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A Recent Examination of the Impact of Selenium Supplementation to Lactating Cattle

AUTHORS DETAIL

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INTRODUCTION

An adequate dietary intake of minerals (macro- and micronutrients) is fundamental for any cellular life on earth. Among micronutrients, selenium has been the subject of a continuous debate when it comes to human as well as animal nutrition. From toxicity to deficiency, research on selenium has come a long way since its discovery in 1817 by the Swedish chemist Jons Jacob Berzelius (Cobo-Angel et al. 2014).

Like any other animal enterprise, selenium is shown to be an indispensable element in dairy nutrition promoting the overall health status of animal viz. improving gut health, regulating immune system, balancing thyroid hormones, contributing to disease resistance and boosting reproductive performance (Séboussi et al. 2016; Arshad et al. 2021; Xiao et al. 2021). All these vital roles of selenium originate from the fact that it is incorporated in range of selenoproteins (Labunskyy et al. 2014) which are directly or indirectly involved in antioxidant defences (Sun et al. 2019). Research has established that synthesis of selenoproteins is affected by the nutritional level of selenium (Han et al. 2021). Thus, low levels of selenium in diet or, more precisely reduced selenoprotein synthesis in body ultimately affects various metabolic processes (Pedrero and Madrid 2009).

Dietary supplementation of different selenium compounds to farm animals also enhance the nutritional quality of final food product. All these valuable contributions in livestock make selenium a fascinating nutrient, and any half-measures in its supplementation would have far reaching consequences other than compromised animal health and production (Salman et al. 2013; Ianni et al. 2019).

Requirement

Ruminants exclusively depend on diets of plant origin as source of fiber along with other nutrients. These plants, via conversion of selenium salts to different organic forms (mainly selenomethionine) and their subsequent non-specific incorporation into plant proteins, introduces the selenium into human and livestock diets (Calamari et al. 2010). Most of the world soils are deficient in selenium, and different forages grown on them are unable to meet animal requirements (Filley et al. 2007; Sordillo 2013). Moreover, extensive farming strategies along with the legislature prohibiting the use of selenium-based fertilizers inflict lower selenium levels in the soil which consequently translate into lower intake by livestock, thus, necessitating external supplementation of selenium (Davy et al. 2016).

The National Research Council (2001) has set dairy cattle selenium requirement at 0.3 mg/kg feed (DM basis) irrespective of age, physiological stage of animal and selenium form (Oltramari et al. 2014). These propositions most probably intended to prevent the element deficiency in animal rather than health optimization or toxicity prevention (Sordillo 2013). National Research Council (2005) recognized 5 mg selenium/kg feed (DM basis) as maximum tolerable level for ruminants. For dairy nutrition, United States (Food and Drug Administration, 2003) and Canada (Canadian Food Inspection Agency 2015), limit external selenium supplementation to 0.3mg/kg dry matter regardless of the form used, which is roughly equivalent to 3 mg selenium per animal per day. In the European Union, cattle can be fed diets with a maximum of 0.5 mg/kg DM of total dietary selenium with 0.2 mg/kg DM organic selenium at the most (EFSA 2013). Recently, Hendriks and Laven (2020) compared selenium allowances for dairy cattle raised in New Zealand with other parts of the world; attributing to dominant pasture-based diet for better part of the year with adequate vitamin E and polyunsaturated fats. They recommended that feeding the cattle at 0.03 mg selenium/kg DM should be enough.

