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Review

Selenium: An Essential Micronutrient for Sustainable Dairy Cows Production

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Abstract: This review article discusses the importance and effects of Selenium (Se) in sustainable dairy cows' production. The Se is an important micronutrient in dairy cows. It is one of the important feed derived antioxidants. It participates in important enzymes and enzyme reactions to improve metabolism, growth, and the defense system of the body, which results in the improved health of animals, particularly that of the mammary gland and reproductive system, thereby improving productive and reproductive performance. The Se is usually deficient in soil due to current extensive farming strategies, so its supplementation is generally advised. Supplementation of Se in organic form is generally preferred over inorganic form due to its better incorporation and uptake, resulting in improved performance. Kidneys, liver, testis, and lungs are important sites for Se storage. The Se is excreted in urine, feces, exhaled breath, loss of skin, and hair cells. Although Se supplementation plays an important role in the profitability of dairy cows, its excess intake is toxic and should be avoided.

Keywords: selenium; cow; production; reproduction; nutrition

1. Introduction

Selenium (Se) is a nonmetal with the atomic number 34. In the periodic table, the element is located in the fourth period [1,2]. Se was discovered by a Swedish chemist, Jons Jacob Berzelius, in the year 1817 [3]. It is regarded as trace element due to its low content (0.05 ppm) in the earth's crust [4,5]. The Se can occur in organic as well as inorganic form [6]. Inorganic forms of Se include metal selenides, elemental selenium, and selenates (IV) and (VI). Organic forms of Se include selenium amino acids, methyl compounds, selenoproteins, selenocysteine, and selenomethionine [7].

Se was first reported as an essential nutrient for animals by Schwarz and Foltz [8]. In biological samples, Se is present in the form of selenomethionine and selenocysteine [9]. Se plays an important role in animals and human health [10]. In the human body, Se plays a significant role in various biochemical and physiological processes [11].

In farm animals, adequate Se intake prevents various disorders like white muscle disease, mulberry heart disease, dietary necrotic liver degeneration, parturition problems, retention of placenta, *post*-parturient paraplegia, and early embryonic mortality [12]. In cattle, Se supplementation reduces postpartum reproductive disorders like ovarian cysts and metritis [13]. Se also plays an important role in udder health, preventing clinical and subclinical mastitis [14]. Se is a structural component of important proteins involved in defense mechanisms [15]. Further, Se occupies an important part in these proteins [16]. The body cannot produce Se by itself. Forage is a natural source of Se for animals [17]. Selenium is usually deficient in the soil, and the current extensive farming strategies tend to favor Se deficiency [18]. The soil Se concentration differs to a great extent even within small areas.

Therefore, in livestock animals, Se supplementation is advised so that the minimum intake level is certain [19]. Dairy cattle require Se at the rate of 300 μg/kg DM [13]. Recently, several studies have recommended that organic Se is superior to the inorganic form of Se in dairy cattle [20].

2. Absorption, Distribution, Metabolism, and Excretion of Se

Mechanisms of Se homeostasis are important because the element is potentially toxic as well as an essential micronutrient [21]. The Se is absorbed from the small intestine. Organic Se is obtained by the body from selenized yeast and basal feed ingredients in the form of seleno-amino acids (i.e., selenocysteine and selenomethionine), while inorganic selenium supplementation provides selenate and selenite. Seleno-methionine (Se-Methionine) is absorbed via methionine transporter system, selenate is absorbed by active transport system while absorption of selenite mostly takes place by passive diffusion [22]. Rate of absorption of organic Se is higher than inorganic Se [23]. Inorganic Se is mostly reduced to insoluble elemental Se or is readily absorbed into feed particles in the digestive tract [24], resulting in excretion of most of the Se [25]. In contrast, most of organic Se (in form of Se-Methionine) is incorporated in rumen microorganisms so less elemental Se is formed.

