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Role of transition metals in biological systems

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Abstract

Transition metals play pivotal roles in various biological systems, contributing to essential functions ranging from catalysis to signaling. This paper explores the multifaceted roles of transition metals in biological contexts, elucidating their involvement in enzymatic reactions, electron transfer processes, and metalloprotein function. Through intricate coordination chemistry, transition metals facilitate critical biological processes such as oxygen transport, DNA replication, and cellular respiration. Understanding the intricate interplay between transition metals and biomolecules is crucial for deciphering the mechanisms underlying numerous physiological and pathological phenomena. Moreover, insights into the role of transition metals in biological systems hold immense promise for the development of innovative therapeutic interventions and biomimetic technologies.

Keywords: Transition metals, biological systems, coordination chemistry, metalloproteins, enzymatic reactions

Introduction

Transition metals represent a class of elements that exhibit unique chemical properties, making them indispensable components of biological systems. Their ability to undergo redox reactions, coordinate with biomolecules, and catalyze a diverse array of biochemical processes underscores their significance in life processes. The intricate interplay between transition metals and biological molecules forms the foundation of numerous vital functions within living organisms.

In recent years, extensive research has delved into unraveling the roles of transition metals in biological systems, illuminating their involvement in crucial physiological processes such as oxygen transport, cellular respiration, and DNA synthesis. Transition metal ions serve as cofactors in a myriad of enzymes, modulating their catalytic activities and facilitating substrate binding. Moreover, metalloproteins, which harness the unique properties of transition metals, play key roles in signal transduction, gene regulation, and immune response.

Understanding the fundamental principles governing the interactions between transition metals and biological molecules holds immense promise for various scientific disciplines. From elucidating the molecular mechanisms of diseases to developing novel therapeutic agents and biomimetic catalysts, the study of transition metal biology continues to inspire groundbreaking discoveries.

This research paper endeavors to explore the intricate roles of transition metals in biological systems, highlighting their chemical versatility, structural diversity, and functional significance. By synthesizing current knowledge and recent advancements, this paper aims to contribute to a deeper understanding of the profound impact that transition metals exert on the complexity of life processes.

In the following sections, we will delve into the coordination chemistry of transition metals, their roles as cofactors in enzymatic reactions, the structural features of metalloproteins, and the implications of transition metal biology in health and disease. Through this exploration, we endeavor to shed light on the dynamic interplay between transition metals and biological systems, paving the way for future discoveries and innovations in both fundamental science and applied research.

Objectives

1. Investigate the diverse roles of transition metals in biological systems, encompassing enzymatic catalysis, electron transfer processes, and structural stabilization of biomolecules.

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2. Explore the coordination chemistry underlying the interactions between transition metals and biological ligands, elucidating the principles governing metal binding specificity and affinity.
3. Examine the structural and functional diversity of metalloproteins, highlighting their contributions to essential cellular processes such as metabolism, DNA replication, and signal transduction.
4. Assess the implications of transition metal biology in human health and disease, discerning the roles of metal ions in pathophysiological conditions and exploring therapeutic strategies targeting metal-dependent pathways.
5. Synthesize existing knowledge and recent advancements in transition metal biology to provide insights into the development of biomimetic catalysts, metal-based drugs, and diagnostic tools for biomedical applications.
6. Identify key research gaps and challenges in the field of transition metal biology, proposing avenues for future investigations aimed at unraveling the complex interplay between metal ions and biological systems.

Literature Review

Transition metals, characterized by their variable oxidation states and coordination chemistry, have long captivated the interest of researchers in the field of bioinorganic chemistry due to their indispensable roles in biological systems. The investigation into the involvement of transition metals in biological processes dates back to the pioneering work of biochemists such as Hugo Theorell and Fritz Lipmann in the mid-20th century, who elucidated the enzymatic functions of metal cofactors such as iron, copper, zinc, and manganese.

One of the earliest discoveries highlighting the importance of transition metals in biology was the identification of hemoglobin and myoglobin as oxygen-carrying proteins containing iron (II) heme groups. The reversible binding of oxygen to the iron center enables the efficient transport and delivery of oxygen throughout the body, essential for aerobic respiration and cellular metabolism.

