

Role of Selenium in Ruminants Health and Reproduction

Abstract

Selenium (Se), a micro element was well known for its toxicity at earlier times. But, presently it is listed to be an essential mineral which is required for sound health, better immunity, and efficient reproductive functions of livestock. There is variation in the status of Se in animals and plants across the world based on different geological conditions. Se concentrations of plants are closely related with those of its soil concentration. The deficiency of Se is associated with many health problems viz increased neonatal mortality, lowered immunity poor suckling reflex and white muscle disease in animals. There is significant role of Se in the reproduction of animals. The selenoproteins such as, Glutathione peroxidase 4 (GSH-Px4) and SELENOP have a regulatory role in male reproduction. GSH-Px4 has distinct antioxidant and structural properties and is expressed in testes. The peroxidation of Leydig cells is protected by SELENOP. The specific role of Se involves development of seminiferous tubules, growth of testicular tissues, in process of spermatogenesis, steroidogenesis and in synthesis and secretion of reproductive hormones like follicular stimulating hormone (FSH) and luteinizing hormone (LH). In female reproduction, the supplementation of Se may reduce the incidence of metritis and ovarian cysts and decreases the embryonic mortality. Currently, due attention is given on dietary Se supplementation through different (inorganic, organic and nano) forms of Se

Keywords: Selenium, neonatal mortality, energy metabolism, animal health

Introduction

Minerals are inorganic substances that cannot be synthesized in body, but are required in small amount to support different metabolic functions of body [1]. Majorly, 22 minerals are required for animals. Out of which, 15 are micro minerals and 7 macro minerals [2]. “Trace minerals, though required in small quantities (less than 100 mg/kg dry matter) have critical roles in immune function, oxidative and energy metabolism in ruminants which are directly or indirectly involved in growth, production and reproduction” [3]. “Commonly used trace minerals are cobalt, copper, iodine, iron, manganese, molybdenum, Se and zinc” [4]. “Among these, Se is currently acknowledged to be an essential dietary trace element required for various body functions such as growth, reproduction, immune system and protection of tissue integrity” [5]. White muscle disease (WMD) was the first recognized condition associated with Se deficiency. WMD causes new born mortality, especially in ruminants, and impaired production condition in growing and adult animals. Selenium is also required for synthesis of thyroid hormone and it is also very important for converting T4 (thyroxin inactive form) to T3 (active form). Some minerals such as Nickle, Chromium, arsenic and Vanadium are known to clearly have a role in animal health but the exact biochemical nature is unknown and its essentiality have weak evidences[6] [7] [8] [9].

Status of Selenium in ruminant

“The Se status of animals and plants is highly related to its concentration in soil. Agricultural production system in developing countries is under pressure to fulfil the requirement of growing population, leading to unjustified use of fertilizers that has resulted in severe deficiency of micro minerals in soil. The deficiency of Se in soil and crop plants has been reported in many countries like India, China, Turkey and Pakistan” [10]. ~~The concentrations of Se in plant material are highly correlated with those in the soil.~~ “Fertilization of soil with Se containing fertilizers will increase Se concentrations in plants” [11]. ~~The Se status in animals and plants varies markedly around the world as a result of different geological conditions. High Se concentrations are associated with some phosphatic rocks, organic rich black shales, coals, and sulphide mineralization, whereas most other rock types contain very low concentrations.~~ “Globally, Se deficient soils are far more widespread than are seleniferous ones” [12]. “Animal health is affected by either Se deficiency or its excess in the diet, the intake of Se being dependent on the amount of Se taken up by plants as bioavailable Se” [13].

Chemical Nature

“Se is a naturally occurring metalloid element and its essentiality in trace amount has been proven in human and animal health. It was first identified in 1817 by the Swedish chemist, Jons Jakob Berzelius. It has chemical and physical properties intermediate between metals and non-metals and is similar to those of sulphur, arsenic and tellurium, all of which are in Group VI of the periodic chart of the elements” [14]. “Like Sulphur, Se can exist in different oxidation states as selenide (2-), Se (0), selenite (4+) and selenate (6+), respectively. It behaves antagonistically with Copper and Sulphur in humans and animals inhibiting the uptake and function of these elements” [15].

