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Advances in the Study of Copper (II) Complexes with Amino Acids: Synthesis, Characterization, and Applications

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Abstract: ***Because of their distinct structural characteristics and functional adaptability, copper (II) complexes with amino acids have emerged as a key component of coordination chemistry breakthroughs. These complexes have promising medicinal qualities, resemble biological systems, and support industrial and environmental advancements. This review explores the various uses of copper (II)-amino acid complexes as well as their production and characterisation methods. Through the integration of historical perspectives and state-of-the-art research, the paper highlights the transformative impact of these complexes on environmental sustainability, agriculture, and medicine.***

Keywords: copper, amino complex, therapeutic properties, characterization techniques, environmental sustainability

1. Introduction

The study of the structure and reactivity of metal compounds with different ligands, synthetic techniques, and the pursuit of practical applications are all included in the broad topic of chemistry of organometallic compounds today. As long as the target complex remains an independent unit even in solution, despite the possibility of partial dissociation, practically any molecule that can coordinate with the transition metal atom or atoms can be utilised as a ligand.

For ages, the importance of copper in biological systems has been recognised. The discovery of copper-dependent enzymes like cytochrome c oxidase and superoxide dismutase in the 20th century led to the recognition of copper's biochemical significance, although ancient societies utilised it for its antibacterial qualities. These enzymes make use of copper's capacity to be able to exist in many oxidation states, which helps redox reactions that are essential for breathing and cellular defences. In the middle of the 20th century, research on copper complexes with amino acids accelerated. These complexes are used as models to understand biological processes because they resemble metalloproteins and are made up of a copper ion coordinated with amino acids and other ligands. The discovery of ternary complexes, in which copper coordinates with two distinct ligands, broadened the field of study and revealed uses in environmental cleanup, drug development, and catalysis.

For this reason, the information in the review will be categorised based on the catalytic reactions that these ligands are used in rather than the type of ligand molecules (i.e., α-amino acids, peptides or polysaccharides, or Schiff bases). Furthermore, in order to achieve better results, in many cases molecules of ligands of one nature such as α-amino acids were modified by molecules of a different nature, such as sugars.

Key milestones include:

- Alfred Werner's coordination theory, which laid the foundation for understanding metal- ligand interactions.
- The Irving-Williams series, which explained the stability trends of transition metal complexes, with copper occupying a unique position due to its electronic configuration.
- Advances in spectroscopic and computational techniques that allowed detailed characterization of copper complexes.

Synthesis of Copper (II) Complexes

Solution-Based Methods

Solution-based synthesis involves the reaction of copper salts with amino acids and secondary ligands in aqueous or mixed solvents. Factors such as pH, temperature, and ligand concentration significantly influence the outcome. For instance:

- Acidic conditions favor the formation of monomeric complexes, while neutral or slightly basic conditions promote polymerization.
- The choice of secondary ligands, such as 2,2'-bipyridine or 1,10-phenanthroline, introduces steric and electronic effects that alter the geometry of the complexes.

Historical studies demonstrated the role of solvent polarity in determining the crystallinity and stability of the complexes. Modern techniques include controlled precipitation and solvent evaporation to yield high-purity crystals suitable for X-ray diffraction studies.

Mechanochemical Techniques

Mechanochemistry, particularly ball milling, has revolutionized the synthesis of copper complexes. This solvent-free approach reduces environmental impact and enhances reaction efficiency. By varying the milling time and force, researchers can control the particle size and structural properties of the resulting complexes.

A notable example is the synthesis of $[Cu(l\text{-}Ala)(H_2O)(bipy)]_2SO_4 \cdot 2H_2O$, which exhibits enhanced thermal stability and bioactivity compared to its solution-synthesized counterpart.

Electrochemical and Potentiometric Approaches

Electrochemical methods enable the synthesis of copper complexes under precise redox conditions. Potentiometric titration provides valuable data on stability constants, guiding ligand selection for specific applications. These techniques are particularly useful for studying copper-amino acid interactions in real-time, simulating physiological conditions.

Characterization Techniques

Spectroscopic Methods

- *UV-Vis Spectroscopy*: Provides information on electronic transitions within the d-orbitals of copper, revealing the ligand field strength and coordination geometry.
- *Infrared (IR) Spectroscopy*: Identifies functional groups involved in coordination. Shifts in the carboxylate (COO^-) and amine (NH_2) stretching frequencies indicate ligand binding.
- *Electron Paramagnetic Resonance (EPR)*: Highlights the Jahn-Teller distortion commonly observed in copper (II) complexes, offering insights into the electronic environment around the metal center.

X-ray Crystallography

X-ray diffraction remains the most definitive method for determining the structure of copper complexes. Early studies revealed simple geometries like square planar and tetrahedral arrangements, while modern research has uncovered intricate architectures, including coordination polymers and porous frameworks.

Thermal and Computational Analysis

Thermal analysis techniques, such as thermogravimetric analysis and differential scanning calorimetry, elucidate the stability and decomposition pathways of complexes. Computational approaches, including density functional theory, provide molecular-level insights into electronic structures, reactivity, and potential biological interactions.

2. Applications

Medical Applications

- *Antimicrobial Properties*: Copper complexes disrupt bacterial membranes and generate reactive oxygen species, making them effective against drug-resistant pathogens.
- *Anticancer Potential*: Ternary complexes with DNA-binding ligands exhibit selective cytotoxicity, opening avenues for chemotherapy. The Casiopeínas family of copper complexes has shown promise in clinical trials for their anticancer activity.
- *Diagnostics and Imaging*: Copper complexes with fluorescent properties are being developed as probes for imaging biological tissues.

Environmental Applications

- *Water Treatment*: Copper-amino acid complexes chelate heavy metals and organic pollutants, enhancing their removal from wastewater.
- *Soil Remediation*: These complexes influence copper's bioavailability in soils, promoting plant uptake while reducing toxicity.

Industrial and Agricultural Uses

- *Catalysis*: Copper complexes catalyze reactions such as oxidative coupling, hydroamination, and C-H activation, critical for green chemistry initiatives.
- *Fertilizers*: Micronutrient fertilizers containing copper-amino acid complexes enhance plant growth and resistance to diseases, particularly under stress conditions.

Historical Perspective

Copper complex research has progressed from fundamental theory to real-world uses:

1) The conceptual foundation for comprehending metal-ligand interactions was established by Werner's coordination theory (1893).
2) The nature of chemical bonding in transition metal complexes was clarified by Pauling's work in the middle of the 20th century.
3) The remarkable stability of copper in coordination compounds was brought to light by the discovery of the Irving-Williams series.
4) Accurate characterisation of complicated structures was made possible by advancements in technology, including mass spectrometry and nuclear magnetic resonance (NMR).

3. Conclusion

Amino acid and copper (II) complexes are a great illustration of how fundamental research and practical applications can coexist. Because of their versatility in both structure and function, they are very helpful in environmental science, agriculture, and medicine. Future research should focus on developing ligands with particular properties, examining synergistic effects in multi-ligand systems, and expanding applications in cutting-edge fields like nanotechnology and renewable energy.

The role of non-precious metal complexes derived from polysaccharides, peptides, diols, or amino acids in catalytic organic synthesis is also expected to be covered in additional publications in the near future. The goal to reduce the cost of technology and the planned utilisation of valuable resources are the primary explanations for these metals, which are essential in scientific domains.

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