

PHYSIOLOGICAL FUNCTION OF ZINC

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ABSTRACT

Zinc is an essential trace element that plays a pivotal role in numerous physiological processes, making it indispensable for human health. It is a key cofactor for over 300 enzymes involved in critical biological functions such as DNA synthesis, protein metabolism, immune response, and wound healing. Zinc's structural and catalytic properties enable its participation in diverse enzymatic reactions, including those involving antioxidant defense and cellular signaling pathways. Furthermore, zinc influences gene expression by stabilizing the structure of zinc-finger proteins, which regulate transcriptional activity. The dynamic regulation of zinc within cells, governed by specific transporters and binding proteins, ensures its availability for metabolic activities while preventing toxicity. Zinc deficiency can lead to growth retardation, immune dysfunction, and impaired healing, highlighting its vital role in maintaining physiological balance. This abstract emphasizes zinc's multifaceted contributions to biological systems and its potential implications in therapeutic and nutritional interventions.

Keywords: Zinc, Therapeutic, transcriptional, Nutritional

INTRODUCTION

Zinc plays a multifaceted role in biological systems and inorganic chemistry, serving as a vital trace element essential for numerous physiological processes. In the human body, zinc contributes significantly to enzymatic functions, protein synthesis, and cellular metabolism. It is particularly concentrated in tissues such as the brain, where its role extends to neurotransmission and synaptic plasticity. Despite its abundance, zinc cannot be stored in the body, necessitating a balance between dietary intake and excretion to maintain optimal physiological functions. Excess zinc is primarily excreted through the gut and, to a lesser extent, through urine, skin, and hair.

From an inorganic chemistry perspective, zinc's ability to form stable coordination complexes with biomolecules highlights its importance in enzymatic catalysis and structural stabilization of proteins. Zinc-dependent enzymes, such as superoxide dismutase, play critical roles in redox reactions and maintaining cellular homeostasis. Additionally, the HSAB (Hard and Soft Acids and Bases) principle provides insights into zinc's chemical behavior, emphasizing its preference for binding with ligands containing nitrogen or sulfur, which is critical for its functionality in biosystems.

The interplay between zinc's biological and chemical roles underscores its significance in maintaining health and driving biochemical processes. Understanding its function not only sheds light on its physiological importance but also opens avenues for therapeutic and industrial applications, emphasizing its status as a cornerstone of life and chemistry.

LITERATURE REVIEW

Federica Arrigoni et.al (2021) Density Functional Theory (DFT) in conjunction with a wide range of basic functions is one example of a recent quantum chemistry (QM) approach that has been used to study a few bio-inorganic systems. Here, density-functional theory (DFT) has shown to provide dependable (semi-quantitative) descriptions of many features of transition metal complexes that are either important components of naturally occurring enzymes or artificially constructed to imitate enzyme activity. Coacacen, a well-known synthetic oxygen carrier, is the first example taken into consideration. It is N, N'-ethylenebis (acetylacetonatiminato)Co(II). The following are findings from a density-functional theory (DFT) investigation of Coacacen: unbound, penta-coordinated with an appropriate axial ligand, and hexa-coordinated bound to dioxygen. The issues of the electrical structure of Coacacen derivatives have been studied for a considerable amount of time, mostly by experimental means. Renato Ugo's group conducted the first bio-inorganic system investigation in the 1970s on coacacen. Also, our research group of Italy's University of Milano-Bicocca is now investigating the "modern" difficulties of bio-inorganics, thus we will provide a brief overview of them: copper's interaction with amyloid β -peptides and the model compounds that describe the catalytic cycle of Fe-Fe hydrogenases.

Madhuchhanda Mohanty et.al (2023) To better molecular docking simulation is a well-known and used computer tool for understanding the molecular interactions between two molecules. This paper looks into several case studies that illustrate how the docking approach has been used to organic, inorganic, and hybrid systems. The databases and technologies needed for the docking investigation and its applications are described here. In order to comprehend the binding processes, the article explains the notion using different docking methods, different types of docking models, and different intermolecular interactions and their functions. This review concludes by discussing the benefits and drawbacks of dockings.

