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Assessing the Biological Activity and Characterization of Chelates of Pyridoxal Derivatives with Transition Metals

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Abstract

This study delves into the intriguing realm of pyridoxal derivatives' chelation with transition metals, assessing both their biological activity and structural characterization. Pyridoxal derivatives are essential cofactors in numerous biochemical processes, making their interactions with transition metals of considerable interest in bioinorganic chemistry.The research begins by elucidating the structural aspects of these chelates, shedding light on their coordination geometries and bonding interactions. Characterization techniques such as spectroscopy and crystallography are employed to unravel the intricate details of these complexes, providing essential insights into their stability and reactivity. In parallel, the study explores the biological activities of these chelates, focusing on their potential impact on biological systems. Understanding how these complexes influence enzymatic reactions, cellular processes, or metal transport mechanisms is crucial for unraveling their roles in living organisms and their potential applications in medicinal chemistry or bioinorganic catalysis. the research investigates the potential for these chelates to serve as biomimetic models for enzymatic reactions involving pyridoxal derivatives. Such insights could pave the way for the development of novel catalysts or therapeutic agents, expanding our understanding of both chemistry and biology.

Introduction

The field of bioinorganic chemistry explores the intricate interplay between biological molecules and transition metals, shedding light on the crucial roles these elements play in living organisms. Within this context, the study titled "Assessing the Biological Activity and Characterization of Chelates of Pyridoxal Derivatives with Transition Metals" embarks on an intriguing journey to investigate the biological properties and structural characteristics of chelates formed by pyridoxal derivatives with transition metals. This research endeavors to

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bridge the gap between chemistry and biology, unraveling the mysteries of these complexes and their potential implications for both disciplines. Pyridoxal derivatives, derived from vitamin B6, are integral cofactors in a myriad of enzymatic reactions essential for life. Their versatility in facilitating various biochemical processes, such as amino acid metabolism and neurotransmitter synthesis, underscores their significance in biology. However, their interactions with transition metals have remained a captivating enigma, holding the promise of unveiling novel insights into the bioinorganic world. At the outset, this research seeks to delve into the structural aspects of these chelates, aiming to elucidate the coordination geometries and bonding interactions that govern their stability and reactivity. Employing cutting-edge characterization techniques, such as spectroscopy and crystallography, the study endeavors to unravel the intricate details of these complexes. This structural exploration is pivotal in comprehending the fundamental nature of pyridoxal derivative-metal interactions.

This investigation explores the biological activities of these chelates, focusing on their potential impact within biological systems. Understanding how these complexes influence enzymatic reactions, cellular processes, or metal transport mechanisms is fundamental in unraveling their roles in living organisms. The knowledge gleaned from these biological assessments could have far-reaching implications, extending from fundamental biochemical understanding to applications in medicinal chemistry and bioinorganic catalysis. the research delves into the possibility of these chelates serving as biomimetic models for enzymatic reactions involving pyridoxal derivatives. By mimicking the behavior of native cofactors, these complexes might offer pathways to the development of innovative catalysts or therapeutic agents, advancing our understanding of both chemistry and biology. this study stands at the intersection of two dynamic fields: chemistry and biology. By assessing the structural characteristics and biological activities of chelates formed by pyridoxal derivatives with transition metals, it aims to provide a holistic perspective on these intriguing complexes. The potential applications and insights emerging from this research hold the promise of enriching our understanding of the intricate relationship between biological molecules and transition metals.

