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ROLE OF ESSENTIAL METAL IONS IN HUMAN PHYSIOLOGY AND SYNTHETIC MODELS FOR BIO-MIMETIC CATALYSIS

Widyan Flayih Hassan
Republic of Iraq Ministry of Education
General Directorate of Education Baghdad Karkh 1st
widyanflayeh@gmail.com

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Abstract. The importance of metal ions in enzyme catalysis and human health is a crucial subject, with applications in biochemistry, clinical medicine and nutrition, highlighting the importance of the metal ions in physiological and metabolic activities. Metal ions, such as zinc, magnesium, iron, copper and manganese, are important cofactors in many enzymes, important aspects of protein structure, and metabolic pathway regulation. They are involved in vital biochemical pathways, alongside oxidative phosphorylation, DNA synthesis, neurotransmission and antioxidant defence, and, therefore, play an important role in maintaining cellular function and overall health. The biological functions of these steel ions, especially their ability to catalyse the transfer of electrons, to stabilise transition states and to undergo redox reactions makes them essential for enzyme activity. The imbalance of the concentration of metallic ions due to deficiency, toxicity or absorption disorders is linked to the occurrence of many diseases such as anaemia, neurological diseases, immune diseases, metabolic diseases, and cardiovascular diseases.

Keywords: Metal Ions ,Enzyme Catalysis, Human Health, Biochemical Processes ,Metalloenzymes,

1. Introduction

Metal ions play an essential role in enzyme catalysis and health, and they are important components of the biochemical processes essential for life. They are important cofactors, mainly responsible for increasing the stability of enzymes, their affinity to the substrate, and the efficiency of their catalytic activity by taking part directly in chemical reactions. Metalloenzymes are a wide variety of biologically important enzymes, which require metal ions (zinc (Zn^{2+}), magnesium (Mg^{2+}), manganese (Mn^{2+}), copper (Cu^{2+}) and iron (Fe^{2+}/Fe^{3+})) to achieve different physiological functions. The zinc ion is, for instance, a part of carbonic anhydrase that plays a pivotal role in the regulation of acid-base balance in the reversible

conversion of carbon dioxide to carbonic acid, and of metalloproteases that may have a critical role in protein metabolism. Magnesium is vital in ATP-dependent enzymes for the stability of the phosphate group, the improvement of enzyme function and the reinforcement of intracellular signalling pathways [1]. Iron plays an important role in cellular respiration and in the production of metabolic energy as it is part of haemoglobin and cytochromes which are used for transportation of oxygen and electron transfer. Copper is an antioxidant mineral that helps neutralise damaging free radicals, preventing oxidative damage to cells and tissues, as it is part of the enzymes used for this purpose, such as superoxide dismutase. Manganese is involved in enzyme activities associated with antioxidant activity and bone strengthening. The ratio of those metal ions is important because an imbalance may result in a serious health issue. Iron is an example, with anaemia being caused by a deficiency of iron, mainly as a result of decreased oxygen transport and fatigue, while too much iron can cause organ damage as in hemochromatosis. A deficiency of zinc has been associated with immune and nervous system dysfunction, and an excess of copper (as in Wilson's disease) leads to high concentrations in the vital organs. Besides their physiological role in plants, metal ions also have applications in the medical field including gadolinium-based contrast agents used in MRI to improve diagnosis and platinum-ions in chemotherapeutic agents like cis-platinum, which target human cancer cells in order to block the replication of DNA. Furthermore, the uptake and regulation of metal ions play an important role in metabolic homeostasis, and in preventing diseases caused by disruption of metal ion homeostasis [2].

2. Aims and goals

To investigate the essential function of metal ions in enzyme catalysis and human health, analysing their biochemical roles, physiological importance, primarily linked to health consequences, and their medical uses.

3. Metalloenzymes

Biological systems have evolved to use certain metal ions, such as zinc (Zn^{2+}), magnesium (Mg^{2+}), iron (Fe^{2+}/Fe^{3+}), copper (Cu^{2+}) and manganese (Mn^{2+}), as co-factors in enzyme processes, which enhances catalytic efficiency and the stability of protein structure. These metallic ions are characteristic and essential in enzymes, known as metalloenzymes, and which in physiological conditions will not work without the presence of these ions. Magnesium is necessary for ATP hydrolysis, plays a significant role in mobile energy metabolism and is very important in haemoglobin and cytochromes for oxygen transport and electron transfer, respectively, for efficient cellular respiration.Zinc is essential for the catalytic function of metalloproteases and carbonic anhydrase, which aid in the degradation of protein and in acid-base balance. Copper, which is part of enzymes like superoxide dismutase, protects the cells from oxidative stress by neutralising free radicals, while manganese is involved in the antioxidant defence mechanisms and bone formation. Such a need for these steel ions is not limited to enzymatic processes, but can cause significant physiological perturbations if they are lacking or in excess. For example, iron deficiency is associated with anaemia, which can impair oxygen transport and cause fatigue, while iron overload (hemochromatosis) can result in damage to organs from oxidative stress. Zinc deficiency is associated with immune disorders and cognitive impairment, while an overload of copper in the body, such as occurs with Wilson's disease, causes toxic levels to build up in the liver and brain, causing neurological and hepatic problems. Optimum concentrations of metallic ions in cells and tissues require a fine regulation, which is effected by special transporters and storage proteins. Steel ions can also be found to have physiological roles and more recently, they have been

