Biological Aspects of Selenium in Farm Animals

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ABSTRACT : In 1957, Schwarz and Foltz discovered that selenium (Se) was an essential trace mineral and nutritionists then started extensive studies to figure out the metabolic function of this element which has been called as toxic mineral. The discovery that glutathione peroxidase (GSH-Px) contained Se demonstrated a biochemical role for Se as an essential trace element. The major physiological function of Se containing GSH-Px is thought to maintain low levels of H_2O_2 and other hydroperoxides in the cell to prevent tissues from peroxidation damages. It is known that the GSH-Px activity is increased when animals were fed high dietary levels of Se. Chemical properties of Se have much in common with sulfur (S) therefore Se would follow the sulfur pathways in its metabolism in animal body. Two sources of Se are available for supplementation of Se in animal feed. Inorganic Se can also exist in selenide (-2), elemental (0), selenite (+4) and selenate (+6) oxidation state with other minerals. When sulfur in S containing amino acids is replaced by Se, organic Se can be made and named "seleno" prior to the name of S containing amino acid, i.e. selenomethionine. Selenium deficiency affects humans as well as animals and dysfunctions such as exudative diathesis, retained placenta, mastitis, liver necrosis, Keshan disease, numerous diseases and cancer. From several centuries ago, Se toxicity was recognized in various animal species and much of the current toxic Se levels has been established largely based upon the controlled toxicity studies used inorganic Se. Toxic effects of Se in animal result in reduced feed intake, growth retardation, ataxia, diarrhea, alopecia and sloughing of hooves. However, several experiments demonstrated that Se deficiencies or toxicities were varied by dietary Se levels and sources. Recent studies demonstrated that the incidence of colorectal and prostate cancer was reduced by approximately 50% when humans consumed 200 μg of Se daily. ***(Asian-Aust. J. Anim. Sci. 2003. Vol 16, No. 3 : 435-444)***

Key Words : Selenium (Se), Antioxidant, GSH-Px

INTRODUCTION

The element selenium (Se) was named by the Swedish chemist J. J. Berzelius in 1818 after its discovery in the residue of sulfuric acid preparations from a mining operation. The early interest in Se was related to its properties as a toxic element. Marco Polo in his travels in western China about the year 1295 A. D. was perhaps the first to describe a disease syndrome resulting from ingestion of seleniferous plants (Rosenfeld and Beath. 1964). He reported a poisonous plant that, if eaten by horses, caused the hooves to drop off (Rosenfeld and Beath, 1964). Loss of hair and nails in humans presumably suffering from chronic selenosis was also described in Colombia by Father Pedro Simon in 1560 (Benavides and Mojica. 1965). Of greater concern, however, was the association of human fetal malformations that was occurring by the consumption of the local foods. In the United States, the toxic role of Se was investigated in certain soils in the Dakotas (Franke, 1934; Moxon, 1937).

Since 1949, three substances had been known to protect rats from a fatal liver necrosis condition (vitamin E, cystine, and Factor 3). Selenium's beneficial role in animal nutrition thus began in 1957 with the finding by Schwarz and Foltz (1957) that a factor in yeast would prevent liver necrosis in rats. It was therefore not until 1957 that Se was discovered to be the active agent of Factor 3. Selenium has since been found to be at the active site of glutathione peroxidase (GSH-Px) (Flohe et al., 1973). Selenium has also been discovered in several bacterial and other Se-containing enzymes (Arthur et al., 1990; Read et al., 1990). All presently known Se-containing enzymes and proteins contain the selenoamino acid, selenocysteine (Hawkes et al., 1985).

Selenium has an atomic number of 34, and atomic weight of 78.96 in the VIa group of elements of the periodic table which also includes oxygen (O) and sulfur (S). Selenium is thus a semi-metal (or metalloid), which has very similar chemical properties to S. It exists in several allotropic forms including a red powder, red crystals, a dark brown moss, and a silver gray form produced after extensive heating at 200 to 220 °C. Elemental Se (Se^0) can be further reduced to selenide(Se^{-2}) or oxidized to selenite(Se^{+4}) state. Selenium can be volatilized under acidic conditions, and care therefore must be taken to prevent the loss of Se during its analysis. Elemental Se burns in air to form SeO_2 which emits a characteristic odor resembling rotting horseradish. Elemental Se is not soluble

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in water. but many of its salts (selenites and selenates) are water soluble (Bennett. 1983).