Jamila Musa (2024) New approaches to environmental cleanup and long-term sustainability are emerging from the field of inorganic chemistry. In this study, we will look at some of the new uses for inorganic substances and materials, and how important they are in combating global warming, pollution, and resource loss. Solar cells and batteries are examples of sustainable energy technologies covered in this study, which focuses on how inorganic nanomaterials might be integrated into these systems to improve efficiency and lessen their environmental effect. Research on transition metal complexes for toxic waste degradation and resource recovery provides further evidence of the relationship between environmental science and inorganic chemistry. Contributing to the advancement of green chemistry concepts, the review delves into the function of inorganic compounds in the creation of environmentally friendly products and procedures. Finally, the field's future directions and difficulties are discussed, with a focus on how multidisciplinary research and cooperation are necessary to fully harness inorganic chemistry's promise for a sustainable future.

Younis O. Ben Amer et.al (2020) A 1:2 reaction between benzidine and O-methoxy benzaldehyde was used to create Bis (2-methoxy benzylidene) biphenyl-4,4'-diamine Schiff base. Iron (II) and Cr (III) complexes were created using this ligand. We used mass spectroscopy, infrared spectroscopy, In order to investigate each of the produced chemicals, we used ^1H NMR and elemental analysis. The proven production of the suggested structures includes both the free ligand and complexes.

THE ROLE AND DISTRIBUTION OF ZINC IN THE BRAN

The body is unable to store zinc. Multiple mechanisms exist for the excretion of endogenous zinc,

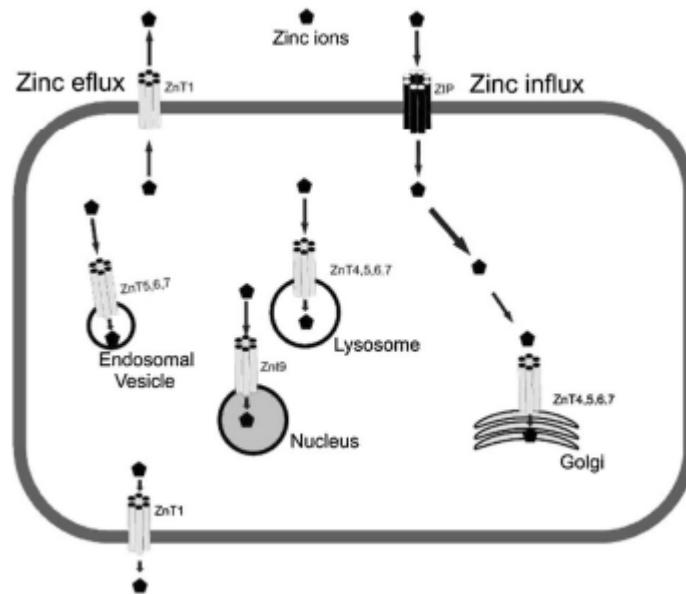


Fig. 1 Possible role of zinc transporters in cells

such as the reproductive organs, integument, kidneys, and sperm. The gut is the primary site of zinc excretion. Zinc is excreted in small quantities in urine, shed skin, new hair growth, sperm, and menstruation. Sloughed epithelium cells and unabsorbed zinc from the food and the body are both eliminated in feces. Dietary zinc loss in stool amounts to one milligram per day for low-zinc diets and five milligrams per day for high-zinc diets. Zinc is eliminated from the body via the urine due to its high concentration. Nitrogen loss via urine is correlated with high zinc losses; stress, infections, burns, severe surgeries, and trauma all contribute to nitrogen loss through urine. Protein catabolism might be one possible cause for this occurrence.

