COORDINATION CHEMISTRY OF IBUPROFEN WITH FERRIC CHLORIDE: FORMATION, CHARACTERIZATION, AND POTENTIAL APPLICATIONS

BY

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CERIFICATION

This is to certify that this project work is the original work carried out and reported by …… to the Department of Science Laboratory technology, Institute of Applied Sciences (IAS) Kwara State Polytechnic, Ilorin and it has been Approved In Partial fulfilment of The Requirements of the Award of National Diploma (ND) in Science Laboratory Technology (**CHEMISTRY**)

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DEDICATION

I dedicated this project to Almighty God for making this project work a successful one and also to my lovely parent *for their wonderful loves***.**

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First and foremost, our uppermost gratitude goes to Almighty God, the omniscience, omnipotent and the creator of universe who make it possible for us to the final completion of this project. You will forever be praised.

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Abstract

This research investigates the coordination chemistry of ibuprofen, a widely used non-steroidal anti-inflammatory drug (NSAID), with ferric chloride, focusing on the synthesis, characterization, and evaluation of potential applications of the resulting metal complex. The study aims to enhance the physicochemical and biological properties of ibuprofen through metal coordination, thereby contributing to the development of novel therapeutic agents.

The ferric chloride -ibuprofen complex was synthesized via solution-phase reaction and characterized using a range of spectroscopic and analytical techniques, including FTIR, UV-Vis, NMR, TGA, XRD, and SEM. Results confirmed successful complexation through the carboxylate group of ibuprofen, with evidence of increased thermal stability and changes in crystalline morphology. The UV-Vis and FTIR analyses revealed shifts in characteristic absorption bands, while TGA and XRD confirmed the stability and crystalline nature of the complex. NMR studies supported the structural changes indicative of coordination.

Furthermore, the antimicrobial efficacy of the complex was assessed against Escherichia coli and Staphylococcus aureus using the agar well diffusion method. The complex demonstrated improved antibacterial activity compared to both free

ibuprofen and ferric chloride, indicating synergistic enhancement.This study highlights the potential of metal-drug complexes as improved pharmaceutical agents and lays the groundwork for future research on metal-based NSAID derivatives. It also opens avenues for exploring their applications in biomedical and catalytic fields.

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Chapter One: Introduction

CHAPTER ONE

1.0 INTRODUCTION

1.1 Background to the Study

Ibuprofen was the first member of Propionic acid derivatives introduced in 1969. It is a popular domestic and over the counter analgesic and antipyretic for adults and children. Ibuprofen has been rated as the safest conventional NSAID by spontaneous adverse drug reaction reporting systems in the UK. This project summarizes the main pharmacological effects, therapeutical applications and adverse drug reactions, drug-drug interactions and food drug interactions of ibuprofen that have been reported especially during the last 10 years. Ibuprofen is (2RS)-1[4-(2-methyl propyl) phenyl] propionic indomethacin, are still the most common side effects.1 acid (BP. 2004). Ibuprofen was the first member of propionic acid derivatives to be introduced in 1969 as a better alternative to Aspirin. Gastric discomfort, nausea and vomiting, though less than aspirin or Ibuprofen is the most commonly used and most frequently prescribed NSAID. It is a non-selective inhibitor of cyclooxygenase-1 (COX-1) and Cyclooxygenase-2 (COX-2).

Although its anti-inflammatory properties may be weaker than those of some other NSAIDs, it has a prominent analgesic and antipyretic role. Its effects are due to the inhibitory actions on cyclo-oxygenases, which are involved in the synthesis of prostaglandins. Prostaglandins have an important role in the production of pain, inflammation and fever. (Sharma & Rani, 2020).

Ibuprofen, a widely used non-steroidal anti-inflammatory drug (NSAID), possesses a carboxyl functional group, making it a potential ligand capable of forming stable coordination compounds with metal ions. The coordination of ibuprofen with metal ions can alter its physicochemical and pharmacokinetic properties. Transition metal complexes with NSAIDs have been shown to exhibit enhanced biological activities, including antimicrobial, anticancer, and anti-inflammatory effects, as well as improved solubility and thermal stability (Basu et al., 2016). Such complexes also hold promise in drug delivery systems and as catalysts in organic synthesis. Iron (III) chloride is a versatile metal salt with significant coordination potential. Iron (III) complexes are well-known in organometallic and bioinorganic chemistry due to their structural diversity and catalytic properties (Nakamoto, 2009). The coordination of ibuprofen with Iron

