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Selenium (Se): Versatile Element in the Overall Health of the Animal – A Review

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Abstract. Animal health is a major determinant of the degree of success in intensive animal production systems. A balanced diet as it relates to the sufficiency of trace nutrients, such as selenium therefore becomes very important. This is because Se is a very critical dietary essential trace-mineral for both humans and farm animals. Se is a very versatile element in the health of animals as it is a component of various proteins, including glutathione (GSH) system, involving glutathione peroxidase (GSH-Px) and other selenoproteins that play significant functions in the body of the animal. Selenoproteins are almost ubiquitous in its health-related functions as it is involved in the protections of cells from oxidative damages occasion by free radicals leading to many chronic diseases. Additionally, they are involved in the proper metabolism of thyroid hormones and the control of reproduction functions. They are also neuro-protective and anti-carcinogenic. Se is also very important in the functions of the immune system as it causes the stimulation of the immune system for the purposes of protecting the animal. In exhibiting these characteristics, Se liaises or works in synergy with the lipid-soluble vitamin E to produce effective antioxidants' defenses for the body. To this point therefore, Se deficiency could be very detrimental to the survival of the animal as judged by its multi-farious functions in the overall health of the animal. This paper covers most of these functions.

Key words: Selenium, Selenoproteins, Immune System and Animal Health

Introduction

Selenium was discovered a long time ago. However, it was recognized as an important trace mineral in the diets of animals about 63 years ago (Schwarz & Foltz, 1957). Following its recognition Se was seen to have prevented white muscle disease in the sheep (Oldfield, Schubert & Muth, 1960), liver necrosis, cardiac myopathy and exudative diathesis in other animal species (NRC, 1983). Nevertheless, it was in 1973 that Se was demonstrated to be a component of the glutathione peroxidase (GSH-Px) enzyme with identified biological evidence of Se function in the body (Rotruck et al., 1973). From this period onward, investigations further revealed that Se plays different essentials' roles in livestock production in terms of animal performance and health. Many different data in the literature also confirmed that Se and vitamin E work synergistically in their biological functions in eliciting overall improved performance and health of the animal. Se sources are various. For instances, Se is available in alkaline soils, grains/other plants and commercial sources are also available. Since the recognition of the important roles of Se in livestock production, at present Se has come to be known and implicated in the performance and health of the animal. Therefore, the objectives of this paper are to excavate the different areas and modes of actions of Se in the overall health of the animal. There are two major areas Se is implicated in eliciting or supporting the overall health of the animal, including improved performance. These are the roles of Se in seleno-proteins and its role on the immune system of the animal, respectively.

Se and Seleno-Proteins

The seleno-proteins family includes at least 20 groups (Kohrle et al., 2000). However, at present only 10 of the seleno-proteins have been fully characterized and described. Amongst them the most discussed is the GSH-Px. GSH-Px roles are to protect hemoglobin and fatty acids from being oxidized and also scavenges for free radicals implicated in lipid peroxidation.

To this extent, the target substrates of GSH-Px are reduced glutathione (GSH), hydrogen peroxides (H_2O_2) and other peroxides, such as phospholipid hydro-peroxide. According to the findings of Arthur (2000) four isoforms of GSH-Px have been identified and characterized in mammals: classic GSH-Px also referred to as cytoplasmic peroxidase. This enzyme is ubiquitous as it is present in all body tissues, plasma (PL-GSH-Px), extracellular enzyme found mostly in the kidneys and liver, gastrointestinal (GI-GSH-Px) and phospholipid-hydroperoxide (PH-GSH-Px) concerned with the protection of cell membranes, phospholipids against oxidation and participation in the production of prostaglandins and catecholamines and of course the sperm nuclei GSH-Px (SN-GSH-Px), respectively.

The major primary functions of these peroxidases are linked to the removal of hydrogen peroxide and thus detoxification due to hydrogen peroxide and lipid peroxidation. Hydrogen peroxide is an intracellular messenger and redox regulator and can thus play some needed roles in the activation of key transcription factors; thus it is thought that regulation of the fragile regional redox balance is a major function of GSH-Px enzymes (Brigelius-Flohe, 1999) whereas the sole function of the SN-GSH-Px is more related to protamine thiol cross-link in sperm maturation (Pfeifer et al., 2001). The GSH-Px enzymes are present in all mammalian tissues where oxidative stress can possibly occur (Kohrle et al., 2000). Nevertheless, it is mostly the cytoplasmic GSH-Px that exhibits the role of emergency GSH-Px and thus most concerned for preventing the negative effects associated with oxidative stress (Kohrle et al., 2000). GSH-Px enzymes are well-known to be implicated in the regulation of pro-inflammatory cytokine production. The involvements of GSH-Px enzymes in the regulation of the biosynthesis of leukotrienes, thromboxanes and prostaglandins are significantly implicated in the regulation of inflammatory events and PH-GSH-Px is capable of inducing cytokine transcriptional gene activation (Kohrle et al., 2000). Although the various GSH-Px perform their protective functions in concert each of them elicits it anti-oxidant protection at different sites and locations. For instance, GI-GSH-Px provides a barrier against hydro-peroxide resorption in the gut (Brigelius-Flohe, 1999). To this point, a recent study has shown that the digestive tract is a major site for antioxidant cum pro-oxidant interaction in the body system (Surai, 2002).

