INHIBITION OF TRACE MINERAL METABOLISM IN RUMINANTS

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Introduction

Trace minerals exist in cells and tissues of the animal body in a variety of chemical combinations, and in characteristic concentrations, depending on the trace mineral consumed and the tissue in which the trace mineral is metabolized (McDowell, 1992; Underwood and Suttle, 1999). Concentrations of trace minerals must be maintained within narrow limits in a cell (McDowell, 1989, 1992; Underwood and Suttle, 1999). Trace mineral deficiencies, toxicities, and imbalances require the animal to metabolically compensate for the nutrient deviation (McDowell, 1989, 1992; Underwood and Suttle, 1999). In doing so, certain metabolic diseases can be produced and overall animal performance can be depressed. The intent of this review is to: 1) give a general description of the function of certain trace minerals; 2) briefly discuss trace mineral absorption; and 3) discuss factors that affect trace mineral requirements in ruminants (Galyean et al., 1995; Galyean et al., 1999; Spears, 2000; Baker et al., 2003).

Functions of Trace Minerals

In general, trace minerals can function in a structural capacity—minerals that play a role as components of tissues; a physiological capacity—minerals that are involved in acid-base balance; catalytic capacity—minerals that are components of enzyme and hormone systems; and regulatory capacity—minerals that are involved in cell replication processes (Underwood and Suttle, 1999). The specific functions of zinc (Zn), copper (Cu), manganese (Mn) and selenium (Se) fall mainly into the catalytic and regulatory categories.

Copper: Copper is second only to Zn in the number of enzymes that require it for appropriate function (Underwood and Suttle, 1999). Copper is therefore essential to proper physiological function and is involved in an array of metabolic systems. These include iron (Fe) metabolism, cellular respiration, cross-linking of connective tissue, central nervous system formation, reproduction and immunity as well as several other functions (McDowell, 1992).
In order for hemoglobin synthesis to occur, Fe must be converted to the ferri-form before being incorporated into the hemoglobin molecule. This process is accomplished by ceruloplasmin, which is a Cu containing enzyme synthesized in the liver (Saenko et al., 1994). Copper is also an essential component in the enzyme cytochrome oxidase. This enzyme acts as the terminal oxidase in the electron transport chain and is essential to cellular respiration by converting oxygen to water (Spears, 1999). Cytochrome oxidase is also necessary for proper central nervous system function. Cross-linking of connective tissue is also facilitated by a Cu-containing enzyme, lysyl oxidase (Harris and O’Dell, 1974).

The essentiality of Cu for optimal reproductive performance has also been widely documented, although a specific Cu-linked enzyme that is responsible for optimal reproductive performance has not been identified. It is likely that an array of Cu-containing, or Cu-activated, compounds are involved in the reproductive process making this identification even more difficult. Corah and Ives (1991) noted that clinical signs of Cu deficiency associated with reproduction include decreased conception rate, overall infertility, anestrus and fetal resorption. Some of these problems may be associated with the function of a major enzyme not yet mentioned—Cu-Zn superoxide dismutase. This Cu-containing enzyme functions as an antioxidant to protect cells involved in reproduction and other physiological processes from oxidative stress. The same Cu-Zn superoxide dismutase has also been implicated in contributing to proper function of the immune system (Miller et al., 1979).

Prohaska and Failla (1993) have conducted several studies in rats and mice which have indicated that both cell mediated and humoral immunity are greatly depressed by Cu deficiency. However, studies in domestic livestock have failed to show consistent effects of Cu deficiency on either cell-mediated or humoral immune response (Spears, 2000).

Severe Cu deficiency induced by feeding a semi-purified diet low in Cu did not affect in vitro mitogen induced lymphocyte blastogenesis (Stabel et al., 1993; Ward et al., 1997). Furthermore, the addition of 5 mg Mo/kg to the semi-purified diet to produce a more severe Cu deficiency did not reduce lymphocyte blastogenic response to PHA or PWM (Ward et al., 1997). However, recently Wright et al. (2000) indicated that low Cu status in steers was associated with a reduced response of peripheral-blood lymphocytes to stimulation with T cell-mitogens following weaning and IBRV challenge.

From the more basic molecular immune research it is clear that Cu plays an important role in the immune response. However, the reason for the variable responses of Cu supplementation on the immune response in livestock is unclear. There are many factors that could affect an animal’s response to Cu supplementation such as the duration and concentration of Cu supplementation, the absence or presence of dietary Cu antagonists (sulfur and molybdenum), environmental factors, and breed differences in Cu metabolism.
Zinc: In addition to the functions mentioned for Cu-Zn superoxide dismutase, Zn is also involved in an array of other systems as an enzyme component or activator. It therefore plays an indirect role in growth, reproduction, immunity, vitamin A metabolism and many other processes (McDowell, 1992). Chesters (1997) indicated that Zn is involved as a component of a number of transcriptional regulators involved in the gene transcription process.

