

Investigation of Ternary Nickel (II) Complexes with Amino Acids and Diols: Stability, Biological Implications, and Structural Insights

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Abstract: *The synthesis, stability, and possible uses of ternary complexes of nickel (II) with histidine, adenine, and other diols or amino acids are investigated in this work. Potentiometric techniques were used to establish stability constants, exposing patterns based on coordination environments and ligand structures. Increased stability in compounds with π - electron systems or aromatic ligands points to important roles in environmental and biological processes. These discoveries open the door for uses in catalysis and medication development by shedding light on nickel's function in enzymes and its interactions with biological macromolecules.*

Keywords: Ternary complex, nickel, amino acids, Potentiometric techniques, ligand, catalysis and medication

1. Introduction

In many biological systems, nickel is an essential trace element that plays a crucial role, primarily as a cofactor in various enzymes. These include urease, hydrogenase, and methyl - coenzyme M reductase, which are vital to processes such as nitrogen metabolism, energy conversion, and methane biosynthesis. Nickel's ability to adopt versatile coordination geometries and oxidation states makes it uniquely suited for these biological functions. Among its numerous chemical forms, Ni (II) complexes with amino acids and diols have gained significant attention due to their roles in metal ion transport, enzymatic catalysis, and inducing structural modifications in proteins and nucleic acids.

Ternary complexes, which incorporate two distinct ligands coordinated to a central metal ion, provide a sophisticated framework for simulating biological coordination environments. By mimicking these natural systems, they enable researchers to gain valuable insights into the mechanisms underlying biochemical processes and explore potential therapeutic applications. Mixed ligand systems exhibit enhanced stability compared to their binary counterparts due to synergistic effects arising from heteroatoms and π - electron interactions. These effects contribute to a more robust coordination network and facilitate fine - tuning of their physical and chemical properties. Of particular interest is the interplay of diols' oxygen donor groups and histidine's aromatic imidazole ring, which creates diverse coordination conditions that influence the overall stability and reactivity of the complexes. Such flexibility in coordination chemistry highlights the potential of ternary Ni (II) complexes to serve as models for studying metalloproteins and to inform the development of nickel - based drugs or catalysts.

This publication compiles the findings of recent studies on Ni (II) ternary complexes, emphasizing their coordination behaviour, stability, and functionality. The review also evaluates the implications of these findings, offering insights into their potential applications in fields such as enzymology, drug discovery, and environmental remediation.

2. Materials and Methods

2.1 Materials

L - histidine, adenine, and various diols (e. g., ethane diol, propane - 1, 2 - diol) were obtained and purified. Nickel (II) chloride was used as the Ni (II) source. Amino acids including aspartic acid, glutamic acid, and leucine were employed to investigate their interactions with Ni (II) in aqueous systems.

2.2 Nickel (II) Chloride

Nickel (II) chloride hexahydrate ($\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$) served as the source of Ni (II) ions. It was selected for its high solubility and stability in aqueous media, making it ideal for complex formation studies. This compound's role as a central coordinating species allows it to form stable bonds with various ligands, enabling the investigation of ternary complex systems.

2.3 L - Histidine

L - histidine, an essential amino acid, was used as a primary ligand. Its imidazole side chain provides a nitrogen donor atom, facilitating strong coordination with Ni (II). Histidine's aromatic character and ability to form π - bonds enhance the stability of ternary complexes. The compound was obtained in high purity and used without further modification.

2.4 Adenine

Adenine, a purine base, was included for its biological relevance and strong interaction with metal ions. Its nitrogen - rich structure, including the exocyclic amino group and imidazole - like ring, makes it an effective ligand for Ni (II). Adenine is particularly significant in mimicking nucleotide - metal interactions.

2.5 Diols

Various diols, including ethane diol, propane - 1, 2 - diol, and 2 - butene - 1, 4 - diol, were employed as secondary ligands.

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These bidentate ligands, with their oxygen donor atoms, create five - and six - membered chelate rings upon coordination. Diols differ in their flexibility and electronic properties, influencing the stability of the resulting complexes. Among these, 2 - butene - 1, 4 - diol demonstrated the highest stability due to its π - electron system.