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In dairy, a single fixed recommendation for dietary selenium seems irrational. The generally accepted recommendation (0.3mg/kg DM) may not be sufficient for cattle at a particular stage (transition period) or when animal is under stress (heat stress) (Gong and Xiao 2021). During the pre- and postpartum period in cows, beneficial role of dietary selenium at slightly higher concentrations than recommended have already been tested in many studies (Kamada 2017; Khalili et al. 2019). Based on various factors viz. animal productivity, body vitamin E status, ingestion of polyunsaturated fatty acids, ambient temperature etc. Suttle (2010) articulated a hierarchy of selenium requirement in cattle which suggested that it is the balance between anti- and prooxidants at any stage or time which determines selenium demand of animal. Increase in body oxidant state will increase the body selenium requirements and vice versa (Hendriks and Laven 2020). A good deal of published studies also stated manifold increase in milk selenium concentration when cattle were fed with supra-nutritional quantities of selenium (Givens et al. 2004; Walker et al. 2010; Sun et al. 2021). However, farmers and legislation authorities must be attentive to the threat posed by such high levels of selenium in animal diets to avoid any environmental hazard. For this, considerable attention should be given to the form of selenium present in the feed supplement.

Sources (inorganic vs. organic)

A great deal of information has been accumulated over a span of years indicating the paramount importance of dietary form of selenium when it comes to bioactivity and metabolic fate of the element (Suttle 2010). In general, there are two selenium sources in cattle diets: (A) native feedstuffs mainly comprising roughages and grains (may include drinking water), and (B) supplemental selenium primarily via mineral premixes or salt blocks. Typically, feedstuffs of plant origin contain selenomethionine accounting for 55-65% of selenium (Whanger 2002) whereas external supplemental sources exist in either inorganic (salts of selenite and selenate) or organic form (selenium yeast or pure selenomethionine preparations) (Surai 2006; Silvestre et al. 2007) (Fig. 1).

Various studies have been made to assess the role of inorganic and organic selenium in dairy nutrition, based specifically on bioavailability, state of production and reproduction, body antioxidative status, tissue accumulation, udder health, milk transference, dam-calf transfer efficiency, toxicity risk assessment and environmental pollution. Most often, such comparative analyses showed notable positive responses with organic forms. Therefore, in recent years, utilization of organic selenium supplements in livestock nutrition has gained considerable interest, however, relatively low prices of inorganic salts still entangle the usage of organic supplements in practical farming (Weiss 2005; Sun et al. 2017).

The bio-efficiency of organic forms revolve around their selenomethionine content rather than total selenium levels (Juniper et al. 2019). Surai et al. (2017) summarized the commercial selenium products into three generations: inorganic selenium salts being the first but outdated one; selenium yeast, pure selenomethionine and Zn-selenomethionine comprising the second generation; hydroxy-selenomethionine, the third generation. Limited productivity of inorganic forms, complications in producing yeast products with constant selenomethionine levels, and instability (oxidation) of the pure selenomethionine supplements paved the way for hydroxy selenomethionine products. They also questioned eligibility of nano selenium as organic supplement along with chelated selenium products viz. glycinates, proteinates and various amino acid complexes, as these are not the methionine bound forms.

Other than application of selenium into ruminant diets via mineral premixes, there have been attempts to increase the selenium concentration of native forages using selenium-based fertilizers (Cun et al. 2015; Séboussi et al. 2016). However, due to the narrow window between selenium toxicity and necessity, there are legislative restrictions, and not all the countries allow the use of selenium fertilizers (Tremblay et al. 2015). In any case, learned decisions involving selenium supplementation in an optimal form and amount are vital in any livestock enterprise to prevent deficiency diseases along with toxicity and environmental pollution.

Absorption and Metabolism

In dairy cattle, metabolic fate of dietary selenium is complicated by the rumen physiology when compared to non-ruminants. Thus, rumen is the major determinant of the nutritional value of given selenium source, even though duodenum is the part involved with most of the absorption. Metabolic fate of ingested selenium from different dietary sources in dairy cattle is shown in Fig. 2. Young ruminants absorb dietary selenium with almost similar efficiency as non-ruminants (Freer 2007; Salles et al. 2017).