Selenium is widely distributed in the environment (waters, soil. and air) though generally in very low concentration. (≤ 1 μg/g). The Se content in limonite rocks sometimes reaches 0.5 mg/g. and 2.6 mg/g in vanadium-uranium rock (Rosenfeld and Beath. 1964). Data on Se-containing rocks are derived from North and South America. Canada. Columbia. Mexico. Australia. New Zealand. Ireland, Bulgaria. Germany, USSR and Mediterranean countries (Rosenfeld and Beath, 1964). Some ground or mountain and waters are reported to contain elevated concentrations of Se (e.g., Colorado channels or subterranean waters in the region Orsk). Selenium and its compounds have found broad technological applications; these include the chemical industry (catalyst), electronics (for production of semiconductors. photocells. and rectifiers). machine industry (for obtaining high-grade steel). glass industry (for staining or coloring of glass), rubber industry (for acceleration of vulcanization). and various pharmaceutics (veterinary Se preparations in treatment of Se deficiency). In agriculture, the organoselenium compounds are used as bactericides. fungicide. and herbicides (Bem, 1981).

INORGANIC AND ORGANIC SELENIUM

Inorganic Se

Alexander and Whanger (1983) showed that at equal Se intakes by rats. selenite produced higher GSH-Px in all tissues than did the Se from raw. cooked. or canned-tuna Se. The supplementation of sodium selenite (200 μg/d for 8wk) resulted in 118 % increase in cytotoxic lympocyte-mediated tumor cytotoxicity and 82.3 % increase in natural killer cell activity when compared to baseline values (Kiremidjian-Schumacher et al.. 1994). This apparently was related to the ability of the nutrient to enhance the expression of receptors for the growth regulatory lymphokine interleukin-2. and consequently. the rate of cell proliferation and differentiation into cytotoxic cells. This indicates that the immunoenhancing effects of Se in humans require Se supplementation above the repletion levels produced by normal dietary Se intakes.

It has been reported that both sodium salt forms of Se (i.e., selenite and selenate) are of potential danger to humans because of their high water solubility when in direct contact with skin and mucous membranes; hence. toxic responses might occur (Echevarria et al., 1988b). Calcium selenite is also considered toxic if it is inhaled or swallowed or when it comes into contact with skin. but its solubility is less rapid than that of sodium selenite and thus presents less immediate danger to humans. Mahan and Magee (1991) reported that calcium selenite responded similarly as sodium selenite when tissue Se concentrations and serum GSH-Px activities of weanling swine were fed at approved. marginally toxic. and toxic dietary Se levels. Selenium bioavailibilities in young chicks and lambs were similar when calcium or sodium selenite have been fed during both short (< 10 d) and long (40 or 80 d) time periods (Echevarria et al.. 1988a; Henry et al.. 1988).

Organic Se

The major Se component of nonaccumulator plants such as grains and grasses. appears to be the proteinaceous amino acid, selenomethionine (Frankenberger and Karlson, 1992). The organic Se found in feed ingredients is comprised of several organic forms but selenomethionine represents about 50 % of the Se in cereal grains (Olson and Palmer, 1976). However, in Se accumulator plants. *Astragalus*. Se is incorporated into nonproteinaceous amino acids such as Se-methylseleno- cysteine. selenocystathione. selenocystine. and selenohomocysteine (Trelease and Beath. 1949; Shibata et al.. 1992).

Gabrielsen and Opstvedt (1980) reported that selenomethionine had 78% of the availability when compared to sodium selenite. This was followed by fish meals (48% for capelin and 34% for mackerel), corn gluten meal (26%). and soybean meal (18%). The relatively low availability reported for fishmeal Se might be related to the lower level of antioxidants in the diets (Cantor et al., 1975a. 1975b) or the higher concentration of heavy metals.

