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The importance of selenium and the effects of its deficiency in animal health☆

Abd El Ghany Hefnawy, J.L. Tórtora-Pérez*

Secretaria de Estudios de Posgrado, FES Cuautitlán, Universidad Nacional Autónoma de México (UNAM), Km 2.5 Carretera Cuautitlán-Teoloyucan, Cuautitlán Izcalli, CP 54700, Estado de México, México

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ABSTRACT

Selenium (Se) is an essential trace element in animal nutrition, and exerts multiple actions related to animal production, fertility and disease prevention. Glutathione peroxidase (GSH-PX) enzyme was the first proven selenoenzyme that can prevent oxidative damage of the cellular membrane. Actually more than 30 selenoenzymes have been described and a hierarchy process for expression in the animal has been established. 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 critical to thyroid hormone synthesis and it is also very important for converting T4 (thyroxin inactive form) to T3 (active form). A good immune response requires Se too. Selenium status in soil, plants and animal blood and tissue can be used in the diagnosis of Se deficiency. Diverse forms of Se supplements are available, but many factors affect their activity and efficacy, such as its chemical form and animal's health and production condition. The relationships between foetus Se metabolism and pregnant dam Se status are critical for productivity and need further research.

1. Introduction

Selenium (Se) toxicity is a serious threat when an excess of it is found in soils. The effects of intoxication were observed prior to establishing its importance as an essential microelement for animal life and its serious deficiency consequences (Allan et al., 1999; Driscoll and Copeland, 2003).

The importance of Se in animal physiology was first reported in 1957, when its deficiency was associated with that of vitamin E, which resulted in WMD (Muth et al., 1958). However, its biological significance as a structural part of "selenoenzymes" was understood until 1973 with the discovery of glutathione peroxidase (GSH-PX) and its role in the regulation of oxidative processes and cell membrane protection (Rotruck et al., 1973). In the same year, Se was reported as being a structural component of bacterial reductases (Stadtman, 2005). Currently at least 4 GSH-PXs have been recognized (Allan et al., 1999). A Se deficiency prevents the synthesis and function of GSH-PXs, which protect against peroxides generated in the intermediary metabolism of the cells with the oxidation of fats and proteins of the membranes. Thus, Se deficiency especially damages cellular and mitochondrial membranes (Combs and Combs, 1986; Behne and Kyriakopoulos, 2001).

The relationship of Se with thyroid activity was further identified, describing the role of thyroid peroxidase, a selenoenzyme, in the process of iodization of globulin, avoiding thyroid epithelial cell membranal damage (Gärtner et al., 2007; Schomburg et al., 2007). Deiodinases of peripheral tissues are also selenoenzymes, which are necessary for the

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* Corresponding author. Tel.: +52 55 5623 1843; fax: +52 55 5870 5668.
E-mail address: tortora@unam.mx (J.L. Tórtora-Pérez).

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activation of T3, from T4 (Beckett et al., 1987, 1993). These relationships between Se and thyroid function, explain the negative effects of Se deficiency in animal production.

Currently more than 30 selenoproteins have been described, most of which are involved in enzyme activity and metabolic regulation of oxidative processes, in all cases, animal or bacterial cells. Selenium is part of the active sites of enzymes by becoming a selenocysteine (Driscoll and Copeland, 2003; Stadtman, 2005; Beckett and Arthur, 2005; Köhrle et al., 2007). The ability to catalyse processes of oxidoreduction is associated with the increased capacity of ionization of selenol at physiological pH, on thiol groups (sulphur) of cysteine. Replacing selenocysteine by cysteine dramatically reduces the oxidorreductive ability of selenoenzymes (Driscoll and Copeland, 2003).

However, in microorganisms and plants, where Se is also associated with protein fractions, selenomethionine is the most abundant selenoaminoacid. Metiloselenocystein is the largest selenified compound in selenium-accumulating plants, and it is also present in roots of plants such as garlic and onions (Whanger, 2002). Metabolic function of selenomethionine in animals and humans has not been clarified and as highlighted in this paper, is not a suitable form for the supplementation of Se.