Importance of the Study

By unraveling the complex interactions between pyridoxal derivatives and transition metals, this research contributes to our fundamental understanding of essential biochemical processes. These derivatives are crucial cofactors in numerous enzymatic reactions vital for life, and

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comprehending how they interact with transition metals illuminates the underlying mechanisms of these biological processes. The study's exploration of the biological activities of these chelates opens the door to potential advancements in medicine, offering the prospect of developing novel pharmaceuticals and therapeutic agents. This research also embodies the interdisciplinary nature of bioinorganic chemistry, bridging the divide between the chemical and biological sciences. It enriches our knowledge of how metals function within biological systems, with implications extending to materials science, catalysis, toxicology, and environmental science. Additionally, the investigation of these chelates as biomimetic models unveils opportunities for catalytic applications, potentially revolutionizing industrial processes. Ultimately, this study promises to advance our understanding of both the molecular intricacies of life and the versatile applications of chemistry in addressing critical challenges across multiple scientific disciplines.

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-methyl

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pyridin-4-yl)methylene)benzohydrazideinvolves 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 answer of 2.0gm (14.48 mmoles) of 4-hydroxybenzoic corrosive in 25mL ethanol, a synergist amount of concentrated H2SO4 was added and the blend was warmed on a heated water shower to reflux for 10 hours. The mélange of the response was removed with ethylacetate. The natural layer was flushed with NaHCO3 that was saturated.The natural layer was dried out over anhydrous Na2SO4, 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.

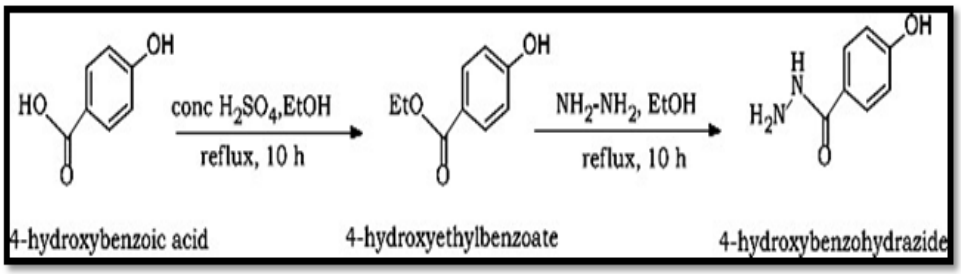

Fig. 1:Synthesis of 4-hydroxybenzohydrazide

Step-2: Synthesis of 4-hydroxy-N′-((3-hydroxy-5-(hydroxymethyl)-2-methylpyridin-4-yl)methylene)benzohydrazide

4-hydroxy-N′-((3-hydroxy-5-(hydroxymethyl)-2-methylpyridin-4-yl)methylene)benzohydrazide was prepared by dissolving 0.50gm (2.45mmoles) of pyridoxal hydrochloride in 25mL hot ethanol, then 0.25mL (2.45mmoles) of triethylamine was added,followed by the addition of 0.37gm (2.45mmoles) of 4-hydroxybenzohydrazide. Two

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hours were spent refluxing the mixture in a heated water bath. The progression of the reaction was monitored using TLC with a 1:10 mixture of methanol and chloroform.The solid yellow compound separated by filtration was collected, rinsed with double-distilled water, dried, and recrystallized with absolute ethanol. It was determined that the compound has a melting point between 187 and 190 degrees Celsius.

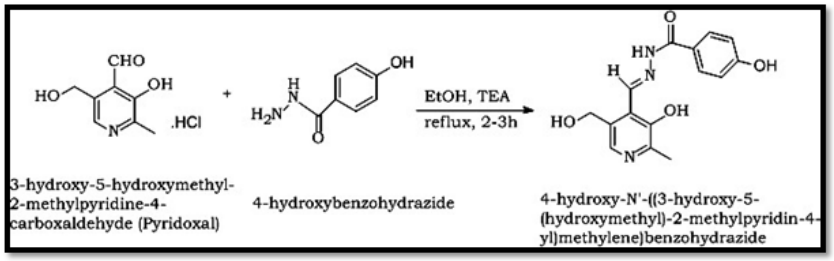

Fig.2 Synthesis of 4-hydroxy-N′-(3-hydroxy-5-(hydroxymethyl) -2-methylpyridin-4-yl)methylene)benzohydrazide