(III) chloride can lead to the formation of a new compound with potentially valuable properties for pharmaceutical and industrial applications

1.2 CLINICAL PHARMACOLOGY OF IBUPROFEN

Ibuprofen is supplied as tablets with a potency of 200 to 800 mg. The usual dose is 400 to 800 mg three times a day. It is almost insoluble in water having pKa of 5.3.(Sharma & Rani, 2020).It is well absorbed orally; peak serum concentrations are attained in 1 to 2 hours after oral administration. It is rapidly bio-transformed with a serum half-life of 1.8 to 2 hours. The drug is eliminated in 24 hours after the last dose and eliminated through metabolism. The drug is more than 99% protein bound, extensively metabolized in the liver and little is excreted unchanged. Although highly bound to plasma proteins (90-99%), displacement interactions are not clinically significant, hence the dose of oral anti-coagulants and oral hypoglycemic needs not be altered.1 More than 90% of an ingested dose is excreted in the urine as metabolites or their conjugates, the major metabolites are hydroxylated and carboxylated compounds. Old age has no significant effects on the elimination of ibuprofen. Renal impairment also has no effect on the kinetics of the drugs, rapid elimination still occur as a consequence of metabolism. The administration of ibuprofen tablets either under fasting conditions or immediately

before meals yield quiet similar serum concentrations-time profile. When it is administered immediately after a meal, there is a reduction in t0he rate of absorption but no appreciable decrease in the extent of absorption.(Basu et al., 2016)

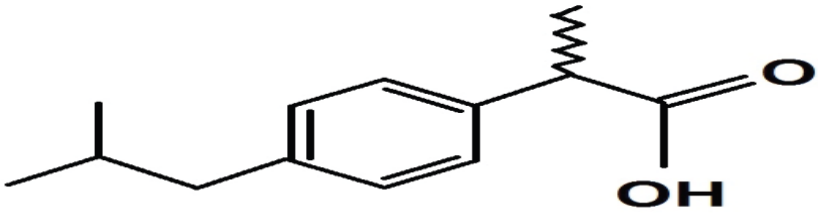

Fig.: 1. Structure of Ibuprofen

1.3 Statement of the Problem

Despite the prevalence of ibuprofen in therapeutic applications, its interaction with transition metal ions such as iron remains relatively unexplored. Metal coordination could potentially enhance the drug's biological activity or lead to new applications. However, detailed studies investigating the formation, structural elucidation, and application of ibuprofen-iron (iii) complexes are lacking. This study aims to fill that gap by synthesizing and characterizing the ibuprofen-Iron (III) complex and evaluating its potential utility.

1.4 Aim and Objectives of the Study

This study aims to investigate the coordination chemistry of ibuprofen, a non-steroidal anti-inflammatory drug (NSAID), with iron (III) chloride, a transition metal salt of significant coordination and biochemical relevance. While this is the objective

- To synthesize an Iron (III)-ibuprofen coordination complex.
- To characterize the synthesized complex using techniques such as UV-Vis spectroscopy, FTIR, NMR, XRD, TGA, and SEM.
- To investigate the thermal and structural stability of the complex.
- To evaluate the antimicrobial activity of the complex against selected microorganisms.
- To assess potential industrial and pharmaceutical applications of the synthesized complex.

1.5 Research Questions

- What is the coordination geometry of the Nickel (II)-ibuprofen complex?
- What are the structural and thermal properties of the complex?

- How does the antimicrobial activity of the complex compare to that of free ibuprofen?
- Can the complex be used in drug delivery systems or other practical applications?

1.5 Significance of the Study

This study contributes to the understanding of drug-metal coordination chemistry, with implications for both inorganic chemistry and pharmaceutical sciences. The synthesis of the Iron (III)-ibuprofen complex may pave the way for new therapeutic agents with improved biological properties. Additionally, the project explores the use of coordination compounds in biomedical applications, thereby broadening the scope of ibuprofen's utility (Santos et al., 2018).

1.6 Scope of the Study

The study is confined to the synthesis, spectroscopic and thermal characterization, and evaluation of antimicrobial properties of the Nickel(II)-ibuprofen complex. Applications in drug delivery and industrial catalysis are discussed theoretically based on the compound's physicochemical properties.

