Selenium Supplementation Efficacy in Small Ruminants: A Review

Review Article

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ABSTRACT

This review is aimed at highlighting the role of selenium (Se) in enhancing the antioxidant status in the blood, immune response, reproductive performance, rumen fermentation, as well as feed efficiency, and weight gain in small ruminants. Selenium is supplied in small ruminant's diet in organic form, inorganic form, or selenium nanoparticles (nano-Se). Each form of Se is metabolized differently and exhibits different levels of bioavailability with nano-Se having the highest bioavailability followed by organic Se. A sufficient supply of Se in small ruminant's diet is important to maintain the proper functioning of the antioxidant defense system which reduces the detrimental effects of free radicals in cells thereby preventing the incidence of metabolic diseases. The ability of Se to improve the antioxidant capacity of the cells also helps to strengthen the immune response of animals and ameliorate the detrimental effects of heat stress. Selenium has also been proven to modify rumen fermentation and microbiota which translated to improved feed efficiency and enhanced weight gain. However, the activities and bioavailability of Se are limited by several factors including the rumen microbiota, the form of Se, and competition with other minerals. Further studies need to investigate the effects of Se on rumen microbiology and heat stress in small ruminants.

KEY WORDS antioxidant, glutathione peroxidase, immunity, rumen fermentation, selenium.

INTRODUCTION

Selenium (Se) is an essential trace mineral in livestock due to its role in health and the prevention of nutritional disorders. The supplementation of Se is practiced worldwide in ruminants kept under an intensive system of production (Ahmadi *et al.* 2018; Ahmadi *et al.* 2019; Pan *et al.* 2021). Moreover, several farmers in developing countries are becoming aware of the need to include exogenous Se sources in livestock diets (Suganthi *et al.* 2019). This has been attributed to the low level of Se in soils resulting in Se deficiency in available grains and forages (Suganthi *et al.* 2019; Mojapelo *et al.* 2021). The concentration of Se in forages and grains varies widely depending on the soil's Se content and geographical location (Zhang *et al.* 2018). In ruminants, Se is required in minute amounts but it plays a key role as a constituent of about 30 seleno-proteins which are responsible for its biological functions (Niwinska and Andrzejewski, 2017). Selenium is a major component of many enzymatic structures and seleno-proteins like glutathione peroxidase 1, glutathione peroxidase 4, iodothyronine-5-deiodinase, and thioredoxin reductase 1 (Kachuee *et al.* 2019; Lee *et al.* 2019). Glutathione peroxidases (GSH-Px) and Seleno-protein W1 are seleno-proteins that play a vital role in the antioxidant defense system of the animal (Rezaei and Dalir-Naghadeh, 2009) by protecting

immune cells from oxidative damage (Carr *et al*. 2020; Ghaderzadeh *et al*. 2020; Wang *et al*. 2021a). Seleno-protein W1 is also used as a biomarker to measure the efficiency of Se as a source of seleno-protein production (Kipp *et al*. 2013). The majority of the seleno-proteins identified in livestock were found to be associated with stress responses, antioxidant system, immune system, and inflammatory processes in the body (Guo *et al*. 2018; Taheri *et al*. 2018; Kachuee *et al*. 2019; Lee *et al*. 2019; Surai *et al*. 2019; Ianni *et al*. 2020; Zhuang *et al*. 2020; Libera *et al*. 2021). Probably due to its role in several physiological processes in the animal's body (Taheri *et al*. 2018; Zhang *et al*. 2018; Mousaie, 2021), the supplementation of Se was reported to improve the rate of maturity in kids (Mojapelo and Lehloenya, 2019), increase the milk yield in does (Rashnoo *et al*. 2020), enhance feed efficiency in lambs (Mousaie, 2021), and improve semen quality in bucks (Mojapelo *et al.* 2021). Inadequate supply of Se in small ruminants can result in several metabolic diseases such as retarded growth, weakened immune system, low feed efficiency, and reproductive failures, (Ianni *et al*. 2019; Sun *et al*. 2019; Lizarraga *et al*. 2020). On the other hand, the increased concentration of Se beyond the required amounts leads to Se toxicity in livestock (Taheri *et al*. 2018). In livestock, Se deficiency is more common than Se toxicity (Ensley, 2020), but for normal physiological processes, an optimal level of Se should always be maintained (Sun *et al*. 2019). However, Se has a very narrow safety margin, thus making it the only element with a legal limit, above which Se toxicity occurs (Ensley, 2020). This review is therefore aimed at summarizing the roles of Se on blood antioxidant status, immune response, reproductive performance, rumen fermentation, as well as feed efficiency, and weight gain in small ruminants.

