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A Review on Properties of Selenium in Animal Nutrition

Review Article

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ABSTRACT

The early interest in selenium (Se) focused on its toxicity, but since 1957 it has been recognized as an essential dietary element. The diet is the major Se source and approximately 80% of dietary Se is absorbed, depending on the type of food consumed. In several regions of the world, the content of Se in diets has been estimated as insufficient. The dietary requirement for Se for most species is about 0.3 ppm. Deficiencies of Se in animals have been confirmed under natural grazing conditions in many countries. Symptoms of deficiencies such as white muscle disease occur primarily in young calves or lambs born in low Se regions and thus we need to provide sufficient amounts in animal diets. Numerous studies have demonstrated that Se plays an important role in animal health. Therefore, this review gives a brief outline of the current information on the physical, chemical and metabolic properties of Se, oxidative stress, antioxidant defense, dietary requirement, deficiency, toxicity and effects of Se on fertility and performance.

KEY WORDS glutathione peroxidase, nutrition, requirements, selenium, trace elements.

INTRODUCTION

Selenium is a non-metal element with an atomic number of 34 (Berzelius, 1818; Kabata-Pendias, 1997). This trace element is present in the earth's crust at an average of 90 µg/kg and levels are greater in carbonate rocks, volcanic and sedimentary soils (global average 0.4 mg/kg) and may subsequently then accumulate in various plants (Mehdi *et al.* 2013). The properties of Se lie between sulphur and tellurium and it exists in 5 oxidation states (–2, 0, +2, +4 and +6) with chemical forms such as selenide, selenite and selenate and is often associated with sulphur containing compounds (Wallschläger and Feldmann, 2009; Mehdi *et al.* 2013). The nutritional value of Se was established in 1957 (Oldfield, 2002). Selenium is an essential trace element, and its importance for animal health and productivity has been well confirmed. It affects many physiological functions. As a component of mammalian enzymes such as glutathione peroxidases (Reich and Hondal, 2016) and selenoproteins (Allmang and Krol, 2006), it have a key role in a variety of biological processes including antioxidant defense (Tapiero *et al.* 2003), fertility (Foresta *et al.* 2002; Kommisrud *et al.* 2005), thyroid metabolism (Arthur *et al.* 1993; Arthur and Beckett, 1999), immune function (Spallholz, 1990; Turner and Finch, 1991; Shini *et al.* 2015), carcinogenesis (Rayman, 2005), endocrine function (Kohrle *et al.* 2005), cardiovascular disease (Salonen *et al.* 1982) and muscle development and function (Brown and Arthur, 2001).

Physical and chemical properties of selenium

Physical properties

Selenium is a naturally occurring element within the oxygen group (Group VIA; Fordyce, 2005), has an atomic mass of approximately 79 and has six natural isotopes, ^{74}Se, ^{76}Se, ^{77}Se, ^{78}Se, ^{80}Se and ^{82}Se. It is a chalcophile (sulphur-loving)

element and replaces S in common sulphide minerals such as pyrite, chalcopyrite, pyrrhotite and sphalerite. The chemical and physical properties of Se are intermediate between those of metals and non-metallic elements (Johnson *et al.* 2010) and it also forms several rare minerals including crookesite (Cu, Ti, $Ag)_2$ Se), berzelianite (CuSe) and tiemannite (HgSe; Fordyce, 2005; Johnson *et al.* 2010).

Chemical properties

Selenium was discovered in 1817 by Jones Jacob Berzelius and exists as elemental Se (Se^0), selenide (Se^{2-}), selenite (SeO_3^{2-}) and selenate (SeO_4^{2-}). The six natural stable isotopes of Se are ^{74}Se (0.87%), ^{76}Se (9.02%), ^{77}Se (7.58%), ^{78}Se (23.52%), ^{80}Se (49.82%) and ^{82}Se (9.19%) (Girling, 1984).