Oral bioavailability of Se-Methionine is, therefore, greater than that of inorganic Se [26]. In blood, Se is bound to low density lipoprotein (LDL), very low-density lipoprotein (VLDL), albumin, and α and β-globulins [27]. Most of the Se in body fluids and tissues is present either in the form of Se-methionine or selenocysteine [28]. In cattle, kidneys are the site of the highest density of Se, and muscles are the site of the highest concentration of Se [29]. The highest amount of Se is stored in the kidneys followed by the liver, testis, and lungs [30]. Liver, heart, and skeletal muscles are most sensitive to Se deficiency [29]. The liver is considered the Se storage organ to which a considerable amount of Se is directed during absorption for accumulation [31]. In cattle, concentration of Se rises in serum two to six days following increased supplementation in diet [32].

Various organic and inorganic Se sources are first transformed to inorganic selenide before synthesis of Se-cysteine which, in turn, contributes to the bioactive component of Selenoproteins. Following absorption, Se-Methionine can be found in plasma methionine pool and blood proteins as it is transported to body tissues. One of example of the transportation is extraction of large amounts of methionine by the mammary gland for milk protein synthesis, resulting in a large quantity of Se in milk, which is beneficial to the neonate and human consumers [33]. With an increase in Se intake in Se deficient animals, the concentration of Se in tissues and the whole body rises sharply due to accumulation of Se in tissues as selenoproteins until adequate body Se status is achieved. However, the rate of Se excretion increases once the body requirement for Se has been fulfilled, thereby reducing its further accumulation [34]. The liver plays an important role in Se excretion [35]. Excretion of Se is important for regulation of whole-body Se [34]. Se is excreted in urine, feces, exhaled breath, loss of skin, and hair cells [36]. Polymethylation of selenide takes place before excretion. Dimethyl selenide is excreted in feces and breath, while the cation $(CH_3)_3Se^+$ is excreted in urine [31]. With an increase in the amount of dietary Se supplementation, the concentration of Se excretion in urine and feces increases. However, the form of Se intake does not influence the concentration of Se excreted [37].

3. Role of Se in Antioxidant Defense Mechanism

Oxidation is a process in which loss of electrons occurs [38]. Oxidation reactions are very important for life, but they can also have detrimental effects [39]. These reactions may produce reactive oxygen species (ROS) [40]. ROS can cause oxidative damage and cell death in case of excessive production [41]. ROS damage macromolecules of the cells leading to lipid peroxidation, nucleic acid, and protein alterations. Formation of ROS is considered as a pathobiochemical mechanism involved in progression or initiation phase of various diseases. To maintain correct cell signaling, radical scavenging enzymes must maintain a threshold level ROS inside the cell. Otherwise, increased ROS production not only causes excessive signals to the cells, but also directly damages key components in signaling pathways [42]. Animals with high productive performance are more susceptible to oxidative stress, resulting in their lower productive and reproductive performance [43].

Under stress conditions, the antioxidant system of the body requires dietary antioxidant supplementation via water/feed, as it cannot deal with excessive ROS formation properly [44]. Antioxidant is a natural or man-made substance that may prevent or delay some types of cell damage [39]. Antioxidants play a significant role in the body's defense system against reactive oxygen species (ROS) [45]. Se is one of the important feed derived antioxidants [43]. Se is an important part of 25 selenoproteins identified in animals [43]. More than half of these proteins are involved in redox balance and antioxidant defense of the body [44]. Important families of selenoproteins include iodothyronine deiodinases, thioredoxin reductases, and glutathione peroxidases (GPX) [45]. The GPX, for example, protects cells against oxidative injury [46]. Activity of this enzyme is better in cows fed Se supplemented diets compared to cows fed Se deficient diets [47–49].