2.6 Amino Acids

Amino acids such as aspartic acid, glutamic acid, leucine, and phenylalanine were used to study their role in ternary complexes. These amino acids were chosen for their diverse side chain functionalities, ranging from polar (aspartic acid) to nonpolar (leucine) and aromatic (phenylalanine). Their interaction with Ni (II) provided insights into ligand - specific stability trends.

2.7 Solvents and pH Control

All experiments were conducted in aqueous media. The pH was controlled using lithium hydroxide and nitric acid to ensure optimal conditions for complex formation. pH values around 7 - 8 were maintained, as this range supports the formation of stable Ni (II) complexes without significant hydrolysis.

2.8 Analytical Techniques

Potentiometric titrations were employed to determine stability constants (β_{MAB} , β_{MAB2} , β_{MA2B}). Spectroscopic methods, including UV - Vis and NMR, were utilized to analyze electronic transitions and molecular structures. These techniques provided critical data for understanding the coordination environment and electronic properties of the complexes.

2.9 Synthesis of Complexes

Ternary complexes were synthesized by mixing Ni (II) with histidine and diols or amino acids in controlled molar ratios. The pH was adjusted to ~ 7 using lithium hydroxide to facilitate complex formation. Resulting complexes were isolated by filtration and crystallized for analysis.

2.10 Analytical Techniques

Potentiometric titrations determined stability constants (β_{MAB} , β_{MAB2} , β_{MA2B}). Magnetic susceptibility and spectroscopic methods, including UV - Vis and NMR, elucidated structural details. Stability constants were calculated using established equations relating binary and ternary systems.

3. Results and Discussion

3.1 Stability Trends

Ternary complexes of the type MA2B exhibited higher stability than MAB2, attributed to increased nitrogen coordination from histidine's imidazole group. Among diols, 2 - butene - 1, 4 - diol - containing complexes displayed the highest stability, likely due to π - electron contributions.

Complexes with adenine and amino acids followed stability trends influenced by ligand basicity and steric factors.

3.2 Biological Implications

The enhanced stability of ternary complexes suggests roles in biological metal ion transport and enzyme activation. Ni (II) complexes with histidine mimic active sites in enzymes like Ni - SOD, crucial for oxidative stress management. Similarly, ternary systems with adenine model interactions with nucleic acids, aiding in understanding DNA repair and potential metallodrug applications.

3.3 Structural Insights

Spectroscopic analysis revealed that ligands' electronic properties and spatial arrangements significantly affect complex stability. Imidazole nitrogen from histidine formed strong bonds with Ni (II), while diol and amino acid side chains contributed secondary interactions, stabilizing the complexes.

3.4 Environmental and Catalytic Applications

The coordination chemistry of Ni (II) also has implications for environmental remediation. For instance, Ni (II) - based complexes can act as catalysts in organic transformations and degradation of pollutants. The high stability of these complexes in aqueous environments makes them suitable candidates for such applications. Studies indicate that ternary complexes with diols could improve the efficiency of catalytic cycles in both industrial and environmental settings.

3.5 Comparative Analysis with Other Metals

Comparing Ni (II) with other transition metals, such as Cu (II) and Zn (II), reveals distinct advantages in terms of stability and specificity. Ni (II) 's coordination properties allow for unique interactions with biological ligands, offering specialized roles in enzymes and other biomolecules. This comparative analysis highlights the niche functions of Ni (II) in biological and chemical systems.

3.6 The Role of pH and Environmental Conditions

The pH and ionic strength of the medium play a crucial role in determining the stability of Ni (II) complexes. At higher pH levels, ternary complexes exhibit increased stability due to reduced competition with protons for binding sites on the ligands. This pH - dependent behavior is significant in biological contexts, where local pH variations can influence metal - ligand interactions.

3.7 Potential in Drug Design

The specificity and stability of Ni (II) - based ternary complexes make them promising candidates for drug design. These complexes can serve as scaffolds for metallodrugs, targeting DNA or enzymes involved in diseases such as cancer or bacterial infections. Advances in understanding their coordination chemistry could facilitate the development of targeted therapies with minimal off - target effects.