In addition to oxygen transport, transition metals serve as cofactors in a diverse array of enzymes, catalyzing a multitude of biochemical reactions vital for cellular function. For instance, the zinc ion in carbonic anhydrase facilitates the hydration of carbon dioxide, while the iron-sulfur clusters in the electron transport chain mediate electron transfer reactions essential for ATP production during oxidative phosphorylation.

The structural diversity of metalloproteins further underscores the versatility of transition metals in biological systems. Metalloenzymes such as cytochrome c oxidase and nitrogenase showcase intricate metal-binding sites that are finely tuned to accommodate specific substrates and catalytic reactions. Furthermore, metalloproteins play critical roles in signaling pathways, DNA repair mechanisms, and metal ion homeostasis, highlighting the far-reaching implications of transition metal biology in cellular regulation and organismal physiology.

Recent advancements in spectroscopic and computational techniques have provided unprecedented insights into the molecular mechanisms governing transition metal-dependent processes in biology. High-resolution crystallography and spectroscopic methods such as X-ray absorption spectroscopy and nuclear magnetic resonance spectroscopy have enabled detailed structural characterization of metalloprotein

complexes, elucidating the coordination geometries and electronic properties of metal centers within biological environments.

Moreover, interdisciplinary approaches integrating biochemistry, molecular biology, and synthetic chemistry have facilitated the design and synthesis of metal-based probes and therapeutics for imaging, diagnosis, and treatment of diseases. Transition metal complexes have emerged as promising candidates for anticancer drugs, antimicrobial agents, and contrast agents for medical imaging modalities, leveraging their unique electronic properties and reactivity profiles.

Despite significant progress, many questions remain unanswered regarding the precise roles of transition metals in biological systems and their implications for human health and disease. Future research endeavors aim to unravel the intricacies of metalloprotein function, decipher metal ion signaling pathways, and develop innovative strategies for targeted manipulation of transition metal biology in biomedical contexts.

In summary, the interdisciplinary study of transition metal biology continues to captivate scientists across various disciplines, offering fertile ground for exploration and innovation at the interface of chemistry, biology, and medicine. By elucidating the fundamental principles governing the interactions between transition metals and biological molecules, researchers seek to unravel the mysteries of life and harness the potential of metal-based systems for addressing pressing challenges in health and biotechnology.

Existing System

The existing understanding of transition metal biology within biological systems represents a dynamic landscape shaped by decades of interdisciplinary research efforts spanning biochemistry, biophysics, and molecular biology. Transition metals, owing to their unique electronic configurations and coordination chemistry, occupy central positions in various biological processes, exerting profound influences on cellular function and organismal physiology.

At the molecular level, the existing system elucidates the intricate mechanisms underlying metalloprotein function and metal ion homeostasis. Metalloproteins, ranging from metalloenzymes to metalloregulatory proteins, harness the catalytic and regulatory capabilities of transition metals to orchestrate a myriad of biochemical reactions and signaling pathways. For example, the iron-sulfur clusters in ferredoxins facilitate electron transfer reactions in photosynthesis and respiration, while copper ions in metallochaperones facilitate copper delivery to cuproenzymes involved in neurotransmitter synthesis and antioxidant defense.

Moreover, the existing system encompasses a comprehensive understanding of metal ion transport and trafficking mechanisms within cells, governed by a network of transporters, chaperones, and metal-binding proteins. Transition metal ions such as zinc, copper, and iron are tightly regulated to maintain cellular homeostasis, with dysregulation often associated with pathological conditions such as neurodegenerative diseases, cancer, and metabolic disorders.

The existing system also encompasses a wealth of structural and spectroscopic data elucidating the coordination geometries, ligand interactions, and electronic properties of transition metal complexes in biological environments. High-resolution X-ray crystallography, nuclear magnetic resonance

spectroscopy, and advanced spectroscopic techniques have provided unprecedented insights into the structural dynamics and functional implications of metalloprotein assemblies, guiding the rational design of metal-based therapeutics and diagnostic agents.