Forms of Se

Selenium is usually included in the diets of sheep and goats in the form of organic and inorganic Se (Table 1 and Table 2). Examples of organic Se used in small ruminants include selenomethionine (Davis *et al*. 2017; Erdogan *et al*. 2017; Kachuee *et al*. 2019; Paiva *et al*. 2019; Suganthi *et al*. 2019) and selenium yeast (Se-yeast) (Czauderna *et al*. 2017; Paiva *et al*. 2019; Mousaie, 2021). A common source of inorganic Se in sheep and goats is sodium selenite and sodium selenate (Czauderna *et al*. 2017; Davis *et al*. 2017; Kachuee *et al*. 2019; Paiva *et al*. 2019; Khalili *et al*. 2020). In the body system, both organic and inorganic Se sources are converted to selenide which is later transformed into Se-cysteine and this is an important constituent of seleno-proteins (Ullah *et al*. 2020). However, these two forms of Se exhibit different metabolic potentials in ruminants (Khalili *et al*. 2020). The organic Se is reported to have a

higher absorption rate and bioavailability, increased tissue storage, and less toxicity in the animal's body when compared to the inorganic forms (Groce *et al*. 1973; Ortman and Pehrson, 1997; Danielsson *et al*. 2012; Davis *et al*. 2017). This could be attributed to the slow absorption of organic Se in the body, which is similar to that of amino acids. In addition, some organic Se such as Se-yeast has a bioavailability of about 120% to 200% when compared with the inorganic Se sources (Muegge *et al*. 2017). However, the inorganic Se is usually absorbed and metabolized in a similar rapid pattern as other trace mineral elements (Groce *et al*. 1973) and it is reported to be more toxic than the organic Se. Some of the soluble Se salts like Na_2SeO_3 and Na_2SeO_4 are considered highly toxic while the poorly soluble Se salts such as elemental Se, SeS_2, diphenyl selenide, and Na_2Se are less toxic (Ullah *et al*. 2020).

The efficacy of Se nanoparticles (nano-Se) on the performance of small ruminants has been investigated (Kachuee *et al*. 2019; Lee *et al*. 2019; Ghaderzadeh *et al*. 2020; Nateq *et al*. 2020) and the results seemed promising. Their mode of action is via stimulating the activities of selenoenzymes (Kachuee *et al*. 2019). This technology enhances the bioavailability of Se by increasing its surface area (Arshad *et al*. 2021). Nanoparticles occur in the natural environment and range between 1 to 100 nm in size (El-Naby *et al*. 2020). Due to their small sizes, nano-Se have higher absorption rates in the gut which improved their biological activities within the animal's system (Patra and Lalhriatpuii, 2020). The smaller the nano-Se the higher the activity (Hosnedlova *et al*. 2018). The smaller sizes and increased surface area allow nano-Se to exhibit greater mucosal permeability and higher intestinal absorption (Libera *et al*. 2021). Selenium nanoparticles have also been reported to possess higher bioavailability, increased tissue storage, higher surface charge, and reactivity, enhanced antioxidant effect, increased binding properties reduced antagonism with other minerals, and less toxicity than the organic and inorganic sources of Se (Hosnedlova *et al*. 2018; Khalil *et al*. 2019; Patra and Lalhriatpuii, 2020; Han *et al*. 2021; Libera *et al*. 2021). These distinctive characteristics of nano-Se make them the preferred form of Se in many biomedical applications (El-Naby *et al*. 2020).

Effects of Se blood antioxidant status

Antioxidants are important in scavenging free radicals and inhibiting oxidative damage in the cells (Sun *et al*. 2019; Ghaderzadeh *et al*. 2020). Inadequate production of antioxidants or excessive production of free radicals can cause oxidative stress in livestock (Gong and Xiao, 2018; Sun *et al*. 2019). Reactive oxygen species (ROS) are free radicals that are usually produced in the body during energy production or increased activities of NADPH oxidase can damage body cells when they accumulate (Gong and Xiao, 2018).