In the referred condition above, specific GI-GSH-Px would likely be the main protective factor against lipid hydro-peroxides present in feed. During feed compounding and storage polyunsaturated lipids are often oxidized which is capable of inducing health-related concerns, especially reduced growth and productive/reproductive traits in production animals and possibly immune-competence (Kanazawa & Ashida, 1998). Here, it should be clearly stated that oxidized lipids can react with transition metals present in feed as feed supplements to produce free radicals. These formed free radicals in turn can react with both natural and synthetic anti-oxidants found in feed to form lipid hydroperoxides. It is the GI-GSH-Px that would prevent the peroxides from having access into the blood circulation. This has been demonstrated in rats (Kanazawa & Ashida, 1998). Therefore, the take home message here is that GSH-Px activities are dependent on adequate dietary concentrations of Se in the diet. This is also an indication that its deficiency would be detrimental to the health of the animal.

Additionally, iodothyronine deiodinases are another sets of selenoenzymes which play some important functions by modulating the conversion of thyroxine (T_4) into 3,5,3-triiodothyronine (T_3) which is the metabolically active form of the thyroid hormone or into the reverse 3,5,3-triiodothyronine (rT_3) the inactive hormone. The type 1,5-iodotyronine deiodinase is found in the liver and kidneys. The thyroid gland produces the hormone (T_3). This hormone has been confirmed in the brain and in the pituitary glands in ruminants. The type 2,5-iodotyronine deiodinase is present in the brain and pituitary glands of all animal species. Its role is to catalyze the transformation of T_4 into T_3 in tissues that are unable to capture the circulating T_3. The type 3,5-iodotyronine deiodinase converts T_4 into rT_3 and T_3

into diiodothyronine found in the brain, skin and placenta and is responsible for inactivating thyroid hormones (Chadio et al., 2006). These observations therefore, support the fact that Se deficiency is capable of obstructing the stated conversions processes which can hinder the normal functions of the thyroid hormone. In this way, it is an indication that low levels of Se can affect the biological functions of the thyroid (Hess & Zimmerman, 2004).

Again, it has been demonstrated that thioredoxin reductase is a selenoprotein enzyme present in all mammals. In the presence of electrons taken from NADPH thioredoxin catalyzes the reduction of oxidized thioredoxin and then transfers the redox capacity of thioredoxin to cell proteins (Lu, Berndt & Holmgren, 2009). Furthermore, it is now known that the physiological roles of thioredoxin reductase have been better elucidated; therefore, it is now known that thioredoxins are capable of donating electrons to redox enzymes, including ribonucleotide reductase and thioredoxin peroxidase. Thioredoxins are involved in DNA transcription and binding. They also act as growth factors, inhibitors of apoptosis and hydro-peroxidase reducers (Arner & Holmgren, 2000).

Another selenoprotein identified as selenoprotein P is involved in an important function in the body. Selenoprotein P and plasma GSH-Px are the mainly known plasma selenoproteins. The presence of this selenoprotein has been confirmed in the blood, liver, heart, kidneys and testes from the studies of Brown and Arthur (2001). Selenoprotein P binds heparin proteoglycans in cells and the intercellular matrix as well as binding of metal ions. In these ways, selenoprotein P protects endothelial cells against oxidants' insults (Persson-Moschos, 2000). Furthermore, selenoprotein P concentrations sparingly decrease during selenium deficiency compared to GSH-Px and therefore is capable of exerting more protections to the animal (Hill et al., 1996).

Selenoprotein identified as selenoprotein W mostly found in muscles, spleen, testes, heart and brain. Its roles are implicated in muscle differentiation and development by protecting myoblasts against oxidative stress (Loflin et al., 2006). The protein present in sperm mitochondria is a special selenoprotein that determines the integrity of sperm tails; therefore, in selenium deficiency its concentrations decreases significantly leading to weakened sperm motility resulting in poor spermatogenesis process in the animal (Pfeifer et al., 2001). Other selenium-containing proteins are selenoprotein K, an antioxidant in cardiomyocytes, selenoprotein M and H with neuroprotective activities, selenoprotein N that promotes muscle function, selenoprotein S involved in the protection against colorectal cancer in humans (Sutherland et al., 2010). There are many other selenoproteins identified in the body but their functions have not been classified but might not be unconnected to antioxidant properties.