Ruminal metabolism of inorganic selenium involves the conversion of selenate (firstly reduced to selenite) and selenite to low molecular insoluble forms which are supposedly not well utilized by animal and are excreted from the body (Salles et al. 2017). Literature also showed synthesis of selenoamino acids (predominantly Se-cysteine) in rumen from selenite, which are later incorporated into microbial protein. Besides, some quantities of ingested selenate and selenite also pass the rumen unchanged and are absorbed in lower part of the gastro-intestinal tract by active and passive pathways, respectively. In a trial with mid-lactation cows, Wei et al. (2019) found selenium apparent absorption of 49.5 and 59.7% with sodium selenite and hydroxy analogue of selenomethionine, respectively. Poor absorption of inorganic selenium could be attributed to the ruminal environment where microorganisms reduced them to insoluble forms. Niwińska and Andrzejewski (2017) unveiled that coating of

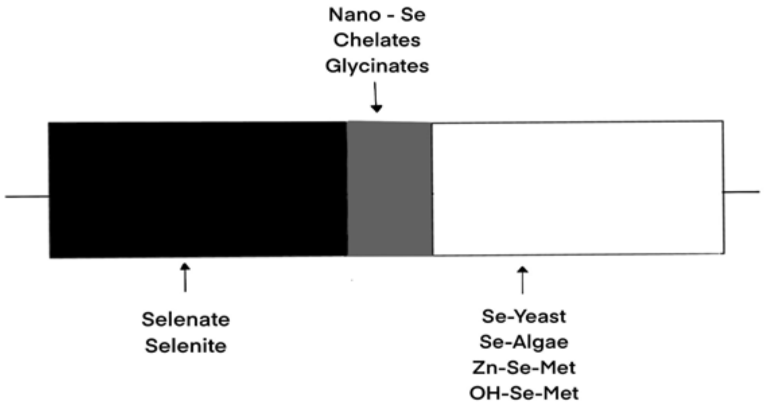

Fig. 1: Major commercialy available selenium supplement

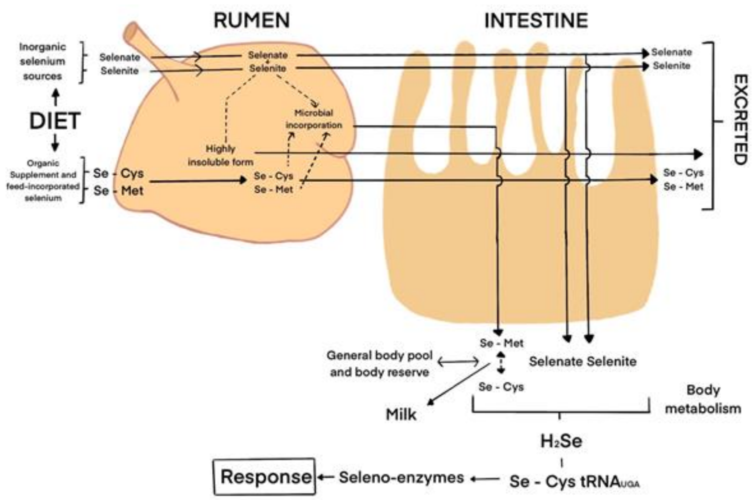

Fig. 2: Metabolic fate of ingested selenium from different diatetary sources in dairy cattle.

inorganic selenium sources with rumen insoluble compounds could increase their availability, supposedly by increasing their incorporation into microbial proteins instead of being reduced to insoluble forms.

Conversely, organic forms packed with selenoamino acids (mainly selenomethionine) encounter fewer alterations in rumen than inorganic sources. Selenomethionine and selenocysteine, upon reaching the small intestine, are absorbed following the routes similar to methionine and cysteine. A higher proportion of selenium from selenomethionine is incorporated into microbial protein than selenite (Mainville et al. 2009). Weiss (2005) stated that greater amounts of selenium as selenomethionine escape the rumen with selenium yeast feeding than selenite or selenate.

The increase uptake of selenium by ruminal microbes might be the reason behind improved bioavailability of selenium in small intestine of ruminants (Hall et al. 2012). Furthermore, in a comparison between selenium yeast and selenium-fertilized forages, Séboussi et al. (2016) reported higher selenium availability from forages and suggested higher digestibility of selenium fed with biofortified forages than selenium yeast, although cattle intake of selenium was higher in forage diets. Nonetheless, in addition to the variable digestion of forages and yeast wall, they attributed these results to longer ruminal retention time of forages and better selenium dispersion in the ration and rumen leading to better selenium accumulation into microbial proteins.

