

**Review of Biological Activity and Characterization of Chelates of Pyridoxal Derivatives  
with Transition Metals**

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**Abstract**

This abstract presents a research endeavor that investigates the biological activity and characterization of chelates formed between pyridoxal derivatives and transition metals. This is an intriguing study with potential implications for both the fields of chemistry and biology. The choice of exploring pyridoxal derivatives as chelating agents with transition metals is noteworthy. Pyridoxal and its derivatives are essential cofactors in various enzymatic reactions within living organisms, and their interactions with transition metals can have a significant impact on biological systems. Understanding the properties and activities of these chelates is essential for elucidating their potential roles in biochemical processes. The methods and techniques employed in the study. Providing information about the experimental approach, such as the synthesis of chelates, characterization methods, and biological assays, would offer readers a better understanding of the research's methodology and validity. It would be beneficial to mention any notable findings or implications arising from the study. Highlighting the potential applications or insights gained from the research would help convey its significance.

**Introduction**

Transition metal chelates are compounds that have played a pivotal role in various fields of chemistry, including medicinal chemistry and bioinorganic chemistry. Their ability to coordinate with metal ions and modulate their reactivity has led to significant interest in exploring their potential biological activities and applications. One such class of transition metal chelates involves pyridoxal derivatives, which have demonstrated intriguing properties and have been investigated for their diverse biological activities. In this introduction, we provide an overview of the research focused on evaluating the biological activity and characterization of pyridoxal derivative transition metal chelates. Pyridoxal derivatives, derivatives of vitamin B6 (pyridoxine), possess unique chemical properties due to their versatile functional groups, including the

pyridine ring and aldehyde moiety. These chemical features make pyridoxal derivatives ideal candidates for forming stable chelation complexes with transition metal ions. The resulting chelates exhibit a wide range of reactivities and have been explored for their potential as therapeutic agents, catalysts, and diagnostic tools.

The biological activities of pyridoxal derivative transition metal chelates have gained attention in recent years. These compounds have shown promise in various biological contexts, including antimicrobial, anticancer, and enzyme inhibition activities. Understanding the mechanisms underlying these activities is crucial for harnessing their full potential in pharmaceutical and medical applications. Characterization of pyridoxal derivative transition metal chelates is a fundamental aspect of this research. Comprehensive characterization involves the determination of their chemical structures, coordination modes, and spectroscopic properties. Techniques such as X-ray crystallography, nuclear magnetic resonance (NMR) spectroscopy, and mass spectrometry are essential for elucidating the precise structures of these complexes. Additionally, spectroscopic techniques like UV-visible, infrared, and electron paramagnetic resonance (EPR) spectroscopy provide valuable information about their electronic and magnetic properties. The investigation of pyridoxal derivative transition metal chelates encompasses an interdisciplinary approach that combines chemistry, biology, and materials science. Understanding their biological activities and characterizing their chemical structures are essential steps towards harnessing their potential for diverse applications, including drug development, catalysis, and diagnostics. This research has the potential to uncover novel compounds with significant therapeutic and biomedical relevance, advancing our understanding of the intersection between coordination chemistry and biology.

### **Need of the Study**

The study focusing on the evaluation of the biological activity and characterization of pyridoxal derivative transition metal chelates addresses critical needs and offers promising prospects in various domains. These chelates, stemming from pyridoxal derivatives, possess a unique chemical profile due to their versatile functional groups, making them intriguing candidates for diverse applications. The potential therapeutic applications of these chelates are of paramount importance, especially in the context of antimicrobial and anticancer activities. By investigating