3-nitro-N′-((3-hydroxy-5-(hydroxymethyl)-2-methylpyridin- 4-yl)methylene)benzohydrazide (PLNBH)

The synthesis of 3-nitro-N′-((3-hydroxy-5-(hydroxymethyl)-2-methylpyridin-4-yl)methylene)benzohydrazidewas carried out in two steps.

i) Step-1: Synthesis of 3-nitrobenzohydrazide

ii) Step-2: Synthesis of3-nitro-N′-((3-hydroxy-5-(hydroxymethyl)-2-methylpyridin-4-yl)methylene)benzohydrazide

i) Step-1: Synthesis of 3-nitrobenzohydrazide

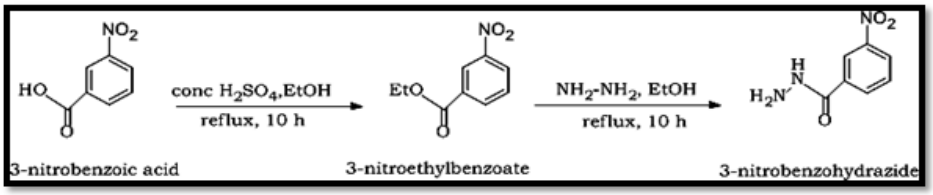

Fig. 3 : Synthesis of 3-nitrobenzohydrazide

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ii) In ethanol, 3.0g (17.94 mmoles) of 3-nitrobenzoic corrosive was disintegrated, and 2-3 beads of concentrated H2SO4 were added.The resultant arrangement was warmed for 10-12 hours in a bubbling water shower. The mélange of the response was weakened with ethylacetate. Isolating and washing the natural layer with immersed NaHCO3.The natural layer was got dried out over anhydrous Na2SO4, separated, and vanished to create 3-nitroethylbenzoate. The combination was refluxed for 9 hours after 0.6mL of hydrazine-hydrate (12.0mmoles) was added to 2.34g of 3-nitroethylbenzoate (12.0mmoles) broke up in 25mL of ethanol. The compound was separated into ethylacetate and dissipated to create 3-nitrobenzohydrazide [1]. Attention was used to screen the response's advancement. The compound's dissolving point was 177 to 179 degrees Celsius.

iii) Step-2: Synthesis of 3-nitro-N′-(3-hydroxy-5-(hydroxymethyl)-2-methylpyridin-4-yl)methylene)benzohydrazide

3- nitro-N′-(3-hydroxy-5-(hydroxymethyl)-2-methylpyridin-4- yl)methylene)benzohydrazide was prepared by dissolving 1.0gm (4.92mmoles)of pyridoxal hydrochloride and0.89gm(4.92mmoles) of 3- nitrobenzohydrazidein 25mL of ethanol.Add 0.50mL (4.90 mmoles) of triethylamine to the above mixture, and allow it to reflux for 2-3 hours.To obtain the pure compound, the yellow solid was filtered and rinsed with water. 80% ethanol was used to dry and recrystallize the substance. The compound's purity was evaluated by TLC using a mixture of methanol and DCM (1:9).The compound had a melting point of 205 to 210 degrees Celsius.