Table 1 Performance of sheep supplemented with Se

S/N	Animal	Physiological state	Se forms	Dose	Duration	Key findings	Source
1.	Assaf ewes	Lactating ewes	sodium selenite anhydrous	1,000 IU of α-tocopherol and 0.4 mg of Se daily	11 weeks	Increased proportions of long-chain fatty acids in the milk of ewes. Decreased concentrations of short-chain fatty acids and medium-chain fatty acids in the milk.	(Pulido *et al.* 2019)
2.	Cor-riedaleram lambs	Growing lambs	Selenate or Selenite	0.35 mg of Se in 1 kg of basal diet	35 day	Reduced concentration of long-chain polyunsaturated fatty acids in the peri intestinal fat compared to the unsupplemented group and group fed carnosic acid. The addition of carnosic acid and selenate increased the ratio of hypocholesterolemic: hypercholesterolemic fatty acid and decreased the atherogenic index	(Bialek *et al.* 2020)
3.	Crossbred (Suffolk×Polypay) ram lambs	8–12 weeks old whether lambs	Sodium selenite (inorganic Se) or selenomethionine (SeMet, organic Se)	1, 2 or 3 mg/kg body weight	7 days	The group given selenomethionine had higher Se concentrations in the serum and whole blood than those supplemented with sodium selenite. Se levels in serum and whole blood of lambs given selenomethionine required higher Se concentrations to reach a peak than lambs dosed with sodium selenite.	(Davis *et al.* 2017)
4.	Kermaniram lambs	7 months of age	Se-enriched yeast	Se at 0.6 or 1.2 mg/kg DM	8 weeks	Improved feed efficiency of rams when compared to those in the unsupplemented group. Enhanced total antioxidant capacity and glutathione peroxidase activity in the blood.	(Mousaie, 2021)
5.	Crossbred (Hu×Small Tailed Han) lambs	6 months old	Se-enriched yeast	Se at 0, 3, 6, 9, and 12 μg/kg body weight per day	15 days	Improved dry matter intake and dry matter digestibility when compared to the unsupplemented group.	(Pan *et al.* 2021)
6.	Moghaniram lambs	3 months old	Nano-Se	Se at 1 and 2 mg/kg DM	90 days	Increased levels of glutathione peroxidase and superoxide dismutase in blood than the unsupplemented group. Upregulation of glutathione peroxidase 1 and selenoprotein W1 in the liver of rams fed with Nano-Se compared with the unsupplemented group.	(Ghaderzadeh *et al.* 2020)
7.	-	Matured rams	-	Se at 5, 10, 15 and 20 mg/kg DM	350 days	Enhanced Sperm morphology compared with the unsupplemented group.	(Piagentini *et al.* 2017)
8.	Cor-riedaleram lambs	82–90 days old	Se-yeast or sodium selenate	Se at 0.35 g/kg DM as Se-yeast or 0.35 g/kg DM as sodium selenate	35 days	Reduced levels of saturated, mono- and polyunsaturated fatty acids, thrombogenic-saturated fatty acids, and atherogenic-saturated fatty acids. In addition to increased levels of Se and malondialdehyde in blood when compared with the unsupplemented group.	(Czauderna *et al.* 2017)
9.	Crossed breed lambs (Charollais×Suffol)	217 days old	Sodium selenite converted to nano-Se by lactic acid bacteria (Selage)	Se at 2 mg/kg DM	8-10 weeks	Increased concentrations of Se in the faeces, wool, blood, and muscle of lambs in the group fed with Selage compared to lambs fed Silage.	(Lee *et al.* 2019)

Continuation of Table 1 Performance of sheep supplemented with Se

S/N	Animal	Physiological state	Se forms	Dose	Duration	Key findings	Source
10.	Suffolk ram lambs	90 days old	Sodium selenite, Se-yeast, or Se-Methionine	Se at 0.2, 0.8 and 1.4 mg/kg DM	84 days	Increased levels of Se in the liver and serum of lambs when compared with the unsupplemented group. Lambs fed organic Se sources had a higher concentration of Se in the muscle than the group fed sodium selenite. Lams fed sodium selenite had a higher activity of hepatic GSH-Px than the group fed organic sources.	(Paiva *et al.* 2019)
11.	Ghezelram lambs	2–3 years old	Nano-Se (*in vitro*)	Se at 1 and 2 μg/mL	30 days	The inclusion of Se at 1 μg/mL increased the semen quality and decreased the percentage of abnormal sperms when compared to 2 μg/mL nano-Se and unsupplemented groups. The inclusion of Se reduced lipid peroxidation in the groups as compared with the unsupplemented animals.	(Nateq *et al.* 2020)
12.	Dohne Merino ram lambs	9–12 weeks old	-	Vitamin E at 200 mg/kg and Se at 0.2 mg/kg DM	60 days	The feed intake and weight were higher than that of the unsupplemented group.	(Maraba *et al.* 2018)
13.	Moghani lambs	Pregnant ewes	pellet of Se	Pellets of Se (with a release rate of 0.3 mg Se per day)	120 days	Improved the birth weight, weaning weight as well as a higher daily weight gain of their lambs when compared to the group receiving iodine pellets and the unsupplemented group.	(Zarbalizadeh-Saed *et al.* 2020)
14.	Norduz ewes	Pregnant ewes	Organic Se (63% selenomethionine)	Se at 0.150, 0.300, and 0.450 mg/kg DM	57 days	Increased concentration of Se in the placenta, serum, and colostrum than the unsupplemented group	(Erdogan *et al.* 2017)
15.	Indian local breed ram lambs	5–6 months old	Se-yeast	Se at 0.5, 1.5 or 4.5 g/kg DM	90 days	Increased expression of glutathione peroxidase 1 (GPX1) and GPX3 in the blood than the unsupplemented group. The group fed Se at 1.5 and 4.5 g/kg DM had an increased expression of Selenoprotein P and Selenoprotein W1, respectively when compared to the unsupplemented group.	(Suganthi *et al.* 2019)
16.	Merinoland-schafewes	Pregnant ewes	organic Se (Se-yeast) or inorganic Se sodium selenite	Se at 0.3 mg/kg DM	4 months	Increased levels of Se in the blood when compared to the unsupplemented group.	(Novoselec *et al.* 2017)
17.	Oula rams	1-year-old	Se-yeast	Se at 0, 0.2, 0.4, and 0.8 mg/kg DM	35 days	Improved feed conversion ratio and a higher dry matter intake as compared to the unsupplemented group.	(Wang *et al.* 2019)

Examples of ROS include hydroxyl radicals (OH-), superoxide anion radicals (O^-_2), and hydrogen peroxide (H_2O_2). During oxidative metabolism, H_2O_2 is produced and it infiltrates the cells to cause oxidative stress. The excessive production of ROS can also activate cellular apoptosis which could destroy nucleic acids, proteins, and lipids within the cell (Surai *et al.* 2019; Wang *et al.* 2021b).

