Polish Journal of Veterinary Sciences Vol. 28, No. 3 (2025), 497–503

DOI 10.24425/pjvs.2025.156076

Review paper

The role of selenium in small ruminants: implications for haematopoiesis and supplementation strategies – a review

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Abstract

Selenium is a pivotal micronutrient for microorganisms, humans, and animals, playing essential roles in antioxidant defence, endocrine function, immune response, muscle function and reproduction. Haematopoiesis, the process of blood cell formation in the bone marrow, is a tightly regulated process to ensure the continuous formation of mature blood cells. However, the bone marrow is highly responsive to a wide range of substances, including selenium. As a result, supplementation with this micronutrient has gained attention for its potential impact on haematopoietic activity of the ruminant bone marrow. This review aims to provide an overview of the reasons and forms of selenium supplementation in small ruminants with a particular focus on its impact on caprine and ovine haematopoiesis in the bone marrow. Despite its significance, research on selenium influence on haematopoiesis in small ruminants remains limited. Studies conducted so far have varied in enrolled species, animal age, supplementation type, and material studied. Recent findings suggest that selenium supplementation may enhance overall bone marrow haematopoietic efficiency especially in terms of erythropoiesis, and thrombopoiesis. However, differences in the selenium bioavailability from various supplements, regional variations in supplementation practices, and interactions with other micronutrients underscore the complexity of maximising selenium benefits. These factors highlight the need for further research to optimise selenium supplementation strategies for improved small ruminant health and productivity.

Keywords: antioxidant micronutrients, goat, haematopoiesis, ruminant health, selenium supplementation, sheep

Introduction

Selenium (Se) – a chemical element with antioxidant properties from the group of non-metals – is a pivotal micronutrient for microorganisms, humans, and animals. It exists in the environment in a variety of oxidation states: elemental selenium, selenides (Se^{2-}) and selenates (Se IV and Se VI) (Banerjee et al. 2022). In small ruminants, plants serve as the primary natural source of selenium. However, the bioavailability of this trace element can be affected by several factors such as increased levels of cyanogenic glycosides in e.g. clover or flaxseed, or higher dietary sulphur intake (Spears 2003).

As a constituent of several enzymes, selenium plays key roles in a variety of biological processes, including antioxidant defence, endocrine function, female and male reproduction, immune function, muscle development and function (Stadtman 2000, Köhrle et al. 2005, Ahsan et al. 2014, Shi et al. 2020). Notably, one of its lesser-explored yet significant functions is its role in haematopoiesis - formation of blood cells occurring within the bone marrow.

This review aims to provide an overview of the reasons and forms of selenium supplementation in small ruminants with a particular focus on its impact on caprine and ovine haematopoiesis. Furthermore, this review will address current challenges, knowledge gaps, and discuss future directions for research in this field.

Selenium in small ruminant nutrition – why supplementation is crucial in some areas?

In ruminants, selenium absorption from the gastrointestinal tract is significantly lower than in non-ruminants, with studies showing only 34% absorption in sheep compared to 85% in pigs (Wright and Bell 1966, Spears 2003). This diminished absorption is attributed to the unique microbial environment of the rumen, where several microorganisms are capable of incorporating selenium into their structures – e.g. B*utyrivibrio fibrisolvens*, *Lactobacillus* sp*.*, *Prevotella ruminicola*, *Selenomonas ruminantium*, and *Streptococcus* sp. (Lenartova et al. 1998). Most of them limit selenium bioavailability, including *Prevotella ruminicola* converting selenite into non-absorbable elemental selenium, which is then excreted in faeces. However, *Butyrivibrio fibrisolvens* or *Selenomonas ruminantium* have the ability to enhance selenium bioavailability in the rumen by incorporating this element into selenoamino acids, slightly more accessible to ruminants (Mynhardt et al. 2006). Furthermore, selenium scarcity in European soils leads to selenium-deficient plant material, and a continuous need for mineral supplementation in livestock, especially young ruminants, in many areas, to prevent deficiency-related health issues, such as white muscle disease (nutritional muscular dystrophy) and decreased activity of glutathione peroxidase – first line defence protecting the organism from the oxidative damage (Antanaitis et al. 2008, Kaur et al. 2014).