introduced in medical therapies, such as diagnosis and therapy. The majority of the contrast agents used in Gadolinium are used to enhance the performance of the MRI to be able to see all the internal structures very clearly; platinum-based chemotherapy agents (e.g. cisplatin) halt growth in the majority of cancer cells by preventing the process of DNA replication and causing the cells to die (apoptosis).Moreover, the uptake and utilization of metal ions are relevant in the human health and nutrition and the diets should be well balanced with adequate supplementation of the essential trace elements to avoid the deficiency and related diseases. The study of the role of the metallic ions in the catalysis of enzymes has spread beyond the boundaries of biochemistry and biotechnology and now entered the field of pharmaceutical research where new generation of enzyme-based drugs, bio-engineered catalysts and innovative drug formulations are being invented. The newfound understanding of these interactions between enzymes and the metal ions would translate into biomedical research from precision reactions that utilize these enzymes to the development of new biomedical technology to combat certain diseases related to the metal ion, to the improvement of metabolic engineering. Metal ions in medicine, nutrition and biochemistry are therefore a multiparametric topic, which also involves the binding of metal ions to each other, in order to emphasize the importance of metal ions to life, wellness and human health. The organism would have to maintain high specificity of ion transporters, storage proteins, etc. for ion homeostasis in order to maintain its physiological function and/or to avoid toxicity. This is not to mention of the many pharmaceuticals, biotechnology and medicinal compounds to which steel ions have a wide range of applications.

4. Literature Review

From Jomova (2021) critical metals play essential roles in human life, enabling balance and helping cellular function. The twenty fundamental elements have ten of which are metals: Na, K, Mg, Ca, Mn, Fe, Co, Cu, Zn, and Mo. These metals are involved in enzymatic activities, electron transport and metabolism. The transition metals like iron and copper undergo redox reactions and require careful control to prevent oxidative stress and prevent the development of disease such as Diabetes, Cardiovascular Diseases, Alzheimer's and Parkinson's. Metalloenzymes like Cu, Zn-SOD and catalase catalyse the critical metabolic reactions at physiological costs. However, the presence of differences in these metals, both deficit or excess, can result in pathological conditions. Besides, there could be interactions between important and non-essential parts (like Chromium) that could impact natural processes. Cr (III) has been associated with fat and glucose metabolism, while Cr (VI) is known to be a carcinogenic agent. Other micronutrients like boron, silicon, vanadium, nickel and tungsten are required for certain species, but not the entire world. A multidisciplinary approach is required to understand the processes of metal homeostasis, which includes bioinorganic chemistry, biophysics and biology. Research on the chemistry of essential elements such as their ligand-binding characteristics, mobility and oxidation state have enhanced the development of treatments for metal-associated diseases. Advances in systems biology will also help to uncover the effects of metallic ions on human health, essential for improving recovery strategies. The inter-disciplinary approach can help to better understand the relationship between metals, metal homeostasis and the broader implications of those relationships and their importance to disease prevention and management.

Heavy metals pose a significant risk to human health because they can be absorbed into the body through ingestion, breathing in or absorption through the skin. Heavy metals have the ability to disrupt basic biological processes at low concentrations,

unlike other essential metals such as Na, K, Mg, and Ca. Harmful metals damage protein and enzyme function by disrupting the correct function of the protein/enzymes by binding to functional groups (e.g. thiols) and/or by oxidating the side chains of amino acids and altering the conformation of the enzyme and/or by replacing key metal ions in enzyme. This disturbance could cause damage to DNA and membranes that would affect the cells' function. Micronutrients, such as Zn, Cu, Fe and Mn, are important for metabolic processes, but excess or deficiency can be harmful. Heavy metals could be enzyme co-factors or inhibitors, and could alter biochemical pathways. The body depends on a proper balance of metals to function properly, as nearly half of all enzymes need them to function correctly for metabolism. Excessive levels of heavy metals in the environment is a worldwide problem and urgent need for application of effective remediation technologies to reduce its harmful effects.Bioremediation techniques such as chelation therapy and microbial remediation are among the methods that are being considered to help reduce heavy metal toxicity.