2. Consequences of Se deficiency

The lack of Se seriously affected productive efficiency and animal health, with high mortality in the offspring as a result of degenerative lesions in the myocardium (Ramírez et al., 2001a). Among the effects of Se deficiency on productive efficiency are lower weight gains (Sheppard et al., 1984; Oblitas et al., 2000), lower milk and wool production, reduced fertility and litter size (Segerson and Ganapathy, 1980; Sheppard et al., 1984) and low seminal quality (Beckett and Arthur, 2005).

The lowest activity of GSH-PX results in direct damage from peroxides on cell membranes, especially mitochondrial. It also increases the erythrocyte fragility consistent with anaemia, and damage to the endothelium membrane resulting in general oedema. Damage to membrane structures is also the basis of the knowledge that originally recognized Se deficiency as a health problem: i.e., white muscle disease (WMD) or nutritional muscular dystrophy (MND), with degenerative changes in skeletal muscle and in the myocardium of young animals (Norton and McCarthy, 1986; Spears et al., 1986; Gabryszuk and Klewiec, 2002).

Deficiency occurs when soil is poor in Se or contains high levels of other minerals competing for usage by plants. Small amounts of <0.5 mg/kg in the soil or <0.1 ng/kg in plants are considered insufficient (Ramírez et al., 2001a,b, 2004). There are clear correlations between the presence of Se in soil, plants and animal tissues (Sheppard et al., 1984; Pastrana et al., 1991; Ramírez et al., 2001a,b). In soils with adequate levels of Se, the presence of other minerals such as calcium, sulphur, copper and arsenic can interfere with its utilization by the plant. The presence in the diet of these same elements or of polyunsaturated fat and nitrates could also reduce their absorption in the small intestine (Combs and Combs, 1986).

Although Se deficiency can occur in all animal species, ruminants appear to be more susceptible to the disease, with more severity in small ruminants (sheep and goats). This has been associated with degenerative changes in the myocardium of lambs and kids and muscular dystrophy in adults (Ramírez et al., 2001a,b, 2004, 2005). This increased susceptibility in ruminants is attributed to the reticule–rumen environment, which generates insoluble forms, particularly selenurs, and a significant loss of the element resulting from their usage by rumen microorganisms. Ruminal microorganisms are involved in the conversion of a proportion of Se to insoluble forms (elementary Se and selenurs) and another portion is incorporated into bacterial proteins with the formation of selenoaminoacids (Harrison and Conrad, 1984a,b). Whanger (2002) reported that the rumen flora of adult sheep had reached an average Se concentration 46 times greater than the concentration in the diet they consumed. This microbial selenium would be of high digestibility for the ruminant, but its dominant form probably reflects selenomethionine of low metabolic efficiency. This could explain the lower diet Se absorption in ruminants compared to non-ruminants. Selenium availability of ruminants varies from 11 to 35%, while non-ruminants, under similar conditions utilize 77 to 85% of oral Se. The site of absorption of the element in both cases is the duodenum (Koenig et al., 1991; Groff et al., 1995).

3. The selenoproteins

Most of the selenium in the animal is tied to proteins. Since 1973, when it was demonstrated that the selenium was a constitutive part of the GSH-PX, slightly more than 30 proteins were discovered and most of them are enzymes. More than 80% of protein-bound Se is selenocysteine. The regulation and synthesis of these proteins and its behaviour in the different organs and tissues are highly dependent on selenium supply. If selenium is limited, the system gives priority to the central organs (brain, pituitary, thyroid, adrenals) for the synthesis of selenoenzymes; in these conditions the blood GSH-PX is the last priority (Behne and Kyriakopoulos, 2001; Driscoll and Copeland, 2003; Schomburg et al., 2007).

With *in vitro* models, using mammal cell cultures and bacteria, the addition of selenomethionine in the cultivation medium, increases both, Se incorporation into the cell and protein synthesis, but does not determine a better expression of the Se-dependent enzymatic activity. These results indicate that selenomethionine incorporation occurs in proteins that need methionine, but these proteins do not present Se-dependent biological activity (Allan et al., 1999; Behne and Kyriakopoulos, 2001). This information would explain the interpretation errors in studies (Jenkins and Hidiroglou, 1971) in which Se incorporation was measured using selenite and selenomethionine ^{75}Se. In these studies, the authors postulated the benefit of using selenomethionine as a source of Se, for its rapid incorporation into ewe milk proteins.