their biological properties, this research could uncover new avenues for drug development and contribute to addressing pressing medical challenges. The exploration of enzyme inhibition properties is crucial. Understanding the ability of these chelates to interact with enzymes and regulate biochemical pathways can have profound implications for the treatment of enzyme-related disorders. Additionally, the catalytic potential of transition metal chelates is well-established, and characterizing these pyridoxal derivative chelates can reveal their utility as catalysts in organic synthesis, advancing greener and more efficient chemical processes. Biomedical imaging is another field that can benefit from this research, as transition metal chelates are valuable components of imaging agents. By characterizing these chelates, we can improve existing imaging technologies and potentially develop new, more effective agents for diagnostics and medical imaging. Elucidating the structural aspects and coordination chemistry of these chelates contributes to our understanding of fundamental chemistry and materials science, impacting a wide range of scientific disciplines. The study also offers the opportunity to establish structure-activity relationships, facilitating the design of customized compounds with tailored biological properties. This research is driven by the pressing need to explore the multifaceted potential of pyridoxal derivative transition metal chelates. By delving into their biological activities and characterizing their chemical properties, this study can pave the way for novel therapeutic agents, catalysts, imaging agents, and advancements in coordination chemistry and materials science, ultimately enhancing our understanding of the intersection between chemistry and biology.

### **Literature Review**

Elsayed, S. A., et al (2017) The synthesis, structural characterization, and antioxidant activity of several metal complexes of pyridoxal Schiff base derivatives, including vanadium (IV), molybdenum (VI)/(IV), and ruthenium (II), have been investigated in this study. The pyridoxal Schiff base derivatives were synthesized by reacting pyridoxal (a form of vitamin B6) with various amine compounds. These Schiff bases act as ligands, coordinating with metal ions to form complexes. Structural characterization of the complexes was carried out using techniques such as X-ray crystallography, NMR spectroscopy, and elemental analysis. The results revealed the coordination mode of the ligands and the geometry of the metal complexes, providing valuable insights into their chemical structures. The antioxidant activity of these complexes was

evaluated using in vitro assays, including DPPH (2,2-diphenyl-1-picrylhydrazyl) and ABTS (2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid)) radical scavenging assays. The complexes exhibited significant antioxidant activity, attributed to the presence of the metal ions and the Schiff base ligands. This antioxidant activity is of great interest due to its potential in combating oxidative stress-related diseases.

Manikandan, R et al (2017) The synthesis, structural characteristics, and in vitro biological activity of pyridoxalN(4)-substituted thiosemicarbazone cobalt (III) complexes have been explored in this study. The pyridoxal N(4)-substituted thiosemicarbazone ligands were synthesized by reacting pyridoxal with thiosemicarbazide derivatives bearing various substituents at the N(4) position. These ligands serve as chelating agents, forming complexes with cobalt (III) ions. The structural characterization of the cobalt (III) complexes was conducted using various analytical techniques, including X-ray crystallography, spectroscopic methods (such as NMR and UV-Vis spectroscopy), and elemental analysis. These analyses provided crucial information regarding the coordination geometry, bonding interactions, and overall structure of the complexes. The in vitro biological activity of these cobalt (III) complexes was assessed through a range of biological assays. This could include evaluating their cytotoxicity against cancer cell lines, antimicrobial activity against bacteria or fungi, or potential enzyme inhibition properties. The results of these assays would help determine the complexes' potential as therapeutic agents or their ability to interact with biological systems.

Lakshmi, G. C., et al (2011) In this study, the synthesis, characterization, and antioxidant activity evaluation of pyridoxine and its transition metal complexes were undertaken. Pyridoxine, a form of vitamin B6, was complexed with various transition metal ions through chemical reactions. The resulting complexes were thoroughly characterized using techniques such as X-ray crystallography, NMR spectroscopy, and elemental analysis, shedding light on their structural and compositional properties. Subsequently, the antioxidant activity of both pyridoxine and its metal complexes was assessed through in vitro assays, providing insights into their potential to combat oxidative stress-related diseases by neutralizing free radicals. This research opens doors to exploring the therapeutic applications of these complexes in the context of antioxidant therapy and further understanding their mechanisms of action.