To kill phagocytized bacteria, neutrophils must provide a high oxidizing intracellular environment, but at the same time they must also maintain a balance between reactive oxygen metabolites (H_2O_2 and superoxide [O^{2-}]) so that cell damage and death can be avoided [33]. In neutrophils of Se deficient cattle, GPX activity and oxygen consumption is lower than normal [50]. This results in oxidative injury of body cells [46]. Due to healthy GPX activity, destruction of cellular proteins and necrosis can be avoided, as it neutralizes the effects of lipid hydroperoxide and hydrogen peroxide [51]. Organic Se is superior to inorganic Se in improving antioxidant status in dairy animals [44].

4. Role of Se in Milk Production

General health of the animal, health of the mammary gland, environmental conditions such as insufficient nutrient intake, intensity of production system, and low corporal condition directly influence milk production [52]. Production can be improved in lactating dairy cows by supplementation of organic trace minerals [53]. Se is one of the trace minerals [54]. It is an essential element in ruminant nutrition [54,55]. Deficiency of Se impairs the immune function, leading to a higher risk of illness including that of the udder, which results in lower milk production [56].

Se helps to decrease linear somatic cell count scores [14]. Se affects innate and adaptive immune responses of the mammary gland through humoral and cellular activities [57]. It improves the bactericidal effects of milk and blood neutrophils [58]. It, therefore, prevents the incidence of mastitis [59]. In short, higher milk production in response to supplementation of Se is due to improvement in immune system brought about by Se [60].

Se yeast also improves feed digestibility, resulting in improved milk production [61]. There is a better incorporation and uptake of selenium when it is supplemented as selenium yeast [56]. Yeast based Se retains higher in tissues than inorganic Se and ensures sufficient Se availability for disease reduction [62]. Supplementation of Se in yeast form increases milk production by 24.8% [63]. When Se is supplemented along with vit E, a payback of 0.21 US cents/animal/day can be increased [64].

5. Role of Se in Feed Intake, Feed Utilization, and Body Growth

Feed intake is a critical factor for milk production of dairy cattle. The intake generally declines under heat stress to reduce metabolic heat production [65]. Feeding management is one of the key factors to enhance feed intake of dairy cows. [66]. Supplementation of diet with supranutritional Se and vit E enhances feed intake in heat stress condition by improving antioxidant status and thyroid hormone activity [67]. Se supplementation also improves growth performance in heifers, especially during the early stages of growth [68]. Se participates in important enzymes and enzyme reactions [69,70]. For example, Se helps in the expression of iodothyronine deiodinases, which regulate active T3 hormone production in peripheral tissues and the thyroid gland to improve metabolism and growth [71]. Thyroid peroxidase is also a selenoenzyme important for the process of iodization of globulin, thus avoiding damage to the thyroid epithelial cell membrane [72,73].

Supplementing Se enhances organic matter (OM) and crude protein (CP) intake [74]. Se supplementation improves total digestible nutrients (TDN) intake [68]. A higher TDN intake improves microbial efficiency in cattle. Due to differences in metabolism, the organic form of Se has better bioavailability compared to the inorganic form [75]. Supplementation of Se in yeast form improves digestibility of dry matter (DM), organic matter (OM), crude protein, neutral detergent fiber (NDF), and acid detergent fiber [76]. Se yeast improves feed digestibility in lactating dairy cows [61].

6. Role of Se in Cattle Reproductive Performance

Reproductive performance, such as age at first calving and calving interval, are important for improving productivity and profitability of dairy cows [77]. Trace minerals play very important roles in improving reproductive health and performance [78]. Fertility in dairy cows is getting worse in recent years, so enhancement of the conception rate has become an important issue. Although multiple factors are responsible for the declining fertility, improving the function of corpus luteum (CL) is one of the focuses of recent studies [79]. The function of CL is very important for reproduction according to many researchers [79]. For example, it was found that a reduced level of progesterone (P4) in plasma during the ovulatory follicles' growth is associated with decreased conception rate [80], and a low level of plasma progesterone in the blood was associated with low survivability of the embryo during early pregnancy [81]. Progesterone concentration in blood plasma of dairy cows supplemented with selenium enriched yeast shows an early increase compared to cows to which no selenium is fed [79]. Se increases proliferation of bovine corpus luteal cells by degrading lipid peroxides resulting in increased progesterone concentration [82]. This improved luteal function helps in preventing early embryonic death [83]. So, Se supplementation improves fertility by reducing embryonic death during the first month of gestation [13].