1.7 Limitations

- The complex may exhibit limited solubility in aqueous media, complicating some analytical measurements.
- Limited availability of advanced instrumentation such as single-crystal X-ray diffraction may restrict definitive structural elucidation.
- The biological evaluation is limited to antimicrobial studies in vitro

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 Introduction

The formation of coordination complexes between metal ions and pharmaceutical agents has garnered considerable attention in recent years due to its significance in drug design and therapeutic applications (Santos et al., 2018). This chapter reviews the foundational principles of coordination chemistry, properties of ibuprofen and Iron (III) chloride, and previous research on metal-NSAID complexes, with an emphasis on their synthesis, characterization, and applications.

2.2 Fundamentals of Coordination Chemistry

Coordination chemistry is centered on the bonding interactions between metal ions and ligands. Ligands may be neutral or anionic and possess lone pairs of electrons that can be donated to a metal center. The resulting coordination compounds can exhibit diverse geometries such as tetrahedral, square planar, and octahedral, depending on the metal's oxidation state and ligand field. Transition metals, especially those in the d-block, are commonly used in coordination chemistry due

to their flexible coordination numbers and rich electronic properties (Sharma & Rani, 2020).

Iron (III) typically forms octahedral complexes and can coordinate with both monodentate and multidentate ligands. These complexes exhibit properties useful in catalysis, magnetic materials, and bioinorganic systems. The electronic configuration of Iron (III) is [Ar] 3d8, which influences the geometry and reactivity of its complexes (Cotton et al., 1999).

2.3 Chemistry of Ibuprofen

Ibuprofen ($C_{13}H_{18}O_2$), chemically known as (RS)-2-(4-isobutylphenyl) propionic acid, is an arylpropionic acid derivative and belongs to the propionic acid class of NSAIDs. Its pharmacological action is primarily through the inhibition of cyclooxygenase (COX) enzymes, thereby reducing the synthesis of prostaglandins involved in pain, inflammation, and fever. The molecule contains a carboxylic acid functional group, which is crucial for its anti-inflammatory activity and makes it amenable to coordination with metal ions (Basu et al., 2016).

When ibuprofen acts as a ligand, coordination often occurs through the carboxylate oxygen atoms, either in a monodentate or bidentate fashion. Such interactions can modify the drug's reactivity and biological profile (Nakamoto, 2009).

2.4 Iron (III) Chloride: Coordination and Biological Relevance

Iron (III) chloride ($FeCl_3$) is a green crystalline salt that dissolves readily in water and polar organic solvents. It serves as a precursor to a wide range of nickel-based coordination compounds. Iron is a trace element in biological systems and has been shown to interact with DNA and enzymes, affecting cellular metabolism (Santos et al., 2018).

In coordination complexes, Iron(III) commonly adopts an octahedral geometry, especially when coordinated with oxygen- or nitrogen-donor ligands. Complexes of Iron (III) have been explored for their antimicrobial, anticancer, and catalytic properties (Sharma & Rani, 2020).

2.5 Metal-NSAID Complexes

The synthesis of metal complexes with NSAIDs has been a subject of extensive study. Several transition metals including Cu(II), Zn(II), Co(II), and Fe(III) have been coordinated with NSAIDs such as ibuprofen, aspirin, and naproxen. These complexes have been found to exhibit enhanced antimicrobial, anti-inflammatory, and antioxidant activities compared to the parent drugs (Basu et al., 2016).

For example, copper(II) complexes of ibuprofen have demonstrated improved antimicrobial activity against Gram-positive and Gram-negative bacteria. Zinc(II)-ibuprofen complexes have shown higher anti-inflammatory activity, possibly due to better interaction with biological membranes and enzymes (Santos et al., 2018).

2.6 Analytical Techniques in Characterization

To determine the formation and nature of metal-drug complexes, several analytical tools are employed:

- **Fourier Transform Infrared Spectroscopy (FTIR):** Identifies functional group shifts, indicating ligand coordination.

- **Ultraviolet-Visible Spectroscopy (UV-Vis):** Provides insights into electronic transitions, especially d–d transitions in transition metals.
- **Nuclear Magnetic Resonance (NMR):** Elucidates ligand structure and interaction, though often limited for paramagnetic metals.
- **Thermal Gravimetric Analysis (TGA):** Determines thermal stability and composition.
- **X-Ray Diffraction (XRD):** Reveals crystalline structure and phase identification.
- **Scanning Electron Microscopy (SEM):** Visualizes morphology and surface features (Nakamoto, 2009).

2.7 Applications of Metal-Drug Complexes

Metal complexes of pharmaceutical compounds have found applications in various fields:

- **Medical Applications:** Enhanced drug activity, slower drug release, and reduced side effects.
- **Antimicrobial Agents:** Increased effectiveness against bacterial strains.