Some commercial forms of Se are H_2Se, metallic selenides, SeO_2, H_2SeO_3, SeF_4, $SeCl_2$, selenic acid (H_2SeO_4), Na_2SeO_3, Na_2SeO_4 and various organic Se compounds (Zayed and Terry, 1994). Selenium in the +4-oxidation state can occur as selenium dioxide (SeO_2), SeO_3^{2-}, or selenious acid (H_2SeO_3), while in the +6-oxidation state, Se is in the form of selenic acid (H_2SeO_4) or SeO_4^{2-} salts (Chilimba, 2011).

The chemical identity of elemental Se, selenite, selenate, and selenomethionine is reviewed in Table 1, as adapted from ATSDR (ATSDR, 1996; ATSDR, 2003).

Metabolic properties of selenium

Scientific attention to Se results from its role in the prevention and therapy of different diseases such as cancer (Clark *et al.* 1996). Because Se is a component of several selenoproteins and selenoenzymes with essential biological functions, it is important for many cellular processes, especially in the antioxidant protection of cells against oxidative stress (Letavayová *et al.* 2008). Also, Se in the form of selenite and organic selenium from selenized yeast was shown to prevent harmful effects, such as lipid peroxidation, DNA and RNA oxidation in rats (Ishrat *et al.* 2009) and mice (Lovell *et al.* 2009).

For animals, Se is an essential micronutrient that acts as a component of the unusual amino acids, selenocysteine (Se-Cys) and selenomethionine (Se-Met) and functions as a co-factor for the reduction of antioxidant enzymes, including glutathione peroxidases and certain forms of thioredoxin reductase (Berry *et al.* 2002).

Adequate amounts of Se will decrease the risk of myopathy, immunodeficiency (Hartikainen, 2005). In addition to its role as an antioxidant, Se has been shown to affect the fatty acid composition in mouse muscle and chicken eggs (Crespo *et al.* 1995; Czauderna *et al.* 2004; Pappas *et al.* 2005).

Oxidative stress and antioxidant defense

When the generation of reactive oxygen species (ROS) in a system exceeds the capacity to neutralize and eliminate them, then oxidative stress may occur (Sies, 2015). The ROS are chemically reactive molecules, including superoxide anions, hydrogen peroxides, hydroxyl radicals and nitric oxide derivatives, and are generated in all aerobic organisms through several pathways (Kulkarni *et al.* 2007). The imbalance can result from a lack of antioxidant capacity caused by disturbance in production, distribution, or by an overabundance of ROS from endogenous sources or environmental stressors.

Extensive oxidation increases the production of unstable compounds known as free radicals, such as those derived from molecular oxygen which leads to oxidative stress (Levander and Beck, 1997). If they are not eliminated, they will damage the biological components in the body and lead to lipid peroxidation, protein carbonylation and DNA strand breakages, ultimately causing various clinical consequences (Stone *et al.* 2010).

Free radicals are delineated by an unpaired electron that makes them highly reactive and short-lived. Copper and iron donate electrons to molecular oxygen, producing more than one species (superoxide, hydroxyl radical, and singlet oxygen) of radicals with varied reactivities; the hydroxyl radical is one of the most reactive species. Free radicals are not just product in normal cellular functions, indeed they can occur via many reactions, such as those happening upon exposure to certain chemicals, radiation (including ultraviolet light), air pollutants, inflammation and high-fat diets. Exposure of a healthy cell to free radicals is known to damage structures and consequently to interfere with functions of enzymes and critical macromolecules (Kumar and Priyadarsini, 2014).

For a free radical produced within a cell will seek another electron within the surrounding cell to become paired and stable. However, the outcome of such interaction is the formation of other free radicals derived from components of nucleic acids, lipids, carbohydrates, and proteins. Over time, animal cells have developed defense mechanisms that provide protection against oxidative damage induced by free radicals.