Therefore, the accumulation of ROS is seen as the cause of several metabolic diseases and there is a need to increase the synthesis of radical scavenging enzymes capable of neutralizing the excess ROS within the cell (Ullah *et al.* 2020). Research has shown that an exogenous supply of Se is important to prevent the buildup of these ROS in animal cells (Muegge *et al.* 2017).

Table 2 Response of goats supplemented with Se

S/N	Animal	Physiological state	Se forms	Dose	Duration	Key findings	Source
1.	Polish white or fawn improved does	Lactating	Sodium selenite or Se-yeast	Inorganic Se at 0.7 mg/goat/day or organic Se at 0.6 mg/animal/day	7 months	The milk yield, milk fat yield, and milk protein yield were increased by the Se-yeast treatment while the somatic cell count decreased when compared to goats supplemented with sodium selenite	(Reczyńska *et al.* 2019)
2.	Crossbred goats (Alpine×local breed) does	Lactating	Se-yeast	Se at 0.1 mg/kg DM	42 days	An increased proportion of long-chain fatty acids, unsaturated fatty acids, and medium-chain fatty acids when compared to the unsupplemented group.	(Mitsiopoulou *et al.* 2021)
3.	Crossbred (Anglonubiana×Toggenburg) does	Non-lactating goats	Se-yeast	Se at 0.04 g/animal/day	42 days	The endogenous heat was reduced by decreased respiratory thermolysis and increased erythrocyte levels when compared to the unsupplemented group.	(Silveira *et al.* 2021)
4.	-	Pregnant does and kids	Intra-ruminal bolus containing Se	Se at 0.25 mg/animal/day	Given once at four weeks pre-partum	Increased milk yield, milk fat percentage, milk component yield, milk Se and iodine concentrations compared to the unsupplemented group. An increased Se concentration in serum and a higher activity of the glutathione peroxidase in the blood in the does and their kids when compared to the unsupplemented group.	(Rashnoo *et al.* 2020)
5.	Khalkhali does	Pregnant does and kids	Selenomethionine, nano-Se, and sodium selenite	Se at 0.6 mg/animal/day	4 weeks	Increased blood Se concentration compared to the unsupplemented group. The goats fed nano-Se had a higher Se level in the blood and serum than goats fed selenomethionine and sodium selenite.	(Kachuee *et al.* 2019)
6.	Guanzhong dairy does	Lactating does	Sodium selenite or Se-yeast	Sodium selenite at 0.2 and 0.4 mg/kg DM; Se-yeast at 0.2 and 0.4 mg/kg DM; Sodium selenite at 0.2 mg/kg DM mixed with Se-yeast at 0.2 mg/kg	90 days	Increased milk production, Se-yeast being more effective than sodium selenite. Se concentration and glutathione peroxidase activity were increased but Se-yeast is more effective than sodium selenite.	(Zhang *et al.* 2018)
7.	Saanen buck kids	2-2.5 months old	Sodium selenite	Se at 0.34 mg/kg body weight	150 days	Increased semen volume and enhanced semen quality when compared to the unsupplemented group. An increased level of luteinizing hormone and testosterone when compared to the unsupplemented group.	(Mojapelo and Lehloenya, 2019)
8.	Iranian native does	Pregnant does	0.3 mg organic Se (Selenomethionine) or 0.3 mg organic Se (sodium selenite)	Organic Se at 150 mg/animal/day or inorganic Se at 1 mg/animal/day	45 days	The group fed selenomethionine recorded a higher dry matter intake, organic matter intake, and crude protein intake than the unsupplemented group. The feeding of selenomethionine or sodium selenite improved the crude fat digestibility in does when compared to the unsupplemented group.	(Taheri *et al.* 2018)
9.	Saanen bucks	11–12 months old	Sodium selenite	Se at 0.34 mg/kg DM	4 months	Feeding sodium selenite to bucks (0.34 mg Se/kg) increased the levels of serum glutathione peroxidase as compared to the unsupplemented group and group given adrenocorticotropic hormone. The bucks fed sodium selenite at 0.34 mg Se/kg had a higher semen volume, and better semen quality when compared to the unsupplemented group.	(Mojapelo *et al.* 2021)

This action is due to the production of some enzymes that participates in the defense system such as coenzyme Q, GSH-Px, and thioredoxin (Surai *et al*. 2019). These enzymes eliminate excess ROS thereby maintaining a balance between the synthesis and elimination of free radicals (Mudron and Rehage, 2018; Surai *et al*. 2019; Libera *et al*. 2021). Glutathione peroxidase is an enzyme that protects the intracellular fluids from damage caused by free radicals which makes it a great antioxidant. It safeguards the development and structure of the mitochondrial capsule by forming cross-links between itself and other proteins (Khalil *et al*. 2019). Glutathione peroxidase also reduces H_2O_2 to H_2O (Han *et al*. 2021) and destroys lipid peroxides that are synthesized by free radicals and other products of oxidative metabolism (Lizarraga *et al*. 2020). The seleno-cysteine present in GSH-Px 1 is utilized for decreasing the reactive oxygen species and intracellular hydrogen peroxide produced by the cells during oxidative respiration (Ghaderzadeh *et al*. 2020). Hence, due to the role of GSH-Px in the antioxidant system, it is widely recognized as a biomarker for oxidative stress in ruminants (Han *et al*. 2021) and GSH-Px activity in the whole blood is a reliable index to predict long-term Se status in livestock (Juniper *et al*. 2019). In addition to the GSH-Px, serum malondialdehyde (MDA) is used to estimate the level of lipid peroxidation (Khatti *et al*. 2017). Malondialdehyde is produced from lipid peroxidation in the cells and is used as a marker to indicate oxidative stress in cells. An increased concentration of MDA suggests a high level of oxidative stress (Gaweł *et al*. 2004). Studies investigating the efficacy of Se administration of blood on blood glutathione peroxidase status are highlighted below.