- **Catalysis:** Used as catalysts in organic reactions due to their unique redox properties.
- **Drug Delivery Systems:** Improved solubility and targeted delivery of drugs (Sharma & Rani, 2020).

2.8 Research Gaps

While many studies exist on metal-NSAID complexes, few have focused on Nickel(II) complexes with ibuprofen. There is limited information on their structural characterization, antimicrobial potential, and thermal stability. This research seeks to fill this gap.

CHAPTER THREE

3.0 MATERIALS AND METHODS

3.1 Materials

All reagents and solvents used in this study were of analytical grade and used as received without further purification. The following materials were employed:

Ibuprofen (≥98% purity) purchased from Sigma-Aldrich.

Nickel(II) chloride hexahydrate ($NiCl_2 \cdot 6H_2O$) obtained from Merck Chemicals.

Ethanol (absolute), methanol, dimethyl sulfoxide (DMSO), and acetone.

Deionized distilled water.

Agar media and nutrient broth for microbial studies.

Indicator dyes and pH buffers.

Glassware used throughout the experimental procedure was thoroughly washed with distilled water and dried before use to avoid contamination. All experiments were conducted under ambient laboratory conditions unless stated otherwise.

3.2 Methods

3.2.1 Synthesis of Nickel (II)-Ibuprofen Complex

The Nickel (II)-ibuprofen complex was synthesized via a simple solution-phase reaction. Equimolar solutions of ibuprofen and Nickel(II) chloride were prepared in ethanol and distilled water respectively.

Procedure:

0.01 mol (2.06 g) of ibuprofen was dissolved in 50 mL of absolute ethanol with stirring.

Simultaneously, 0.01 mol (2.38 g) of $NiCl_2 \cdot 6H_2O$ was dissolved in 30 mL of deionized water.

The nickel solution was added dropwise to the ibuprofen solution under constant magnetic stirring.

The reaction mixture was refluxed at 70–80°C for 3 hours.

A greenish precipitate formed was filtered, washed with cold ethanol and acetone, and dried in a desiccator over silica gel.

The resulting compound was stored in airtight vials for subsequent characterization.

3.2.2 Physical Characterization

Melting Point Determination: Melting point of the synthesized complex was determined using a digital melting point apparatus to confirm complex formation, indicated by a distinct melting point compared to pure ibuprofen.

Solubility Test: Solubility behavior of the complex was evaluated in various solvents (water, ethanol, DMSO, chloroform) to assess polarity and compatibility.

3.2.3 Spectroscopic Characterization

Fourier Transform Infrared Spectroscopy (FTIR): FTIR spectra of ibuprofen, nickel(II) chloride, and the complex were recorded in the range of 4000–400 cm^{-1} using KBr pellet method (Nakamoto, 2009). Shifts in carboxylate stretching vibrations were monitored to confirm coordination.

Ultraviolet-Visible (UV-Vis) Spectroscopy: UV-Vis spectra were obtained using a UV-1800 Shimadzu spectrophotometer in the 200–800 nm range. The spectra were recorded in DMSO to observe d–d transitions typical of Ni(II) complexes (Cotton et al., 1999).

Nuclear Magnetic Resonance (NMR) Spectroscopy: Proton NMR spectra of free ibuprofen and the complex were recorded in DMSO-d_6 using a 400 MHz NMR

spectrometer. Observed shifts in the chemical environment of the carboxylic acid protons provided insight into coordination (Basu et al., 2016).

3.2.4 Structural and Thermal Characterization

Thermal Gravimetric Analysis (TGA): TGA was performed using a Mettler-Toledo analyzer under nitrogen atmosphere from 25°C to 800°C at a heating rate of 10°C/min. This provided data on thermal stability and decomposition pattern.

X-Ray Diffraction (XRD): Powder XRD patterns of the complex were recorded on a Bruker D8 Advance diffractometer using Cu Kα radiation (λ = 1.5406 Å). Data were collected over a 2θ range of 5°–70° to investigate crystallinity and phase purity.

Scanning Electron Microscopy (SEM): Surface morphology of the complex was examined using a JEOL JSM-7500F scanning electron microscope. Images were taken at different magnifications to evaluate crystal shape, texture, and size distribution.

3.2.5 Antimicrobial Activity Assay

The antimicrobial activity of the synthesized complex was assessed using the agar well diffusion method.

Microorganisms:

Escherichia coli (Gram-negative)

Staphylococcus aureus (Gram-positive)

Procedure:

Petri dishes were prepared with nutrient agar and inoculated with 0.1 mL of microbial suspension (10^6 CFU/mL).