The brain likely has the greatest concentration of zinc of any organ in the body, with the probable exception of pancreatic b islets. The forebrain gray matter has levels of this element that reach 60-90 ppm, the highest in the brain. Because of its somewhat lower zinc levels (26-40 ppm), white matter has the second-highest level. This could be because of the reduced water content in this area. It is worth noting that synaptic vesicles of some glutamatergic neuron terminals contain a substantial amount of zinc (10–15%) in the brain. The majority of brain zinc is found in presynaptic vesicles and may be seen histochemically using Timm's sulfide-silver staining technique; however, over 80% of total brain zinc is bound to zinc metalloproteins. Spotting a zinc-selective fluorescent quinoline derivative, N-(6-methoxy-8-quinolyl)-para-toluene sulfonamide (TSQ), and modified Timm's staining both demonstrate the presence of a zinc entity that is voluntarily accessible in a significant portion of the neuropil across

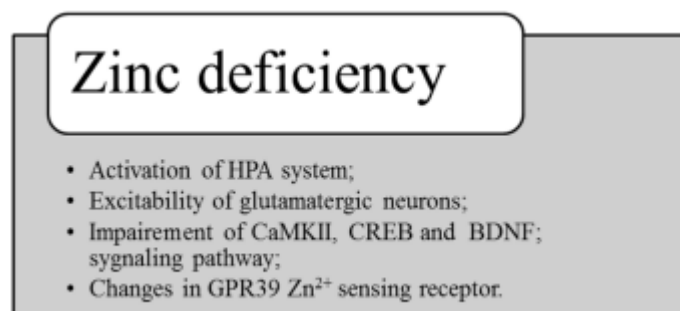


Fig. 2 Possible mechanisms in zinc deficiency

It is located in the brain's cortex. Certain regions of the brain exhibit more pronounced zinc staining than others. These regions include the dentate gyrus, CA1-4 radiatum, oriens and mossy fibers, subiculum, amygdala, thalamus, and striatum. On the other hand, the concentration of staining is much lower in the cerebellum, brain stem, and spinal cord.

Maintenance treatment is necessary to keep the levels of copper and zinc balanced after copper reduction. Therefore, zinc salts or low-dose chelators are used. Zinc salts inhibit copper absorption in the intestines by promoting the production of endogenous metallothionein, a copper chelator. Within a few days, the desquamation of enterocytes excretes copper bound to metallothionein via stool. As a therapeutic tool, zinc salts are ideal for use throughout prior to the onset of symptoms, since there are few adverse effects and the use of zinc salts inhibits the progression of its deficiency.

Table 1 Effects of the zinc deficiency in different part of body

The organ	Effects of zinc deficiency	Source
Brain	Neuropsychiatric disorders	[17, 23, 59, 61, 132, 133]
	Neurosensory disorders	[16, 60, 132, 134, 137]
	Decreased nerve conduction	[132, 135]
	Mental lethargy	[14, 16, 17, 136]
Thymus	Thymic atrophy	[4, 63, 64, 69, 71]
Skin	Skin lesions	[9, 10, 16, 20, 136]
	Acrodermatitis	[13, 16, 17, 28, 31, 34]
	Decreased wound healing	[16–18]
Reproductive system	Hypogonadism	[16, 17, 33]

Coordination complexes may be readily formed by any of these elements due to their free s- and p-orbitals and partly unoccupied d-orbitals, which allow them to establish extra donor-acceptor bonds inside the complexes and function as ideal complexing agents. The exceptional complex-forming capability of transition biogenic metals gives them unique characteristics (Table 2). Transition bio-metals effectively play the role of "organizers of life" when they form complexes with various bioligands found in living organisms".