Irrespective of the form absorbed (selenite, selenate, Se-Met, Se-Cysteine), selenium must be metabolically reduced to inorganic selenide which is then used in the synthesis of Se-Cysteine-tRNA, an active centre for various selenoenzymes (Suzuki and Ogra 2002; Surai 2006). Direct insertion of absorbed Se-Cysteine is not possible as it doesn't possess correct tRNA for selenoenzyme synthesis. So, it must be reduced to selenide which would be used in the Se-Cysteine-tRNA formation (Weiss 2005). Selenomethionine, after absorption, could enter 'general methionine pool', thus, non-specifically incorporating into different body proteins providing a means of reversible selenium reserves which can be later utilized as an endogenous selenium supply for synthesis of selenoenzymes (Schrauzer 2003; Burk and Hill 2015). The selenium homeostasis in body is primarily achieved

by the reserves of selenomethionine in kidney and liver. Before these reserves could be used in the biosynthesis of specific selenoproteins, selenomethionine must be catabolized to Se-Cysteine-tRNA for insertion into the active site of selenoenzyme (Weiss and Hogan 2005). Metabolism of hydroxy-selenomethionine, a precursor of selenomethionine, is also similar to that of selenomethionine (Surai et al. 2017).
To put it briefly, dietary intake of protein (quantity and quality) and its influence on microbial protein synthesis would impact the microbial incorporation of different selenium sources in the rumen. Also, inorganic selenium sources are exclusively associated with the production of selenoenzymes whereas fate of organic sources is split into two pathways viz. specific production of selenoenzymes and non-specific incorporation into different body proteins containing methionine/cysteine. It also highlights the build-up of greater body reserves of selenium with organic supplementation which would be beneficial to animal in times of stress or high demand (Gong and Xiao 2018; Gong and Xiao 2021).
Apart from the body tissue reserves, dairy cattle also deposit absorbed selenium into milk protein (casein) (Weiss and Hogan 2005). It is generally agreed that mineral status of dam is vital in determining the status in its offspring (Hostetler et al. 2003). Hair selenium content could also be used as long-term indicator of animal selenium status (Weiss et al. 1990). Other routes through which selenium leaves the body include feces, urine and exhalation. In ruminants, owing to their ruminal metabolism, major excretory pathway for dietary selenium is feces instead of urine which is major route in non-ruminants. Endogenous losses such as intestinal sloughing along with secretions of bile, pancreas, plasma, and saliva should also be accounted in fecal excretion when estimating true absorption of the mineral (Cruickshank 2021).
The presence of antagonists in the dietary milieu further complicates the circuitous route of selenium metabolism in ruminants. Many nutrient interactions involving vitamin E, sulphur, proteins, lipids, ascorbic acid and various microelements influence animal selenium requirements. Sulphate is less likely to hinder selenomethionine absorption as compared to inorganic supplements (Weiss and Hogan 2005), suggesting the plausibility that known antagonists of selenium might not treat the organic and inorganic supplements as same. Additionally, some other minerals have also been reported interfering with selenium absorption viz. copper, calcium, arsenic and cobalt (Goff 2018). Some intrinsic factors present within certain feedstuffs (i.e., soybean meal, millet, alfalfa) as well as the ratio between concentrate and forages also affect selenium availability to ruminants. Diversity of microbial populations and variation of the rumen fermenting environment with roughage and concentrate diets could be attributed to these manipulations (Spears 2003; Goff 2018).
Dietary supplementation of selenium to animals always results in a net gain of the element in environment. Therefore, caution should be taken to avoid disturbances in different agricultural production systems (Walker et al. 2010).