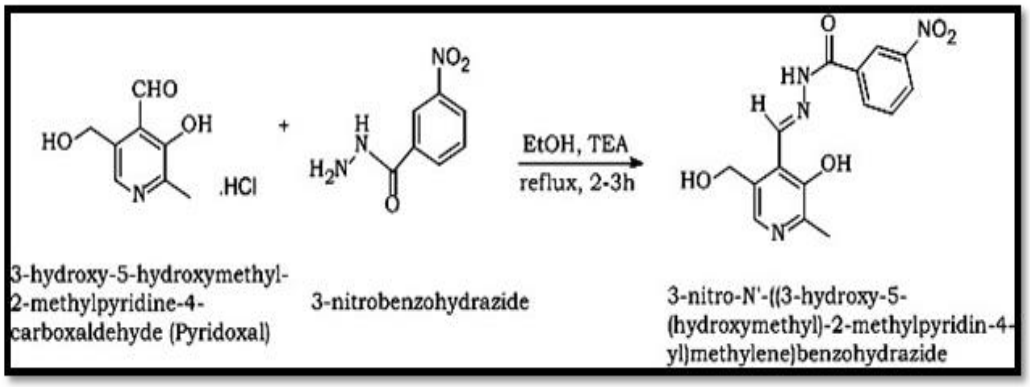

Fig.4: Synthesis of 3-nitro-N′-(3-hydroxy-5-(hydroxymethyl) -2-methylpyridin-4-yl)methylene)benzohydrazide

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2,4-dichloro-N′-((3-hydroxy-5-(hydroxymethyl)-2-methylpyridin-4-yl) methylene)benzohydrazide (PLDCBH)

The synthesis of the compounds involves two steps.

i) Step-1: Synthesis of 2,4-dichlorobenzohydrazide
ii) Step-2: Synthesis of 2,4-dichloro-N′-((3-hydroxy-5-(hydroxymethyl)-2-methylpyridin-4-yl)methylene)benzohydrazide

i) Step-1: Synthesis of 2,4-dichlorobenzohydrazide

To a solution of 2.0 grams (10.47 mmoles) of 2,4- dichlorobenzoic acid in ethanol, a catalytic amount of concentrated H2SO4 was added, and the mixture was refluxed for 9 to 10 hours. The reaction mixture was diluted initially with ethylacetate and then with water. The organic layer was extracted and rinsed with saturated NaHCO3.To obtain 2,4-dichloroethylbenzoate, the compound was filtered. 1.75g (7.91mmoles) of 2,4- dichloroethylbenzoate was dissolved in ethanol, 0.4mL (7.90mmoles) of hydrazine-hydrate was added, and the mixture was refluxed over a hot water immersion for 11 hours. Using absolute ethanol, the solid 2,4-dichlorobenzohydrazide obtained in step [1] was filtered, dehydrated, and recrystallized. TLC was used to verify the compound's purity, and the product's melting point was discovered to be between 180 and 182 degrees Celsius.

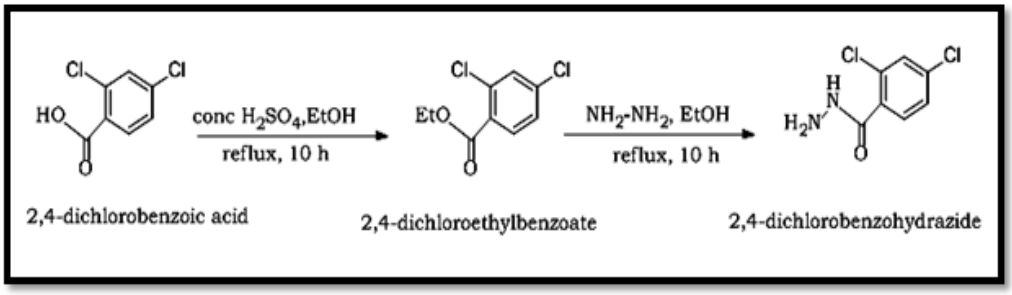

Fig.5: Synthesis of 2,4-dichlorobenzohydrazide

i) Step-2: Synthesis of 2,4-dichloro-N′-(3-hydroxy-5-(hydroxymethyl)-2-methylpyridin-4-yl)methylene)benzohydrazide

In 20mL ethanol, 0.50g (2.45mmoles) of pyridoxalhydrochloride and 0.50g (2.45mmoles) of 2,4-dichlorobenzohydrazide were dissolved. The solution was then added 0.24mL of

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triethylamine (2.45mmoles) and refluxed for 2 hours in a heated water bath. The reaction medium was poured into water and ethyl acetate was used to extract it. The solid compound of pure yellow hue was obtained by washing the organic layer with water and concentrating it under reduced pressure. Using 90% ethanol, the substance was re-crystallized. Using a 5:1 mixture of chloroform and methanol, TLC was used to monitor the progression of the reaction.The melting point of PLDCBH was determined to be 221-225 degrees Celsius.

