete loss of ligand from the complex in the temperature range of 338 - 380 °C, leaving nearly 7.49% cobalt oxides as end residue. The corresponding DTG temperatures for the consecutive second, third and fourth steps are 268.38 °C, 284.05 °C, and 357.21 °C respectively.

The thermogram of the complexes showed that the complexes are stable up to 100 °C and no weight loss occurs before this temperature. This is in agreement with the spectroscopically determined stability constant of both complexes, which did not show any change up to 40 °C (Table 4.1), and this infers that the metal complexes can be used for different biological applications. The proposed chemical formulas of the complexes are therefore in line with TGA data. Accordingly, the thermal decomposition of the Co(II) complex exhibits three degradation steps.

The thermogram of the Fe(III) complex (Figure 4.13) showed four decomposition steps in the temperature range of 50 to 778 °C. The first step of decomposition occurs within a temperature range of 100−130 °C, which shows a mass loss of 9.26% (calcd. = 9.26%) that corresponds to the loss of two water molecules. The second step of decomposition occurs within a temperature range of 150−510 °C, which is accompanied by a weight loss of 19.89% (calcd. = 20.71%) corresponding to the loss of C_2H_4ClOH molecules.6,68 The third step of degradation occurs in the temperature range of 535−778 °C and is accompanied by a weight loss of 51.43% (calcd. = 51.0%) corresponding to the loss of the $C1_2H_{12}N_3$ species of the quinoline ring. The actual mass loss from these steps is 80.58%, which is close to the calculated value of 80.97%.69. Thereafter, the compound showed a gradual decomposition up to 778 °C with a weight loss of the organic moiety. The weight of the residue corresponds to the respective iron oxide about 19.42% (calculated = 19.03%) (Damena et al., 2022).

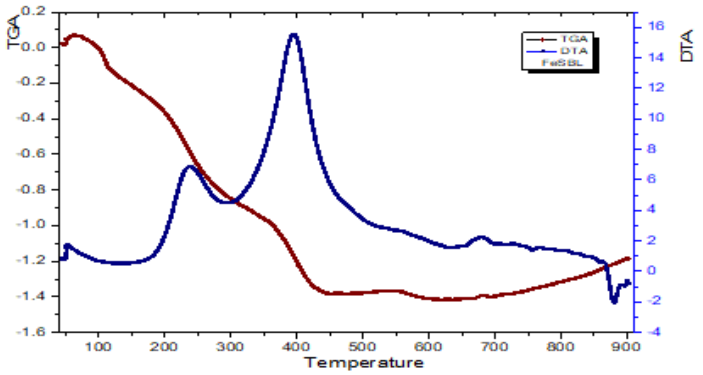


Figure 13. TGA-DTA graph of Fe(III)- (SBL) complex

4.8. X-ray Diffraction Analysis

X-ray powder diffraction study of the substances has become a valuable tool for the characterization of complexes in the field of coordination chemistry. Crystal structure determination from powder diffraction data is much more difficult and complicated than from single crystal data. This is because; there is the collapse of the three dimensions of crystallographic information onto the single dimension of a powder diffraction pattern. Although the single crystal approach is much more suitable and straightforward than the powder diffraction technique for structure determination, the formation of single crystal for all the chemical complexes is not accessible.

The study conducted an X-ray diffraction (XRD) analysis to investigate the crystal system of the metal complexes. The analysis was performed using Ultima IV X-ray diffractometer. Powder diffraction patterns of metal complexes were recorded over the range of $2\theta = 5^0$–80^0 at wavelength 1.5406$\boldsymbol{A}$. The XRD results of the Co(II) and Fe(III) complexes are presented in Fig. 4.14 and 4.15.

Single crystal growth of the synthesized SBL and its metal complexes were unsuccessful, so their crystallinity was assured by X-ray powder diffraction study. X-ray diffractogram of Co(II)-SBL complex was relatively very poor quality and diffusive. This broad bump behavior observed in the XRD of the Co (II) complex suggests that the material is amorphous or poorly crystalline, which may impact its properties and biological activity.

