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## **Original Article**



Nutrition for immunity: Role of minerals for optimizing immune system and functions of animals

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# INTRODUCTION

Minerals are essential for optimizing functioning of immune system of animals and plays critical roles as components of body tissues (bone, nerve and muscle) and their functions. Minerals are vital for functional integrity of body tissues of animals by means of varieties of chemical combinations and concentrations to maintain optimal growth, health and productivity of animals (Underwood and Suttle, 1999). Deficiency of minerals adversely affect certain homeostatic mechanisms of the body and is manifested as metabolic diseases affecting physiological and immune functions of the animals.

## Immune system and mechanisms

Immune system of animal body creates numbers of different cells and molecules to protect from disease causing pathogens. The generated cells and molecules can recognize foreign molecules or pathogens to create appropriate immune response called 'effector response' and to induce 'memory response' to eliminate pathogens and to prevent future infections, respectively.

Immune system of animal body has two components, namely innate or non-specific immunity and acquired or specific immunity. Animals acquire innate or non-specific immunity by birth and is species specific. It gives protection against pathogens from entering the body. Innate immunity has four sub-systems, namely, a). Anatomic (skin), which is one of the first line of defenses against invading pathogens, b). Physiologic, which is manifested by changes of body's temperature, pH of body fluid and oxygen tension etc. to prevent entry of infectious agents, c). Phagocytic i.e. engulfment and killing of invading pathogens by macrophages and neutrophils, and d). Inflammatory, which is also another response of immune system to prevent infection or invasion by pathogens. Inflammation creates physical barrier against the spread of pathogens or infection and promotes healing of damaged tissues by pathogen clearance. Cytokine barriers of innate immunity include 'interferons' which are secreted by pathogen-infected cells to protect non-infected cells from

infection. The *interferons* regulate signals that initiate and constrain inflammatory response to pathogen and injury.

The acquired or specific immunity develops when an animal's immune system encounters invading pathogens or when receives antibodies from another source. There are two types of acquired or specific immunity – adaptive and passive immunity. The adaptive immunity develops when animals encounter infection or vaccination. The passive immunity develops when animals receive antibodies or toxin rather than making them through its own immune system. The acquired or specific immunity can also be subcategorized as humoral and cell-mediated immunity. Humoral immunity is the adaptive immunity manifested by production of antibodies by B-lymphocytes which are secreted by plasma cells. The cell-mediated immunity does not involve antibodies but associated with the activation of macrophages, NK-cells, T-lymphocytes to release cytokines in response to an antigen or invading pathogen.

### Role of minerals on immunity and immune functions

Minerals are important components of animal diet influencing nutritional status of animals which critically determines immune status of animals. A balanced diet with balanced mineral status is essential for optimum health and productive performance of animals and also for effective immune system and efficient immune functions. Many minerals, directly or indirectly, are involved with immune system and functions of animals.

#### **Magnesium and immunity**

Magnesium is the most abundant divalent cation in living cells and bony matrix regulating numbers of cellular functions. It binds with proteins, nucleic acid and nucleotides in the cells. Magnesium is cofactor for many enzymes, activates several enzymes and plays important roles in membrane function and intracellular signaling. It also involves in the synthesis and replication of RNA and DNA and secretion of enzymes and hormones. Magnesium is essential for oxidative phosphorylation, transmembrane movement of ions and muscle contraction. Magnesium helps in stabilizing cell membrane structure and membrane potential.

Magnesium influences both innate and adaptive immunity of animals. Magnesium modulates macrophages in their response to cytokines. Magnesium helps in reducing cytokine production by stimulating toll-like receptor (TLR), which is for increased 1kBa level. Magnesium plays role in development, differentiation and proliferation of lymphocytes (Feske et al., 2012). Fas-induced apoptosis is magnesium-dependent process. The Fas receptor is a death receptor on the surface of cells that leads to apoptosis if it binds its ligand. Magnesium influences T-lymphocyte function as their proliferation is dependent on Mg<sup>2+</sup> transporter TRPM7 and deficiency of magnesium inhibits T-lymphocyte development and also early cell death. Magnesium regulates phosphoinositic metabolism, which is an important intracellular signaling system involving in a variety of cellular functions, such as growth factor signaling, membrane trafficking, and cytoskeleton regulation; thus, involving indirectly in various immune cell functions. In acute inflammatory condition, magnesium favors metabolic activities of T-lymphocytes.