Furthermore, the existing system includes computational modeling and simulation approaches aimed at deciphering the thermodynamics and kinetics of metalloprotein-ligand interactions, predicting metal binding sites, and elucidating the mechanisms of metalloenzyme catalysis. Molecular dynamics simulations, density functional theory calculations, and quantum mechanics/molecular mechanics methods offer powerful tools for interrogating the energetics and dynamics of transition metal-mediated processes, complementing experimental observations and guiding hypothesis-driven research endeavors.

Proposed System

The proposed system builds upon the foundation of existing knowledge in transition metal biology, aiming to address current research gaps and expand the frontiers of understanding in this dynamic field. By integrating cutting-edge experimental techniques, computational methodologies, and interdisciplinary approaches, the proposed system seeks to unravel the complexities of transition metal-mediated processes in biological systems and leverage this knowledge for innovative applications in biomedicine and biotechnology.

One key aspect of the proposed system involves the elucidation of metalloprotein structure-function relationships at atomic resolution. Advanced structural biology techniques, including cryo-electron microscopy, time-resolved X-ray crystallography, and single-molecule spectroscopy, will be employed to capture the dynamic conformational changes and transient intermediates underlying metalloprotein function. By elucidating the structural determinants of metal binding, substrate recognition, and catalytic activity, researchers aim to gain deeper insights into the molecular mechanisms driving biological processes mediated by transition metals.

In parallel, the proposed system emphasizes the development and implementation of high-throughput screening platforms and computational tools for the discovery and characterization of novel metalloproteins and metal-based therapeutics. Utilizing combinatorial chemistry, directed evolution, and bioinformatics approaches, researchers will explore the vast chemical space of transition metal complexes and metalloprotein variants, with the goal of identifying molecules with enhanced catalytic efficiency, specificity, and biocompatibility.

Moreover, the proposed system integrates systems biology and network analysis techniques to elucidate the global regulatory networks and metabolic pathways modulated by transition metals in biological systems. By leveraging multi-omics data integration, mathematical modeling, and network inference algorithms, researchers aim to decipher the hierarchical organization and emergent properties of metalloprotein networks, uncovering novel biomarkers and therapeutic targets for precision medicine applications.

Furthermore, the proposed system explores the therapeutic potential of transition metal-based compounds for the treatment of human diseases, including cancer, neurodegenerative disorders, and infectious diseases. Through structure-guided drug design, medicinal chemistry optimization, and preclinical validation studies, researchers seek to translate fundamental discoveries in transition metal

biology into clinically relevant interventions with improved efficacy, safety, and selectivity.

Lastly, the proposed system emphasizes the importance of interdisciplinary collaboration and knowledge dissemination in advancing the field of transition metal biology. By fostering partnerships between academia, industry, and healthcare institutions, the proposed system aims to accelerate the translation of basic research findings into tangible solutions that address pressing societal challenges and improve human health outcomes.

In summary, the proposed system represents a holistic and forward-thinking approach to transition metal biology, encompassing innovative experimental methodologies, computational strategies, and translational applications. By embracing complexity and embracing diversity, the proposed system aims to unlock the full potential of transition metals as versatile tools for understanding life's intricacies and transforming the landscape of modern medicine and biotechnology.

Methodology

Literature Review: Conduct a comprehensive review of existing literature on transition metal biology, including research articles, review papers, and textbooks. Synthesize key findings, identify research gaps, and delineate the scope of the study based on established knowledge and emerging trends in the field.

Experimental Design: Design experiments to investigate the roles of transition metals in biological systems, focusing on specific metalloproteins, enzymatic pathways, and cellular processes of interest. Define clear research objectives, hypothesis-driven experimental approaches, and selection criteria for model systems and experimental conditions.

Synthetic Chemistry: Synthesize transition metal complexes and metalloprotein variants using synthetic chemistry techniques, including coordination chemistry, organometallic synthesis, and protein engineering methods. Characterize the chemical composition, structural properties, and spectroscopic features of synthesized compounds using analytical techniques such as nuclear magnetic resonance spectroscopy, mass spectrometry, and X-ray crystallography.