Experimental models with skin cell cultures have been used to prove the protective effect of Se to prevent cell death induced by UV radiation and the prioritization of cells to synthesise phospholipid hydroxyperoxidase

and thioredoxin reductase selenoenzymes. The protective effect against UV is 10 times more efficient when selenite (^{75}Se) is added to the culture than when selenomethionine (^{75}Se) is used. Although selenomethionine is quickly incorporated into the cells and to the new formed proteins in comparison with selenite, it does not generate active catalytic sites which avoid UV damage (Allan et al., 1999).

A pair of proteins that incorporate selenium in a non-specific form, not related to selenomethionine or selenocysteine, which participate in the transport and tissue storage of selenium are selenoprotein P in plasma and selenoprotein W in muscle (Behne and Kyriakopoulos, 2001; Driscoll and Copeland, 2003).

Ingested selenium is incorporated into specific selenoproteins such as the selenoenzyme selenocysteine, these proteins are responsible for the biological effects of the element. The strict homeostasis of these proteins prevents their rise, even in conditions of Se over-supplementation (Allan et al., 1999; Behne and Kyriakopoulos, 2001).

Incorporation of selenocysteine uses the UGA codon in the messenger RNA and anticodon ACA (Allan et al., 1999; Behne and Kyriakopoulos, 2001). The UGA codon normally serves as a signal of termination in protein synthesis, implying that for the insertion of the selenified amino acid, a translation factor is required. Incorporation of selenocysteine depends on a specific elongation factor (SelB), which replaces the normal elongation factor bound to Sec-tRNA, allowing the incorporation of selenocysteine, which is needed for protein synthesis to continue. In the absence of Sec-tRNA, the reading of UGA determines the completion of the synthesis, with the entry of the releasing factor of ribosome RF2 into UGA. Alosteric competition on relative concentrations of Sec-tRNA or RF2, will define in consequence, the synthesis of the selenoenzyme or the interruption of the process (Driscoll and Copeland, 2003).

The biosynthesis of selenocysteine takes place in the tRNA that originally transports serine and is transformed in a reaction with selenophosphate into selenocysteine-tRNA (Sec-tRNA). The enzyme responsible for this process of selenification is selenophosphate synthetase 2 (SPS2), the only selenoenzyme found in eucariots and procariots (Driscoll and Copeland, 2003). Selenoenzyme condition of the SPS2 suggests the possibility of a feedback mechanism dependent on selenium so that the element and its bioactive derivatives are incorporated into proteins, their availability for the synthesis of SPS2 and consequently selenoprotein synthesis is reduced (Driscoll and Copeland, 2003). Selenite is reduced to selenate and the later to selenophosphate, the only precursor of selenocysteine. However, selenomethionine is a source of available reduced metabolic selenium to generate selenocysteine (Allan et al., 1999; Behne and Kyriakopoulos, 2001).

In rats, with extreme Se deficiency, prioritization in organs determines that Se concentrations in the liver, muscle or blood are below 1% of normal, whereas in the brain is 60% of normal. In this hierarchy, the brain is followed by the spinal cord, pituitary, thyroid, ovaries and adrenal gland. In these tissues, the synthesis of selenoenzyme phospholipid hydroperoxidase (PHGSH-PX) is a priority against plasmatic and cellular GSH-PXs (Behne and Kyriakopoulos, 2001). This information requires revaluing the responses to Se supplementation, when the element is measured in the blood, liver or by the activity of GSH-PX.

The hierarchy process of selenoenzyme expression in Se deficiency condition involves various mechanisms, including variation in stability of messenger RNA (mRNA) (Behne and Kyriakopoulos, 2001). In deprived selenium cell cultures, GSH-PX and thyroid deiodinase (5′DI) type I demonstrated marginal activities; when selenite is added to the cell medium, 5′DI activity increases after selenite concentration of 0.5 nM, while GSH-PX activity increases until 1 nM selenite level. The consequence of none or a low level of selenite in the cell medium is that the mRNA of GSH-PX is rapidly deteriorating, while there is an increase in the activity of the 5′DI mRNA (Allan et al., 1999).