An enriched Se-yeast product has been produced by feeding a yeast strain with a high S requirement with sources of inorganic and organic Se (Mahan. 1995). Because S and Se are chemically similar, Se is incorporated into yeast cell protein structures by replacing the S with Se. Kelly and Power (1995) demonstrated that approximately 94% of the Se in the Se-enriched yeast source was organically incorporated into one of several seleno-amino acid analogs. the major one being selenomethionine. Bird et al. (1997), however. reported that selenomethionine accounted for no more than 20% of all Se-containing materials in selenized yeast. In addition to selenomethionine. the other compounds that had been identified included selenocystine. Se-methylseleno cysteine and selenoethionine (representing ~20%). On top of that. there were several unidentified peaks that combined to represent 40-50% of the total when more sophisticated analytical method. high performance liquid chromatography-inductively coupled plasma-mass spectrometry (HPLC-ICP-MS) (Bird et al., 1997). The dietary supplementation with the Se-enriched yeast product resulted in the increase retention of Se in all tissues, and changes in distribution and retention of Cu. Zn. Mn. and Fe in rat tissues (Djujic et al., 1995). The aspects of Se absorption and excretion were varied by Se sources. The apparent digestibility of Se

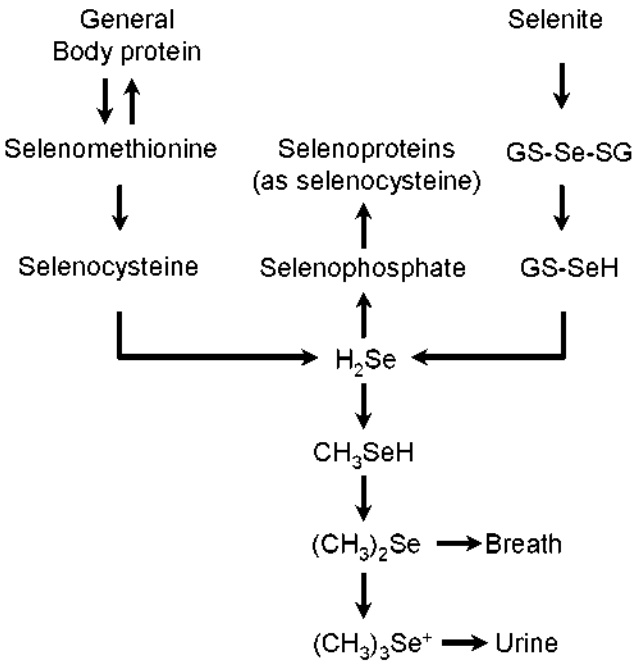

Figure 1. Selenium metabolic pathway (Ganther, 1986)

increased when pigs were fed inorganic Se (sodium selenite) compared to organic form but Se retention tended to be higher when organic Se was provided. Urine was the main route of inorganic Se excretion while the fecal route when the organic form was provided (Kim and Mahan, 2001c, Figure 1).

GLUTATHIONE PEROXIDASE (GSH-PX)

Studies of Se-dependent protection against rat red blood cell hemolysis was conducted in the laboratory of W. G Hoekstra and culminated in 1973 with the discovery that rat red cell GSH-Px is a selenoenzyme (Rotruck et al., 1973). Shortly thereafter, Flohe et al. (1973) reported that bovine blood GSH-Px contained one Se atom per subunit. Since then, this enzyme has been purified from a number of sources including human tissues, and has shown to contain Se in each case. It has a wide distribution in animal cells and is present in the mitochondria cytosol (Burk, 1983). Nutritional deficiency of Se results in a decline in tissue Se-dependent GSH-Px activity. Rat liver activity falls to undetectable levels after only 4 weeks of a Se-deficient dietary regimen (Hafeman et al., 1974). Other tissues experience a more gradual decline in GSH-Px activity. These observations indicate that a major biochemical effect of Se is to maintain GSH-Px activity.