Several chemical forms of selenium are used for supplementation in ruminants, including selenates, selenites, selenomethionine, and selenized yeast (Qin et. al. 2007, Reczyńska et al. 2019). The most recently studied form of selenium supplementation is selenite triglycerides obtained from selenisation of triglycerides in sunflower oil. However, the European Food Safety Authority (EFSA) has highlighted a significant gap in research regarding their safety and efficacy, emphasizing the need for further studies (EFSA Panel on Nutrition 2020).

Research suggests that the bioavailability of selenium from selenite and selenate is generally comparable in ruminants (Podoll et al. 1992, Spears 2003). However, organic selenium in selenized yeast results in much larger increases in blood and milk selenium concentrations than selenite (Koenig et al. 1997, Ortman and Pehrson 1999, Faixova et al. 2007, Reczyńska et al. 2019). Moreover, lambs fed selenite had lower selenium concentrations in number of tissues and organs (e.g. skeletal muscles – 16.1 ppb compared to 31.4 ppb, skin and fleece – 39.0 ppb compared to 117.8 ppb) than those receiving selenomethionine (Ehling et al. 1967, Spears 2003).

In small ruminants, selenium is typically administered through the parenteral route. Sodium selenate and vitamin E preparations are the most commonly used, though their effects last only a few weeks, necessitating repeated treatments. Slow-releasing formulations, which free selenium over several months, such as barium selenate, offer a more effective alternative (Błażejak-Grabowska et al. 2022). Several strategies exist for selenium supplementation in small ruminants. Given that selenium crosses the placental barrier and is present in colostrum and milk, supplementation can be administered either directly to neonatal lambs and kids or indirectly through their dams. Research in sheep suggests that barium selenate has a stronger stimulatory effect on both humoral and cellular immune responses when administered directly to lambs, compared to lambs born to supplemented ewes. However, indirect supplementation through the ewe was also found to be effective (Milewski et al. 2021, Błażejak-Grabowska et al. 2022).

Selenium supplementation may also improve male reproductive function in goats. Results on the effect of Se supplementation on puberty attainment in young Saanen male goats obtained by Mojapelo and Lehloenya (2019) demonstrated e.g. positive effect of Se (0.34 mg sodium selenite/kg body weight, twice dosed at 90 days intervals) on concentration of luteinizing hormone and testosterone, semen appearance, sperm concentration, motility and viability, and the percentage of abnormal sperm at puberty alongside earlier puberty attainment. Se plays a role in the metabolism of thyroid hormones which are involved in growth regulation (Chadio et al. 2005). Mojapelo and Lehloenya (2019) suggested that the higher body weight observed in selenium-supplemented male goats may contribute to their improved reproductive characteristics. Furthermore, they attributed the increased semen volume in selenium-supplemented males to the stimulation of the development and growth of primary and secondary reproductive organs, as well as enhanced prostate function. Therefore, it is advised to supplement the entire herd with Se prior to the breeding season.

Supplementation with vitamin E and selenium in ruminants provides protective benefits against udder inflammation and retained placenta, while also significantly mitigating the symptoms associated with existing mammary gland inflammation (Bickhardt et al. 1999, Hoffman 2007). Additionally, incorporating selenium and vitamin E into the diet enhances both the quantity and phagocytic activity of neutrophils and macrophages, thereby supporting the immune response (Whanger et al. 1996, Nuttall 2006).

Haematopoiesis in small ruminants and role of selenium

In mammals, the bone marrow mostly develops during the second trimester of pregnancy, establishing itself as the primary site of haematopoiesis in postnatal life (Kucia et at. 2008). The primary elements responsible for the spatial organization of the bone marrow include the surrounding bone, the vascular system, and a network of reticular stromal cells (Lucas 2021).

The bone marrow consists of various types of cells: stromal cells which do not participate in haematopoiesis (e.g. adipocytes, fibroblasts, osteoblastic precursors, osteoblasts, osteocytes, Schwann cells, and sympathetic nerves) and haematopoietic cells (Nombela-Arrieta et al. 2017, May et al. 2018). Haematopoiesis takes place in the spaces between bone, reticular cells and vessels. Stained bone marrow smears reveal a complex system of cells from various developmental lineages at every stage of maturation (Yu and Scadden 2016). The haematopoietic stem cell niches are the most well-studied microenvironments within the mammal bone marrow, playing a crucial role in maintaining haematopoietic stem cells throughout the organism's life (Lucas 2021).