Results and Discussion

All of the substances were yellow solids that were soluble in ethanol, methanol, DMF, and DMSO and stable at room temperature. TLC was used to verify the compounds' purity.Table 3.1 presents the physical constants and elemental analysis data.

TABLE - 1. PHYSICAL CONSTANTS AND ANALYTICAL DATA OF LIGANDS

Compound	Molecular Formula	M.pt. °C	Elemental Analysis Found (calc) %C	%H	%N
PLHBH	$C_{15}H_{15}N_3O_4$	187-190	59.51 (59.74)	4.64 (4.97)	13.73 (13.93)
PLNBH	$C_{15}H_{14}N_4O_5$	205-210	54.73 (54.55)	4.31 (4.24)	16.84 (16.97)
PLDCBH	$C_{15}H_{13}N_3O_3Cl_2$	221-225	50.95 (50.84)	3.78 (3.67)	11.62 (11.86)
PLFBH	$C_{15}H_{14}N_3O_3F$	176-180	59.63 (59.41)	4.76 (4.62)	13.95 (13.86)
PLTMBH	$C_{18}H_{21}N_3O_6$	203-205	57.45 (57.63)	5.41 (5.69)	11.19 (11.27)

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

IR spectrum

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The IR spectrum of the PLHBH [1] showed, stretching bands corresponding to 3336cm-1 ν(O-H) due to phenolic-OH, amide ν(N-H) band at 3150cm-1, 2900cm-1corresponds to ν(NH+),1662cm- 1attributed to ν(C=O), azomethine at 1602cm-1 ν(C=N), ν(C-O)phenolic stretching band at1270cm-1 and 3020cm-1is due to aromatic ν(C-H). At 620 cm-1 and 414 cm-1, the pyridine ring bending vibrations were seen.

UV-Visible

The PLHBH's UV-visible spectrum revealed strong peaks at 31948 cm-1 and 28985 cm-1, which correspond to the pyridinering and benzohydrazide moiety's n- and -* transitions, respectively.