Living cells with a self-defense system can protect against oxidative stress through antioxidant mechanisms. Two types of antioxidants exist, internal and supplementing antioxidants. Internal antioxidants are enzymes like superoxide dismutase and glutathione peroxidase (GPx), which are synthesized within the cells and act as a primary defense system against free radicals (Szymonik Lesiuk *et al.* 2003), whereas some antioxidants like vitamins and Se are a secondary defense system.

Table 1 Chemical identity of elemental selenium, selenite, selenate and selenomethionine

	Selenium	Sodium selenite	Sodium selenate	Selenomethionine
Synonyms	Elemental selenium; Selenium base; selenium dust; Colloidal selenium; Selenium homopolymer	Disodium selenite; Disodium selenium trioxide; Selenious acid disodium salt; Sodium selenium oxide	Disodium selenate	Methionine, seleno; 2-amino-4-(methylselenyl) butyric acid; 2-amino-4-(methylseleno) butanoic acid
Formula	Se	Na_2SeO_3	Na_2SeO_4	$CH_3Se(CH_2)_2CH(NH_2)COOH$
Molecular weight	78.96	172.95	188.94	196.11
Color	Metallic gray to black; Hexagonal crystals	White tetragonal crystals	Colorless rhombic crystals	Transparent, hexagonal sheets or plates; Metallic luster of crystals
Physical state	solid	Solid	Solid	Solid
Melting point	144 ˚C; 221 ˚C	No data	No data	D, L form: 265 ˚C (decomposes) L form: 266-268 ˚C (decomposes)
Boiling point	685 ˚C	No data	No data	Not applicable
Density (g/cm^3)	4.81 (20 ˚C)	No data	3.213 (17.4 ˚C)	No data
Water solubility	insoluble	Soluble	84 g/100 mL at 35 ˚C	L form: 5 g/100 mL
CAS number (No.)	7782-49-2	10102-18-8	13410-01-0	1464-42-2

The GPx and other selenium containing enzymes are the major Se containing internal antioxidants that help in the neutralization of highly reactive free radicals (Kieliszek and Błażejak, 2013). The GPx converts reduced glutathione to oxidized glutathione while reducing peroxides by converting them to harmless alcohols, thus maintaining membrane integrity (Kunwar *et al.* 2007; Kieliszek and Błażejak, 2013).

Redox potential of the Se compounds provides important information about antioxidant activity (Indira Priyadarsini *et al.* 2013). A balance between the formation of free radicals and protection against cellular damage is essential for normal cellular processes induced by these species. Cells will enter a state of oxidative stress when that balance is disrupted by excessive generation of damaging species or low levels of antioxidants. Following exposure to oxidative stress, the cell could die or repair the damage. However, if the damage continues, the cell will enter a state of genetic instability that can lead to chronic diseases like cancer (Garewal, 1997).

Selenium requirement, deficiency and toxicity

Requirement

For optimal health in our herds and flocks, we have to add adequate Se to animal diets, where a deficiency can be demonstrated. The dietary requirements for selenium in domestic animals as summarized by the National Research Council (NRC) are shown in Table 2.

The maximum Se tolerance in animal diets for the major livestock species, established by the NRC is 2 mg Se kg^{-1} but this guideline does not consider the chemical forms of the element.

Table 2 Dietary requirements of selenium for domestic animals

Species	Requirement	Reference
Dairy cattle	0.3 (mg/kg DM)	NRC (2001)
Beef cattle	0.1 (mg/kg DM)	NRC (1984)
Sheep	0.5 mg/kg LWG/AC	NRC (2007)
Goat	0.5 mg/kg LWG/AC	NRC (2007)
New world camelids	0.74 mg/kg LWG/AC	NRC (2007)
Chickens (0-8 wk)	0.3 (mg/kg DM)	NRC (1984)
Turkeys (0-8 wk)	0.2-0.3 (mg/kg DM)	NRC (1994)

LWG: live weight gain; AC: absorption coefficient (forages=0.31 and concentrates=0.60) and DM: dry matter.