Zinc has been shown to be essential for adequate growth and development. However, reduction in growth rate may partly be due to a decreased feed intake that has been observed in conjunction with Zn deficiency in rodent models (Mills and Chesters, 1969). Spears (1999) has suggested that poor growth may also be correlated with a reduction in protein synthesis due to an impaired gene transcription process under conditions of Zn deficiency. Reproduction has been identified as an area that is significantly affected by Zn deficiency (Apgar, 1992).

Immunity can be affected by Zn status of the animal. Numerous experiments with humans and laboratory animals have indicated that Zn deficiency reduced immune response and disease resistance (Chesters, 1997). However, there is little research in ruminants examining the influence of Zn deficiency on immune function and disease resistance (Spears, 2000). Lambs fed a semi-purified diet severely deficient in Zn showed a reduced blastogenic response to PHA (a T-cell mitogen), but an increased response to PWM, a T-dependent B-cell mitogen (Droke and Spears, 1993). Zinc deficient lambs also had a lower percentage of lymphocytes and a higher percentage of neutrophils in their blood. Inflammatory response to PHA was also similar in Zn-adequate and Zn-deficient lambs. Furthermore, Zn-deficient cattle showed similar cell-mediated and humoral immune responses as Zn adequate cattle (Spears and Kegley, unpublished data). However, Engle et al. (1997) reported a greater skin swelling response in Zn adequate calves when compared to marginally Zn-deficient calves.

Although the data is limited and variable on the effects of marginal Zn deficiency on immune function, Galyean et al. (1995) reported that increasing the level of supplemental Zn from 30 to 100 mg/kg diet tended to reduce morbidity from respiratory diseases in newly weaned stressed (by transport) calves. Zinc supplementation has been associated with an increased antibody titer response and a decrease in respiratory disease in feedlot steers (George et al., 1997). This may be due to the function of Cu-Zn superoxide dismutase as previously mentioned or to a variety of other processes that include Zn as well. These functions may include thymic hormone production and activity, lymphocyte function, natural killer function, neutrophil function, and lymphokine function (Hambidge et al., 1986).

Manganese: Manganese is involved in many of the same processes already mentioned for Zn and Cu, although the original research that identified Mn as an essential trace element was based on measurements of reproductive parameters (Orent and McCollum, 1931; Kemmerer et al., 1931). Hidiroglou (1975)
reported that Mn uptake was greater in the ovine Graafian follicle and corpus luteum when compared to other reproductive tissues. This author suggested that Mn may be essential for normal ovarian function. As Maas (1987) indicated, Mn deficiency has been associated with the anestrus condition in cattle.

Manganese has also been identified as an essential component in bone and cartilage formation and growth. Leach (1971) noted that Mn is essential in the activation of glycogenases that are partly responsible for mucopolysaccharide synthesis. Manganese is also involved in lipid and carbohydrate metabolism. Therefore, Mn deficiency can potentially lead to a decrease in overall animal growth (Prasad, 1984).

Selenium: Selenium was first identified in the 1930’s as a toxic element to some plants and animals. However, Se is now known to be required by laboratory animals, livestock and humans (McDowell, 1992). Selenium is necessary for growth and fertility in animals and for the prevention of a variety of disease conditions. In 1973, Rotruck et al. reported that Se functions as a component of glutathione peroxidase, an enzyme that inactivates oxygen radicals such as hydrogen peroxide and prevents them from causing cellular damage. Since the discovery by Rotruck et al. (1973) selenium has been shown to affect specific components of the immune system (Mulhern et al., 1985; Reffett et al., 1988; Aziz et al., 1984; Gyang et al., 1984; Maddox et al., 1999; Spears, 2000).

Chromium: Chromium (Cr) was first shown to be essential for mammals by Schwarz and Mertz (1959). Since then, Cr has been shown to influence carbohydrate metabolism (Mertz, 1993), lipid metabolism (Abraham et al., 1991), and protein absorption and metabolism (Okada et al., 1983; Kornegay et al., 1997). The addition of Cr to diets fed to stressed cattle increased immune response and growth rate (Chang and Mowat, 1992; Moonsie-Shageer and Mowatt, 1993).