Biochemical Assays: Perform biochemical assays to assess the catalytic activity, substrate specificity, and kinetic parameters of metalloenzymes and metal-binding proteins. Utilize enzymatic assays, spectroscopic assays, and substrate profiling techniques to quantify reaction rates, substrate turnover, and product formation in the presence of transition metal cofactors.

Biophysical Characterization: Employ biophysical techniques to investigate the structural dynamics and ligand interactions of metalloprotein complexes in solution. Utilize techniques such as circular dichroism spectroscopy, fluorescence spectroscopy, and surface plasmon resonance spectroscopy to probe protein folding, ligand binding, and protein-protein interactions mediated by transition metal ions.

Cellular and Molecular Biology Studies: Perform cellular and molecular biology studies to elucidate the physiological roles of transition metals in living organisms. Utilize cell culture models, genetic manipulation techniques, and

molecular imaging approaches to study the effects of transition metal deficiency or excess on cellular signaling pathways, gene expression profiles, and cellular functions.

Computational Modeling and Simulation: Employ computational modeling and simulation techniques to elucidate the structural and energetic properties of transition metal complexes and metalloprotein-ligand interactions. Use molecular docking, molecular dynamics simulations, and quantum mechanical calculations to predict metal binding sites, explore reaction mechanisms, and analyze metal coordination geometries.

Data Analysis and Interpretation: Analyze experimental data using statistical methods, data visualization tools, and computational algorithms. Interpret experimental results in the context of established biochemical principles, structural models, and theoretical frameworks, drawing meaningful conclusions and identifying correlations between transition metal biology and biological function.

Validation and Reproducibility: Validate experimental findings through independent replication studies, control experiments, and comparison with published data from reputable sources. Ensure experimental reproducibility, transparency, and adherence to ethical guidelines and scientific standards throughout the research process.

Integration and Synthesis: Integrate experimental results from diverse methodologies to construct comprehensive models of transition metal-mediated processes in biological systems. Synthesize experimental observations, theoretical insights, and computational predictions to generate novel hypotheses, propose mechanistic models, and advance our understanding of transition metal biology in health and disease.

By employing a multifaceted methodology encompassing experimental, computational, and integrative approaches, this research aims to elucidate the intricate roles of transition metals in biological systems and pave the way for future discoveries and innovations at the interface of chemistry, biology, and medicine.

Contrast of Different Studies

Enzymatic Catalysis: While some studies focus on the catalytic mechanisms of transition metal-dependent enzymes such as carbonic anhydrase and cytochrome c oxidase, others explore the structural and functional diversity of metalloenzymes across different biological systems. Contrasts arise in the specific metal cofactors utilized, the substrate specificities exhibited, and the regulatory mechanisms governing enzymatic activity, highlighting the versatility and complexity of transition metal-mediated catalysis in biological processes.

Metalloprotein Structure-Function Relationships: Various studies elucidate the structural determinants of metalloprotein function, including metal coordination geometries, ligand binding affinities, and conformational dynamics. Contrasts emerge in the structural motifs and metal-binding sites observed across different metalloprotein families, reflecting evolutionary adaptations and functional specialization within diverse biological contexts.

Metal Ion Homeostasis and Cellular Signaling

Investigations into metal ion transport, storage, and sensing mechanisms highlight contrasting regulatory strategies employed by organisms to maintain metal ion homeostasis and coordinate cellular responses to environmental stimuli. While some studies focus on the role of metalloregulatory proteins in transcriptional regulation and metal ion sensing, others examine the interplay between transition metals and redox signaling pathways in oxidative stress response and cellular signaling cascades.

Biomedical Applications of Transition Metals: Contrasts arise in the therapeutic potential of transition metal-based compounds for the treatment of human diseases, including cancer, neurodegenerative disorders, and infectious diseases. While some studies emphasize the cytotoxic effects of metal-based drugs targeting DNA replication and protein synthesis pathways, others explore the use of metalloenzyme inhibitors and metalloprotein mimetics for targeted intervention and precision medicine applications.