The understanding of Se-dependent GSH-Px was complicated in 1976 by the discovery of a non Se-dependent GSH-Px activity (Lawrence and Burk, 1976). The glutathione S-transferases account for the non-Se-dependent GSH-Px activity (Prohaska and Ganther, 1977). These enzymes are found in fewer cell types than Se-dependent GSH-Px. In rat liver, glutathione S-transferase is present in the cytosol, mitochondria, and microsomes. Their GSH-Px activity in the microsomes appears to be lower than that in the other sites (Burk et al., 1982). Rat liver glutathione S-transferase activity is 50 to100% higher in Se-deficient male rat liver cytosol than in the control and presumably also non-Se-dependent GSH-Px activity (Lawrence et al., 1978). The reason for this increase is unknown, but it may compensate for losses of Se-dependent GSH-Px. Therefore, these enzymes should be increased during a Se deficiency. Observations from studies with rats (Hill et al., 1987; Lawrence et al., 1978) are consistent with this hypothesis. Whereas, Se-deficient birds (Xu and Diplock, 1983; Kim and Combs, 1992) and fish (Bell et al., 1986) with severely reduced tissue GSH-Px activities have not shown increased glutathione S-transferase activities. Kim and Combs (1992) demonstrated that the increase in glutathione S-transferase activity did not to occur in Se-deficient chicks unless they were also deficient in vitamin E.

Lawrence and Burk (1978) reported the presence of both Se-dependent and Se-independent GSH-Px activities in pig livers. Approximately 67% of the total liver GSH-Px activity of the pig was Se-independent, whereas the data of Meyer et al. (1981) suggested that 45 to 60% was Se-independent. The amount of Se-independent GSH-Px activity was fairly consistent at the different dietary Se levels, the relative percentage of Se-independent activity was greatest for those fed .1 ppm Se because of the lower Se-dependent GSH-Px activity (Meyer et al., 1981). These results suggest that the increase in total liver GSH-Px activity largely reflected the increase of the Se-dependent form of the enzyme, as there was no further increase in activity at higher dietary Se levels.

The glutathione S-transferases catalyze the conjugation of electrophilic compounds and metabolites with glutathione, thereby constituting one of the major detoxification mechanisms in the liver. Some of these enzymes have nonSe-dependent GSH-Px activity.

Although the Se-dependent and non Se-dependent GSH-Px carry out the same general reaction, many of their characteristics differ (Burk and Lawrence, 1978). Selenium-dependent GSH-Px destroys both H_2O_2 and organic hydroperoxides. Non Se-dependent GSH-Px does not metabolize H_2O_2 and it accumulates (Lawrence and Burk, 1978). The enzyme also has higher apparent Kms toward organic hydroperoxide substrates than does Se-dependent glutathione peroxidase.

The major physiological function of Se dependent GSH-Px is thought to maintain low levels of H_2O_2 and other hydroperoxides in the cell to prevent tissues from peroxidation damage.

Accumulation of these reactive substances could lead to impaired function or destruction of the cell. Experiments in which H_2O_2 or organic hydroperoxides were added to isolated cells or perfused livers demonstrated that the GSH-Px functions in intact cells (Sies et al., 1972; Eklow et al., 1981). The H_2O_2 concentration in the cell may be regulated by Se-dependent GSH-Px acting in concert with catalase (Jones et al., 1981).

The role of the GSH-Px in the metabolism of the organic hydroperoxides is not clear. Fatty acid hydroperoxides should be the major organic hydroperoxide form in the cell. They serve as substrates for both GSH-Px when present in the unesterified form (Pierce and Tappel, 1978), but may not be available to the enzymes when esterified in phospholipids (McCay et al., 1976), which are the likely form found in the cell. Consequently, it cannot be stated with certainty that the GSH-Px metabolize fatty acid hydroperoxides in the cell. Sies and Moss (1978) suggests that Se dependent GSH-Px may help regulate mitochondrial substrate oxidation. Oxidation of pyruvate was shown to decrease when hydroperoxide was being metabolized by Se-dependent GSH-Px but no decrease was found when Se deficient mitochondria were used. This indicates that the selenoenzyme may have more subtle functions than the destruction of hydroperoxides.