Effects of Se on blood glutathione peroxidase status

The concentration of GSH-Px in the blood is a good indicator of the Se status of the animal and can be a cheaper alternative to assessing blood Se levels (Juniper *et al*. 2019; Diyabalanage *et al*. 2020). It can also be used to assess the level of oxidative stress in cells (Han *et al*. 2021). The administration of Se in sheep and goats has been effective in stimulating the activities of glutathione peroxidase in the blood. In goats, the administration of Se resulted in increased activity of GSH-Px in the serum of the treated groups when compared to the unsupplemented group (Rashnoo *et al*. 2020; Mojapelo *et al*. 2021). Similarly, in sheep, the supplementation of organic and inorganic Se (Paiva *et al*. 2019) increased the activity of GSH-Px (Paiva *et al*. 2019; Suganthi *et al*. 2019; Mousaie, 2021), in addition to iodothyronine deiodinases, seleno-protein P, and seleno-protein W1 (Suganthi *et al*. 2019) in the blood of the treated lambs when compared to the unsupplemented group. In another study on lambs, the addition of nano-Se

in their diets increased the activities of superoxide dismutase and GSH-Px in the blood in addition to an upregulation in the expression of seleno-protein W1 and GSH-Px 1 in the liver when compared to the unsupplemented group and lambs fed conjugated linoleic acid (Ghaderzadeh *et al*. 2020). The efficacy of vitamin E (Vit E), and sodium selenite administration intravenously was investigated and the results revealed increased activity of GSH-Px in the blood of the treated rams (Mahmoud *et al*. 2013).

Effects of Se on heat stress

The supplementation of Se in ruminants is known to ameliorate the detrimental effects of heat stress on the animal. Heat stress accelerates the accumulation of free radicals in the cells thereby resulting in the destruction of DNA, lipids, and proteins including those cells associated with immune response in the body (Patra and Kar, 2021). The negative effects of heat stress on the humoral and cellular immune response are linked to the alteration of cytokine expression and increased production of cortisol during a severe incidence of heat stress thereby causing oxidative stress as well as immunosuppression (Patra and Kar, 2021; Zheng *et al*. 2021). In a study on lambs exposed to heat stress, the supplementation of Se and vitamin E improved the feed intake and weight gain of lambs when compared to the unsupplemented group (Chauhan *et al*. 2016). The administration of Se injection in sheep under heat stress decreased the rectal temperature by 0.3 ˚C in the treated group when compared to the unsupplemented group. In addition, the animals in the treated group recorded an increased blood eosinophil count and decreased weight loss as compared to the unsupplemented group (Alhidary *et al*. 2012). In a related study, Alhidary *et al*. (2015) supplemented Se and vitamin E to heat-stressed sheep and reported a decreased weight loss in the treated group in addition to increased antioxidant status. This suggests that the amelioration of the negative effects of heat stress on the animals is due to an increased antioxidant defense system stimulated by Se supplementation.

Effects of Se on the immune system and health of small ruminants

A sufficient supply of Se in small ruminants is important to maintain the proper functioning of the antioxidant defense system (Muegge *et al*. 2017). An enhanced antioxidant system in animals will reduce the detrimental effects of ROS thereby preventing the incidence of metabolic diseases, especially during the periparturient period in female animals (Gong and Xiao, 2018). Oxidative stress can weaken the host immune system and trigger inflammatory responses thereby resulting in clinical symptoms such as mastitis, embryonic degeneration, encephalomalacia, liver necrosis, cardiomyopathy, and myopathy (Gong and Xiao,

2018; Mudron and Rehage, 2018; Libera *et al.* 2021). Selenium is absorbed as seleno-protein (mainly selenocysteine) which is important for the synthesis of GSH-Px by the body (Muegge *et al.* 2017). The importance of GSH-Px in neutralizing the activities of ROS in the cells and ensuring a balance between the synthesis and elimination of free radicals cannot be overemphasized (Mudron and Rehage, 2018; Surai *et al.* 2019; Libera *et al.* 2021). Hence, it is imperative to maintain a sufficient supply of Se to ensure continuous synthesis of seleno-proteins and GSH-Px (Muegge *et al.* 2017). Selenium plays a key role in the function of the immune system and its shortage will negatively affect the animal's immune defense system (Prince *et al.* 2017). Selenium improves the immunity of animals via both humoral and cellular immune activities (Khalili *et al.* 2020; Wang *et al.* 2021a). This is achieved through stimulation of the cytokines secretion and enhancement of the proliferation as well as differentiation of lymphocytes (Wang *et al.* 2021a).