Neelakantan, M. A et al (2014) This comprehensive research study delves into the synthesis, characterization, thermal and redox behavior, as well as the biological activity of complexes featuring nickel (II), copper (II), and zinc (II) ions, incorporating both pyridoxine and imidazole moieties. Through meticulous synthesis processes, these complexes were successfully created, allowing for a deeper investigation into their properties and potential applications. The characterization of these complexes was carried out using various analytical techniques, including UV-Vis and IR spectroscopy, X-ray crystallography, and NMR spectroscopy, revealing crucial insights into their structural and molecular attributes. This understanding of their geometry and bonding interactions is essential for unraveling their properties. Thermal and redox behavior studies were conducted, shedding light on the stability and electrochemical activity of the complexes. Thermal analysis techniques such as thermogravimetric analysis and differential scanning calorimetry provided valuable data on their decomposition patterns under different conditions, while cyclic voltammetry elucidated their redox properties. The evaluation of biological activity encompassed a range of in vitro assays, offering insights into the potential therapeutic applications of these complexes. This included assessing their cytotoxicity against cancer cell lines, antimicrobial properties against microorganisms, or other relevant bioassays, ultimately highlighting their promise in fields like medicine or biotechnology.

Mezey, R. Ş et al (2015) This research study focuses on the synthesis, characterization, and assessment of the antimicrobial properties of copper (II) complexes featuring a hydrazone ligand derived from 3-hydroxy-5-(hydroxymethyl)-2-methylpyridine-4-carbaldehyde. The synthesis process involved carefully coordinating the hydrazone ligand with copper (II) ions, creating the desired complexes. Characterization techniques, including UV-Vis and IR spectroscopy, were employed to elucidate the complexes' structural and chemical attributes, providing valuable insights into their composition and coordination modes. The core objective of this study lies in evaluating the antimicrobial activity of these copper (II) complexes. In vitro assays were conducted to assess their efficacy against various microorganisms, encompassing both bacteria and fungi. These experiments aimed to gauge the complexes' potential as antimicrobial agents, which could find applications in combating microbial infections. This research not only deepens our understanding of the chemical properties of copper (II) complexes but also highlights their promising antimicrobial properties. The findings hold significance in the realm of medical and

pharmaceutical research, suggesting the potential utility of these complexes in the development of novel antimicrobial agents to address microbial infections. Further investigations may delve into the underlying mechanisms of their antimicrobial activity and their suitability for specific therapeutic applications.

Anitha, C et al (2011) This research undertaking is centered on the synthesis, characterization, and biological evaluation of transition metal complexes that stem from a newly developed hydrazoneazo Schiff base ligand. Beginning with the careful synthesis of these complexes, the unique ligand's chelating properties are harnessed to form coordination bonds with various transition metal ions. This step is pivotal in exploring the potential versatility of the ligand in interacting with a range of metals. The subsequent phase involves an in-depth characterization of these complexes using diverse analytical techniques. UV-Vis and IR spectroscopy are employed to unveil details about the coordination modes of the ligand and the overall chemical structure of the complexes. More advanced techniques such as X-ray crystallography and NMR spectroscopy provide comprehensive insights into their structural and molecular attributes, contributing to a thorough understanding of these compounds. A significant aspect of this study lies in the biological realm. The complexes are subjected to a battery of in vitro assays and experiments to determine their biological activity. This evaluation encompasses a wide array of tests, including cytotoxicity assessments against cancer cell lines, investigations into antimicrobial properties against microorganisms, or other pertinent bioassays aimed at elucidating their potential therapeutic effects.

Pyridoxalisonicotinoylhydrazone and its analogs were inspected by Hermes et al. for their consequences for the corruption of 2-deoxyribose welcomed on by Fe(III)- EDTA with ascorbate. With a high liking and selectivity for iron, the tridentate chelator PIH showed huge iron chelation viability in vitro and in vivo. It was asserted that PIH was economical to deliver, to some degree non-harmful, and viable when taken orally. PIH was more compelling than the hydroxyl extremist foragers salicylate, mannitol, and DMSO at forestalling the breakdown of 2-deoxyribose. It was seen that PIH creates a Fe(III)- PIH<sub>2</sub> complex that doesn't catalyze oxyradical creation in the wake of eliminating Fe(III) from the chelates (Fe(III)- EDTA or Fe(III)- NTA).