Until recently, researchers knew little of the effect of Se deficiency on glutathione metabolism. Liver glutathione concentration is measured by determining the rate of synthesis of the compound in the liver and the rate of glutathione release into the bile and blood (Bartoli and Sies, 1978). Experiments with isolated hepatocytes and perfused livers indicate that Se deficiency markedly accelerates glutathione synthesis in rat liver (Hill and Burk, 1982) which is balanced by an increased glutathione concentration into blood. There appears to be no effect of Se deficiency on the release of glutathione into the bile. Liver cysteine concentration is lowed in the Se-deficient rat (Hill and Burk, 1982), presumably because cysteine is used in the synthesis of glutathione. Glutathione concentration in blood plasma is two to three times higher in Se-deficient rats than in the controls as a result of the increased release of the compound into the blood. At present it is not known why Se deficiency increases hepatic glutathione turnover. The increase may be in compensation for the loss of plasma GSH-Px activity. Alternatively, glutathione could be lost from the liver cell as a consequence of faulty regulation of its release. Little is known about the mechanism and regulation of glutathione release into the blood (Burk, 1983).

Glutathione peroxidase activity in certain tissue (kidney, heart) may therefore be a more accurate indicator of Se adequacy than is Se content of the tissue (Chow and Tappel, 1974).

Thompson and Fraser (1983) suggested that erythrocyte GSH-Px would be the most sensitive indicator particularly at lower levels of Se uptake. However, GSH-Px does not appear to be a sensitive index of excessive dietary Se intake (Goehring et al., 1984b). Blood GSH-Px data demonstrate that excess sodium selenite elevates GSH-Px to a level that is possibly greater than the animal's physiological requirement of this enzyme. The plateauing of GSH-Px activity while serum Se concentration continued to rise suggests that the Se requirement had been met.

In dietary liver necrosis, a clear-cut relation between GSH-Px levels in the liver and the development of liver necrosis has been established. During the latent phase of dietary liver necrosis, i.e., 6 to 8 days before death, the GSH-Px activity in livers are reduced by 80 to 90 %. A single injection of selenite (50 μg Se/100 g of body weight) is sufficient reestablish normal enzyme levels within 1 to 2 days. The 6 to 8 day time lag indicates that Se is not simply incorporated into a preexisting apoenzyme, but that the enzyme is synthesized *de novo* (Schwarz, 1976).

Glutathione peroxidase is not the only enzyme affected in Se deficient pigs. Pigs fed low Se diets had elevated serum glutamic oxaloacetic transaminase (sGOT), serum glutamic-pyruvic transaminase (sGPT) and serum lactic acid dehydrogenase (LDH) activities, reflecting oxidative damage to cells which results in their subsequent release into the circulatory system. Selenium supplementation prevented increases in sGOT and sGPT (Ewan and Wastell, 1970). In addition, supplemental Se decreased the elevation of LDH activity (Ewan and Wastell, 1970).

SELENIUM DEFICIENCY

Selenium deficiency is related to several nutritional disease conditions in animal and humans. The pathological changes found in animals include growth retardation, skin lesions and hair loss, visual defects, reproductive disorders, pancreas atrophy, liver necrosis and dystrophy of the skeletal muscle and of the heart muscle. The occurrence, in animals of Se-responsive endemic deficiency diseases in various parts of the world is an excellent example of the interrelation between the geochemical environment and geographic pathology of a nutritional inadequacy. White muscle disease in sheep and cattle is a widespread, naturally occurring form of muscular dystrophy caused by a Se deficiency (Schwarz, 1976). In humans, a low-Se status may lead to cardiomyopathy and muscular disorders. A role of Se in cardiovascular disease, osteoarthropathy and cancer has been discussed, but a direct relationship between Se deficiency and these diseases have yet to be established (Behne et al., 1994).

Selenium deficiency markedly affects glutathione metabolism and some glutathione-dependent enzymes. Selenium deficiency results in drastic decline in Se-

dependent GSH-Px activity, which can produce a rise in cellular H_2O_2 concentration. Higher levels of H_2O_2 can still be disposed of through cellular catalase activity (Jones et al., 1981). The higher steady-state level of H_2O_2 probably will emerge as an indication of a Se deficiency. This has not been measured directly. It is not clear what effect the loss of Se-dependent GSH-Px has on fatty acid hydroperoxides in the cell because of the uncertainty over their metabolism and the presence of the nonSe-dependent GSH-Px. Selenium-dependent GSH-Px may play a metabolic regulatory role as proposed by Sies and Moss (1978). Consequently, a Se deficiency may decrease the ability of the mitochondria to adjust to changes in substrate concentrations and result in a higher H_2O_2 production.