Essentiality of Selenium

Se is earlier categorised as a toxic element, has now been proved to be an essential mineral in trace quantities for proper health, immunity, and reproductive functions of animals. The essentiality of Se was proved for the first time from the work that liver necrosis in rats [16] and exudative diathesis in chicks could be prevented by supplements of Se. Se is required to maintain normal physiological functions and provides a significant dietary source of antioxidant defenses [17]. “It is necessary for maintaining the vital functions of humans and animals. Majority of the Se is found bound to tissues and blood in the form of selenoproteins. It is a constituent of at least 25 selenoproteins with various physiological properties like antioxidant, anti-inflammatory and chemoprotective” [18]. “The most important are glutathione peroxidases (GSH-Px-1, GSH-Px-6), thioredoxin reductases (TrxR1–TrxR3), iodothyronine deiodinases (ID1–ID3), selenophosphate synthetase, Selenop, and selenoprotein W. Se acts as a cofactor of the GSH-Px family of enzymes which is an antioxidant enzyme. Specifically, Se-dependent GSH-Px enzyme recycles glutathione, reducing lipid peroxidation by catalysing the reduction of peroxides, including hydrogen peroxide. In general, all these enzymes in their reduced state catalyse the breakdown of lipid hydroperoxides and hydrogen peroxides in cells” [19]. The inflammatory response is regulated by GSH-Px and selenoprotein P.

Important role of selenium in health and reproduction

Se has specific role in enhancing the immune response in farm animals [20]. Se deficiency has been reported to decrease humoral immune response and neutrophil killing activity in cattle without any clinical signs [21]. Moreover, [22] reported that “dietary Se supplementation increases antibody titre, neutrophils killing activity and reduces morbidity and mortality in beef cattle. Se improves phagocytosis in white blood cell populations”. “Se has improved the passive immunity by enhancing immunoglobulin G (IgG) absorption in the new born lamb” [23]. The improvement of immune response might be due to improved antioxidant status [24]. “The selenoproteins, especially GSH-Px4 (Glutathione peroxidase) and SELENOP (Selenoprotein-P) had significant functions in the male reproductive systems. GSH- Px4 is distinctly expressed in testes and has both an antioxidant as well as a structural role; the latter context is evident from a fact that it constitutes over 50% of mitochondrial capsule (as an oxidatively inactivated protein) in midpiece of mature sperm” [25]. “During the initial process of spermatogenesis GSH-Px4 protects the plasma membrane of sperm from oxidative damage however, in the later phase, through cross linkage with proteins in midpiece region, it provides the integrity to the sperm midpiece by becoming a structural component of mitochondrial sheath circumventing the flagellum, which is an essential component for sperm stability and motility. SELENOP serves as a transport protein for Se and is also expressed in vesicle like structures in the basal region of the Sertoli cells” [26]. “Reactive oxygen species (ROS) are constantly produced and are products of normal metabolism and the reproductive tissues are constantly exposed and during the fertilization process spermatozoa normally pass through an area of high oxygen level” [27]. “The polyunsaturated fatty acids (PUFA) of sperm membrane are highly susceptible to lipid peroxidation caused by reactive oxygen species (ROS) overproduction” [28]. These damages deteriorates the quality of semen and sperm integrity. Intensive lipid peroxidation eventually results in sperm motility and viability loss [29]. Several defence mechanisms including antioxidant help in counteracting ROS detrimental effects and maintain sperm motility and viability [30]. The physiological activity of the cytoplasmic antioxidant enzymes are very low in sperm cells [31], and the small amount of the cytoplasm in their heads and tails makes them susceptible to oxidative stress. On contrary, the seminal plasma is a vital source of antioxidants, including glutathione peroxidase (GSH-Px), superoxide dismutase (SOD), uric acid and vitamin E [32]. “Activity of Se-dependent phospholipid hydroperoxide GSH-Px (PH-GSH-Px, GSH-Px4) is very pronounced in late (meiotic) spermatogenic cells, where it acts as a structural protein in sperm heads, whereas the nuclear form GSH-Px4 contributes to chromatin condensation” [33].