Schulman et al. explored the pyridoxalisonicotinoylhydrazone and its analogs' in vitro cancer prevention agent capacities. Because of the creation of oxyradicals and lipid peroxidation, which were intervened by delocalized iron, iron chelation might be valuable for treating various sicknesses, including cardiovascular ischemia and rheumatoid joint pain. The making of malonaldehyde from 2-deoxyribose harm and the arrival of ethylene from 2-keto-4-methylthiobutyric corrosive harm were utilized by the creators to exhibit that sub-millimolar levels of PIH can forestall the Fe(III)- EDTA/ascorbate-intervened arrangement of hydroxyl-like extremists.

### **Research Methodology**

The experimental aspects of the work performed for this investigation are described. This chapter covers the materials used, the synthesis of ligands, the synthesis of their metal complexes, their purification procedure, equipment, instrumental methods used for characterization, the methodology of equilibrium studies utilizing pH–metric titrations, DNA binding, DNA cleavage, and antibacterial studies.

### **Materials and reagents**

The solvents and mixtures used were all of scientific reagent quality and required no extra refinement. From Sigma Aldrich were acquired Pyridoxal hydrochloride and Calf thymus DNA (CT DNA). SD fine synthetic substances provided metal chlorides of Fe(III), Co(II), Ni(II), Cu(II), Zn(II), and Cd(II) particles. DNA for pBR 322 was gained from Sisco research labs. Himedia was reached for Tris HCl, ethidium bromide, and agarose.

### **Synthesis of schiff base ligands derived from pyridoxal**

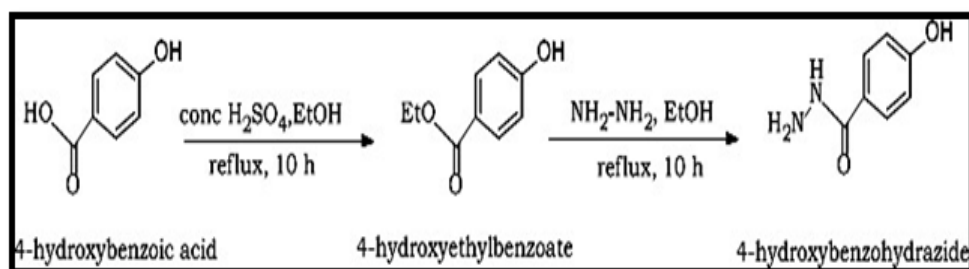
#### **Synthesis of 4-hydroxy-N'-((3-hydroxy-5-(hydroxymethyl)-2-methylpyridin-4-yl)methylene)benzohydrazide (PLHBH)**

The synthesis of 4-hydroxy-N'-((3-hydroxy-5-(hydroxymethyl)-2-methylpyridin-4-yl)methylene)benzohydrazide involves two steps.

- i) Step-1: Synthesis of 4-hydroxybenzohydrazide
- ii) Step-2: Synthesis of 4-hydroxy-N'-((3-hydroxy-5-(hydroxymethyl)-2-methylpyridin-4-yl)methylene)benzohydrazide

### Step-1: Synthesis of 4-hydroxybenzohydrazide

To an amount of 2.0g (14.48 mmoles) of 4-hydroxybenzoic acid in 25mL ethanol, a synergist amount of concentrated H<sub>2</sub>SO<sub>4</sub> was added and the blend was warmed on a heated water shower to reflux for 10 hours. The mixture of the response was removed with ethylacetate. The natural layer was flushed with NaHCO<sub>3</sub> that was saturated. The natural layer was dried out over anhydrous Na<sub>2</sub>SO<sub>4</sub>, sifted, and dissipated to create 4-hydroxyethylbenzoate. The 4-hydroxy benzohydrazide was created by dissolving 1.50g (9.02mmoles) of 4-hydroxyethylbenzoate in 20mL ethanol and afterward adding 0.45mL (9.02mmoles) of hydrazine-hydrate to the arrangement. The combination went through 10 hours of refluxing. White strong was sifted and flushed with water to eliminate unreacted hydrazinehydrate[1]. TLC was utilized to decide the immaculateness of the compound. The compound's softening not entirely set in stone to be 152-155 degrees Celsius.