Selenium deficiency can also cause an increase in hepatic glutathione S-transferase activity (Burk, 1983). This should provide more binding sites to allow increased "storage" of compounds such as bilirubin, heme, and other organic anions. More importantly, the increased glutathione synthesis should increase the ability of the liver to detoxify substances via the glutathione conjugation pathway. The Se deficiency-induced increase in hepatic glutathione synthesis depletes cellular cysteine, so it may impair cellular process such as protein synthesis that requires cysteine. It increases plasma glutathione concentrations due to an increased rate of glutathione release by the liver (Burk, 1983).

Van Vleet et al. (1973) demonstrated an effective preventative injection dosage for Se deficiency of .06 mg Se per kg body weight in 1-week-old piglets. Mahan et al. (1973) reported excellent results when 1 mg of Se was intramuscularly injected in 3-to 4-week-old swine.

Deficiencies of Se in cattle and sheep have been observed under natural grazing conditions in many countries of the world. Overt signs of Se inadequacy such as white muscle disease (nutritional muscular dystrophy) occur primarily in young calves or lambs when born to Se deficient dams. Infertility has increased in ewes grazing pastures low in Se. Selenium deficiency has not generally occurred in older animals such as finishing beef cattle and lactating beef cows (Ammerman and Miller, 1975). Subclinical deficiencies of Se are not easily determined and an inadequacy of the element may be limiting maximum animal performance under certain circumstances of drylot feeding.

Selenium was originally considered as a toxic element, but in 1957 Schwarz and Foltz recognized Se to be the effective component of "factor 3" which prevented liver necrosis in rats. Schwarz and Foltz (1957) further demonstrated that Se prevented exudative diathesis in chicks. Selenium deficiency in chicks caused reduced egg production and hatchability in poultry (Cantor and Scott, 1974) poor growth, and increased mortality and gizzard myopathy in young turkey poults (Scott et al., 1967). Pancreatic fibrosis also occurred in severe Se deficient chicks (Noguch et al., 1973; Thomson and Scott, 1970). Chicks fed the Se-free diet showed severe degeneration and fibrosis of the pancreas even when the diet was supplemented with all nutrients known to be required, including high levels of vitamin E (Thomson and Scott, 1970). Bartholomew et al. (1998) demonstrated that heterophils and monocytes were increased in Se deficient chicks, whereas, lymphocytes, basophils, and Hb decreased. Selenium deficient chicks had coagulative necrosis of myocytes accompanied by scattered hemorrhage. In addition, the ratio of myeloid-to-erythroid (M:E) from erythroid hyperplasia in femoral bone marrow decreased in Se deficient chicks because of increased immature erythroid cellular elements (Bartholomew et al., 1998).

SELENIUM TOXICITY IN POULTRY

Since the settlement of western South Dakota and northern Nebraska in the 1890s, residents of certain regions observed poor hatchability of chicken eggs (Franke et al., 1934). Embryos were found with many types of deformities. Legs, toes, wings, beaks, and eyes were often malformed, rudimentary, or entirely lacking (Franke and Tully, 1935). Disturbances in the normal processes of bone and cartilage formation were evident. Hatchlings exhibited down that appeared greasy or wiry and never became fluffy. Investigations of the disease which began in 1929 led to cooperative work with the U. S. Department of Agriculture. These studies led to the discovery of toxic levels of Se in locally grown wheat as well as in the soil upon which it was grown (Moxon, 1937). The chick embryo is very sensitive to Se poisoning because egg hatchability is reduced by high dietary Se concentrations of Se that are too low to produce selenosis symptoms in other farm animals (Rosenfeld and Beath, 1964). The toxicity of Se is affected by several factors associated with diet, gender, and previous exposure to the element (Levander, 1972). Among the diet are related factors that affect Se toxicity are level and type of protein, dietary levels of heavy metals, other trace elements, inorganic sulfur, methyl group donors, and antioxidants (Combs and Combs, 1986). By injecting selenite into the air cell of eggs before incubation, Franke et al. (1936) induced teratogenic effects on the embryos. The highest frequencies of abnormalities resulted when the Se dosage was .7 ppm of egg yolk plus egg white; however, amounts as low as .01 ppm produced some monstrosities. Embryo deformities produced by Se toxicity resemble those induced by X-rays, various chemicals, high and low temperatures, and centrifugal force (Trelease and Beath, 1949). Latshaw (1975) reported that Se from selenite was deposited more in the yolk than in the albumen. However, Kinder et al. (1995) demonstrated that dietary Se would affect egg albumen