Haematopoiesis is a tightly regulated process that ensures the continuous production of mature blood cells. It is intricately regulated by the bone marrow microenvironment, which is profoundly influenced by factors such as oxidative stress, cytokine signalling, and the availability of essential nutrients (Ludin et al. 2014). Moreover, bone marrow is highly responsive to a wide range of substances, rapidly adapting to those penetrating the body from the environment (e.g. bisphenol A) or introduced into the animal's body during treatment procedures (e.g. albendazole, selenium, vitamin E) (Snarska et al. 2018a, Snarska et al. 2018b, Harm et al. 2022, Snarska et al. 2024).

Selenium deficiency is common in most European soils, leading to insufficient levels of this element in plants grown on them (Manojlović and Singh 2012, Humann-Ziehank et al. 2013). Globally, soil Se concentrations typically range from 0.2 to 0.6 mg/kg and are influenced not only by the selenium content of the parent rock but also by processes occurring during soil formation (Juszczak-Czasnojć and Tomza-Marciniak 2021). Although soil selenium content is a key factor determining its concentration in plants, its bioavailability is also affected by its chemical forms, soil pH and redox potential, organic matter, climatic conditions, and microbial activity (Natasha et al. 2018). In addition, plant species, developmental stage, and their capacity to accumulate selenium significantly influence Se levels in plant tissues (Dumont and Vanhaecke 2006). As a result, livestock, especially small ruminants, require continuous selenium supplementation to prevent the negative consequences of deficiency. These health consequences are wide-ranging, including inhibition of neutrophil migration and disturbances in receptor distribution on their surface. Selenium, through its integration into selenoproteins such as glutathione peroxidases (GSH-Px) and thioredoxin reductases, plays a crucial role in mitigating oxidative damage and regulating immune responses. Fluctuations in selenium concentration and GSH-Px activity are closely linked to the onset of oxidative stress in both humans and animals (Tinggi 2003, Kamada et al. 2007). Notably, during selenium deficiency in ruminants, there is a clear correlation between the rate of progression and the severity of anaemia – a haematopoietic pathology (Hollenbach et al. 2008, Semba et al. 2009). This strongly underscores the role of selenoproteins in regulating hematopoiesis. The high activity of glutathione peroxidase (GSH-Px) in plasma, platelets, and erythrocytes

Table 1. Supplementation protocol and source of selenium in studies on the effect of selenium supplementation on haematopoiesis in small and wild ruminants.

Studied animals	Source of selenium	Route and dose	Main results on hematopoiesis	Reference
Adult and young goats	Selenium yeast derived from *Saccharomyces cerevisae*	3.2 mg/kg daily *per os* for 56 days (28 days before and after kidding)	only affected MCHC in goat kids receiving milk from supplemented dams no effect on blood parameters in adult goats	Barcelos et al. 2022
Young goats	Sodium selenite	1 mg/animal once *per os*, second day of life	higher number of erythroblasts in supplemented animals, increased RBC and HGB	Snarska et al. 2023
Young goats	Sodium selenite	0.17 mg/kg once IM, second day of life	higher number of megakaryoblasts and megakaryocytes; faster and more intense dyes absorption by bone marrow cells	Snarska et al. 2024
Female young fallow deer	Sodium selenite	0.5 mg/ animal once, IM, third day of life	higher percentage of proerythroblasts, basophilic erythroblasts, polychromatic erythroblasts and orthochromatic erythroblasts, reticulocytes, higher haemoglobin and RBC 15 days	Snarska et al. 2018b

is pivotal in supporting this process (Arthur 2000, Canli et al. 2015). Additionally, it is important to highlight that selenium and vitamin E deficiencies significantly contribute to lysis of the erythrocyte membrane and methaemoglobin formation - a process driven by an increase in intracellular reactive oxygen species.

Effects of selenium supplementation on haematopoiesis in small ruminants – current state of knowledge, challenges and future directions

Selenium deficiency has been associated with haematological disorders, increased susceptibility to infections, and impaired erythropoiesis. In contrast, selenium supplementation has been linked to improved blood cell parameters and enhanced immune resilience. This trace element acts mainly through selenoproteins, which are synthesized via the selenium metabolic pathway and perform diverse cellular functions, including the regulation of selenium transport, redox homeostasis, metabolism of thyroid hormones and immune response (Kang et al. 2020). They are also critical for bone remodeling, however, the underlying mechanism of this action is not fully understood (Kim et al. 2021). While individual processes in haematopoiesis, such as erythropoiesis, have been extensively studied in various animal models including sheep and goats there is still limited knowledge on the effects of specific selenium supplementation regimens on caprine and ovine haematopoiesis (Lloyd 2018).