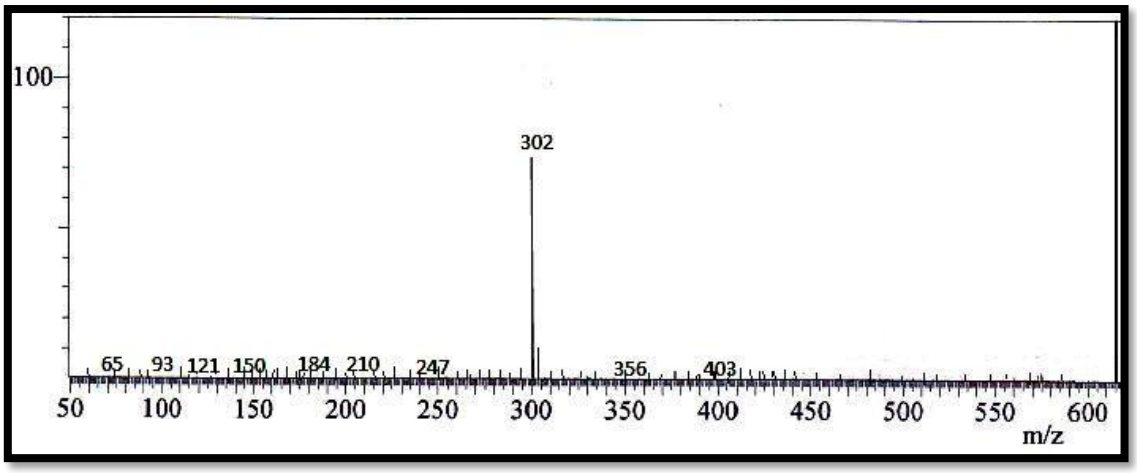

FIG.6 MASS SPECTRUM OF PLHBH

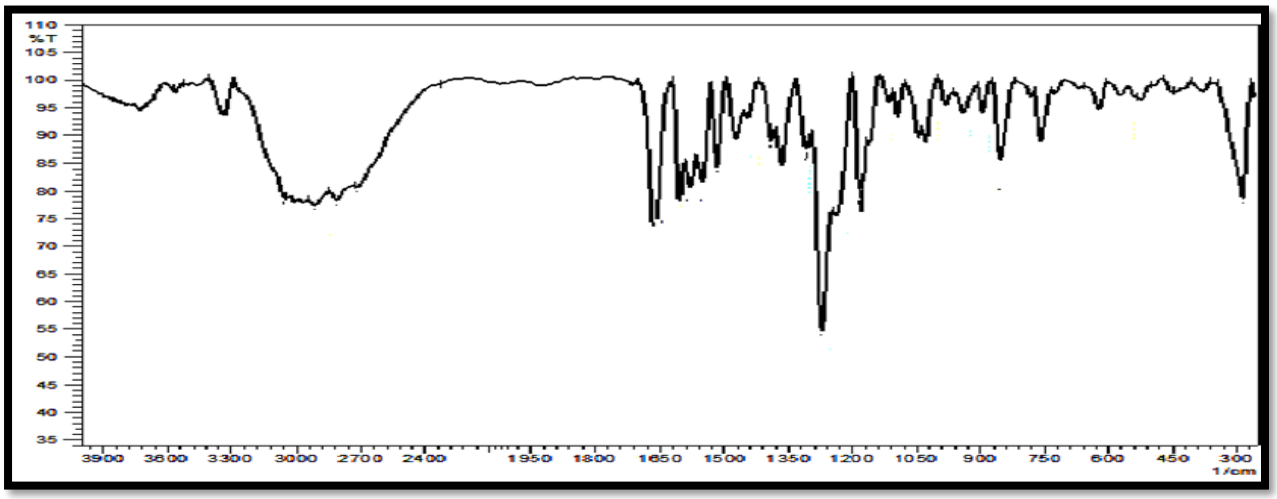

FIG. 7 IR SPECTRUM OF PLHBH

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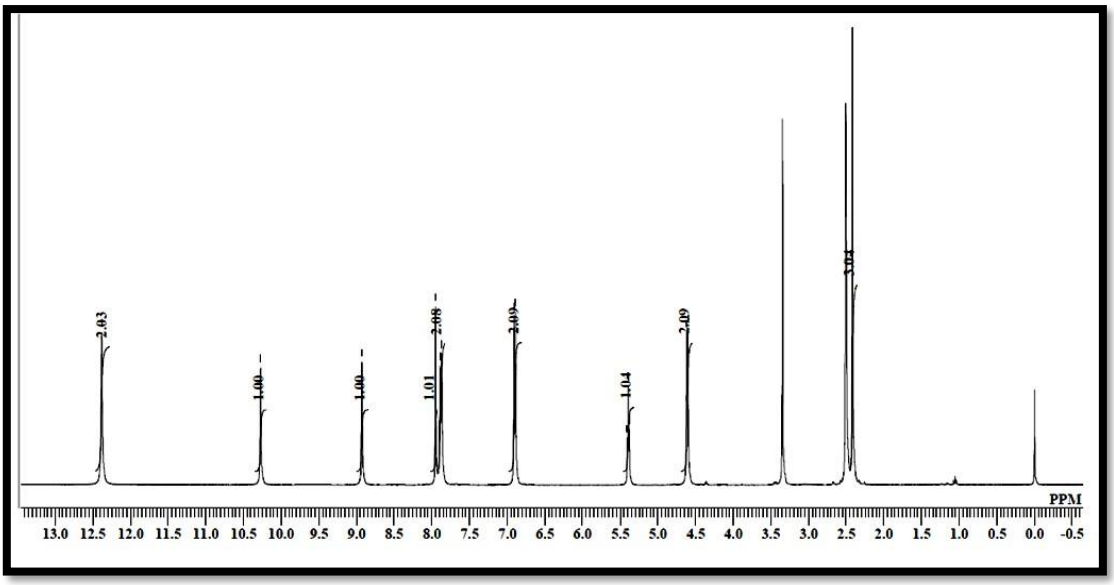