before the yolk Se content because broiler breeder ovum requires approximately 10 days for maturation, whereas the albumen is deposited each time an egg is formed (22 to 26 hours). Within 2 months after supplementation was withdrawn, egg Se levels declined by 50% and it appeared that eggs were acting as an avenue for clearing Se from the hen's bodies (Heinz et al., 1987; Kinder et al., 1995). Feeding 1.4 ppm Se supplementation to emus, resulted in reduced hatchability from 52% to 40% with surviving chicks having a high incidence of leg deformities (Kinder et al., 1995). Ort and Latshaw (1978) demonstrated that 5 ppm Se caused hatchability to decrease in chickens and low egg weights resulted from 7 ppm Se supplementation. Egg production was affected by 9 ppm Se and abnormal embryos occurred at 10 ppm Se in diets.

Selenium content in feathers was increased in proportional to dietary Se. Feathers from chicks fed a diet containing 8 ppm Se were found to contain 3.4 ppm Se (Mertz and Underwood, 1986).

Several studies of aquatic birds feeding in discarded, Se-containing, subsurface agricultural drainage water containing 300 μg Se/L (normal surface waters contains < 1 μg/L) found a high prevalence of embryonic death and deformity as well as death of adult birds (Ohlendorf, 1989).

SELENIUM TOXICITY IN SWINE

Acute Se toxicities in young pigs can result in clinical selenosis disease symptoms similar to those for lambs and calves (Shortridge et al., 1971).

Chronic Se poisoning in pigs is recognized by dullness, lack of vitality, emaciation, roughness of hair coat, loss of hair, soreness and sloughing of hooves, stiffness and lameness due to erosion of the joints of long bones, atrophy of the heart, cirrhosis of the liver and anemia (Underwood, 1977).

Moxon and Mahan (1981) reported that 5 ppm of Se in corn-soybean meal diets reduced the growth and feed intake of weanling swine. Growth rate was the most sensitive indicator of chronic selenosis in swine (Goehring et al., 1984b). Goehring et al. (1984a) did not observe any effect on performance of pigs fed wheat diets containing up to 8.3 ppm Se. They further reported (Goehring et al., 1984b) that hoof lesions developed when 12 ppm Se was provided. This observation is consistent with descriptions of hoof lesions typical of chronic selenosis (Harrison et al., 1983; Goehring et al., 1984b). Wahlstrom et al. (1984) reported separation of the hooves at the coronary band after approximately 4 weeks of feeding 8 ppm inorganic Se to growing pigs.

Sodium selenite administered subcutaneously to 30 to 70 kg swine at 2.0 and 1.2 mg/kg body weight was reported to cause myopathy, increased plasma glutamic oxaloacetic transaminase (GOT) activity, and clinical signs of toxicities including paresis, trembling, and ataxia (Orstadium, 1960; Diehl et al., 1975). Acute oral intoxication in swine was induced experimentally with dosages of 13 to 23 mg Se/kg body weight, as selenite, and resulted in vomiting, diarrhea, paresis, anorexia, trembling, and depression (Miller and Williams, 1940).

A difference in the susceptibility of pigs to Se toxicity has been shown to exist among pigs of different hair color (Wahlstrom et al., 1984). Red pigs fed corn-soy diets containing 5 ppm Se developed severe selenosis, while black or white pigs were only slightly affected. Wahlstrom et al. (1984) suggested that growth rate was the most sensitive index of chronic selenosis in swine and hair selenium content was not in itself a sensitive index of chronic selenosis in swine.