Deficiency

Selenium enters the food chain through plants, which take it up from soil. Volcanic regions of the world that have a low soil content of selenium and that deficiency has been identified.

Acid soils and complexation, often with iron or aluminium, also decrease the uptake of selenium by plants. In low selenium areas, producers have adopted methods like Se fertilization of soils and Se-enriched animal feed to ensure that their animals obtain adequate amounts of Se (Pedrero and Madrid, 2009).

Animal deficiency symptoms and diseases have been identified since the 1950 s on a wide scale in livestock (Reilly, 1996).

Signs of dietary Se deficiency in ruminants include reduced growth and white muscle disease (nutritional muscular dystrophy), a myopathy of heart and skeletal muscle in young animals and poor reproductive performance in older animals (Underwood, 1971; Reilly, 1996). When such signs of deficiency apparent, losses of economic importance have already occurred.

Godwin and Fraser (1966) and Godwin (1968) in studies with sheep, have shown that subclinical cases of nutritional muscular dystrophy can be detected by electrocardiography.

The condition was confirmed following slaughter of young sheep and lambs which had shown abnormal electrocardiograms. Hall *et al.* (2014) have reported that measurement of tissue glutathione peroxidase may be useful in establishing selenium status of the animal. Concentration of Se in various tissues, including liver, kidney, heart and muscle, fluctuates with dietary intake of the element, and results from several studies have been summarized (NRC, 1984; NRC, 2001; NRC, 2007). Andrews *et al.* (1968) have shown that 1.0 ppm in the kidney cortex and 0.1 ppm or more in the liver are indicative of adequate Se in sheep. These authors also suggest that 0.05 ppm selenium in the liver is borderline and that 0.02 ppm represents a severe Se deficiency.

Toxicity

The symptoms of toxicity were probably described long before the discovery of Se. While traveling along the Silk Road to remote parts of China in the middle of 13th century, Marco Polo recorded the presence in the of certain poisonous plants in Shanxi province that had serious effects on livestock that ate them: the hoofs of the animals dropped off (Oldfield, 2002). It is likely that these plants were Se accumulators, which was not recognized until the end of the 1930 s. The occurrence of ‘‘alkali disease’’ was reported in the western United States (Mayland, 1994). The symptoms of Se toxicity were necrotic and sloughed hoofs, hair loss, poor growth and reproduction, and in extreme cases it caused the death of horses grazing on ranches with saline seeps. Researchers identified ‘‘alkali disease’’ as chronic Se toxicosis (selenosis; Hartikainen, 2005). This condition still occurs in ruminants and monogastrics in seleniferous areas. Against this background, it is easy to understand that until the 1950 s, Se had been considered merely as an environmental toxicant (Hartikainen, 2005). Signs of Se toxicity include respiratory distress, restlessness, blindness, staggering, head pressing, anorexia, salivation, abdominal pain, watery diarrhea, convulsions, paralysis and death.

Selenium has an ambivalent reaction ranging from being essential to toxicity, depending on the species, oxidation state and concentration. Cases of Se toxicity are very rare in the literature and the problems related to Se toxicity are much less common than deficiency (Szpunar *et al.* 2003). Selenium poisoning (selenosis) has acute (short-term) and chronic (long-term) forms. Experimental chronic Se toxicity in animals affects the major organs including the liver, spleen, kidneys, heart and pancreas. Multiple factors contribute to chronic experimental Se toxicity including animal species, dietary Se compound administered, and quality of dietary protein, dietary acclimation, and dietary Se concentration. A single oral treatment of 10 to 15 mg of selenium could overdose lambs (Pedrero and Madrid, 2009) and Injection of more than 5 mg nano-selenium can be lethal to lambs (Ghaderzadeh, 2016).