Se supplementation also improves estrous percentage and results in lower age at first conception [84]. Supplementation of diet with organic Se in lactation and transition period improves the immune function and health of the uterus followed by improved reproductive performance [85]. Pregnancy enhances oxidative stress and vitamin E, and Se supplementation reduces the stress [86]. Deficiency of Se is usually associated with a high risk of metritis, retention of placenta, abortion, increased susceptibility to infections, and lower fertility [87]. Se supplementation improves the rate of reproduction. However, results are best when Se is supplemented as Se yeast. There is a better incorporation and uptake of selenium when it is supplemented as Selenium yeast [56].

7. Toxicity and Concluding Remarks

Se is an indispensable micronutrient in animals and is a fundamental part of seleno-enzymes. However, its excess is toxic for animals [88]. Toxicity of Se was described long before its actual discovery. In 1295, Marco Polo observed that in the north-eastern region of China, hooves of animals consuming a particular type of plant became deformed [89]. At the turn of the nineteenth century, it was discovered by US researchers that similar situation arose in cattle due to eating plants containing Se in large quantities [10,90].

Different factors, like routes of administration of Se, species of animals, and chemical forms of the element, influence the severity of Se poisoning. The soluble salts of Se (Na_2SeO_3 and Na2SeO_4) are among the more toxic compounds; seleno-aminoacids and Se inherent in grains are relatively moderately toxic; the poorly soluble forms (e.g., diphenyl selenide, SeS_2, Na_2Se, and elemental Se) are among the least toxic of the Se compounds. Oral administration of Se poses less chances of toxicity than parental administration [91].

Chronic selenosis, often called alkali disease and acute selenosis, popularly known as blind staggers, are the most common form of selenosis [12]. Animals consuming feed containing Se at the rate of 5–8 mg/kg of dry matter are at risk of Se toxicity [92,93]. Livestock within 1 km of toxic farms is at risk of the toxicity. Therefore, blood samples from the livestock within 5 miles of known toxic farms should be tested for levels of Se before supplementation with the mineral [94].

Acute poisoning is not common due to the unpalatability of plants with high Se levels. However, hungry animals may eat such plants and thus suffer from acute poisoning. In cattle, acute poisoning is characterized by watery diarrhea, abnormal posture and movement, labored respiration, indications of abdominal pain, elevated temperature, prostration, and death. Chronic selenium poisoning may result from consumption of seleniferous feed over prolonged periods such as weeks or months. Important signs of the poisoning in cattle include hoof malformations, emaciation, loss of hair, and lameness [95]. In advanced cases, atrophy of the heart, anemia, and liver cirrhosis occur [91]. Excess Se intake impairs some immunological functions [96].

It is concluded from the present review that Se supplementation, especially in organic form, improves immunity, feed utilization, reproductive performance, and milk production in dairy cattle (Figure 1).

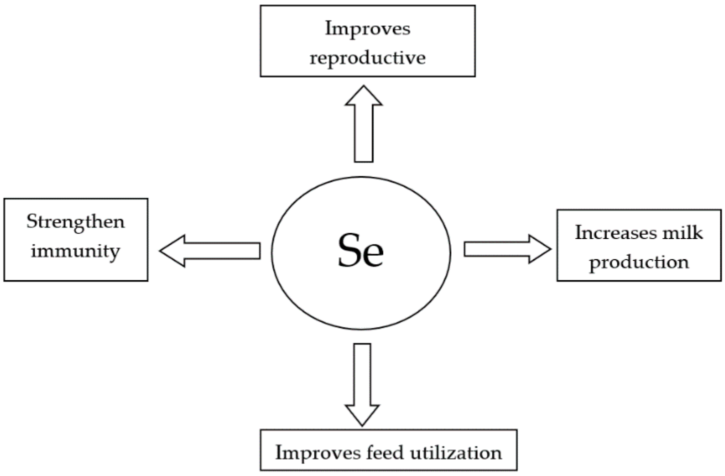

Figure 1. Benefits of Se supplementation in dairy cattle nutrition.