Table 2. Classification of cations in biological systems

Ions	Na ⁺ and K ⁺	Mg ²⁺ and Ca ²⁺	Zn ²⁺	Fe, Cu, Co, Mn, and Mo (in the Form of M ⁿ⁺)
Function	Charge carriers	Solid structures	Acids and catalysts	Catalysts for oxidation–reduction reactions
Characteristics	Mobile	Moderately mobile	Static and inert	Static, inert
Stability in biological systems	Weak stability complexes	Moderate stability complexes	Stable complexes	Stable complexes
Preferred donor atoms	Coordination with donor O atoms	Coordination with donor O atoms	Coordination with donor N atoms	Coordination with donor N and S atoms

One major expectation is that transition metals will participate in oxy-reduction processes. Many well-known bio-compounds, including enzymes, hormones, other proteins, vitamins, and ions of biogenic transition metals, rely on these elements. The majority of these elements found in living things are found in coordination compounds. The metals of life are a common term for the d-elements. The complex chemicals presented in Table 3 are some examples of those that are physiologically active.

Table 3. Metal-containing proteins and enzymes of biogenic metals

Biometal	Biological System/Bioligand
Na	Extracellular cation; buffer systems, osmosis, Na ⁺ /K ⁺ - pump; activator of Na-specific ATP-ase [22]
K	Membrane pumps Na ⁺ /K ⁺ ATPase; activator of pyruvate phosphokinase and K-specific ATPase [23]
Mg	Chlorophyll; activator of phosphotransferase, phosphohydrase [24]
Ca	Ca ²⁺ -ATPase membrane pump; calmodulin transduces Ca ²⁺ signals in cells; calcitonin, aspartates, glutamates [25]
Biometal	Biological System/Bioligand
Mn	Activator of enzymes - pyruvate carboxylase, arginase, cholinesterase, phosphoglucomutase, peroxidase, aminophenol oxidase; glutamine synthetase; Mn superoxide dismutase in mitochondria [26]
Fe	Hematopoietic processes and electron transfer [27].
Fe (heme)	Hemoglobin; cytochromes; catalase; peroxidase; tryptophan, dioxygenase.
Fe (non-heme)	Pyrocatechase, ferredoxins, hemerythrin, transferrin, aconitase.
Co (B ₁₂ coenzyme)	Vitamin B ₁₂ (cyanocobalamin); glutamate mutase, dioldehydrase, methionine synthetase [28].
Co (non-corrin)	Dipeptidase, ribonucleotide reductase.
Cu	Processes of hematopoiesis, respiration, angiogenesis and neuromodulation; Cu-containing metalloproteins and metalloenzymes (about 1% of total proteome): cytochromes, Cu(histidine) ₂ , tyrosinase, amino oxidase, laccase, peroxidase, ascorbate oxidase, ceruloplasmin, superoxide dismutase, plastocyanin, and methionine synthetase [29].
Zn	Processes of reproduction; the enzymes carbonic anhydrase, Zn(gluconate) ₂ , carboxypeptidase, and alcohol dehydrogenase [30].
Mo	Enzymes oxidases: aldehyde, sulfite, molybdopterin, a xanthine oxidases in purine metabolism [31].

Proteins and other biopolymers have natural coordination molecules that are significant in many ways. Biomolecules like heme (a component of hemoglobin) and chlorophyll (a combination of porphyrin and

magnesium (II) ion) rely on metal ions like Mg^{2+} and Fe^{2+} , which are stable complexes formed by the porphyrin system. The cobalamin (vitamin B12) complex includes the cobalt (III) porphyrin element. In metalloenzymes, a wide variety of transition metals bind to specific proteins. Metal ions play an essential role in bioredox catalysis by activating coordinated substrates and contributing to the charge buildup at certain redox-active locations. There are a number of transition metals that may achieve several stable oxidation states; they include molybdenum (IV, VI), copper (I, II), iron (II, III), and cobalt (II, III). For instance, just mentioning the systems that include iron, like catalase and cytochromes, or copper, such as superoxide dismutase and cytochrome c-oxidase, is sufficient. Table 4.3 shows that around 30% of all enzyme systems revolve around biogenic metals. Metals like magnesium and zinc are involved in hydrolysis processes catalyzed by enzymes. Cu, Fe, and Mo, which are metals with varying valences and coordination numbers, control a wide variety of redox reactions.