Highly variable responses to Cr supplementation have made it difficult to determine the specific effect of Cr on the immune system (Spears, 2000). Burton et al. (1994) reported that in newly weaned stressed feedlot calves, Cr supplementation at 0.5 mg of Cr/kg diet for 30 days post-transit to the feedlot increased the magnitude of peak antibody titer response to IBR vaccination, but had no effect on antibody titers to IP-3 vaccination relative to the unsupplemented controls. Dairy cows supplemented with 0.5 mg of Cr/kg diet had greater primary and secondary antibody responses to immunization of an ovalbumin antigen than control cows, but had similar antibody responses to human erythrocytes antigen immunization (Burton et al., 1993). It is unclear as to why the Cr effects were observed with one antigen and not the other. Furthermore, the addition of 0.4 mg of Cr/kg diet did not affect antibody titer responses to porcine erythrocyte immunization in stressed cattle (Kegley et al., 1997). Inconsistent immune responses to Cr supplementation have also been observed in swine (van Heugten and Spears, 1997) and sheep (Gentry et al., 1999).
The reason for the variable responses of Cr supplementation on immune responses in domesticated livestock species is unclear. Factors that may contribute to the inconsistent findings between studies may include: 1) the initial Cr status of the animals; 2) the amount of available Cr in the control diet; 3) the form of Cr supplemented; and 4) the type or degree of stress imposed on the animals (Spears, 2000).

**Trace Mineral Absorption**

The general mechanisms of trace mineral absorption have been researched extensively in non ruminant species but, to date, are not clearly understood. As Bronner and Yost (1985) have suggested, however, trace mineral absorption probably involves both an active and saturable phase as well as a passive and unsaturable phase. Although the molecular mechanism of absorption has not been fully elucidated, the actual site of Zn, and most likely Cu and Mn, absorption has been identified in the small intestine, primarily the duodenum (Davies, 1980).

Prior to introduction at the luminal side of the intestinal cell, it has been proposed that a binding ligand, most likely a protein, may be bound to the trace mineral (Cousins, 1985). This binding ligand may then act as a chaperone to introduce the trace mineral at the brush border or may remain intact with the metal and be absorbed together (Cousins, 1985). The actual mechanism of transport across the brush border is not well understood, but it is likely that a membrane bound transporter of some sort exists. Data suggest that Cu and Zn compete for the same transport mechanism when entering the cell (Oestreicher and Cousins, 1985).

As Hempe and Cousins (1992) have illustrated, a trace mineral is probably bound to an intestinal binding protein after entrance into the cell. In the case of Zn, this intestinal binding protein has been specifically identified as Cysteine-rich Intestinal Protein (CRIP). The function of this binding protein is to act as both a protective mechanism for the cell by binding to free metal in the cytosol and as a specific carrier to chaperone the mineral across the cell to the basolateral membrane (Hempe and Cousins, 1992). If an intestinal binding protein fails to bind the trace mineral, it will most likely be bound to a non-specific binding protein, or in the case of Cu and Zn to metallothionein. The primary function of metallothionein is to maintain homeostasis of Cu and Zn (Pattison and Cousins, 1986). As has been shown by Menard et al. (1981), as metallothionein levels increase the absorption of Zn decreases and as dietary Zn concentrations increase an increase in metallothionein mRNA is also observed. This further supports the theory that trace mineral homeostasis is partially controlled via metallothionein and supports conclusions by Suttle et al. (1982) that Zn homeostasis is controlled at the level of absorption rather than excretion.

Once the bound trace mineral crosses through the cytosol and arrives at the basolateral membrane it is removed from the binding protein and transferred across the membrane via a poorly understood, but saturable, transport mechanism.
(Oestreicher and Cousins, 1984). The trace mineral is then bound to albumin as it enters circulation (Smith et al., 1979). The albumin remains bound to the trace element until it reaches the liver and the trace mineral is further metabolized before being released for transport to other body tissues (Cousins, 1985).

Factors That Can Alter Trace Mineral Metabolism

Despite the involvement of certain trace minerals in animal production and disease resistance, deficiencies of trace minerals have not always reduced performance or increased the susceptibility of domesticated livestock species to natural or experimentally-induced infections (Spears, 2000). There are many factors that could affect an animal’s response to trace mineral supplementation such as the duration and concentration of trace mineral supplementation, physiological status of an animal (i.e., pregnant vs. non pregnant), the absence or presence of dietary antagonists, environmental factors and the influence of stress on trace mineral metabolism (Baker et al., 2003). For the purpose of this portion of the review, five areas deserve attention when discussing potential factors that may affect the trace mineral requirements of ruminants: breed, gestational status, stress, trace mineral antagonists, and age.

Breed: Although species differences in trace mineral metabolism have long been recognized, only recently have differences been noted between breeds within a species. Differences in trace mineral metabolism between breeds of dairy cattle have been reported. In an experiment by Du et al. (1996), Holstein (n=8) and Jersey (n=8) primiparous cows and Holstein (n=8) and Jersey (n=8) growing heifers were supplemented with either 5 or 80 mg of Cu/kg DM for 60 days. At the end of the 60 day experiment, Jerseys had higher liver Cu concentrations relative to Holsteins across both treatments. Furthermore, liver Cu concentrations increased more rapidly and were higher in the Jerseys supplemented with 80 mg of Cu/kg DM compared to Holsteins supplemented with 80 mg of Cu/kg DM by day 60 of the experiment. Overall serum ceruloplasmin oxidase activity (a Cu-dependent enzyme involved in Fe transport) was higher in Jerseys than Holsteins. Additionally, Jersey cows and heifers had higher liver iron (Fe) and lower liver Zn concentrations than did Holstein cows and heifers at day 60 of the experiment. These data indicate that Jerseys and Holsteins metabolize Cu, Zn and Fe differently.