Computational Modeling and Simulation: Contrasts in computational studies stem from differences in modeling techniques, simulation parameters, and theoretical frameworks employed to simulate transition metal-mediated processes in biological systems. While molecular docking and molecular dynamics simulations provide insights into ligand binding and protein dynamics, quantum mechanical calculations offer mechanistic insights into metalloenzyme catalysis and metal-ligand interactions at the atomic level.

By contrasting findings from diverse studies, this research aims to synthesize disparate perspectives, identify common themes, and elucidate underlying principles governing transition metal biology in biological systems. Through integrative analysis and critical evaluation of contrasting evidence, this study seeks to advance our understanding of the multifaceted roles of transition metals in health and disease, providing insights into potential avenues for future research and therapeutic innovation.

Applications

The research on the role of transition metals in biological systems holds significant implications across various scientific disciplines and practical domains. One primary application lies in the development of novel therapeutics targeting metalloenzymes and metal-dependent pathways implicated in human diseases. Transition metal-based drugs offer promising avenues for the treatment of cancer, neurodegenerative disorders, and infectious diseases, leveraging the unique catalytic properties and regulatory functions of metal ions in biological processes.

Furthermore, the insights gained from transition metal biology have profound implications for biotechnological applications, including the design of biomimetic catalysts, biosensors, and bioinspired materials. Transition metal complexes and metalloproteins serve as versatile platforms for catalyzing chemical reactions, detecting biomolecular analytes, and modulating material properties, offering innovative solutions for environmental remediation, energy conversion, and industrial processes.

Benefits

Precision Medicine: Understanding the roles of transition metals in disease pathogenesis enables the development of

targeted therapies tailored to individual patients based on their metal ion profiles and metabolic signatures.

Sustainable Chemistry: Transition metal-based catalysts and processes offer sustainable alternatives to traditional chemical methods, enabling greener and more efficient synthesis routes with reduced environmental impact.

Biomedical Imaging: Transition metal complexes serve as contrast agents for various imaging modalities, including magnetic resonance imaging (MRI) and positron emission tomography (PET), enabling non-invasive visualization of physiological processes and disease states in living organisms.

Drug Discovery: Transition metal complexes exhibit diverse pharmacological properties and modes of action, providing new opportunities for drug discovery and development against challenging disease targets such as drug-resistant pathogens and cancerous cells.

Drawbacks

Toxicity and Side Effects: Some transition metal complexes exhibit inherent toxicity and off-target effects, posing challenges for their clinical translation and therapeutic application in humans.

Biocompatibility and Stability: The biocompatibility and stability of transition metal-based materials and implants present technical hurdles in their integration with biological systems and long-term performance *in vivo*.

Regulatory Challenges: The regulatory approval process for transition metal-based drugs and medical devices involves stringent safety and efficacy requirements, necessitating rigorous preclinical and clinical testing and validation.

Cost and Scalability: The synthesis and production of transition metal-based therapeutics and biomaterials often entail high costs and technical complexity, limiting their widespread adoption and accessibility in clinical practice and industrial applications.

Despite these drawbacks, the continued advancement of research in transition metal biology offers transformative opportunities for addressing pressing healthcare, environmental, and societal challenges, paving the way for innovative solutions and paradigm shifts in medicine, biotechnology, and materials science.

Result and Analysis

The investigation into the role of transition metals in biological systems has yielded multifaceted results, shedding light on the intricate interplay between metal ions and biomolecules across diverse biological contexts. Through a combination of experimental studies, computational modeling, and integrative analysis, key findings emerge regarding the structural, functional, and regulatory aspects of transition metal biology, along with their implications for health and disease.

One notable result is the identification of metalloproteins as central players in cellular function, with transition metal ions serving as essential cofactors in enzymatic catalysis, electron transfer processes, and signal transduction pathways. Structural analysis of metalloprotein complexes reveals intricate coordination geometries and ligand binding motifs,

highlighting the versatility and adaptability of transition metals in facilitating diverse biochemical reactions and molecular recognition events.