Table 4 lists the characteristic properties of acids and bases that are in accordance with the HSAB concept.

Table 5 Characteristics of acids and bases according to the HSAB principle

Type	Acid	Base
Hard	Acceptors with high positive charges,	Donors with low polarizability, high
	low polarizability, and low LUMO energy; difficult to reduce	electronegativity, and low HOMO energy; difficult to oxidize
Soft	acceptors; with lower positive charges,	donors with high polarizability, low
	high polarizability, and high LUMO energy; easily reduced ones.	electronegativity, and high HOMO energy; easily oxidized ones.

By interacting with orbitals that have comparable energies, Lewis acids and bases are able to better explain their preferred binding mode. While dealing with hard reagents, the interaction is mostly electrostatic; while dealing with soft reagents, the preferred contact is covalent. Separation of acids and bases into categories was achieved by comparing the stability of the produced complexes to that of the basic forms. Table 6 provides examples of the major categories.

Table 6 Classification of hard and soft acids and bases

Type	Acid	Base
Hard	Na^+ , K^+ , Mg^{2+} , and Ca^{2+} , Mn^{2+}	H_2O , ROH , F^- , Cl^- , OH^- , $CH_3CO_2^-$, NH_3 , ClO_4^- , CO_3^{2-} , PO_4^{3-} , SO_4^{2-} , and NO_3^-
Intermediate	Fe^{2+} , Co^{2+} , Cu^{2+} , and Zn^{2+}	aniline, pyridine, N_3^- , Br^- , NO_2^- , and SO_3^{2-}
Soft	Cu^+ , Ag^+ , Cd^{2+} , Hg^+ , and Hg^{2+}	I^- , H^- , CO , CN^- , R_3P , R_2S , RSH , SCN^- , alkenes, and $S_2O_3^{2-}$ arenes

When it comes to understanding cation binding in biosystems, The HSAB concept has effectively accounted for the distinct interactions and conflicting responses. By extension, this concept states that a

metal's hardness is proportional to its oxidation state. It has been shown that certain ligands may stabilize oxidative states. We must highlight the potential synergy of the ligands. This indicates that ligands with similar degrees of hardness or softness are more likely to be included in the complex. As a result, biogenic metals that are alkaline or have an alkaline earth composition will combine with organic substances that include carboxyl groups (such as glutamate and lactate) or inorganic ions (such as CO₃²⁻, PO₄³⁻, and SO₄²⁻). The most efficient donor for a given metal is dependent on its oxidation state, however transition metals tend to favor molecules that include nitrogen or sulfur.

CONCLUSION

The study comprehensively explores the critical role of zinc in biological systems and its profound implications in inorganic chemistry, highlighting its indispensable contributions to enzymatic functions, cellular processes, and chemical stability. By analyzing the chemical properties and biological significance of zinc, the research underscores its importance as a trace element essential for maintaining health and biochemical balance. It also delves into the mechanisms governing zinc's behavior in the human body, including its absorption, utilization, and excretion pathways, providing insights into its physiological regulation.

From an inorganic chemistry perspective, the study emphasizes zinc's coordination chemistry and its role in forming stable complexes, which are pivotal for catalytic activities and structural integrity in biomolecules. The findings illustrate zinc's versatility in binding with diverse ligands, reflecting its adaptability and functional importance across biological and chemical domains.

This research highlights the necessity of maintaining adequate zinc levels to prevent deficiencies that can impair vital processes. Furthermore, it underscores the potential applications of zinc in therapeutic and industrial contexts, paving the way for future innovations in medicine, nutrition, and material science. Overall, the study bridges biological understanding and chemical innovation, reinforcing zinc's centrality in sustaining life and advancing science.

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