Metabolism of selenium

During a period of five decades, selenium was found to be an essential micronutrient for many species of animals (Oldfield, 2002). They predominantly absorb it from seeds and roughages. Metabolism of absorbed Se is similar for ruminants and non-ruminants (Ammerman and Miller, 1975). Various consecutive reactions may convert inorganic Se compounds such as selenate and selenite to organic forms and vice versa, and these reactions are enzymatically catalyzed (Ip, 1998). Selenium was reported as a component of a widely dispersed mammalian enzyme, glutathione peroxidase (GSHPx; Brigelius-Flohé and Maiorino, 2013). The Se in GSHPx was found to be present as a selenoamino acid, selenocysteine (Böck *et al.* 1991). This amino acid had also been found earlier in enzymes of bacteria (Cone *et al.* 1976) and is genetically encoded by a universal UGA codon for selenocysteine formed from hydrogen selenide (H_2Se) and serine. The H_2Se plays a central role, formed from glutathione-coupled reactions from selenite (SeO^{2-}_3) via selenodiglutathione (GS-Se-SG) and glutathione selenopersulfide (GS-SeH). The H_2Se is generally needed as a substrate for biosynthesis of selenocysteine (Sec) by cysteine synthases and as a molecule for the transformation into selenophosphate ($H_2SePO^{-}_{3)}$ by selenophosphate synthetase and both are required for the mechanisms and biosynthesis of selenoproteins. Further metabolism of H_2Se involves methylation to methylselenol (CH_3SeH), dimethylselenide ($(CH_3)_2Se$) and trimethylselenonium ion ($(CH3)_3Se^{+}$), the latter both exhaled in the breath and excreted in urine. Alternatively, selenomethionine, which can be combined into proteins in place of methionine, converts to selenocysteine through trans-sulfuration, which in turn is degraded to H_2Se by cysteine lyase (Ip, 1998; Birringer *et al.* 2002).

Effects of selenium on fertility

Genetics, nutrition, management, and environment can affect reproductive performance of animals (Kumar, 2003). Various minerals such as copper, cobalt, selenium, manga-

nese, iodine, zinc and iron can also affect reproductive performance of animals. Trace mineral are critical in nutrition, since even small fluctuations in their levels can have large effects on reproductive health and performance (Hedaoo *et al.* 2008). Reproductive failure may be due to deficiencies or imbalance of trace elements.

Administration of Se in several cases of selenium deficiency has been shown to prevent reproductive problems. Lambing percentages increased in controlled trials with ewes when Se was fed orally in monthly doses beginning 4 weeks before mating and continuing through pregnancy (Hartley *et al.* 1960; Hartley and Grant, 1961; Ghaderzadeh, 2016). Reduced fertility in untreated animals was attributable to embryonic mortality at 20 to 30 days of pregnancy (Andrews *et al.* 1968; Ghaderzadeh, 2016). Ewes grazing on pasture of low Se and high estrogen content were given Se 1 to 2 months before breeding. Their conception rate increased from 49% to 76% (Godwin, 1968). When Se and copper were added to the diet, significant improvement in lambing rate and incidence of twinning in ewes has been reported, conversely the twinning rate was decreased by a Se deficiency with fewer lambs born to the control ewes (Hill *et al.* 1969).

Oxidative damage to spermatozoa is important for male fertility and Se helps to protect against this and plays an important role in maintaining male fertility (Chu *et al.* 1996). Following consumption of Se deficient (0.2 ppm sodium selenite) or Se excessive (1.0 ppm sodium selenite) diets in male mice, elevated levels of lipid peroxidation, malondialdehyde and ROS have been observed (Shalini and Bansal, 2007; Kaushal and Bansal, 2009). The resultant decreased the fraction of motile spermatozoa, spermatozoa concentration, number of motile spermatozoa and increased tailless and headless spermatozoa resulted in harmful effects to semen quality (Hawkes and Turek, 2001). A diet deficient in Se (0.2 ppm sodium selenite) has been shown to reduce glutathione peroxidase (GSH-Px or GPx) activity in mice (Shalini, 2005; Foresta *et al.* 2002) and Moghani lambs (Shalini and Bansal, 2007; Shalini and Bansal, 2008; Ghaderzadeh, 2016), while excess Se (1.0 ppm in a yeast based diet) intake resulted in increased GPx activity, impairing male reproductive potential in mice (Kaur and Kaur, 2000; Shalini and Bansal, 2007; Shalini and Bansal, 2008).