Effects of Se on rumen fermentation, feed intake, and weight gain
The rumen harbors several species of beneficial microorganisms (*Archaea*, *Bacteria*, *Protozoa*, *Fungi*, and *Viruses*) that are responsible for the breakdown of fibrous feeds. These rumen microbiotas interact with each other and their activities are linked to the host's metabolism and performance (Amin *et al.* 2022). In the rumen, Se is either utilized by the microbiota for the synthesis of seleno-amino acids for their use or reduced to elemental Se salts with poor solubility and hence cannot be absorbed by the animal (Niwinska and Andrzejewski, 2017; Ferreira and Petzer, 2019).

The metabolism of Se in the rumen environment depends on the form of Se given to the animal. Although both organic and inorganic Se could be metabolized by rumen microbes into selenite which is further transformed into bacterial protein (seleno amino acids) (Ferreira and Petzer, 2019), the absorption of organic Se by the rumen microbiota is greater than inorganic sources of Se. Due to the powdery form of most inorganic Se, they provide a higher surface area for the action of rumen microbiota and conversion into poorly soluble elemental Se (Niwinska and Andrzejewski, 2017). The action of the rumen greatly reduces the bioavailability of Se in ruminants (about 34%) when compared with non-ruminants like swine (about 85%) (Galbraith *et al.* 2016). The encapsulation of inorganic Se salts has proven to be effective in protecting them from the action of rumen microbiota until they reach the small intestine (Niwinska and Andrzejewski, 2017).

The efficacy of supplementing Se on rumen fermentation and microbiota has been investigated. In a study on goats by Tian *et al.* (2022), the application of metagenomics re-

vealed enrichment in the carbohydrate-binding module and glycosyl transferase pathway in the group supplemented with Se-yeast when compared to the unsupplemented group.

The goats supplemented with Se-yeast also had a higher concentration of propionic acid, isobutyric acid, caproic acid, and isovaleric acids when compared to the unsupplemented group. In addition, the relative abundances of the genera *Sarcina* and *Methanobrevibacter* were found to be reduced by Se supplementation. In another study, the supplementation of sheep with Se-yeast increased the ruminal concentration of total volatile fatty acids and propionate in the treated group as compared to the unsupplemented group. In addition, gene function prediction showed that carbohydrate metabolism and metabolism of other amino acids were upregulated in the rumen of sheep supplemented with Se (Cui *et al.* 2021).

Naziroglu *et al.* (1997) studied the influence of Se and vitamin E supplementation on rumen fermentation parameters in lambs and they reported an increased concentration of acetic acid, butyric acid, propionic acid, and total volatile fatty acids in the rumen of the treated groups when compared to that of the unsupplemented group. In addition, the total protozoa counts, and the relative percentage of *Diplodinium* were also found to be significantly higher in the group supplemented with Se and vitamin E. However, the rumen pH and abundance of *Dasytricha ruminantium* were decreased by the treatment. Similarly, Xun *et al.* (2012) reported a higher concentration of total volatile fatty acids (VFA) and propionate production and a decreased ruminal pH in sheep supplemented with Se as compared to the unsupplemented group.

Hendawy *et al.* (2022) added that Se encourages the growth of cellulolytic bacterial species in the rumen thus resulting in higher VFA production and consequently decreasing ruminal pH.