The growth of testicular tissues, development of seminiferous tubules and the process of spermatogenesis, steroidogenesis synthesis and secretion of follicular stimulating hormone (FSH) and luteinizing hormone (LH) are regulated by Se [34]. Supplementation of Se has been found to improve semen quality by increasing antioxidative defence of seminal plasma in buck [35], boar [36] Boer goats [37] ram [38] and cockerels [39]. Se deficiency had lowered immunity and increased mortality [40]. It may also result in endocrine disorders, especially thyroid dysfunction [41].

Effects of Se sources on health and reproduction of ruminants

Supplementation sources and its bioavailability

“The bioavailability of Se is associated with its forms of supplementation. Generally, Se is utilized as inorganic, organic and nano forms. The form and mode of Se supplementation has an important bearing on its possible ameliorative effects and/or on

general wellbeing and development of organisms” [42]. “Both form and the total intake of Se are equally important with regards to the potential health- related effects. The organic forms of Se have better bioavailability as compared to the inorganic forms” [43]. “It is usually because the common inorganic forms; sodium selenite and sodium selenate must first be converted to hydrogen selenide and then to selenophosphate before they can be utilised in selenoprotein synthesis” [44]. “The sodium selenite (SS) and sodium selenate, are usually added in mineral premixes or or available in injectible form. Organic Se sources are seleno-amino acids (e.g. selenomethionine (Se-Met) and selenocysteine), which are found in Se yeast or in feeds grown on Se-rich soils. Recently, nano-Se has attracted a wide spread attention because of its better bioavailability and low toxic properties” [45] [46]. “Nano minerals improve the bioavailability due to its novel characteristics such as high surface activity, a lot of surfaces active centers, strong adsorbing ability and high catalytic efficiency” [47]. Nano-Se has efficient functions on animal growth, reproduction and immunity systems [48]. “In sheep, Nano-Se had improved ruminal fermentation, nutrient digestibility” [49]. “In addition, some reports on rats and mice demonstrated that Nano-Se had higher efficiency than sodium selenite and other Se sources in up-regulating selenoenzymes, exhibiting lower toxicity” [50]. Subsequent studies also pointed out that “Nano-Se has more beneficial effects to improve activity of glutathione peroxidase, blood biochemical indices with lower toxicity comparing with organic or inorganic Se sources” [51].

Conclusions:

Adequate essential trace mineral intake and absorption is required for a variety of metabolic functions including immune response, reproduction and growth. Se is now recognized as an essential micro element, and its deficiency has been associated with impaired growth, fertility, and poor health especially in farm animals. Diets for ruminant animals are often of plant origin and the Se concentration within plants are reported to be highly variable. Consequently, concentration of Se can be deficient, and Se supplementation may be required. Supplementation of trace elements in animal diets has long been practiced to ensure optimum growth production and improve immune response. Considering the serious impact on the productive efficiency of the affected animals and death in newborns, deficiency should be prevented by supplementation especially in Se deficient regions and deficient animals. Different forms of Se routinely used for dietary supplementation are inorganic, organic and nano Se. The most common inorganic Se sources are sodium selenite (SS) and sodium selenate, which are usually provided in mineral premixes or injected. Organic Se sources are seleno-amino acids (e.g. selenomethionine (Se-Met) and selenocysteine) that are absorbed with better efficiency than the inorganic forms. The recently used are nano forms, novel studies also reported that Nano-Se has more beneficial effects to improve activity of glutathione peroxidase, blood biochemical indices with lower toxicity comparing with organic or inorganic Se sources. There are reports of improved growth, better production performance, reproduction and health in ruminants irrespective of either inorganic, organic and nano forms of Se.

REFERENCES:

1. Eruvbetine D. 2003. Canine Nutrition and Health. A paper presented at the seminar organized by Kensington Pharmaceuticals Nig. Ltd, Lagos.