#### **Immunological functions of Zinc**

Zinc is an essential trace mineral both for innate and adaptive immune system of animals. Zinc functions as antioxidant stabilizing cell membrane as zinc is associated with superoxide dismutase and carbonic anhydrase. Zinc regulates many enzymes and hormones. It is component of transcription factors and involves in the synthesis of RNA and DNA. Mechanistically, zinc is involved in the processes of genetic stability and gene expression (Casadevall et al., 1998). Zinc is present in the cell nucleus, nucleolus and chromosomes, and it stabilizes the structure of DNA, RNA and ribosomes (Wu and Wu, 1987). Zinc has regulatory effect on production of cytokines and hence antibody production. Deficiency of zinc adversely affect immune functions and health of animals.

Zinc is essential for activity of nicotinamide adenine dinucleotide phosphate oxidase of neutrophil granulocytes controlling functioning of both innate and adaptive immune system (Hasegawa et al., 2000; DeCoursey et al., 2003 and Bonaventura et al., 2015). Zinc also has significant role in natural killer cells functions.

Zinc is component of hormone thymulin secreted by thymus regulating formation, maturation and function of T-lymphocytes influencing adaptive immunity of animals. Zinc is also important for T-cell differentiation process (Sheikh et al., 2010); and its deficiency is directly related with immune dysfunction. Deficiency of zinc is also associated with reduced maturation of B-lymphocytes and hence immune response. Zinc can influence production and signaling of various inflammatory cytokines resulting increased oxidative stress and systemic inflammatory responses for its deficiency for increased expression of IL-1 $\beta$ , IL-1 $\alpha$  and IL-6. Zinc inhibits production of proinflammatory cytokines. Zinc inhibits NF-kB signaling pathway resulting apoptosis, innate and adaptive immune responses and inflammatory processes, inhibiting expression of pro-inflammatory cytokines such as TNF- $\alpha$ , IL-1 $\beta$  and IL-6.

### Role of copper in immunity of animals

Copper is associated with both humoral and cellular immune function as its deficiency influence thymus and its function. Neutropenia and decreased numbers of T-lymphocytes are reported for copper deficiency. Copper is important cofactor for oxidative balance (Husain and Mahmood, 2019) and regulates transfer of electrons to oxygen. Copper is essential for pathogen growth and hence growth of pathogens can be prevented by limiting the availability of copper to diseased animals.

#### Iron and immunity

Iron is indirectly involved in modulating immune system of animals. Iron helps in B-lymphocyte proliferation, T-lymphocyte function and adaptive immune responses. Both deficiency and excesses of iron is harmful for animals. As evident from studies, excess iron may favor growth and proliferation of invading pathogens. Thus, iron has role both in host defense and pathogen proliferation. Innate immune system affects invading pathogens within hours of infection by reducing available iron. This process is driven by inflammatory cytokines to host invasion, stimulating an increase in circulating levels of the hepatic derived peptide, hepcidin, which functions to modulate and degrade the activity of the ferroportin iron export channels (Nemeth and Ganz, 2009). Degradation of ferroportin iron export channels is effective in restricting iron availability for use by

pathogens and this results sequestration of iron with macrophages, enterocytes and hepatocytes which reduces any extracellular iron levels that could be used for microbial growth (Ganz and Nemeth, 2015).

Animal's immediate response to infection is to restrict extracellular availability of iron to invading pathogenic organisms. Thus, optimal iron status indirectly helps to ensure better immunocompetence of animals which allows an appropriate immune response to invading pathogens.

#### Role of selenium

Selenium is component of glutathione peroxidase and therefore, as antioxidant and maintains homeostasis in animals. Glutathione peroxidase is essential for optimal functioning of thyroid gland and to protect the thyroid gland by removing the excess hydrogen peroxide. It also regulates inflammation and immunity playing important role for optimal immune functions of the body. Selenium toxicity occurs at intakes of >900  $\beta$ g/day; whereas, deficiency occurs at < 19  $\beta$ g/day. Deficiency is known to induce cardiomyopathy, reduced immune function, skeletal muscle myopathy, osteoarthropathy, and make body susceptible for diseases. Selenium deficiency may activate increased inflammatory cytokines via inducible nitric oxide synthetase pathway.

#### Role of chromium

Chromium is known to influence metabolism of carbohydrates, protein and lipids in animals. Chromium influences immune functions of animals by reducing serum cortisol and increasing serum IgM and total immunoglobulins. It was also reported that chromium supplementation increased antibody titer response to infectious bovine rhiontracheitis vaccination in newly weaned stressed feedlot calves (Burton et al.,1994) and greater primary and secondary antibody responses to immunization in dairy cows. Factors influencing immune responses for chromium supplementation in animals include the initial chromium status of the animals, the amount of available chromium in the diet, the form of chromium supplementation and the type or degree of stress imposed on the animals (Spears, 2000).

#### CONCLUSION

It is evident that minerals are crucial for proper functioning of immune system of animals. Dietary supplementation at right amount and proportion is essential for optimum bioavailability of minerals and their functioning to optimize immunity, health and productivity of animals.

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