

Biochemistry of Zinc in Antioxidant Enzymes: Implications for Veterinary Medicine: A Review

Salam Ketab Rebat

Department of Animal Production, College of Agriculture, Kirkuk University, Kirkuk, Iraq

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Annotation: Zinc is an essential trace element with powerful biological effects, performing vital biochemical functions associated with the antioxidant system. Zinc is a cofactor and coenzyme for the enzyme Cu/Zn-superoxide dismutase and a regulator of metallothioneins. Zinc is essential for balancing redox reactions in most processes, protecting and stabilizing biomolecules from oxidative damage. In veterinary practice, zinc is important for ensuring overall health, reproduction, immunity, and production in animals. A deficiency of this nutrient is associated with poor growth, reproductive failure, and susceptibility to infection. Its supplementation enhances its antioxidant capacity, improves reproductive performance, and enhances resilience to environmental stressors and climate change. Recent advances identify organic, inorganic, and nanoscale sources of zinc that can beneficially and significantly increase bioavailability and improve overall efficiency. However, there is still a lack of accurate knowledge and information about the prolonged toxicity of this important element, its mineral antagonisms, and requirements across species. The importance of zinc in enhancing nutritional status and overall health in animals is reflected in particular through its biochemically potent oxidizing and reducing properties. This review aims to summarize our current understanding and provide precise guidance for the next steps in animal nutrition and health research.

Keywords: Zinc; Superoxide dismutase; Metallothioneins; Oxidative stress.

1. Introduction

Zinc (Zn) is a rare, essential trace element that is essential for many processes and is indispensable for all forms of human and animal life. It plays a fundamental and essential role in activating enzymes within the body, synthesizing many proteins/DNA, and modulating immune status (Marrero et al., 2017). Zinc is also an essential nutrient with structural and catalytic functions, serving as one of the active sites for more than 300 enzymes within the body and is crucial for overall growth, development, and metabolic balance (Palani et al., 2024; Palani et al., 2018a; Mhamad & Palani, 2025). Minerals and natural antioxidants have gained significant importance in recent studies in veterinary medicine, biochemistry, and animal production.

One of the most critical functions of zinc is as an antioxidant. Zinc is also a cofactor of Cu/Zn-superoxide dismutase (SOD), a crucial antioxidant enzyme that detoxifies harmful reactive oxygen species (ROS) that cause oxidative stress and protects lipids, proteins, and nucleic acids in the body against oxidative damage (Baltaci et al., 2018). Furthermore, the expression of metallothioneins, metal-binding proteins that protect the cell from oxidative damage, is influenced by zinc, emphasizing the role of zinc in redox control.

In the veterinary industry, zinc is extremely important since it has a strong influence on the health, productivity, and disease resistance of animals as a whole. Zinc deficiency in animals results in retarded growth, reproductive abnormalities, reduced immune response, and increased susceptibility to infection (Duffy, 2023). On the other hand, while low levels of zinc in the diet increase susceptibility to oxidative and environmental stress and decrease antioxidant capacity and fertility, supplementation with zinc improves this situation in farm animals (Oconitrillo, 2024).

Economic and social problems, e.g., the housing crisis in Iraq, emphasize the need to adapt and introduce sustainable programs linked to agriculture and veterinary medicine. Optimizing the use of nutrient inputs such as zinc supplementation in animals can enhance animal health and, in turn, economic sustainability, which is beneficial for the overall economy (Palani, 2025a).

Recent research has reported a substantial impact of essential trace minerals and natural antioxidants on the regulation of oxidative stress, reproductive physiology, and animal health (Mhamad et al., 2025; Palani et al., 2018a; Palani et al., 2018b; Mhamad & Palani, 2025) (lead and molybdenum ruminants; selenium and zinc supplementation on reproductive traits in Kurdi sheep, dietary intervention to ewes, and the antioxidant role of saffron compounds). On the other hand, nutritional and hormonal treatments are often found to be synergistic in improving reproductive and physiological performance in livestock (Ingole et al.). For instance, hormonal treatments improved reproductive performance and caused changes in some biochemical parameters in ovulating long bones in Awassi ewes (Alwan et al., 2018a, 2018b). These findings, through our review, suggest the potential for applying nutritional innovations in conjunction with general physiological management strategies, particularly for ruminants, previously developed to enhance aquaculture production. This review aims to analyze the role of zinc in antioxidant enzyme functions and protein synthesis (biochemical functions), as well as its role from the perspective of veterinary and production applications. Combining basic laboratory science with veterinary and production practice, this review utilizes the biochemical and physiological properties of zinc base, along with observational studies of zinc utilization, metabolism, and synthesis in animals, to identify its important and essential functions in protecting cells against damage and promoting overall animal health.