2. Underwood EJ, Suttle NF. 1999. The mineral nutrition of livestock. CABI Publication, New York, USA.
3. Bhalakiya N, Haque N, Patel P, Joshi P. 2019. Role of Trace Minerals in Animal Production and Reproduction. *International Journal of Livestock Research*, 9(9):1-12
4. Soetan KO, Olaiya CO, Oyewole OE. 2010. The importance of mineral elements for humans, domestic animals and plants-A review. *African journal of food science*, 4(5):200-222.
5. Pilarczyk B, Tomza-Marciniak A, Dobrzański Z, Szewczuk M, Stankiewicz T, Gaczarzewicz D, Lachowski W. 2013. The effect of selenized yeast supplementation on some performance parameters in sheep. *Turkish Journal of Veterinary and Animal Sciences*, 37(1):61-67.
6. Keshri A, Roy D, Kumar V, Kumar M, Kushwaha R, Vaswani S. Impact of different source chromium sources on physiological response, blood biochemicals and endocrine status of heat stress in dairy calves. *Biological Rhythm Research*. 2022; 53(1):58-69.
7. Singh A, Kumar M, Kumar V, Roy D, Kushwaha R, Vaswani S. Effect of Nickle supplementation on antioxidant status, immune characteristics and energy and lipid metabolism in growing cattle. *Biological Trace element research*, 2019; 190(1):65-75.
8. Vaswani S, Mani V, Kewalramani N, Kaur H. 2010. Mitigation of adverse effects of arsenic by supplementing vitamin E in crossbred kids maintained at low protein diet. *Indian journal of Animal Nutrition*. 27(4): 346-352.
9. Praveen Kumar Gupta, Shalini Vaswani, Vinod Kumar, Debashis Roy, Muneendra Kumar, Raju Kushwaha, Avinash Kumar, Amit Shukla. Investigations on Modulating Effect of Vanadium Supplementation on Growth and Metabolism Through Improved Immune Response, Antioxidative Profile and Endocrine Variables in Haryana heifers. *Biological trace element research*. 194: 379-389.
10. Gupta PK and Vaswani S. 2020. Basic information about vanadium 'ultra-trace element or occasionally beneficial element' and its various functions in animals: A review article. *J. Entomol. Zool. Stud.*, 8:645-53
11. Rashid A, Ryan J. 2008. Micronutrient constraint to crop production in the near east potential significance and management strategies. *Micronutrient deficiencies in global crop production*, DOI:10.1007/978-1-4020-6860-7_6
12. National Research Council. 2001. Nutrient requirements of dairy cattle. National Academies Press. Washington, DC, USA.
13. Khanal DR, Knight AP. 2010. Selenium: Its Role in Livestock Health and Productivity. *Journal of Agriculture and Environment*, 11:101-106.
14. Fordyce F. 2005. Selenium deficiency and toxicity in the environment. In 'Essentials of medical geology—Impacts of the natural environment on public health' (Eds O Selinus B Alloway JA Centeno RB Finkelman R Fuge U Lindh P Smedley) pp. 373-415.
15. Verma AK, Kumar A, Rahal A, Kumar V, Roy D. 2012. Inorganic versus organic selenium supplementation: a review. *Pakistan journal of biological sciences*, 15(9):418-425.
16. Netto AS, Zanetti MA, Correa LB, Del Claro GR, Salles MSV, Vilela FG. 2014. Effects of dietary selenium sulphur and copper levels on selenium concentration in the serum and liver of lamb. *Asian-Australasian journal of animal sciences*, 27(8):1082