Experiments carried out with adult sows using sodium selenite and revealed that conception rate, litter size, and weight of piglets were reduced by feeding high dietary Se level (10 ppm) to sows (Wahlstrom and Olson, 1959a). The growth rate was more affected after weaning than during the suckling period, where the Se challenge was smaller as the Se content in the milk was low compared to the feed (Poulsen et al., 1989). The performance of weanling piglets was affected by high dietary Se resulting in reduced feed intake and rate of gain (Wahlstrom and Olson, 1959b; Goehring et al., 1984b; Mahan and Moxon, 1984). However, When gilts were fed barley-based diets with high dietary inorganic Se (up to 16 mg/kg feed), there was no detrimental effect on sow conception, the number of piglets born, mortality, and the weight of the whole litter at birth (Poulsen et al., 1989). There was a tendency for a lower body weight of individual piglets at birth by Se supplementation. Colostrum and milk Se content was influenced by dietary Se treatment (Poulsen et al., 1989). The only clinical observation was a circular dark band in the hoofs of some sows fed the high Se supplementation, but the locomotion of the sows and piglets were unaffected (Poulsen et al., 1989). When growing pigs were fed high levels of dietary Se from organic or inorganic forms, organic Se retained more Se in muscle and organs than the group fed inorganic Se. Selenium toxicity observed at 5 ppm Se but selenosis effects were more severe and occurred sooner when inorganic Se was provided (Kim and Mahan, 2001a). A study was conducted to evaluate the effects of feeding high levels of dietary Se from 0.3 to 10 ppm Se from organic and inorganic sources. Both organic and inorganic Se sources were toxic when primiparous sows were fed at 7 to 10 ppm for a prolonged period, but organic Se seemed to express the selenonic effects more on reproductive performance, whereas inorganic Se was more detrimental effects in progeny during lactation (Kim and Mahan, 2001b).

Table 1. Comparison of inorganic and organic Se

	Inorganic Se	Organic Se
Chemical forms	Sodium selenite, selenate	Selenomethionine
	Calcium selenite	Selenocysteine
Biological functions	Increase GSH-Px activity	Increase maternal Se transfer to litter
FDA approval	Approved	Approved 2000 for poultry
		Approved 2002 for swine
Retention	Low efficiency	High efficiency
Excretion route	Urine	Feces
Toxicity	More toxic in growing animal	More toxic in reproductive animal

SELENIUM TOXICITY IN RUMINANT

Early this century, Se was identified as the active component in forages that caused livestock poisoning in South Dakota. The condition had first been recognized many years earlier by Madison, an Army doctor stationed at Fort Randall in what was the Nebraska Territory (Franke, 1934). Reports over the years of Se toxicity, occurred in grazing livestock, and we have been reminded of this problem recently by the occurrence of birth defects in waterfowl hatched on the Kesterson Wildlife Refuge in California. Selenium had concentrated in the shallow ponds by evaporation of subirrigation drainage water from the San Joaquin Valley and was the cause of the problem (Ohlendorf et al., 1986).

When steers were fed 0.28, and 0.8 mg Se/kg body weight (approximately 10 and 25 ppm, respectively) as selenomethionine or sodium selenite, alkali disease occurred at 0.28 and 0.8 mg/kg body weight in the form of selenomethionine and to 0.8 mg/kg body weight in the form of sodium selenite (O'Toole and Raisbeck, 1995). These results demonstrated that the toxic level of inorganic Se was 25 ppm, while was 10 ppm organic Se in ruminant. Consequently, organic Se is more toxic in ruminant compared with inorganic Se. The distinctive histological changes that developed in the hooves, particularly in stratum medium, may account for the dystrophic digital lesions in selenosis. These lesions were accompanies by mild to marked hyperplasia and parakeratosis in laminar epithelium and, to a less extent, in coronary epidermis and loss of the normal abrupt transition between stratum spinosum and stratum corneum. The predominance of epithelial changes in hooves may distinguish Se-induced lesions from those of chronic (corial) changes in addition to irregular hyperplasia of epidermal laminae (Singh et al., 1992; O'Toole and Raisbeck, 1995).

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