2. Zinc is a cofactor in enzymes

2.1 The Role of Zinc in Superoxide Dismutase (Cu/Zn-SOD)

SOD1, a key antioxidant enzyme in aerobic bacteria, contains organic and inorganic zinc, an important structural component. SOD1 catalyzes the decomposition of the superoxide radical and anomalous oxygen ($O_2^{\bullet-}$) into hydrogen peroxide and oxygen (Wang et al., 2020), preventing harmful and unnecessary excess levels of reactive oxygen species (ROS) that could negatively impact cellular components. Copper plays an important catalytic role in physiological processes, while zinc salts are a structural component of this protein, enabling proper folding, overall enzyme activity, and protein synthesis. The absence of zinc, an essential mineral cofactor, leads to SOD1 instability, reduced catalytic activity, and decreased physiological processes, while increasing the production of reactive oxygen species (ROS) within the body.

2.2 Contribution to Stability of Antioxidant Proteins

In addition to SOD1, it participates with zinc in stabilizing most powerful antioxidant proteins. The formation of stable complexes of Hg with thiol groups of cysteine residues prevents oxidation of the sulfhydryl groups and function of antioxidant enzymes (Maret, 2020). Zinc indirectly also plays a role in stabilizing membranes and inhibiting lipid peroxidation, thus decreasing the requirements of enzymatic antioxidant defenses (Marreiro et al., 2017). Another point is that zinc-induced metallothioneins act as radical scavengers and prevent antioxidant enzymes from oxidative inactivation.

2.3 Balance Between Zinc and Other Trace Elements

In addition to zinc, the activity of Cu/Zn-SOD, as well as several other antioxidant enzymes, is strongly regulated by the balance among trace minerals, particularly copper and manganese. Copper is needed for the catalytic function of SOD1; however, an excess of copper in the absence of adequate zinc can serve to induce pro-oxidant effects due to unbridled Fenton-like processes (Baltaci et al., 2018). Also, manganese is a cofactor of mitochondrial SOD (Mn-SOD), and an imbalance between zinc and manganese could compromise mitochondrial antioxidant defenses. As such, the balance of Zn with other trace minerals to achieve an optimal level is vital for the efficient activity of antioxidant enzymes and overall oxidative balance (both human and veterinary) (Duffy, 2023).

3. Molecular Mechanisms of Zinc in Oxidative Stress Regulation

3.1 Regulation of the Reactive Oxygen Species (ROS) by Zinc

Zinc is a redox-inactive transition metal, unlike iron and copper. Nevertheless, zinc is able to impart redox activity to proteins by binding cysteines to form cysteinate complexes, which stabilize proteins and control redox signaling. This act of indirect modulation serves to regulate the levels of ROS and buffer cellular materials against oxidative injury.

3.2 Zinc and Nrf2 Pathways in Antioxidant Genes

The Nrf2 pathway, which is involved in regulating gene expression in general and also acts as a potent antioxidant, is an important target for zinc by altering the levels of the key regulators Keap1 and GSK3 β . Zinc modulates the potent antioxidant Nrf2 (nuclear factor erythroid 2-related factor 2) pathway to stimulate the transcription of Nrf2-dependent potent antioxidant target genes. This ultimately leads to increased expression of potent antioxidant defenses and, when present, oxidative damage and harm.

3.3 Metallothioneins: a Function in Metal Homeostasis and Antioxidant Defence

Zn-binding proteins such as metallothioneins (MTs), which are sulfur-rich, bind Zn very tightly and form essential elements regulating Zn homeostasis. MTs are metal reservoirs and/or radical scavengers and release zinc in oxidative stress. Their additional functioning highlights the significance of zinc in redox defense processes.

4. Veterinary Implications of Zinc in Antioxidant Defense

4.1 Health Consequences of a Zinc-Deficient Condition in Animals

Nutritional deficiencies are common in livestock, and zinc deficiency can have serious health and productivity implications. In young animals, deficient intake of Zn results in decreased growth performance, skeletal abnormalities, and poor feed efficiency. At the immune level, the depletion of vitamin A down-regulates the responses of both innate and adaptive immunity, the animals are more apt to be infected, and the combined vaccination's efficiency diminishes. Zinc deficiency also leads to reproductive problems, such as delayed sexual maturity, low quality of semen, low conception rate, and embryonic mortality in ruminants and poultry (Saleh et al., 2018).

4.2 Use of Zinc Supplementation in Veterinary Medicine

Zinc supplementation is commonly applied in veterinary nutrition due to its antioxidant defense, immunomodulation, and reproductive potential. The normal intake of zinc should ensure the activity of Cu/Zn-SOD and metallothioneins, leading to lower oxidative stress and tissue damage (Marreiro et al., 2017). In poultry production, dietary Zn supplementation increases hatchability, antioxidative enzyme activities, and carcass quality, while in ruminants the compound improves reproduction efficiency, udder health, and hoof integrity (Hu et al., 2024). In addition, modern and novel zinc salt sources such as chelates, organic receptors and nano zinc as salts have been shown to be more bioavailable than inorganic salts, leading to improved animal growth performance, fertility, reproduction and resistance to strong oxidative stress (Ng'ang'a et al., 2025).