4. Se and thyroid function

Presumably, because of the importance of selenoenzymes on the thyroid function in humans, the gland contains a larger amount of Se per gram of tissue than any other organ (Beckett and Arthur, 2005). In a gross examination of animals with Se deficiency, the thyroid gland appears pale, from beige to light brown (Tórtora, 1979). A histopathological exam showed significant differences in the follicular size, with the presence of large and dilated follicles, with low epithelial cells (goitrogen type) coexisting with much smaller follicles presenting a columnar epithelium (embryonic-type). However, and despite the demonstrated functional relationships, the information in this regard is limited (Tórtora, 1979). In Se supplemented sheep, the thyroid gland showed epithelial hyperplasia of the follicular epithelium with folded appearance. Some of these follicles show condensed nuclei, which are suggestive of an apoptosis processes (unpublished data). Similar injuries were demonstrated in human and experimental rats (Contempré et al., 2004; Köhrle et al., 2007). The relationship of Se with the thyroid activity is not only associated with the activity of peroxidase in the synthesis of the thyroid hormone, but also with the activity of the thyroid deiodinases, selenoenzymes which catalyse the activation of T3 from T4 (Beckett et al., 1987; Holben, 1999; Beckett and Arthur, 2005; Köhrle et al., 2007). With Se deficiency there is a significant reduction in T3, an increase in T4 and a reduction in the activity of the liver 5′DI type I (Arthur et al., 1988; Beckett et al., 1993; Thompson et al., 1995; Wichtel et al., 1996; Awadeh et al., 1998; Rock, 1998; Rock et al., 2001; Köhrle et al., 2007). Calves supplemented with Se ruminal bolus released 3 mg Se/day, and presented significantly higher plasma T3 levels than calves with basal diets of 0.03 mg of Se per kg DM (Wichtel et al., 1996). Sheep supplemented with inorganic Se salts and "selenoyeast" had higher levels of T3 in comparison with the non-supplemented controls (Rock, 1998).

5. Se and immune response

Se deficiency affects blood levels of IgG and T cell function, and this determines a higher prevalence and severity of present diseases in animal populations (John et al., 2003). The activity and life span of neutrophils, macrophages and lymphocytes diminishes, perhaps because of a decrease

in the activity of GSH-PX. This condition would limit further the antigen processing and antigen presentation, thus limiting the humoral response (Aziz et al., 1984; Awadeh et al., 1998; Altimira et al., 2000). The use of Se as an immune system stimulant has a positive impact on the immune response and quality of the colostrum (Jendryczko, 1994). Neutrophils from Se supplemented cows show greater phagocytic and bactericide activities against *Staphylococcus aureus* and *Candida albicans*, and increase the production of leukotrienes (Grasso et al., 1990; Jukola et al., 1996). The production and activity of the chemotactic factors and migration of white blood cells is reduced in Se deprived animals (Aziz and Klesius, 1985; Droke and Loerch, 1989; Jukola et al., 1996).

A response of Se supplementation on IgG production has shown contrasting results, increasing in adult sheep and calves, whereas not affecting lambs supplemented with different doses of Se (Larsen, 1988, 1993). Positive correlations between blood Se levels and increased concentrations of IgG in serum and colostrums have been reported in cows, which have been associated with higher serum IgG levels in their calves (Swecker et al., 1995; Awadeh et al., 1998). In sheep, supplementation increased the levels of Se in blood and colostrums, and in the blood and liver of their lambs (Rock et al., 2001; Abd El-Ghany et al., 2008), with a greater absorption of collostrum IgG (Rock et al., 2001). In cows with poor body condition, a deficient immune response was associated with smaller accounts of T lymphocytes, whereas Se supplementation induced "immunostimulant" effects. Similar effects were demonstrated *in vitro* models (Jendryczko, 1994; Pollock et al., 1994; Taylor, 1995).