17. Patterson EL, Milstrey R, Stokstad ELR. 1957. Effect of selenium in preventing exudative diathesis in chicks. *Proceedings of the society for experimental Biology and Medicine*, 95(4):617-620.
18. Sordillo LM. 2013. Selenium-dependent regulation of oxidative stress and immunity in periparturient dairy cattle. Hindawi Publishing Corporation. *Veterinary Medicine International*.
19. Pappas AC, Zoidis E, Surai PF, Zervas G. 2008. Selenoproteins and maternal nutrition. *Comparative Biochemistry and Physiology Part B: Biochemistry and Molecular Biology*, 151(4):361-372.
20. Navarro-Alarcon M, Cabrera-Vique, C. 2008. Selenium in food and the human body: a review. *Science of the total environment*, 400(1-3):115-141.
21. Chauhan SS, Celi P, Ponnampalam EN, Leury BJ, Liu F, Dunshea FR. 2014. Antioxidant dynamics in the live animal and implications for ruminant health and product (meat/milk) quality: role of vitamin E and selenium. *Animal Production Science*, 54(10):1525-1536.
22. Hogan JS, Smith KL, Weiss WP, Todhunter DA, Schockley WL. 1990. Relationships among vitamin E, selenium, and bovine blood neutrophils. *Journal of Dairy Science*, 73(9):2372-2378
23. Hall JA, Bobe G, Vorachek WR, Gorman ME, Mosher WD, Pirelli GJ. 2013. Effects of feeding selenium-enriched alfalfa hay on immunity and health of weaned beef calves. *Biological Trace Element Research*, 156(1-3):96-110.
24. Rock MJ, Kincaid RL, Carstens GE. 2001. Effects of prenatal source and level of dietary selenium on passive immunity and thermo metabolism of newborn lambs. *Small Ruminant Research*, 40(2):129-138.
25. Rossi CS, Compiani R, Baldi G, Muraro M, Marden JP, Rossi R, Pastorelli G, Corino C, Dell'Orto V. 2017. Organic selenium supplementation improves growth parameters, immune and antioxidant status of newly received beef cattle. *Journal of Animal and Feed Sciences*, 26(2):100-108.
26. Foresta C, Flohe L, Garolla A, Roveri A, Ursini F, Maiorino M. 2002. Male fertility is linked to the selenoprotein phospholipid hydroperoxide glutathione peroxidase. *Biology of reproduction*, 67(3):967-971.
27. Olson GE, Winfrey VP, Nagdas SK, Hill KE, Burk RF. 2007. Apolipoprotein E receptor-2 (ApoER2) mediates selenium uptake from selenoprotein P by the mouse testis. *Journal of Biological Chemistry*, 282(16):12290-12297.
28. Fujii J, Iuchi Y, Matsuki S, Ishii T. 2003. Cooperative function of antioxidant and redox systems against oxidative stress in male reproductive tissues. *Asian Journal of Andrology*, 5(3):231-242.
29. Aitken RJ, Buckingham D, Harkiss D. 1993. Use of a xanthine oxidase free radical generating system to investigate the cytotoxic effects of reactive oxygen species on human spermatozoa. *Reproduction*, 97(2):441-450.
30. Makker K, Agarwal A, Sharma R. 2009. Oxidative stress and male infertility. *Indian Journal of Medicine Research*, 129(4):357- 67.
31. Aitken RJ, Baker MA. 2004. Oxidative stress and male reproductive biology. *Reproduction, Fertility and development*, 16(5):581-588.
32. Bilodeau JF, Chatterjee S, Sirard MA, Gagnon C. 2000. Levels of antioxidant defenses are decreased in bovine spermatozoa after a cycle of freezing and thawing. *Molecular Reproduction and Development: Incorporating Gamete Research*, 55(3):282-288.
33. Raijmakers MT, Roelofs HM, Steegers EA, Mulder TP, Knapen MF, Wong WY, Peters WH. 2003. Glutathione and glutathione S-transferases A1-1 and P1-1 in