Selenium and Cancer

Amongst all trace-minerals widely studied, selenium has been shown to possess anti-neoplastic characteristics; this may explain in part why cancer patients show reduced Se blood levels. Furthermore, this can be further explained by findings in agronomy why increased incidences of neoplastic diseases are highly correlated with low soil Se concentrations (Sanz, Romero & Romero, 2000). The modus operandi of Se in exhibiting this quality is related to its antioxidant properties mainly via the redox-dependent regulation of transcription factor functions involved in inhibiting cell growth. Depending on the concentration or dose of Se, it exhibits a stimulatory or an inhibitory impact on the growth of animal tumors which are sensitive to the cytotoxic action of natural killer cells (Koller et al., 1986). Se also has the capabilities of stimulating the production of anti-neoplastic metabolites as well as inhibiting angiogenesis and induces the apoptosis of cancer cells. In these ways Se is an anti-carcinogen agent thereby playing critical roles in the wellness and welfare of the overall health of the animal (Combs & Gray, 1998).

Se and the Immune System

The immune system response to pathogens involves many cell types, such as macrophages, B- and T-lymphocytes. These cells integrate and interact together to exert both cellular and humoral immunogenic responses. Enhanced T-cells proliferation occurs in the presence of Se or vitamin E. Macrophages and T-lymphocytes functions in the engulfing foreign antigens or pathogenic organisms thereby killing and removing them from the body resulting in a better/improved health of the animal. Furthermore, the humoral response enhances the proliferation of serum antibodies secreted by B-lymphocytes. The antibodies so produced functions by binding and getting rid of the body of invading toxic organisms. In all these selenium and vitamin E in concert synergistically modulate the cellular and humoral responses of the animal system.

Selenium as an entity impacts the immune system and selenium compounds trigger humoral immunity mechanisms and thus increases type M immunoglobulins. Thus, it has been demonstrated that Se supplementation of the feed of the animal accelerates good health by speeding up the levels of antibodies thereby eliciting phagocytic activity by neutrophil granulocytes and macrophages and when stimulated with myogens triggers T-lymphocytes' concentrations (Hoffman, 2007). Selenium to a very large extend is indispensable or very essential in the production of the lymphocyte migration inhibition factor and interleukin-2 that speeds up the proliferation and maturation processes and thus the activities of T-lymphocytes (Shrimali et al., 2008). Therefore, T cells are very sensitive to Se deficiency as their cell membranes consist of lipids that are more vulnerable to oxidation than the membrane lipids of B-lymphocytes. To this point therefore, Se deficiency reduces the counts and thus the cytotoxic actions of T-lymphocytes. When this happens, lymphotoxin productions are significantly impeded (Hawkes, Kelley & Taylor, 2001). These observations have been substantiated to in animal model studies. For instance, it has been demonstrated that in cows with significantly low concentrations of lymphocyte proliferation induced by concavalin A suffered and were thus significantly insulted health-wise due to Se deficiency compared with the control animals. However, when the cows with impeded immunity as a result of reduced status of T-lymphocytes were administered with Se supplements they showed a significantly resounding immune-stimulating impact. Se supplementation also intensified blastic transformation of splenic lymphocytes and thus prevented a reduction in lymphocyte proliferation (Ghany-Hefnawy & Tortora-Perez, 2010). From the above discussed, it can be seen clearly that Se is strongly implicated in the well-being of the animal. Therefore, it is not a gainsaying that Se is very ubiquitous and versatile to the overall health of the animal. Table 1 further highlights some nutritional diseases that result due to Se or/and vitamin E deficiency (Levander, Ager & Beck, 1995) stressing the importance of the need for adequate dietary Se and vitamin E in the health of the animal.

Table 1. Nutritional diseases due to selenium or/and vitamin E deficiency

Item	Due to its deficiency in diet	
	Se	Vitamin E
Liver necrosis	+	+
Spar hair coat	+	-
Reduced growth rate	+	-
Lack of sperm motility	+	-
Cataracts	+	-
Fat discoloration	-	+
Diseased uterus	-	+
Poor incisors formation	-	+
Hemolysis	-	+

Poor reproduction in females	-	+

Source: Levander, Ager and Beck (1995)
Note: + = indicates cause or causes of the disease.

Conclusions

Selenium is a trace element but very important in various physiological functions. Se possesses antioxidant characteristics via GSH-Px and many other selenoproteins. It is a quencher of oxidative stress via its proactive impacts on free radicals and also involved in the maintenance of thyroid homeostasis. Se is also a very active player in the modulation of the immune system and therefore strongly implicated in the overall health of the animal implying that Se deficiency can significantly compromise the health and overall well-being of the animal.

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