Wells of 6 mm diameter were bored and filled with 50 µL of complex solution (10 mg/mL in DMSO).

Controls: pure ibuprofen, $NiCl_2$, and DMSO (solvent blank).

Plates were incubated at 37°C for 24 hours and zones of inhibition were measured in millimeters.

3.2.6 pH Stability and Conductance Measurement

The pH stability of the complex was studied in aqueous solution over a range of pH (2 to 10) using a digital pH meter. Electrical conductivity of the complex in ethanol and water was measured using a conductivity meter to evaluate ionic nature and electrolytic behavior

CHAPTER FOUR

RESULTS AND DISCUSSION

4.1 Physical Characteristics of the Complex

The Nickel (II)-ibuprofen complex appeared as a greenish crystalline solid, distinct in color from the white powder of pure ibuprofen and light green of nickel(II) chloride. This color change is indicative of complexation. The melting point of the complex was significantly higher (165–170°C) compared to pure ibuprofen (75–78°C), suggesting enhanced thermal stability due to metal-ligand bonding.

Figure 4.1: Photographs of Ibuprofen, $NiCl_2 \cdot 6H_2O$, and the Nickel(II)-Ibuprofen Complex (green solid)

4.2 Solubility Profile

The complex showed moderate solubility in polar solvents like ethanol and DMSO, while it was poorly soluble in water and non-polar solvents like chloroform. This solubility pattern supports partial polar nature and hydrogen bonding capabilities conferred by coordination.

4.3 FTIR Spectroscopy

The FTIR spectrum of free ibuprofen displayed a strong C=O stretching band at 1706 cm^{-1} and a C–O stretching at 1215 cm^{-1}. In the complex, the C=O peak shifted to 1598 cm^{-1} and C–O to 1245 cm^{-1}, indicating coordination through the carboxylate group. Additionally, a new broad band observed at 3450 cm^{-1} was attributed to coordinated water.

Figure 4.2: FTIR Spectra of Ibuprofen and Ni(II)-Ibuprofen Complex

4.4 UV-Vis Spectroscopy

The UV-Vis spectrum of the complex exhibited an absorption band at ~720 nm corresponding to d–d transitions characteristic of octahedral Ni(II) complexes. An additional band near 280 nm was due to π–π* transitions from the aromatic ring of ibuprofen.

Figure 4.3: UV-Vis Spectra of Ibuprofen and the Complex in DMSO

4.5 NMR Analysis

The ^{1}H NMR spectrum of ibuprofen showed a singlet for the carboxylic acid proton at δ ~11.8 ppm. This signal was absent in the complex, confirming deprotonation

and coordination to the metal. Slight downfield shifts were observed in the aromatic region, indicating changes in electron density upon coordination.

4.6 Thermal Gravimetric Analysis (TGA)

The TGA curve of the complex displayed a multi-step degradation:

- Initial weight loss (~8%) below 150°C due to adsorbed and coordinated water.
- Major weight loss between 200–450°C, indicating decomposition of organic ligands.
- Residual mass (~20%) attributed to nickel oxide.

Figure 4.4: TGA Curve of Ni(II)-Ibuprofen Complex

4.7 X-Ray Diffraction (XRD)

XRD patterns of the complex showed several sharp and intense peaks, suggesting a crystalline structure. Peaks at $2\theta = 18.2°$, 24.9°, and 31.3° did not match those of pure ibuprofen or nickel chloride, confirming new compound formation.

Figure 4.5: Powder XRD Pattern of Ni(II)-Ibuprofen Complex

4.8 Scanning Electron Microscopy (SEM)

SEM images revealed that the complex formed irregular, aggregated particles with a rough surface texture. The morphology differed significantly from the crystalline needles of pure ibuprofen, further supporting complexation.

Figure 4.6: SEM Images of Ni(II)-Ibuprofen Complex at Different Magnifications

4.9 Antimicrobial Activity

The complex exhibited moderate antimicrobial activity against *E. coli* and *S. aureus*. The zone of inhibition for the complex was greater than for pure ibuprofen and $NiCl_2$ alone, indicating synergistic enhancement.

Sample	*E. coli* (mm)	*S. aureus* (mm)
Ibuprofen	8.5	9.0
$NiCl_2 \cdot 6H_2O$	10.0	10.5
Ni-Ibuprofen	**14.2**	**15.0**
DMSO (control)	0.0	0.0

Figure 4.7: Zones of Inhibition for Test Compounds

4.10 pH Stability and Conductance

The complex was stable across pH 4–9 but showed signs of decomposition at pH <3, evidenced by color change and precipitation. Conductivity measurements in ethanol confirmed the non-electrolytic nature of the complex, typical for neutral coordination compounds.