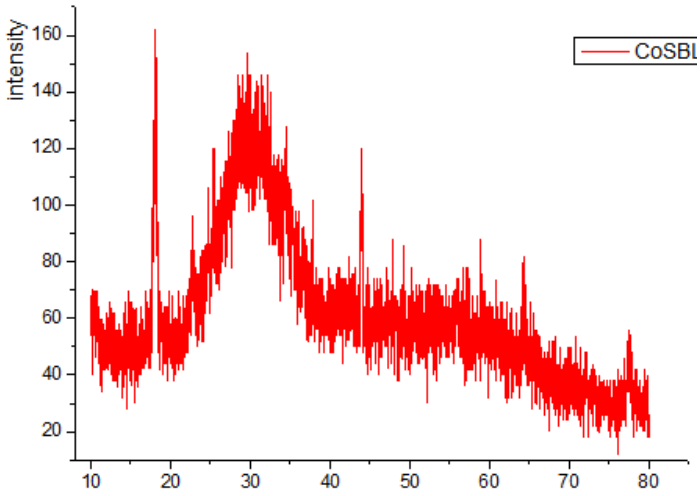


Figure 14. X-ray diffraction patterns of Co(II)-SBL complex

X-ray diffractogram of Fe(III)-SBL complex was relatively well resolved crystalline peaks (Figure 4.15). This sharp crystalline peaks behavior observed in the XRD of the Fe(III) complex suggests its crystalline phase. The formation crystalline phase highly contributes to its distinct properties and biological activity.

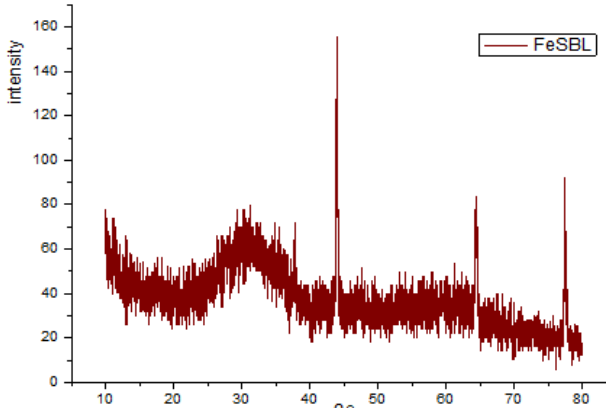


Figure 15. X-ray diffraction patterns of Fe(III)-SBL complex.

4.9. The pH Stability Range of Co(II)-SBL and Fe(III)-SBL Complexes

The pH profile of the tested complexes exhibits well-defined dissociation curves and demonstrates excellent stability across a wide pH range of 5 to 10. This behavior indicates that the presence of our new SBL enhances the stability of all the synthesized complexes. Consequently, the pH range between5 to 10 is deemed suitable for various applications involving these compounds. Moreover,

the obtained results indicate that the synthesized complexes exhibit significantly higher stability compared to free SBL.

4.10 Antibacterial Activities of SBL and its Co(II) and Fe(III) Complexes

The synthesized complexes and their free ligands were screened for their anti-microbial activity against two Gram-positive (Staphylococcus aureus, S.pyogene) and two Gram-negative (Escherichia coli, P. aurega) bacteria, in DMSO using disc diffusion method (Abdel-rahman et al. 2022). It was determined at concentrations of 100 and 200 µg/mL. The ability of the Schiff base ligand and its metal complexes to inhibit the growth of the bacteria was compared to that of the known standard antibacterial drug cephro. The zone of inhibition for each of the compounds against the test organisms was measured in triplicate, and the average is presented as mean ± SD in Table 4.8. The antibacterial activity taken as the inhibition zone diameter is depicted graphically in Figure 4.16 and 4.17.

Table 8. Antibacterial activities SBL and its Co(II) and Fe(III) complexes (diameter of zone of inhibition in mm).

Compound	Conc.(µg/mL)	Gram Positive		Gram Negative	
		S. pyogene	S. aurues	E. coli	P. aureginosa
SBL	100	5.10±0.41	6.05±0.21	6.00±0.408	5.17±0.236
	200	5.50±0.40	7.08±0.31	7.00±0.40	7.00±0.408
CoSBL	100	0.00 ± 0.00	6.67 ± 0.471	6.75 ± 0.204	7.33 ± 0.471
	200	7.33 ± 0.471	7.50 ± 0.408	6.67 ± 0.236	10.33 ± 0.471
FeSBL	100	7.67 ± 0.471	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
	200	9.33 ± 0.00	6.65 ± 0.471	6.75 ± 0.204	7.00 ± 0.00
Cephro	-	28.00 ± 0.816	33.00 ± 0.816	29.67 ± 0.471	30.00 ± 0.816

Except for S. pyogene at 100µg/mL Co(II) complex shows more significant antibacterial activities against both Gram-positive and Gram-negative bacteria than the free ligand at both concentrations of 100 and 200 µg/mL Fe(III) complex shows more activity than its parent ligand in case of S. aurues, E. coli and P. aeruginosa at a concentration of 200 µg/mL Except for S. pyogene, Fe(III) complex shows less activity than its parent ligand in case of S. aurues, E. coli and P. aeruginosa at a concentration of 100µg/mL. The free SBL and metal complexes show less significant

antibacterial activities against both Gram-positive and Gram-negative bacteria than standard antibacterial drug.