The positive effects of Se on rumen fermentation as evidenced in these studies are expected to translate to improved growth performance in the animals (Figure 1). In some studies, investigating the effects of Se on the performance of sheep, the results showed an improved dry matter intake (Maraba *et al.* 2018; Mousaie, 2021; Pan *et al.* 2021), dry matter digestibility (Pan *et al.* 2021), body weight gain (Maraba *et al.* 2018), and feed conversion ratio (Mousaie, 2021) in the treated group when compared to the unsupplemented group. Likewise in goats, pregnant does given Se supplements in their diets recorded an improved weaning weight and average daily gain of their kids (Rashnoo *et al.* 2020; Zarbalizadeh-Saed *et al.* 2020) as well as increased dry matter intake and crude fat digestibility (Taheri *et al.* 2018) when compared to the group that did not receive Se supplements.
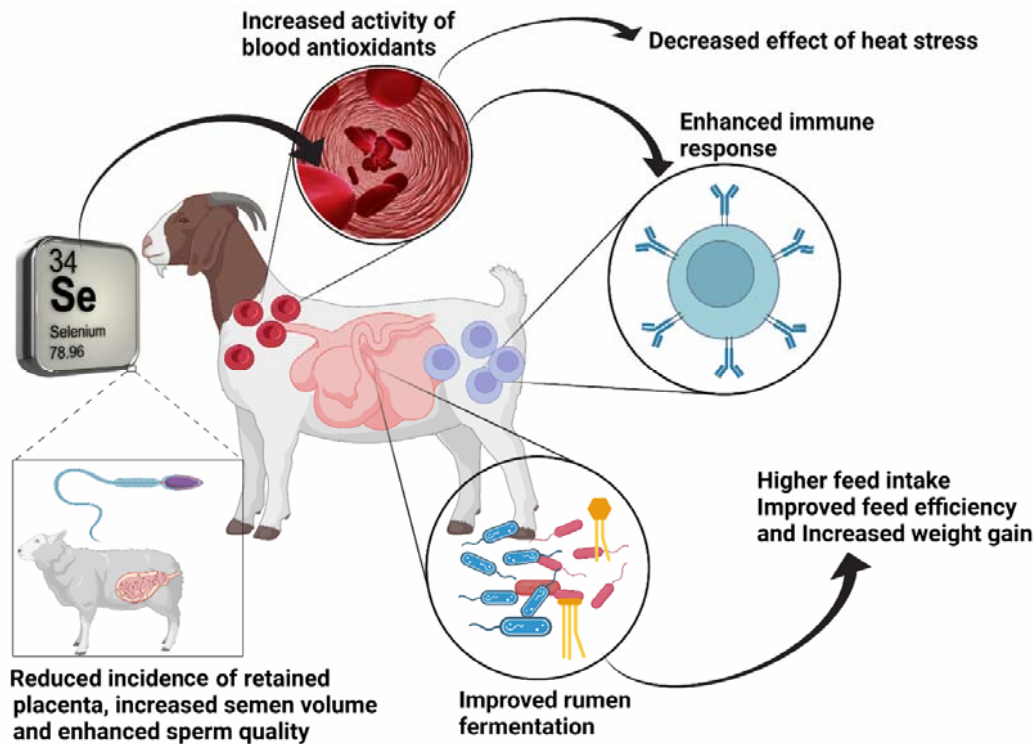
Figure 1 Summary of the role of Se administration in sheep and goats

Effects of Se on milk quality

Similar to the function of Se in the antioxidant defense of cells, selenoproteins also protect polyunsaturated fatty acids particularly linoleic acid, an important component of milk fat, from peroxidation (Ling *et al*. 2017). The activities of GSH-Px were confirmed by an upregulation in the expression of mRNA GPx in the mammary glands thereby suggesting increased antioxidant protection (Han *et al*. 2021). In a study by Pulido *et al*. (2019), the oral administration of α-tocopherol (1000 IU/day) and sodium selenite (0.4 mg/day) to lactating ewes increased proportions of long-chain fatty acids while the concentrations of short-chain fatty acids and medium-chain fatty acids decreased in the milk as compared to that of the unsupplemented group. Similarly, Mitsiopoulou *et al*. (2021) added organic Se (0.1 mg Se-yeast/kg) and vitamin E (60 mg/kg) into the diets containing sesame seed oil and reported an increased proportion of long-chain fatty acids, unsaturated fatty acids, and medium-chain fatty acids in the milk of goats when compared to the unsupplemented group.

The inclusion of Se-yeast into the diets of lactating goats increased the milk yield, milk fat yield, and milk protein yield while the somatic cell count decreased when compared to goats supplemented with sodium selenite (Reczyńska *et al*. 2019). In the same way, the inclusion of organic (Se-enriched yeast) and inorganic (sodium selenite) Se into the diets of goats increased the milk yield.

Interestingly, organic Se was found to be more effective than inorganic Se at 0.4 mg/kg diet (Zhang *et al*. 2018). The efficacy of slow-releasing Se boluses was investigated in lactating goats and the results showed an improved milk yield, milk fat percentage, milk Se, and iodine concentration as well as milk component yields in the treated groups when compared to goats in the unsupplemented group (Rashnoo *et al*. 2020). Although the mechanism of action is unclear this suggests that Se administration in lactating goats could enhance milk yield and yield of milk components.

Effects of Se on reproductive performance in ewes and does

The nutrient requirements, including trace elements, in pregnant animals increase as the gestation stage progresses until it reaches its peak around the late pregnancy period. Hence, there is a need to increase the supply of trace minerals to ewes and does in late pregnancy (Zarbalizadeh-Saed *et al*. 2020).

The appropriate concentration of Se in animal diets is determined by the physiological stage of the animal, the Se status of the animal, and the form of Se (Arshad *et al*. 2021). When Se supplement is given to pregnant ewes, it helps to maintain the Se concentration in the blood and colostrum concentration. The increased Se concentration in the blood also reaches the developing fetus through the pla-

centa and improves the level of Se in the milk (Erdogan *et al.* 2017). Insufficient amount of Se in the animal's diet results in deficiency symptoms which causes great economic losses to farmers. Common symptoms of Se deficiency in ewes and does includes reduced fertility, abortion, and retained placenta (Novoselec *et al.* 2017). In most cases, oxidative stress leads to the incidence of retained placenta, and a sufficient supply of micro minerals including Se and vitamins A, and E have been reported to prevent its occurrence in ruminants (Khalili *et al.* 2020). In support of this, Erdogan *et al.* (2017) supplemented pregnant ewes with selenomethionine and recorded a higher concentration of Se in the placenta, serum, and colostrum than the unsupplemented. In another study, pregnant and lactating ewes supplemented with both organic (Se-yeast) and inorganic (sodium selenite) Se recorded higher levels of Se in the blood when compared to the unsupplemented group (Novoselec *et al.* 2017).