FIG. 8: 1H-NMR SPECTRUM OF PLHBH

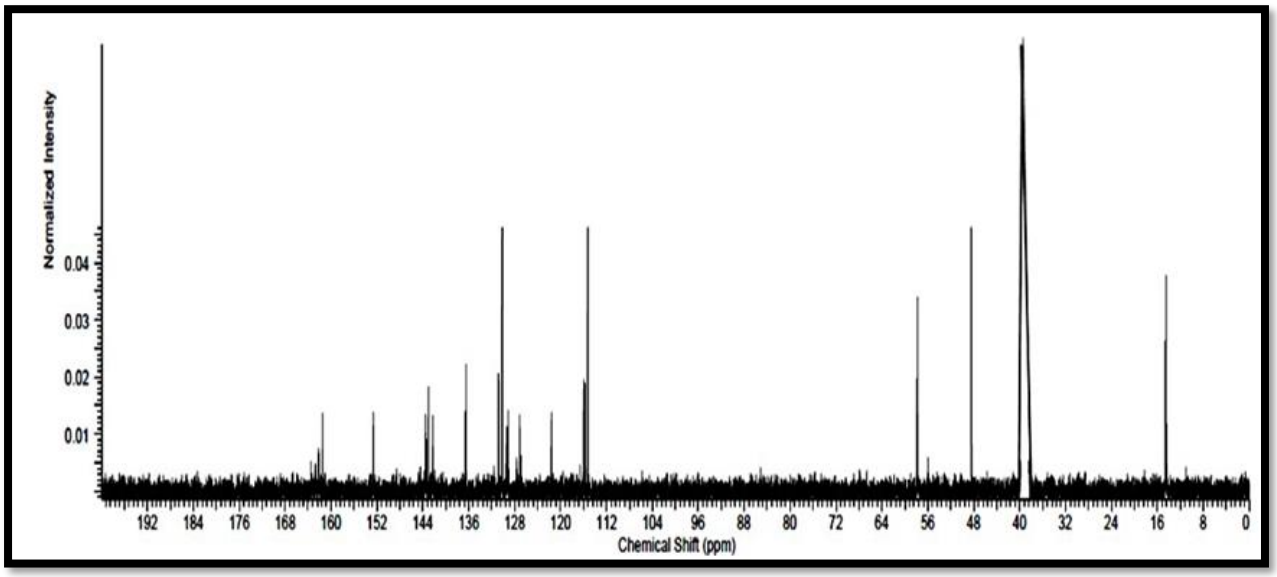

FIG. 9: C NMR SPECTRUM OF PLHBH

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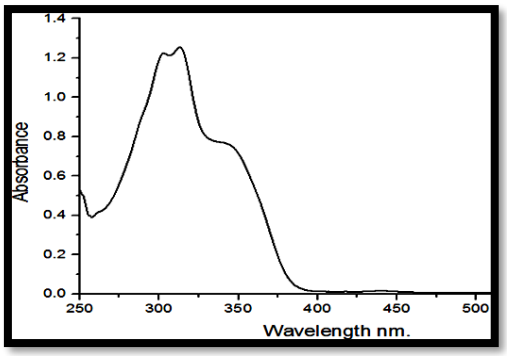