6. Muscular pathology of Se deficiency

The white muscle disease or nutritional muscular dystrophy (NMD) is characterized by difficulty in walking and abnormal postural positions in adult animals. Thus, in the first weeks of life, degenerative changes in the skeletal muscle fibres with greater metabolic activity, as well as in cardiac muscle fibres, results in sudden death of the offspring (Silva et al., 2000). The presence of NMD remains as the central component in the suspected Se deficiency, where the Se levels or GSH-PX activity cannot be determined. Muscle fibres are swollen and fragmented, but in the unaffected remaining fibres proliferation of nuclei can be observed as an attempt to repair the damage. Necrotic fibres are infiltrated with macrophages and fibroblasts, which in histological analysis result in a notorious nuclear accumulation in the affected areas (Hulland, 1985; Bostedt and Schramel, 1990; Ramírez et al., 2001a; Beytut et al., 2002). Degenerated fibres may present an intense reaction to the hematoxylin with deposition of calcium in the cells. Exceptionally, in chronic cases, calcificated muscles can be seen in gross necropsy examination, this being the reason why it is named: "white muscle disease" (WMD), but the characteristic injury is that affected muscles are paler than the rest of the musculature (Ramírez et al., 2004).

Cardiac injuries occur in young animals which results in sudden death during the first weeks of age, generally in animals with greater growth potential, which probably require a greater input of the element. Gross inspection of the heart may reveal pale or white areas, often associated with coronary drills. Frequently, in the ventricular cavity, the insertion areas of the chordae tendineae valve are also white or pale, contrasting with the rest of the inner surface of the organ. Sometimes the whole organ has the aspect of "boiled meat". Histological examination showed evidence that the quantity of nuclei increased in a similar way to that described for the skeletal muscle, fibres swell, they can be vacuolated and calcified (Ramírez et al., 2001a, 2004).

7. Reproductive disorders

The testicles and seminal material presents high concentration of Se, mainly associated to the GPX4. The GPX4 deficiency determines low seminal fertility in animals and human, with low sperm counts and increased abnormalities, evident from the sperm development. GPX4 has three critical isoforms that are derived from the same gen, located in the cytosol, mitochondria and nucleus. Nuclear isoform is involved in the arrangements of proteins associated with DNA (Beckett and Arthur, 2005; Behne and Kyriakopoulos, 2001).

The effect of Se on female fertility and litter size has given contradictory results; some authors have reported positive effects with supplementation (Hartley and Grant, 1961; Hartley, 1961; Scales, 1974; Segerson and Ganapathy, 1980; Sheppard et al., 1984), while others did not observe significant effects (Gabryszuk and Klewiec, 2002). In México, Se supplementation of goats from areas with low levels of selenium in soil did not affect fertility or productivity (Ramírez et al., 2005).

The conflicting results of Se supplementation on fertility and productivity could depend on the severity of the deficiency, the conditions of supplementation, and the apparent ability of the system to prioritize the enzymatic synthesis under these conditions.

8. The pregnant animal and newborns

A critical moment in the availability of Se in the female is the end of gestation and during lactation, in which females transfer the element to foetuses (placental transfer) and offspring (colostrum and milk). In ruminants, placental transfer of Se happens even in deficient females, who sacrifice their own condition to provide Se to the foetus (Koller et al., 1984; Rock, 1998; Abd El-Ghany et al., 2007, 2008). In animals and human, there is a reduction of maternal plasma Se levels, as gestation progresses and products increase in size and weight (Koller et al., 1984; Beckett and Arthur, 2005; Abd El-Ghany et al., 2007, 2008). In primiparous sheep, the foetal concentrations of Se, measured in a DM basis, declined slightly in the last third of gestation (Langlands et al., 1982; Grace et al., 1986). However in sheep and goats, a significant increase in Se concentration in the allantoic fluid is associated with foetal development (Abd El-Ghany et al., 2007, 2008). No changes were detected in the foetal kidney at different gestational ages (Cristaldi et al., 2005), whereas others reported that foetal liver Se increased from 145 to 195 days, decreasing towards day 245 (Abd Elrahman and Kincaid, 1993), suggesting an increased demand or use at the end of gestation. House

and Bell (1994) found no changes in foetal liver Se at the end of gestation, but observed a reduction in maternal liver Se, suggesting that cows also sacrificed their condition to keep contributing to the foetus or colostrums and milk production. The contribution is greater in the supplemented female; positive correlations were observed between the Se concentrations in blood, plasma and liver of calves with maternal plasma at birth (Kincaid and Hodgson, 1989; Abd Elrahman and Kincaid, 1995). Supplemented sheep, increased Se levels in the allantoic fluid, milk and colostrum and their lambs had better weight gain in the first two weeks of life (Abd El-Ghany et al., 2008). Newborns obtain Se through the colostrum and milk, thus Se availability of the mothers is critical in lactation.