The increased inhibition activities can be explained on the basis of Overtone's concept (Anjaneyulu & Rao, 1986) and Chelation theory (Mishra et al., 2012). The normal cell process can also be disturbed by the formation of hydrogen bond through the azomethine nitrogen with the active centers of cell constituents. The differences in the activity of ligand and their metal complexes against microorganisms can be attributed to the variation in the ribosomes of microbial cells and the impermeability of the cells (Raman, Raja, & Kulandaisamy, 2001).

The chelation process decreases the metal atom polarity mainly because of the positive charge of the metal partially shared with nitrogen and oxygen atoms present on the free Schiff base ligand, and there is electron delocalization over the whole complex ring. This enhances the delocalization of the π electrons over the entire complex ring thereby promoting the lipophilicity of the chelate This increases the lipophilic character of the metal chelate and favors its permeation through the lipid layers of the microbial membranes (Mishra et al., 2012).

From Table 4.8, the low activity of some metal complexes is observed. This poor inhibition performance may be attributed to the low lipophilicity, which decreases the ability of the metal complex to penetrate the lipid membrane (Puckett, Ernst, & Barton, 2010). Also, the presence of the metal ions in complexes with azomethine derivatives exhibited more effectiveness in membrane destabilization than the free ligand. This leads to disturbing the structural integrity of the cell and hence eradicating the microorganism (Samanta et al., 2013).

Overall, the inhibition zones of Schiff base ligand and its complexes at different concentrations showed that the complexes had enhanced bactericidal activity than the ligand. Free Schiff base ligand and its complexes exhibited higher antibacterial activity at their higher concentration. The increase in the antibacterial activity of the Co(II) complex may be due to the effect of the metal ion on the normal state of the bacterial cell process (Naeimi, Raeisi, & Moradian, 2017). Research has shown that the structural components possessing additional (C=N) bond with nitrogen and oxygen donor systems inhibit enzyme activity due to their deactivation by metal coordination (Jesmin, Ali, Salahuddin, Habib, & Khanam, 2008).

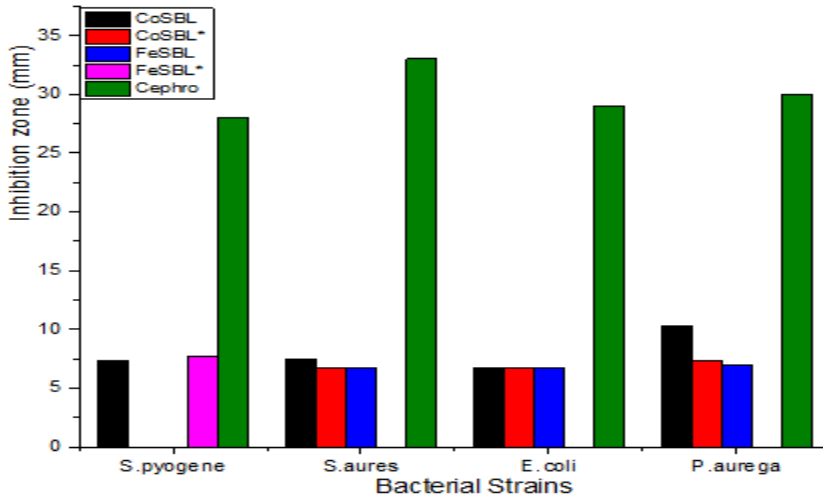


Figure 16. Graphical representation of antibacterial activity of SBL and its Co(II) and Fe(III) complexes.