Feed (nutrient) Digestibilities

Major health beneficial role of selenium is indebted to its antioxidant properties. Similarly, development and operation of rumen is greatly obligated to its microbial efficiency. Research showed that it is possible to raise the antioxidant status of the ruminal microbiome using Se which results in increased microbial proliferation and rumen functioning (Arshad et al. 2021).
Most of the literature strongly agreed that neither the inclusion rate nor the source of selenium affected the feed intake in cows (Wang et al. 2009; Gong et al. 2014; Meyer et al. 2014; Juniper et al. 2019). Furthermore, there are reports of increased digestibilities of dry matter, organic matter, fiber (NDF and ADF), crude protein and crude fat with the addition of selenium in dairy cattle diets (Wang et al. 2009; Wei et al. 2019). Supplementary selenium also exhibited modifications in the ruminal fermentation patterns viz. acceleration in the total volatile fatty acid production especially propionate, and increased consumption of ammonia N by microbes, thus, suggesting improvement in the microbial fermentation rate in the rumen (Wang et al. 2009). On top, high proportions of propionate may potentially be instrumental in gluconeogenesis in dairy cattle during post-partum period (Gong and Xiao 2021), thus improving nutrient metabolism and responding to the challenge of negative energy balance.
In summary, via enhanced activity of microbes or enzymes, supplementation of selenium either inorganic or organic contributes to the act of fermentation in rumen coinciding with improved nutrient digestibilities which might reflect in better growth or enhanced milk yield in dairy cattle.

Selenium Effects on Reproduction

Animal body redox homeostasis is crucial to its metabolic health, especially for high producing cattle during periparturient period (Sordillo 2013; Zhang et al. 2021), and any disturbance in the antioxidant status may led to pathogenesis of different diseases. Selenium is reported to aid in curtailing systemic inflammation response (via downregulation of inflammatory phase proteins) as well as in the optimization of the lipid metabolism (via promotion of glycogenesis) during and after parturition in dairy cattle (Ren et al. 2020; Gong and Xiao 2021).
Supply of adequate selenium to dairy cattle during peri-parturient period may enhance their reproductive performance via better uterine health, prevention of retained placenta, and reduction in open days and number of services per conception (Wilde 2006; Silvestre et al. 2007; Machado et al. 2013). Pre-partum selenium supplementation is also stated to improve cow fertility by avoiding early embryonic deaths, whilst no effects on gestation length are reported. Selenium feeding pre-partum is also linked to improved progesterone levels in cows (Kamada 2017; Ullah et al. 2019) which might be a factor avoiding early embryonic losses.

Inadequate or marginal selenium supply could result in low reproductive performances in dairy cattle i.e., higher incidences of uterine infections, retained placenta, ovarian cyst, anestrous, stillbirth, abortion etc. In case of male cattle, selenium shortage or excess may affect spermatogenesis, resulting in poor semen quality and even infertility (Ahsan et al. 2014).

Milk Biofortification with Selenium Supplementation and its Effect on Milk Yield and Composition

In attempts regarding production of milk biofortified with selenium, plenty of literature is available detailing the superiority of organic selenium over inorganic form (Weiss and Hogan 2005; Wang et al. 2009; Calamari et al. 2010; Walker et al. 2010; Meyer et al. 2014; Séboussi et al. 2016; Zhang et al. 2018). Data on bioactivity of organic selenium showed more efficient transfer of ingested selenium to milk attributable to its retention in milk protein (selenomethionine replacing methionine) via non-specific route. This inevitably amplify the importance of differentiating between the selenium forms used and its dosage rate in the animal ration. In addition to selenium sources, physiological condition of cow is also vital to influence the milk Se levels (Burk et al. 2001).

Literature also showed improvement in milk yield (Juan Eulogio et al. 2012; Li et al. 2019) and modifications in milk components including fat, protein, lactose (Li et al. 2019; Zhang et al. 2020) when dairy cattle were supplemented with different selenium sources.