Selenium deficiency was associated with a significant reduction in testicular weight in rats, impairing reproductive performance (Wu *et al.* 1979). Segerson and Johnson (1980), injected bulls with 50 mg Se and a subsequent 30 mg after three weeks and reported increased of Se concentration in the testis and seminal vesicles, but not in the epididymis. Edens and Sefton (2009) conducted a study in broiler breeder roosters and showed Se at 0.2 mg/kg in feed as sodium selenite or Sel-Plex (Alltech Inc. USA) to be a major factor in male sexual maturation. The roosters fed with Se produced semen at 19 weeks, whereas those fed a non-supplemented diet produced semen at 26 weeks. The roosters fed with organic Se (Sel-Plex) and showed a well-defined hierarchy of spermatogenic cells exhibiting spermatogonia, spermatocytes, spermatids and spermatozoa (Edens and Sefton, 2009). Barber *et al.* (2005) found that Se must act at the reproductive tissue level during spermatogenesis to improve semen quality. This evidence shows that dietary Se in any form could influence the semen quality in human (Scott *et al.* 1998; Hawkes and Turek, 2001), mice (Sánchez-Gutiérrez *et al.* 2007), rat (Wu *et al.* 1979), pigs (Marin-Guzman *et al.* 1997; Lasota *et al.* 2004), rabbit (Castellini *et al.* 2002) and ram (Kendall *et al.* 2002).

Effects of selenium on performance

To our knowledge, many studies have been done about effect of Se on performance. However, many differences can be observed in about their reports. For instant, in a study with nano-selenium on the male Moghani lambs did not see any significant effect on performance (Ghaderzadeh, 2016), that is parallel with other studies that have been done on other species of domestic animals like sheep (Alhidary *et al.* 2012), lamb (Hernandez-Calva *et al.* 2013; Sushma *et al.* 2015), broiler (Chadio *et al.* 2015), beef calve (Richards *et al.* 2011) and calve (Salles *et al.* 2014). So the insignificant difference in these studies might be due to feeding the balanced diet with adequate nutritional practice. In contrast, in several studies the positive effect of Se supplementation (whatever the form) on the animals like broiler (Hu *et al.* 2012), lamb (Kumar *et al.* 2009) and beef calve (Hall *et al.* 2013a; Hall *et al.* 2013b), Quail (egg parameters) (Canoğulları *et al.* 2010; Baylan *et al.* 2011) has been described. The animals that are being reared, may lead to stress due to constant dynamic variations in temperature and humidity in the environment, which causes adverse effects on performance (Niu *et al.* 2009). Heat stress promotes oxidative stress and reduces the activity of thyroid hormones.

Moreover, Se supplementation during heat stress may ameliorate the adverse effects of thermal stress by improving antioxidant status and thyroid hormone activity and do not let decrease the performance parameter compare to control treatments (Alhidary *et al.* 2012).

CONCLUSION

The mammalian system needs a continuous supply of certain trace elements, one of which is Se. Over the last five

decades there have been quite a few achievements in Se nutrition in several species of animals. Among dietary trace elements, Se has been found to have special attributes due to its multifaceted activities. It is a dietary essential, being specifically incorporated into the active sites of several known proteins or enzymes as an amino acid, selenocysteine or GPx enzyme. Knowledge of the importance and management of Se in the immune system, oxidative stress, antioxidant defense and fertility has increased considerably on animals in recent years. Recent evidence underlines the importance to health of adequate Se status, but we have to be careful about requirements and amounts used in diets of animals. At higher dietary levels, many Se compounds can become toxic. All these attributes of Se depend upon the concentration, the chemical form, type and age of the animals.

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