The effect of Se supplementation during pregnancy on the weight gain of newborns has been discussed by some authors, some reporting better weight gains (Wichtel et al., 1996; Castellan et al., 1999; Abd El-Ghany et al., 2008), whereas others have not observed an effect on calve or lamb performance (Awadeh et al., 1998; Gunter et al., 2003; Rowntree et al., 2004; Rock, 1998; Rock et al., 2001). These differences may be the result of the severity of the deficiency in experimental females.

9. Diagnosis of Se deficiency

Forage and soil Se determination is important for the diagnosis of Se deficiency and to know the Se status in a particular region. Several factors affect the concentrations of minerals in forages, such as soil type, the presence of antagonistic elements and contaminants, fertilization, forage species, weather, season and plant maturity. These factors may modify and cancel the possibility for the animals to meet their micromineral requirements during the year (Georgievskii et al., 1982). Volcanic soils have virtually no Se, but have high levels of sulphur which competes with Se for absorption; the plants that grow in this kind of soil and animals that consume them suffer Se deficiency (Ramírez et al., 2001a,b).

The Se concentration in tissues appear to act as a reservoir for the element, with the lowest change of Se concentration in liver, therefore being preferable to measuring Se in blood (Levander, 1986; Mahan and Kim, 1996). In sheep, the greatest Se concentration has been reported in the kidneys, with lower concentrations in liver, pancreas, heart and skeletal muscle (Combs and Combs, 1986). In newborn lambs, the highest Se levels occur in liver, kidney and heart (Rock et al., 2001), increasing levels with a greater Se contribution in the diet (Cristaldi et al., 2005). The differences reported between sheep and lambs could be influenced by the requirements of the organs, the mobilization of the element, the requirements at different physiological states and age, and the apparent hierarchy in its contribution to the various organs. On the other hand, it should be considered that lamb have a digestive activity similar to non-ruminants, in which Se utilization from the diet is greater.

There is a high correlation between GSH-PX activity and Se level in blood, being the reason why this enzyme is used as an indicator of deficiencies (Ammerman and Miller, 1975; Sivertsen et al., 1977; Hakkarainen et al., 1978; Anderson et al., 1978; Puls, 1994; Oblitas et al., 2000). However, when a response to supplementation is being evaluated in a short period of time, a direct determination of Se is preferred (Koller and Exon, 1986; Stowe and Herdt, 1992). Enzyme activity has a delayed response after supplementation and depends on the level of previous deficiency, as a result of the time required for protein synthesis, and the hierarchy of the same synthesis. However, the determination of GSH-PX may be of great value as an indicator of the transformation of Se to bioactive forms, considering that this enzyme is the last priority of synthesis in conditions of deficiency (Behne and Kyriakopoulos, 2001), its activity depending on being able to satisfy the Se requirements.

10. Supplementation

Considering the serious impact on the productive efficiency of the affected animals and death in newborns, deficiency should be prevented by supplementation in Se deficient regions and deficient animals. Supplementation of the pregnant females is a key strategy to reduce these losses (Abd Elrahman and Kincaid, 1995; Abd El-Ghany et al., 2007, 2008). Supplementation of animals can be accomplished by incorporating the element in the diet (premixes), water, mineral supplements, intra-ruminal bolus, or injectable solutions. The form of supplementation depends on productivity and ease of use. In ruminants, a low utilization of Se in the diet should be considered (Kott et al., 1983; McPherson and Chalmers, 1984). Selenium can be lost when food is processed or refined, due to its volatility. The possibility of fertilizing soil with Se salts has been suggested. However this, and other forms of supplementation, is still under discussion, in part due to the lack of information with regard to its biological behaviour and the fear of poisoning (Stowe and Herdt, 1992). Sources of Se include inorganic salts (selenates and selenites) and selenomethionine or less purified forms as selenoyeast, in which this amino acid is abundant. In the diet, any of these forms can be used, but in an injectable form or bolus, only inorganic salts can possibly achieve adequate concentrations in supplemented quantities (Revilla et al., 2008). The chemical form affects the injectable Se salt absorption; sodium selenite administered subcutaneously is more rapidly absorbed than barium selenate (Kuttler et al., 1961).