5.Role of Metal Ions in Enzyme Catalysis

The steel ions play a crucial role in different enzyme reactions as cofactors, helping in the catalysis, binding of the substrate and maintaining the structural stability of the enzymes. Enzyme Kinetics studies reveal that some enzymes such as carbonic anhydrase, superoxide dismutase, and cytochrome oxidase require a specific metal ion for the most efficient functioning. Zinc is also important for the functioning of carbonic anhydrase, as it stabilizes the active site of the enzyme and allows to convert carbon dioxide to bicarbonate. Likewise, ATP is involved with kinases, which need to be phosphorylated for the mobile energy switch. X-ray crystallography and nuclear magnetic resonance spectroscopy of enzyme structure elucidation show that metal ions play a role in enzyme structure stabilization.

6. Impact of Metal Ion Imbalances on Human Health

Clinical research shows that the imbalance in the levels of steel ions in the body have a significant effect on human health [6]. A deficiency of the essential metals, such as iron, zinc and magnesium has been linked to different health problems. For example, anaemia is a condition associated with low level of haemoglobin which results in low level of oxygen transport which is a major cause of iron deficiency.

Iron deficiency can lead to fatigue, cognitive dysfunction, and a weakened immune system, underscoring the essential role of the mineral. The symptoms of iron deficiency include fatigue, impaired mental function, and compromised immunity, highlighting the vital function of iron in the body's health. Low levels of zinc have been associated with reduced immune function, delayed healing and growth delays. Research has demonstrated that zinc is necessary for the activation of enzymes in the body, for DNA synthesis and for growth and immune function. Magnesium is required by over 300 enzymes, some of which are related to blood pressure and nerve signals; therefore, magnesium deficiency has been associated with neurological disorders, muscle cramps, cardiovascular diseases. The good news is, in excess, metal ions are toxic and harmful to organs. Wilson's disease is a genetic disorder in which the body accumulates copper causing hepatic cirrhosis and neurological symptoms - due to the inability of the body to excrete copper.

7. Medical Applications of Metal Ions

The wide use of metal ions in medicine for diagnosis and therapeutic purposes. Pharmaceutical ions based on metals in scientific evaluation and treatment. In combination with cisplatin, metal-containing tablets are very important in many

cancers, as they bind to DNA and disrupt the reproduction of tumour cells. In clinical studies, platinum-based chemotherapy has been found to be highly effective in treating a variety of cancers, but it is also known to have some side effects, including kidney damage. In scientific imaging, the assessment techniques using gadolinium compounds enhance MRI images and make it easier to visualise the structures inside the body. The findings indicate that gadolinium can also be used in diagnostic imaging, but due to its extended time in the body can cause toxicity in patients with impaired renal function. This has kick-started the improvement of potential imaging vendors that have less toxicity. Metal chelation therapy is an important technique employed in two scenarios: in cases of heavy metal toxicity and iron overload. Chelating drugs, which chelate excess iron out of the bloodstream, have been studied for their effect on hemochromatosis [8].

8.Nutritional Importance of Metal Ions

There is a strong relationship between nutrition and the control of metal ions and the prevention of deficiency. The result of the nutritional analysis indicated that leafy greens, lentils and pork are important sources of iron-rich food and good haemoglobin levels. Studies show that heme iron is better absorbed than non-heme iron and it is important to eat a balanced diet. Zinc is observed to be essential for immunity and bioavailable sources of zinc are shellfish, nuts and seeds. The findings also indicate that certain foods will compete with zinc absorption, for example, phytates in whole grains, so it is important to modify food choices as needed for individuals at a higher risk of being zinc deficient [9]. The nuts and seeds and whole grains are rich in magnesium, which is associated with improved cardiovascular health; magnesium helps to control blood pressure and muscle function.

9.Synthetic Models for Bio-Mimetic Catalysis

Synthetic models for biomimetic catalysis have been fabricated that mimic the catalytic process and the active site of natural metalloenzymes, which enriches the understanding of natural metalloenzymes. In fact, researchers seek to replicate the highly selective, efficient and mild reaction conditions of natural enzyme systems via the synthesis of metal complexes, metal-organic frameworks and biomimetic metal nanostructures. Transition metal-containing catalysts are often produced and used to serve as structural and functional mimics to elucidate complex biochemical reaction pathways, and as long-lasting alternatives to natural enzymes in industrial and therapeutic applications.

CONCLUSION

The role of metal ions in enzyme catalysis and health is a crucial research field which is closely related to biochemistry, clinical medicine and nutrition and is fundamental to their physiological role for maintaining metabolic efficiency and physiological balance.The role of the metallic ions (Zn^{2+}, Mg^{2+}, Fe^{2+}, Cu^{2+} and Mn^{2+}) is related to the changes in metabolic pathway, strengthening protein structures and catalysis. They take part in multiple cellular processes such as oxidative phosphorylation, DNA synthesis, neurotransmission, and antioxidant defense, showcasing their role in preserving cellular characteristics and vitality. Serious health diseases such as anaemia, neurological disorders, immunological dysfunctions and metabolic syndromes have been correlated with the Steel ion imbalance.

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