Effects of Se on reproductive performance and semen quality

Both organic and inorganic Se sources have been used to improve the quality of semen and the overall reproductive performance of rams and bucks. During the cryopreservation of semen, the activities of free radicals cause oxidative stress and eventually reduce the viability of the sperm cells as well as their fertilization ability after thawing (Khalil *et al.* 2019). Interestingly, the quality of frozen semen can be enhanced by the addition of Se to the semen extender. In an *in vitro* study on the post-thawing quality of ram semen, the inclusion of nano-Se into semen extender decreased lipid peroxidation and resulted in a lower percentage of abnormal sperms while sperm viability and motility were higher when compared to the unsupplemented group (Nateq *et al.* 2020).

Compelling evidence from several studies on goats revealed that Se supplementation has improved semen volume, and semen quality (Shi *et al.* 2010; Lukusa and Lehloenya, 2017; Mojapelo and Lehloenya, 2019; Mojapelo *et al.* 2021), and increased the levels of luteinizing hormone and testosterone (Lukusa and Lehloenya, 2017; Mojapelo and Lehloenya, 2019) in the treated group when compared to the unsupplemented group. This could be attributed to the ability of Se to enhance spermatogenesis via an association with glutathione peroxidase in the testis (Jamali *et al.* 2019). Similarly, in rams, the administration of Se and vitamin E increased ejaculate volume in the treated group as compared to the unsupplemented group (Baiomy *et al.* 2009; Mahmoud *et al.* 2013). In another study on rams, the efficacy of sodium selenate on reproductive performance was investigated by Marai *et al.* (2009).

The results revealed an increased libido, higher ejaculate volume, and improved sperm motility as well as the sperm-cell concentration in the treated group when compared to the unsupplemented group. Selenium plays a key role in the spermatogenesis and synthesis of testosterone which are vital components of the reproductive life of a male animal (Badgar and Prokisch, 2020). Selenium acts directly on the interstitial cells of the testes or indirectly via the hormones of the anterior pituitary gland to enhance semen volume and sperm quality (Yousef *et al.* 1990). This explains the increased semen volume and higher concentration of testosterone reported in the studies above.

Factors limiting the activities of Se in ruminants

The rumen environment is one of the major factors that limit the activity of Se in ruminants. When sheep were supplemented with dietary Se, the Se in the rumen fluid was found to be insoluble (Badgar and Prokisch, 2020). This could be due to the action of microbes on the Se and converting it to the poorly soluble elemental Se or selenides thus decreasing its bioavailability (Spears, 2003). Another factor that affects the bioavailability of Se in ruminants is the form of Se. Organic, inorganic, and nano-Se are metabolized differently in ruminants. Organic Se is slowly absorbed in the body and has a high bioavailability, increased tissue storage, and less toxicity than inorganic Se (Groce *et al.* 1973; Ortman and Pehrson, 1997; Fairweather-Tait *et al.* 2010; Danielsson *et al.* 2012; Davis *et al.* 2017). However, when compared with the organic and inorganic sources of Se, nano-Se has proven to exhibit higher bioavailability, increased tissue storage, enhanced surface charge, and reactivity improved antioxidant effect, increased binding properties as well as reduced antagonism with other minerals, and less toxicity (Hosnedlova *et al.* 2018; Khalil *et al.* 2019; Patra and Lalhriatpuii, 2020; Han *et al.* 2021; Libera *et al.* 2021).

Due to the similar chemical properties to sulfur, Se has been reported to compete with sulfur. This means that a diet with high sulfur will decrease the bioavailability of Se. In addition, some anti-nutritional factors such as cyanogenic glycosides in forages might limit the availability of Se (Spears, 2003).

Recommendation

The effect of Se on heat stress and immunity is worth investigating. This is due to the relationship between oxidative stress and heat stress. Prospective researchers can compare the effects of different forms and doses of Se on small ruminants exposed to heat stress. In addition, with recent advances in metagenomics and metabolomics, future researchers could employ metagenomics and metabolomics to explore the effects of Se on rumen fermentation and micro-

biology, as well as the interaction between rumen microbiota and Se supplementation in small ruminants.

CONCLUSION

The supplementation of Se in sheep and goats has been shown to improve blood antioxidant status, immune response, reproductive performance, rumen fermentation, as well as feed efficiency, and weight gain. The influence of Se on heat stress and immune response were all associated with its ability to neutralize the free radicals in cells thereby protecting the cells from oxidative stress. This is due to the action of many enzymatic structures and seleno-proteins, especially glutathione peroxidase which is responsible for the reduction of H_2O_2 to H_2O and the elimination of lipid peroxides that are synthesized by free radicals in the cells. Due to the positive correlation of oxidative stress with heat stress, prevention of oxidative stress will automatically translate to a reduced risk of heat stress. Similarly, oxidative stress can weaken the host immune system and activate inflammatory responses thereby resulting in several metabolic diseases. Selenium helps to provide an antioxidant defense to the immune system, stimulates the secretion of cytokines, and enhances the differentiation of lymphocytes. However, factors limiting the bioavailability of Se include the rumen microbiota, the form of Se, and competition with the other minerals.

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