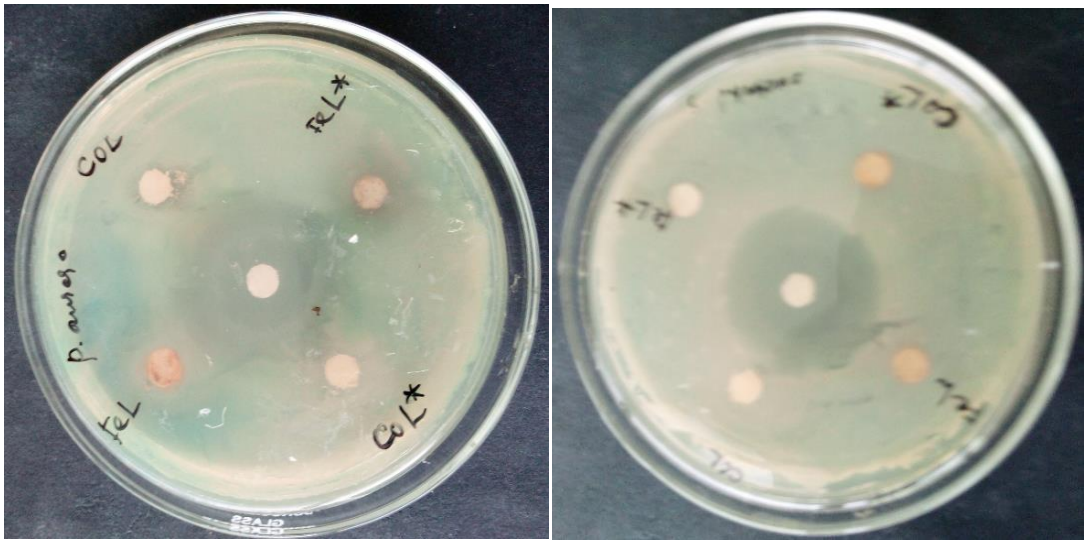


Figure 17. Antibacterial activity of Co(II)-SBL and Fe(III)-SBL complexes

5. CONCLUSION AND RECOMMENDATION

5.1 Conclusion

Growing interest in the success of metal-based drugs as chemotherapeutic agents is the basic foundation of Schiff base research. The present investigation has devoted for the synthesis of Schiff base ligand, (E)-2-{[(7-chloro-2-hydroxyquinolin-3-yl) methylene] amino}-3-phenylpropanoic acid. This has reacted with Co (II) and Fe (III) ions for the formation of their metal complexes. They have been characterized by various physical and spectral techniques, like elemental analysis, conductivity measurement, FT-IR, ^{1}H & ^{13}C NMR, and electronic absorption studies. Their structure characterization has been further validated by XRPD and TGA/DTA. The antibacterial activity study has been accomplished by disc diffusion technique.

Structural analysis of all the Schiff base ligands and metal complexes, by applying spectral techniques has revealed the participation of nitrogen atom of azomethine group, oxygen atoms of carboxylic and pyridine ring group in the legation process with metal ions. Molar conductivity values of the metal complexes is 17.31 and 20.17 Ω^{-1} cm^2mol^{-1} for Co (II) and Fe (III) complexes, respectively and this has recommended electrolytic nature of the complexes. The electronic absorption data nicely support the concerned geometry of the complexes. The powder XRD data of the complexes revealed their non-crystalline nature.

In our work, the antibacterial activity study of all the synthesized ligands and complexes, against the clinical strains of bacterial pathogens, showed moderate inhibition growth. The Co(II) complex showed higher bacterial inhibition growth compared to free Schiff base ligand for all test bacterial strains at both concentrations. At both concentrations, the Fe(III) complex shows lower antibacterial potency compared to free Schiff base ligand for all test bacterial strains. This study with free Schiff base ligand and metal complexes also revealed the strong antibacterial potency against all the bacterial pathogens at their higher concentration. Furthermore, free Schiff base ligand and metal complexes showed less potency than standard antibacterial drug Ciprofloxacin. The Fe (III) complex was found less active with all the bacterial pathogens except S. pyogene bacteria at concentration of 200µg/mL

5.2. Recommendation

Research is a continuous process and the following recommendations are proposed for the future studies.

- Attempts to grow a single crystal of each of these synthesized compounds did not yield fruits; only amorphous solid complexes were generated. Further studies on how to generate crystals of these complexes should be pursued.
- Only bacterial activity for four bacterial strains of the free SBL and synthesized complexes was studied. Antibacterial activity for more other bacterial strains, of these free SBL and complexes should be investigated.
- Other biological activities such as antioxidant, antiviral, anticancer, antifungal, etc., of these free SBL and complexes should be investigated.
- The toxicity tests and MIC of these free SBL and complexes should be explored.
- The *in vivo* antibacterial study of the compounds should be investigated.

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