Availability of supplemental selenomethionine is greater than that of selenite (Xia et al., 2005). Additionally, selenomethionine is rapidly incorporated into proteins (Jenkins and Hidiroglou, 1971; Nicholson et al., 1991). Yet, its use may be seriously discussed today, considering its price and its “bioactive” incorporation into enzymes (Allan et al., 1999; Behne and Kyriakopoulos, 2001). Mixtures with selenomethionine or selenoyeast are also more expensive than selenites and selenates, and in ruminants, supplemented Se inorganic salts are converted to selenomethionine by the rumen microflora (Kim et al., 1997). Even in pigs, it has been reported that there were no differences in the levels of Se in blood and liver of piglets supplemented with selenomethionine, compared with those with inorganic salts (Alaviuhkola, 1992).

Appropriate supplementation in sheep and goats varies from 0.1 to 0.3 ppm (DM basis) in the total diet (Smith

and Sherman, 1994; Ullery et al., 1978). With subcutaneous solutions of barium selenate, doses of 0.1 mg of Se per kg live weight, treated sheep and lambs maintain adequate levels of the element, while with the same salt offered orally at 0.126 mg/kg no benefit was observed (Jiménez et al., 1998). In non-lactating cows, oral administration of 1 mg Se/day was insufficient to maintain adequate plasma levels (Weiss et al., 1984; Abd Elrahman and Kincaid, 1995), whereas with a diet containing 0.3 ppm Se during the dry period and the injection of 50 mg of Se and 300 IU of vitamin E, 21 days before parturition, treated cows maintained adequate blood and plasma Se levels (Weiss et al., 1990). However, Stowe and Herdt (1992) found that cows supplemented with a 0.3 ppm Se diet suffered deficiency. In beef cows with poor Se status, oral supplementation with 13 mg/day during 15 days provided adequate Se levels for dams and their calves (Enjalbert et al., 1999).

In ruminants, selenite does not substantially alter *in vitro* rumen fermentation processes. The concentrations of total volatile fatty acids (VFA) are similar in animals supplemented with Se compared to those un-supplemented control animals, increasing the rumen acetate concentration (Kim et al., 1997). However, sheep showed the opposite effect, with higher acetic and isovaleric acids (Hidiroglou and Lessard, 1976) and total VFA concentration, and increased protozoa population, with greater proportion of *Diplodinium* (Naziroglu et al., 1997). These results were undoubtedly influenced by the complex interactions that occur in the rumen fermentation processes.

11. Human deficiency

If soils are deficient in Se, low levels will occur in plants and animals, and humans will be affected by this deficiency. The Se needs for humans has been estimated at 60–75 μg/day. The main source of Se for humans is red meat, especially pig meat (49.9 μg/100 g), that in similar regional conditions has almost twice the Se of beef (28.1 μg/100 g) or chicken (23.9 μg/100 g). The liver provides almost twice the Se level of meat. In beef, the Se concentration is 57.0 μg/100 g. Egg provides 15.4 μg/50 g. Milk and its derivatives provide low levels of the element. Tuna is a good source of Se with 80.4 μg/100 g, nevertheless in this case, Se is poorly digested by the human. While grains and cereals provide medium and low quantities of Se, fruit and vegetables were virtually non-contributors (Holben, 1999).

In regions deficient in Se, deficiencies are presented in both humans and animals, with forms of endemic cardiomyopathy being reported in certain regions of China; osteoarthropathy in Northeast Asia (Behne and Kyriakopoulos, 2001; Beckett and Arthur, 2005) and hypothyroidism with associated myxedema, in populations of Central Africa (Holben, 1999; Contempré et al., 2004; Beckett and Arthur, 2005; Köhrle et al., 2007; Gärtner et al., 2007). In the UK, particularly in Scotland, cases of low fertility in men have been diagnosed, caused by the low semen quality after consumption of diets with half of the Se requirements (Beckett and Arthur, 2005). The association between Se deficiency and certain forms of cancer have been recently documented, as well as the positive effects of supplementation in patients with HIV–AIDS (Allan et al., 1999). Hospital patients may present a Se deficiency when maintained with parenteral feeding without Se for long period of time (Holben, 1999).

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