Selenium distribution among different milk components is also important. Data showed that selenium is abundantly distributed in milk protein i.e., 55-75% in casein, 17-38% in whey, and around 7% in fat (Van Dael et al. 1991). Research also showed that selenium supplementation has no or little effect on selenium distribution pattern in milk components (Muñiz-Naveiro et al. 2005). Thus, it can be deduced that removing fat from the milk (skimmed milk) would have little effect on selenium concentration of milk.

Deficiency and Toxicity

Selenium deficiency is much dreaded geographically when compared with its toxicity (Khanal and Knight 2010). Generally, dietary intake of selenium lower than 0.05 mg/kg DM in both humans and animals is perceived as insufficient. In ruminants, severe selenium deficiency can trigger nutritional myopathies i.e., white muscle disease, primarily in young calves and selenium-responsive ill-thriftiness. In adult dairy cattle, it is very common to be inflicted with marginal selenium levels which predispose them to various maladies viz. enhanced oxidative susceptibility (reduced antioxidant capacity, poor response to oxidative stress), poor thyroid hormone regulation, inefficient feed utilization, impaired growth, impaired immune function, reproductive disorders (cystic ovaries, metritis, infertility, early embryonic death, retained fetal membranes, high calf mortality, increased number of services per conception, low pregnancy rates), and compromised udder health (clinical and subclinical mastitis, higher milk somatic cell counts, reduced milk production). It is of the essence that proper assessment of body selenium status be made via various indicators (milk, blood, tissue selenium levels) before treating the animals to avoid toxicity (Silvestre et al. 2007; Sordillo 2013; Hendriks and Laven 2020; Ullah et al. 2020; Arshad et al. 2021).

Although, selenium had a profound and lengthy history of toxicity, its occurrence in current livestock setup is uncommon by virtue of proper management practices. Nevertheless, liable to human error, faulty selenium supplementation culminating into excessive intakes by animals can lead to the toxicity syndrome (selenosis). Signs of selenosis may appear with prolonged ingestion of selenium ranging between 5 to 50 mg/kg DM (Kaneko et al. 2008). National Research Council (2005) recognized 5 mg selenium/kg feed (DM basis) as the maximum tolerable level for ruminants. Factors affecting the selenium toxicity may include type of diet, animal sex and species, selenium form and supplementation duration (Arshad et al. 2021). Selenosis is also known as “alkali disease” (chronic) or “blind staggers” (acute) (Zarczynska et al. 2013). Selenium toxicity in livestock is characterized by lethargy, emaciation, loss of hair, roughness of coat, aching and sloughing of hooves, stiffness and joint related lameness, atrophy of the heart, liver cirrhosis, anemia and teratogenic effects along with abortions/stillbirths (Schöne et al. 2013). Apart from incorrect supplementation, selenosis could be an outcome of ingesting ‘selenium accumulator plants’ viz. *Astragalus*, *Atriplex*. In modern dairy, it is very unusual for animals to develop selenosis. Quite contrarily, the bigger task is getting enough to stay healthy and perform optimally (Schöne et al. 2013).

Conclusion

Feeding dairy cattle with supplementary selenium (0.3-0.5 mg/kg DM) is undoubtedly valuable ensuring the optimum intake of this micro element by the animal especially during the periparturient period. A great deal of scientific data showed selenium to be an indispensable element in dairy nutrition promoting the health status of animal viz. improving gut health, regulating immune system, balancing thyroid hormones, contributing to disease resistance, boosting reproductive and productive performances. Moreover, the supplemental selenium potentially enhances the quality of final food product. Organic forms of selenium have been shown to be superior in terms of availability and execution of selenium-dependent responses. Usage of selenium biofortified forages in dairy diets has also been tried and proved beneficial but it is tied to the regional legislature. The overall selenium body status, calculated via different indicators (milk, blood, tissue etc.), assist the nutritionists in maintaining a delicate balance between the dark side (toxicity) and the bright side (productivity) of the selenium. The supra-nutritional doses of organic selenium in dairy cattle diets could aid in the production of functional food, however, its long-term effects on the trichotomy of animal, human and their environment needs further research.

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