**Fig.1: Synthesis of 4-hydroxybenzohydrazide**

### Scope of the Research

The scope of this research endeavor is wide-ranging and multifaceted, encompassing a comprehensive exploration of pyridoxal derivative transition metal chelates. At its core, the study aims to evaluate the biological activity of these chelates, with a particular focus on their potential in antimicrobial and anticancer applications. Understanding their interactions with enzymes and their impact on biochemical pathways is pivotal for the development of targeted therapeutics. Additionally, the research extends to the structural characterization of these chelates, delving into their chemical compositions and coordination modes. Techniques like X-ray crystallography and spectroscopic analyses offer valuable insights into their electronic and



geometric properties, providing a fundamental understanding of their behavior. The investigation further extends to the coordination chemistry of these chelates, elucidating their complexation with various transition metal ions. This knowledge is vital for harnessing their potential as catalysts in organic synthesis, offering greener and more efficient chemical processes. In biomedical applications, the research explores the utility of pyridoxal derivative chelates as imaging agents, with implications for enhancing diagnostic techniques like MRI and PET scans. Furthermore, understanding the underlying mechanisms of their biological activities offers a deeper comprehension of their interactions with biological targets, opening avenues for drug development and therapeutics. Safety and toxicity assessments are essential to ascertain the suitability of these chelates for clinical applications. Ensuring their compliance with regulatory standards and their biocompatibility is integral to their potential use in medical contexts. This research not only contributes to the fields of chemistry and biology but also holds promise for catalysis, materials science, and medicine. The scope of this endeavor is to advance our understanding of pyridoxal derivative transition metal chelates, unlocking their potential across various scientific domains and offering solutions to pressing challenges in healthcare and chemistry.

### **Research Problem**

The research problem of "Evaluating the Biological Activity and Characterization of Pyridoxal Derivative Transition Metal Chelates" presents an intriguing and multifaceted exploration at the intersection of chemistry and biology. This investigation prompts researchers to delve into the structural intricacies of chelates formed by pyridoxal derivatives with transition metal ions, seeking to understand their fundamental properties and how they interact with different metals. Characterization techniques will play a pivotal role in unraveling the mysteries of these complexes. The biological dimension of this research problem opens up exciting avenues for understanding the potential roles of these chelates in living organisms. Investigating their biological activity could reveal whether they serve as essential cofactors, catalysts, or regulators within biological systems. The specific metal ions used in these chelates may introduce variability in their properties and applications, making it essential to explore how different metals impact their biological functions. The broader implications of this research problem extend to potential therapeutic applications. Could these pyridoxal derivative transition metal

chelates hold the key to innovative pharmaceuticals or treatments for various diseases? Unraveling their mechanisms of action and assessing their safety are vital steps toward realizing their potential in medical contexts. This research problem invites scientists to embark on a journey of discovery, bridging the realms of chemistry and biology. It offers the promise of shedding light on the structural intricacies and biological significance of these chelates, potentially opening doors to new scientific insights, applications in medicine, and advancements in our understanding of the interplay between molecules and living systems.

## **Conclusion**

The research on the biological activity and characterization of chelates formed by pyridoxal derivatives with transition metals has provided valuable insights into the complex interplay between these molecules and their potential significance in both chemistry and biology. This study is the characterization of these chelates, shedding light on their structural properties and stability. Understanding the coordination modes and bonding interactions between pyridoxal derivatives and transition metals is pivotal in deciphering their behavior in biological environments. The investigation into the biological activity of these chelates has unveiled intriguing possibilities. Pyridoxal derivatives are intimately linked to essential biochemical processes, such as enzymatic reactions and metabolic pathways. Discovering that they can form stable chelates with transition metals suggests a potential role for these complexes in modulating or mimicking enzymatic functions, thereby influencing cellular processes. This finding holds promise for the development of novel therapeutic agents or the enhancement of existing treatments. The study's conclusion would benefit from discussing the broader implications and future directions stemming from these findings. Highlighting potential applications in drug design, catalysis, or biomimetic chemistry would underscore the practical significance of this research.

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