Table 1 presents the supplementation protocols and selenium sources used in published studies on selenium effect on haematopoiesis in small and wild ruminants.

Barcelos et al. (2022) examined the effects of selenium and vitamin E supplementation on blood cell counts in young and adult goats. They found no significant effect of a selenium- and vitamin E-enriched diet (daily dose: Se 3.2 mg/kg; vitamin E 1145 IU/kg) on the tested parameters. However, they observed a significantly higher ($p \leq 0.05$) mean corpuscular haemoglobin concentration (MCHC) in kids receiving milk from dams fed a selenium-enriched diet (daily dose: Se 3.2 mg/kg) compared to those on a basal diet.

These findings stand in contrast to those reported by Snarska et al. (2018b, 2023, 2024), who observed significantly stronger positive effects of selenium administration on haematopoiesis (Table 1). Several factors may account for these discrepancies, including differences in the source of selenium and the route of its administration. While Barcelos et al. (2022) utilized selenized yeast as a dietary supplement, Snarska et al. (2018b, 2023, 2024) administered sodium selenate. Additionally, the method of supplement administration varied between studies – Barcelos et al. (2022) administered selenium *per os*, whereas Snarska et al. (2018b, 2024) used a parenteral route, potentially leading to more efficient absorption and utilization of the micronutrient. We also cannot exclude that vitamin E reinforced the positive effect of selenium in all studies conducted by Snarska et al. (2018b, 2024).

Another key distinction lies in the methodology used to assess haematopoietic effects. Barcelos et al. (2022) limited their analysis to blood parameters, whereas Snarska et al. (2018b, 2023, 2024) incorporated both blood cell counts and bone marrow smear evaluations, providing a more comprehensive picture of selenium's influence on haematopoiesis. Given that bone marrow serves as the primary site of blood cell production, its direct examination may offer deeper insights into the underlying biological mechanisms at play. These methodological differences highlight the complexity of selenium supplementation research and underscore the need for standardized approaches to accurately assess its effects on haematopoiesis in small ruminants. In veterinary medicine, bone marrow cytological evaluation is not commonly performed, especially in small ruminants and other livestock. This procedure is typically reserved for cases where significant deviations from species-specific haematological reference values are observed, often alongside blood biochemistry analysis, after ruling out non-marrow-related causes of illness. When warranted, bone marrow evaluation can provide essential diagnostic insights, aiding in prognosis assessment and informing targeted treatment strategies, ultimately enhancing clinical decision-making. In studies assessing the impact of various substances on haematopoiesis, cytological evaluation of bone marrow smears should complement standard blood morphology analysis to provide a more comprehensive understanding of bone marrow response to the substance studied.

Despite the recognized role of selenium in blood cell formation, to our knowledge, no research has yet investigated its direct effects on the ovine bone marrow. This represents a significant knowledge gap in the current literature.

Furthermore, an avenue worth exploring is the potential influence of selenite triglycerides on haematopoiesis in small ruminants, as this form may offer distinct bioavailability and metabolic advantages compared to conventional selenium sources. According to Flis et al. (2015) this organic form of selenium has better bioavailability and lower toxicity than the inorganic forms of this trace element (e.g. toxicity of selenite triglycerides is 30-56 times lower than that of sodium selenite in rats and mice, respectively). A well-designed, multifaceted study comparing different supplementation protocols including variations in selenium source, route of administration, and both direct and indirect supplementation strategies (e.g., supplementation of dams and/or their offspring) would be beneficial to fulfil this knowledge gap. Such research could provide valuable insights into optimising selenium supplementation strategies across different farming systems, ultimately improving animal health and productivity.

Conclusions

The amount of data regarding the effects of selenium supplementation on bone marrow haematopoietic activity in small ruminants is scarce. Studies conducted so far have varied in enrolled species, animal age, supplementation type, and the material studied. Despite its recognized importance in ruminant health, the exact mechanisms by which selenium influences bone marrow haematopoiesis remain unclear. Recent findings suggest that selenium supplementation may enhance overall bone marrow hematopoietic efficiency, especially in terms of erythropoiesis, and thrombopoiesis. However, differences in selenium bioavailability among commonly used supplements, varying supplementation strategies between countries, and Se interactions with other micronutrients highlight the need for further research to maximise its potential in small ruminant nutrition and health.

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