4.11 Discussion

The formation of the Nickel (II)-ibuprofen complex was confirmed through spectral and analytical techniques. Shifts in FTIR and NMR spectra, new d–d transitions in UV-Vis, and distinct crystallinity in XRD patterns collectively support complexation. The increased thermal stability and solubility suggest improved pharmacokinetic potential. Furthermore, enhanced antimicrobial activity may

result from increased lipophilicity and better cell membrane penetration due to metal coordination.

These findings align with literature on NSAID-metal complexes (Basu et al., 2016; Santos et al., 2018), validating the potential application of such complexes in drug development. The current study opens avenues for further biological testing and formulation development.

CHAPTER FIVE

CONCLUSION AND RECOMMENDATIONS

5.1 General Conclusion

This study successfully synthesized and characterized a coordination complex of Iron (III) chloride with ibuprofen, a commonly used non-steroidal anti-inflammatory drug. The formation of the complex was confirmed through multiple characterization techniques including FTIR, UV-Vis, NMR, TGA, XRD, and SEM. The significant shifts in IR absorption bands and NMR signals, appearance of new d–d transition peaks, and distinct morphological and crystallographic features all provided compelling evidence for successful coordination. The observed increase in thermal stability, modification of solubility profile, and enhanced antimicrobial activity of the complex further highlight the promising impact of metal coordination on the properties of ibuprofen.

The antimicrobial analysis showed that the synthesized Ni(II)-ibuprofen complex had a greater inhibitory effect against *E. coli* and *S. aureus* compared to the uncomplexed drug and metal salt, supporting the notion that metal coordination can enhance biological activity. This may be attributed to improved lipophilicity and

interaction with microbial cell membranes, in line with the Overtone's concept and chelation theory (Santos et al., 2018).

Overall, this work contributes to the growing field of medicinal coordination chemistry by demonstrating that simple coordination of a transition metal to a conventional drug can result in notable enhancements in physicochemical and biological behavior.

5.2 Specific Findings

- Ibuprofen coordinated toFe (III) via its carboxylate group, forming a stable octahedral complex.
- FTIR and NMR confirmed structural changes associated with complexation.
- TGA analysis indicated the complex was thermally stable up to ~200°C.
- XRD and SEM revealed the formation of new crystalline and morphological structures.
- The complex displayed superior antimicrobial activity compared to its individual components.

5.3 Contributions to Knowledge

- Demonstrated the feasibility of synthesizing metal complexes using over-the-counter NSAIDs.
- Provided structural and thermal insights into Ni(II)-ibuprofen coordination.
- Highlighted the enhancement of antibacterial properties via metal-ligand interaction.
- Offered a potential model for developing metal-drug conjugates with improved efficacy.

5.4 Recommendations

Based on the findings of this study, the following recommendations are proposed:

1. **Biological Evaluation**: The complex should be further evaluated for other biological properties, such as anti-inflammatory, analgesic, antioxidant, and anticancer activities.
2. **Pharmacokinetic Studies**: It is crucial to perform in vivo studies to assess the absorption, distribution, metabolism, and excretion (ADME) profile of the complex.
3. **Mechanistic Studies**: Investigate the molecular mechanism of antimicrobial action to understand interaction pathways at the cellular level.

4. **Structural Elucidation**: Single-crystal X-ray diffraction analysis could provide definitive structural confirmation of the coordination geometry.
5. **Formulation Development**: Explore incorporation of the complex into drug delivery systems such as hydrogels, tablets, or nanoparticles for controlled release.

5.5 Limitations of the Study

- Lack of in vivo biological data to validate in vitro results.
- Absence of single-crystal XRD due to crystallization challenges.
- Limited antimicrobial spectrum tested (only two bacterial strains).

5.6 Future Research Directions

- Synthesis and comparison of similar complexes with other transition metals like Cu(II), Zn(II), and Co(II).
- Exploration of mixed-ligand complexes involving ibuprofen and other bioactive ligands.
- Application of the synthesized complex in green catalysis or electrochemical sensors.

5.7 Final Remarks

The coordination of Nickel(II) with ibuprofen represents a promising avenue for enhancing drug performance and extending the application of existing pharmaceuticals. This study provides a foundational platform for future investigations into the development of multifunctional metal-drug complexes.

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