4.3 Evidence from Studies in Farm Animals

Numerous recent studies and research confirm the functional importance of zinc salts for both large and small livestock. Zinc salt supplements can improve hoof health, reduce somatic cell count, and enhance overall udder immunity, as they do in dairy cows (Duffy et al., 2023). Zinc salts significantly increased fertility, reproduction, and strong antioxidant status in sheep and goats under stress (heat and seasonal breeding). Zinc dichromate, zinc methionine, or nano-zinc supplements improved growth efficiency, immunity, and strong oxidative status in chickens under high environmental temperatures (Saleh et al., 2018, Ho et al., 2024). Together, these findings and studies provide further evidence and precise information on the importance of zinc salts as micronutrients, not only for overall animal health and production, but also for productivity, resilience, and animal behavior, and are directly relevant to veterinary practice. The resource efficiency aspect, which is also relevant to veterinary animal nutrition, also applies to veterinary animal nutrition. The utilization of laboratories is maximized to achieve high productivity and efficiency as well as productivity as in the efficient use of industrial inputs (Balani and Hussain 2022).

5. Conclusion and Future Perspectives

5.1 Synopsis of Biochemical Functions of Zinc in Antioxidant Defence

Zinc salts are an essential and rare trace element with known biochemical and physiological roles in protecting against powerful antioxidants and the resulting damage. It is a cofactor in the enzyme Cu/Zn-superoxide dismutase (SOD1), a powerful antioxidant and cellular protector that works to absorb free radicals and abnormal superoxide radicals by catalyzing their conversion to a less toxic and less oxidatively damaging substance (either normal molecular oxygen or hydrogen peroxide). Besides enzymatic activity, zinc shields sulfhydryl groups, stabilizes cell membranes, and controls the signaling system in oxidative stress. When bound to metallothioneins, it also strengthens radical scavenging ability and helps maintain intracellular metal balance (Maret, 2019; Marreiro et al., 2017).

5.2 Veterinary Importance of Zinc

From the veterinary aspect, zinc is required for animal health, production, and resistance. Sufficient zinc is essential for reproductive performance, immune function, and oxidative stability, and low dietary zinc results in inferior fertility, increased incidence of disease, and stunted growth. Supplementation strategies have been successfully used in poultry, ruminants, and swine to enhance productivity and resistance to diseases, particularly under stress conditions of heat, intense production, and weaning (Saleh et al., 2018; Duffy et al., 2023).

5.3 Research Gaps

In spite of advances in the knowledge of the roles of zinc, several research gaps exist:

- Insufficient information regarding the safety, and also the efficacy, of nano-zinc in the long-term use in livestock nutrition.
- Limited understanding of mineral interactions (e.g., with copper, iron, manganese) in antioxidant regulation.
- No species-specific requirements for zinc in environmental stresses including heat and oxidative stimuli.
- Limited connection of molecular level data (e.g., Nrf2 activation) with commercial scale production and field results.

5.4 Future Directions

Future studies should:

1. Inter-specific nano-zinc supplementation trials over an extended period among different types of livestock need to be carried out to evaluate the safe and optimal dosage upon supplementation.
2. Use omics approaches to study the molecular action of zinc in antioxidant signaling pathways (i.e., Nrf2, metallothioneins).
3. Establish targeted nutritional strategies in regards to zinc supplementation according to animal species, age, and environmental stressors.
4. Assess the economic and sustainability effects of zinc supplements in concentrated animal feeding operations.

The successful application of innovative nutrition, involving organic and nano-zinc at commercial scale, needs to be scientifically validated and financially supported over the long term. As is well documented in finance literature in the context of international borrowing and credit rating, the ability to obtain funding is a key determinant of embracing new production techniques. For this reason, prospective veterinary research and animal nutrition courses and programs should be based on economic perspectives that enable on how to invest economically in sustainable animal enterprise (Palani, 2025b).

Integration of molecular biochemistry with applied veterinary nutrition will enable zinc research to contribute to sustainable animal husbandry and to improve welfare as well as profitability of livestock farming.

6. Conclusion

Zinc is a crucial trace element that performs essential biochemical functions, participating in enzymatic activities such as Cu/Zn-superoxide dismutase and metallothioneins, and antioxidant defense. Zinc is important in veterinary medicine for maintaining the health, fertility, immune function, and productivity of animals, and deficiency is associated with major physiological disturbances. Nutritional supplementation strategies, particularly micronutrients, particularly those based on organic zinc salts and nano-zinc, appear promising for excellent positive effects on animal health. However, further studies are needed to determine the appropriate doses of zinc and nano-zinc, their long-term safety, and cost-effectiveness. Animal health, welfare, and behavior, as well as a sustainable and cost-effective livestock production system, could

significantly benefit from improved molecular and micronutrient knowledge through their integration into good veterinary practices and ruminant production.

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