4. Conclusion

With applications in enzymology, drug discovery, and environmental remediation, ternary complexes of Ni (II) with histidine, adenine, diols, and amino acids exhibit diverse and intriguing coordination chemistry. These complexes demonstrate significant potential due to their structural versatility, stability in aqueous environments, and ability to interact with biological molecules. By exploring their pH - dependent behaviour, researchers can better understand the factors influencing their reactivity and optimize their catalytic and therapeutic properties.

Future research should prioritize advanced analytical techniques, such as X - ray crystallography, nuclear magnetic resonance (NMR) spectroscopy, and computational modelling, to refine structural understanding and unveil subtle electronic and geometric properties. Additionally, systematic studies on their functional applications, including their potential as metalloenzyme mimics, drug delivery agents, or environmental catalysts for pollutant degradation, could significantly enhance their utility. Collaborations across disciplines—combining chemistry, biology, and materials science—could further unlock the full potential of these complexes in real - world applications, paving the way for innovations in sustainable and biomedical technologies

References

- [1] Barone G, Terenzi A, Lauria A, et al. DNA - binding of nickel (II), copper (II) and zinc (II) complexes: structure–affinity relationships. *Coord Chem Rev.*2013; **257** (19 - 20): 2848 - 2862.
- [2] Fricker S. P. Metal compounds in cancer therapy. *Springer Science & Business Media*; 2012.
- [3] Orvig C., Abrams M. J. Medicinal inorganic chemistry: introduction. *Chem Rev.*1999; **99** (9): 2201 - 2204.
- [4] Barry NPE, Sadler PJ. Exploration of the medical periodic table: towards new targets. *Chem Commun.*2013; **49** (45): 5106 - 5131.
- [5] Kalaiaarasi G, Jain R, Puschman H, Poorna Chandrika S, Preethi K, Prabhakaran R. New binuclear Ni (II) metallates containing ONS chelators: synthesis, characterisation, DNA binding, DNA cleavage, protein binding, antioxidant activity, antimicrobial and in vitro cytotoxicity. *New J Chem.*2017; **41** (7): 2543 - 2560.
- [6] Kazemi Z., Moini N., Rudbari H. A., Micale N. A comprehensive review on the development of chiral Cu, Ni, and Zn complexes as pharmaceutical agents over the past decades: Synthesis, molecular structure and biological activity. *Medicinal Research Reviews* 2024.
- [7] Szunyog, G., and et al. A comparative study on the nickel binding ability of peptides containing separate cysteinyl residues. *Dalton Trans.*, 2019; **48**: 16800–16811.
- [8] Lema, J., Ortega, J. A., Martínez, J. D., and et al. Solution equilibria and stabilities of binary and ternary systems of nickel (II) complexes with Di picolinic acid and the amino acids (histidine, cysteine, aspartic and glutamic acids). *J. Solution Chem.*2015; **44**, 2144–2153.
- [9] Radalla, A. M., Potentiometric investigation on complex formation and stabilities of some divalent metal ions with L - cysteine and glycine as ligands in aqueous solutions. *J. Solution Chem.*2021; **50**, 954–967.
- [10] Pyreu, D., Gridchin, S., Thermodynamics of mixed ligand complex formation of copper (II) and nickel ions with glycine and histidine in solution. *J. Solution Chem.*2020; **49**, 239–253.
- [11] Perrin, D. D., Sayce, I. G.: Complex formation by nickel and zinc with penicillamine and cysteine. *J. Chem. Soc. A* 1968.
- [12] Amico, P., and et al. Mixed - metal complexes in solution.3. Thermodynamic study of heterobinuclear copper (II) –L - histidine and –histamine complexes in aqueous solution. *Inorg. Chem.*1981; **20**, 772–777.
- [13] Alemdaroğlu, T., Berthon, G.: Trace metal requirements in total parenteral nutrition: II. Potentiometric study of the metal—ion equilibria in the zinc—histidine, zinc—glycine, zinc—cysteine—histidine, zinc—glycine—histidine and zinc—glycine—cysteine systems under physiological conditions *Bioelectrochem. Bioenerg.*1981; **8**, 49–62.