Furthermore, the analysis of metal ion homeostasis and cellular signaling pathways uncovers intricate regulatory mechanisms governing metal uptake, distribution, and storage within cells. Transition metal ions such as zinc, iron, and copper participate in redox signaling, metalloregulatory networks, and metallochaperone-mediated trafficking, orchestrating cellular responses to oxidative stress, nutrient availability, and environmental stimuli.

In the context of human health and disease, the analysis reveals the dual nature of transition metals as both essential nutrients and potential toxicants. While adequate metal ion levels are crucial for maintaining physiological homeostasis and supporting vital cellular functions, dysregulation or excess of transition metals can lead to oxidative damage, protein misfolding, and pathological conditions such as neurodegeneration, cancer, and metabolic disorders.

Moreover, the analysis highlights the therapeutic potential of transition metal-based compounds for treating human diseases, including metalloenzyme inhibitors, metal ion chelators, and metal-based drugs. Transition metal complexes exhibit diverse pharmacological properties and modes of action, targeting specific molecular pathways and biological targets implicated in disease pathogenesis.

However, the analysis also underscores the challenges and limitations inherent in studying transition metal biology, including technical constraints in experimental manipulation, chemical characterization, and computational prediction of metal-ligand interactions. The inherent complexity of biological systems and the dynamic nature of metalloprotein assemblies pose challenges in elucidating precise molecular mechanisms and predicting system-wide effects of transition metal perturbations.

Conclusion and Future Scope

In conclusion, the exploration of transition metals in biological systems has illuminated the intricate interplay between metal ions and biomolecules, unveiling fundamental principles governing enzymatic catalysis, cellular signaling, and metal ion homeostasis. Through a multidisciplinary approach encompassing experimental, computational, and integrative methodologies, this research has generated valuable insights into the structural, functional, and regulatory roles of transition metals in living organisms.

The findings presented in this research paper underscore the significance of transition metal biology in health and disease, highlighting the therapeutic potential of metal-based compounds for treating a myriad of human ailments, including cancer, neurodegenerative disorders, and infectious diseases. Moreover, the elucidation of metalloprotein structure-function relationships and metal ion signaling pathways offers opportunities for targeted intervention strategies and precision medicine approaches tailored to individual patient profiles.

Looking ahead, the future scope of research in transition metal biology is vast and promising. One avenue for future exploration lies in deciphering the molecular mechanisms underlying metalloprotein assembly, dynamics, and regulation, utilizing advanced structural biology techniques and computational modeling approaches to unravel the complexities of metalloenzyme function in atomic detail.

Furthermore, the integration of systems biology and network

analysis methodologies offers a holistic approach to understanding the emergent properties of metalloprotein networks and the systemic effects of transition metal perturbations on cellular physiology and organismal health. By elucidating the interconnectedness of metal ion signaling pathways, metabolic networks, and regulatory circuits, researchers can uncover novel therapeutic targets and biomarkers for disease diagnosis and intervention.

In addition, the development of innovative methodologies for metal ion sensing, imaging, and manipulation holds promise for advancing our ability to monitor and modulate transition metal biology in real-time, both *in vitro* and *in vivo*. By harnessing the power of chemical biology, nanotechnology, and bioinformatics, researchers can engineer custom-designed metalloproteins, metal-based probes, and drug delivery systems with enhanced specificity, sensitivity, and therapeutic efficacy.

Moreover, the exploration of transition metal biology in non-traditional model organisms and environmental contexts offers insights into the evolutionary origins and ecological roles of metalloproteins, as well as the ecological impacts of anthropogenic metal pollution and environmental stressors on ecosystem health and resilience.

In conclusion, the research presented in this paper represents a stepping stone towards a deeper understanding of transition metal biology and its implications for human health, biotechnology, and environmental sustainability. By embracing interdisciplinary collaboration, technological innovation, and scientific curiosity, we can unlock the full potential of transition metals as versatile tools for deciphering life's complexities and addressing pressing challenges in the 21st century and beyond.

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