- seminal plasma may play a role in protecting against oxidative damage to spermatozoa. *Fertility and sterility*, 79(1):169-172.
34. Flohe L. 2007. Selenium in mammalian spermiogenesis. *Biological chemistry*, 388(10):987-995.
 35. Bedwal RS, Bahuguna A. 1994. Zinc copper and selenium in reproduction. *Experientia*, 50(7):626-640.
 36. Shi L, Zhang C, Yue W, Shi L, Zhu X, Lei F. 2010. Short-term effect of dietary selenium-enriched yeast on semen parameters, antioxidant status and Se concentration in goat seminal plasma. *Animal feed science and technology*, 157(1-2):104-108.
 37. Marin-Guzman J, Mahan DC, Pate JL. 2000. Effect of dietary selenium and vitamin E on spermatogenic development in boar. *Journal of animal science*, 78(6):1537-1543.
 38. Li-Guang S, Ru-Jiea Y, Wen-Bina Y, Wen-Juana X, Chun-Xianga Z, You-Shea R, Lei AS, Fu-Linb L. 2010. Effect of elemental nano-selenium on semen quality, glutathione peroxidase activity, and testis ultrastructure in male Boer ram. *Animal Reproduction Science*, 118:248-254.
 39. Kendall N, McMullen S, Green A, Rodway R. 2000. The effect of a zinc cobalt and selenium soluble glass bolus on trace element status and semen quality of ram lambs. *Animal Reproduction Science*, 62(4):277-283.
 40. Ebeid TA. 2012. Vitamin E and organic selenium enhances the antioxidative status and quality of chicken cockerel semen under high ambient temperature. *British Poultry Science*, 53(5):708-714.
 41. Enjalbert F, Lebreton P, Salat O. 2006. Effects of copper, zinc and selenium status on performance and health in commercial dairy and beef herds:retrospective study. *Journal of Animal Physiology and Animal Nutrition*, 90(11-12):459- 466.
 42. Kohrle J, Jakob F., Contempre B, Dumont JE. 2005. Selenium, the thyroid, and the endocrine system. *Endocrine reviews*, 26(7):944-984.
 43. Pappas AC, Zoidis E, Surai PF, Zervas G. 2008. Selenoproteins and maternal nutrition. *Comparative Biochemistry and Physiology Part B: Biochemistry and Molecular Biology*, 151(4):361-372.
 44. Burk RF, Hill KE. 2015. Regulation of selenium metabolism and transport. *Annual review of nutrition*, 35:109-134.
 45. Kachuee R, Moeini MM, Souri M. 2013. The effect of dietary organic and inorganic selenium supplementation on serum Se Cu Fe and Zn status during the late pregnancy in Merghoz goats and their kids. *Small Ruminant Research*, 110(1):20-2
 46. Xu DX, Shen HM, Zhu QX, Chua L, Wang QN, Chia SE, Ong CN. 2003. The associations among semen quality, oxidative DNA damage in human spermatozoa and concentrations of cadmium, lead and selenium in seminal plasma. *Mutation Research/Genetic Toxicology and Environmental Mutagenesis*, 534(1-2):155-163.
 47. Zhang J, Wang X, Xu T. 2008. Elemental selenium at nano size (Nano-Se) as a potential chemopreventive agent with reduced risk of selenium toxicity: comparison with se-methyl selenocysteine in mice. *Toxicological sciences*, 101(1):22-31.
 48. Wang Y, Yan X, Fu L. 2013. Effect of selenium nanoparticles with different sizes in primary cultured intestinal epithelial cells of crucian carp, *Carassius auratus gibelio*. *International Journal of Nanomedicine*, 8:4007.
 49. Shi L, Xun W, Yue W, Zhang C, Ren Y, Liu Q, Wang Q, Shi L. 2011. Effect of elemental nano-selenium on feed digestibility, rumen fermentation, and purine derivatives in sheep. *Animal Feed Science and Technology*, 163 (2-4):136-142.
 50. Zhang JS, Gao XY, Zhang LD, Bao YP. 2001. Biological effects of a nano red elemental selenium. *Biofactors*, 15(1):27-38.

51. Yaghmaie PA, Ramin S, Asri-Rezaei A, Zamani. 2017. Evaluation of glutathione peroxidase activity trace minerals and weight gain following administration of selenium compounds in lambs. *Veterinary Research Forum*, 8(2):133 – 137.

UNDER PEER REVIEW