Lastly, excessive antioxidant supplementation generally can lead to an increased production of ROS [97,98]. Inorganic Se (selenite) is more toxic than the organic form. Inorganic Se reacts with glutathione, resulting in formation of selenotrisulphides which, in turn, react with other thiols and thus lead to the generation of oxygen free radicals, for example, superoxide anion. Organic Se is converted into selenols. This also results in the generation of oxygen free radicals inducing oxidative stress [88]. Mineral sulphates given in high doses can antagonize Se [94]. Deficiency of Se [99] is a much more common problem than its toxicity.

Table 1 summarizes the effects of the different forms of Se supplementation on productive and reproductive parameters, as well as the health status of dairy cows.

Table 1. Effect of Se supplementation on different parameters of dairy cows. DM: Dry matter; OM: Organic matter; NDF: Neutral detergent fiber; NFC: Non-fiber carbohydrates.

Parameter	Form of Se	Dose of Se	Effect	Reference
Milk production	Organic	0.15 mg/kg DMI	Increased	[61]
	Organic	0.3 mg/kg DMI	Increased	[61,63,64]
	Organic	0.4 mg/kg DMI	Decreased	[63]
Neutrophil function	Inorganic/sodium selenite	10 µM	Improved	[58]
	Organic	0.3 mg/kg DMI	Increased	[33]
Adaptive immunity	Organic	0.3 mg/kg DMI	Improved	[33]
Somatic cell count	Organic	0.3 mg/kg DMI	Decreased	[33]

Table 1. *Cont.*

Parameter	Form of Se	Dose of Se	Effect	Reference
Milk fat	Organic	0.3 mg/kg DMI	Increased	[100]
	Nano particles	0.3 mg/kg DMI	Increased	[100]
	Organic	0.3 mg/kg DMI	Increased	[33]
Milk protein	Organic	0.3 mg/kg DMI	Increased	[100]
	Nano particles	0.3 mg/kg DMI	Increased	[100]
Digestibility (DM, OM, NDF, Ether extract, NFC)	Organic	0.3 mg/kg DMI	Increased	[100]
	Nano particles	0.3 mg/kg DMI	Increased	[100]
Plasma P4	Inorganic	0.5 mg/kg DMI	Increased	[101]
Serum Se	Organic + Inorganic	105 mg/week + 0.3 mg/kg DMI	Increased	[102]
Plasma Se	Organic	0.3 mg/kg DMI	Increased	[33]
Whole blood Se concentration	Organic + Inorganic	105 mg/week + 0.3 mg/kg DMI	Increased	[102]
Serum amyloid A	Organic + Inorganic	105 mg/week + 0.3 mg/kg DMI	Increased	[102]
Erythrocyte glutathione	Organic + Inorganic	105 mg/week + 0.3 mg/kg DMI	Increased	[102]
Serum albumin concentration	Organic + Inorganic	105 mg/week + 0.3 mg/kg DMI	Increased	[102]
Serum cholesterol concentration	Organic + Inorganic	105 mg/week + 0.3 mg/kg DMI	Decreased	[102]
α-tocopherol/cholesterol ratio	Organic + Inorganic	105 mg/week + 0.3 mg/kg DMI	Increased	[102]
Uterine health	Organic	0.3 mg/kg DMI	Improved	[33]
Second service pregnancy rate	Organic	0.3 mg/kg DMI	increased	[33]

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