FIG. 10: UV-VISIBLE SPECTRUM OF PLHBH

Characterization of 3-nitro-N'-(3-hydroxy-5-(hydroxymethyl)-2-methylpyridin-4 yl)methylene) benzohydrazide (PLNBH)

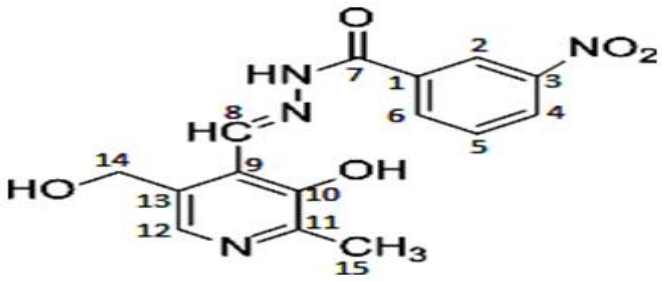

FIG.11 STRUCTURE OF PLNBH

IR spectrum

The IR spectrum of the PLNBH shows, stretching bands at 3630cm-1 ν(O-H)attributed to phenolic-OH, 3246cm-1 ν(N- H)due to amide stretching vibrations, 2895cm-1belong to ν(NH+),1687cm-1attributed to ν(C=O), azomethine at 1614cm-1 ν(C=N), ν(C-O) stretching band at1270cm-1 and 3020cm-1due to aromatic stretching vibrations of ν(C-H), 1365cm-1 assigned to ν(N-O), 1255cm- 1due to ν(C-N) and pyridine ring deformations at 611cm-1and 413cm-1.

UV-Visible spectrum

Conclusion

The research on assessing the biological activity and characterization of chelates formed by pyridoxal derivatives with transition metals represents a significant scientific endeavor with multifaceted implications. This study has not only deepened our comprehension of the intricate

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interplay between pyridoxal derivatives and transition metals but also showcased the transformative potential across several domains. this research contributes to our fundamental understanding of biological processes, shedding light on the roles of pyridoxal derivatives in enzymatic reactions and cellular functions. This knowledge has direct implications for medicine, offering avenues for the development of innovative pharmaceuticals and therapeutic agents that leverage the unique properties of these chelates. the study exemplifies the interdisciplinary nature of bioinorganic chemistry, where insights into coordination chemistry and metal interactions within biological systems have far-reaching applications. Beyond biology and medicine, this research paves the way for advancements in materials science, catalysis, toxicology, and environmental science, impacting a broad spectrum of scientific disciplines. this study not only enhances our understanding of life's molecular intricacies but also offers practical solutions and innovations. It underscores the profound synergy between chemistry and biology and exemplifies how scientific exploration can yield valuable insights and applications that extend well beyond the confines of the laboratory, ultimately benefiting society at large.

Future Work

Future research in the domain of assessing the biological activity and characterization of chelates formed by pyridoxal derivatives with transition metals holds immense potential for scientific progress. Avenues for exploration are abundant, including the investigation of various metal complexes to unravel the full spectrum of their biological activities. Deeper inquiries into the specific biological mechanisms influenced by these chelates are essential, allowing us to connect the molecular-level interactions with broader physiological functions. Quantitative studies are crucial for a more precise understanding, enabling the determination of binding affinities and concentrations under diverse conditions. Transitioning from laboratory experiments to clinical applications is a logical step, as it may pave the way for innovative treatments and therapies based on these chelates. Additionally, the catalytic potential of these complexes deserves further attention, with potential implications for green chemistry and industrial processes. Environmental considerations, particularly in terms of metal detoxification and environmental remediation, warrant dedicated research efforts. Advanced characterization techniques and interdisciplinary collaboration between experts

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from diverse fields can push the boundaries of our knowledge. Moreover, toxicological studies are imperative to ensure the safety of these chelates for both human health and the environment.

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