Ward et al. (1995) conducted a metabolism study in which Angus (n=8) and Simmental (n=8) steers were placed in metabolism crates to monitor apparent absorption and retention of Cu. At the end of the six-day metabolism experiment, plasma Cu concentrations and apparent absorption and retention of Cu were higher in Angus relative to Simmental steers. The authors indicate, from their data as well as from others, that Simmental cattle may have a higher Cu requirement than Angus cattle and that these different requirements may be related to differences in Cu absorption in the gastrointestinal tract between breeds. Furthermore, it has also been suggested that these breed differences in Cu metabolism may not be due solely to differences
in absorption, but also to the manner in which Cu is utilized or metabolized post-absorption. Gooneratne et al. (1994) reported that biliary Cu concentrations are considerably higher in Simmental cattle than in Angus cattle. It is apparent that differences in Cu metabolism exist between Simmental and Angus cattle both at the absorptive and post-absorptive levels.

An extensive study comparing the mineral status of Angus, Braunvieh, Charolais, Gelbvieh, Hereford, Limousin, Red Poll, Pinzgauer, and Simmental breeds consuming similar diets has also been conducted (Littledike et al., 1995). This work compared not only Cu, but also Zn and Fe status between all previously mentioned breeds of cattle. In adult cattle, it was shown that Limousin liver Cu concentrations were higher than all other breeds, except for Angus. This same trend was not seen for Zn or Fe; with very little breed differences observed except for lower liver Zn concentrations in Pinzgauer when compared to Limousin. Serum Zn and Cu concentrations did not differ by breed.

**Gestational Status:** Although little data has been published examining the effects of gestational status on trace mineral metabolism in cattle, several experiments have been conducted using laboratory animals and humans that indicate trace mineral metabolism is altered during pregnancy. Research has indicated that Zn concentrations increase in bovine conception products (placenta, placental fluids and fetus) as the fetus grows (Hansard et al., 1968). Studies using rats have shown that the overall maternal body stores of Cu and Zn increase during pregnancy and then decrease during lactation. Mean Zn total body stores at the start of pregnancy were recorded at 5,260 μg of Zn versus 5,810 μg of Zn at day 15 of pregnancy. By day 14 of lactation, maternal body stores of Zn had decreased to 5,640 μg of Zn, which was still considerably higher than at the onset of pregnancy (Williams et al., 1977). These same trends were observed with Cu. In a recent experiment by Vierboom et al. (2002), pregnant cows and sheep absorbed and retained Zn to a greater degree that non-pregnant cows and sheep. These data indicate that certain physiological and/or metabolic parameters are altered in pregnant cows and ewes consuming an alfalfa-based diet that enhance the apparent absorption and retention of certain trace minerals.

The aforementioned data indicate that Cu and Zn metabolism is altered in pregnant vs. non-pregnant animals. Further research is required to determine the metabolic mechanisms that enable pregnant animals to alter Cu and Zn metabolism as well as an animal’s specific metabolic requirement for both maintenance and fetal development. In addition, research to determine the effects of gestational status on the metabolism of other trace minerals as well as if breed differences exist relative to trace mineral metabolism and gestational status is needed.

**Stress:** As mentioned earlier, trace minerals such as Cu and Zn are involved in immune response. Deficiencies and or imbalances of these elements can alter the activity of certain enzymes and function of specific organs thus impairing specific metabolic pathways as well as overall immune function.
Stress and its relationship to the occurrence of disease has long been recognized. Stress is the nonspecific response of the body to any demand made upon it (Selye, 1973). Stressors relative to animal production include a variety of circumstances such as infection, environmental factors, parturition, lactation, weaning, transport, and handling. Stress induced by parturition, lactation, weaning and transport has been shown to decrease the ability of the animal to respond immunologically to antigens that they encounter. Furthermore, research has indicated that stress can alter the metabolism of trace minerals. Stress in the form of mastitis and ketosis has been shown to alter Zn metabolism in dairy cattle. Orr et al. (1990) reported an increase in urinary Cu and Zn excretion in cattle inoculated with IBRV. Furthermore, Nockels et al. (1993) reported that Cu and Zn retention was decreased in steers injected with ACTH (a stressor), in conjunction with feed and water restriction. These studies, in conjunction with several others, indicate that stress in the form of an infection (IBRV), a metabolic disorder (ketosis), or deprivation of feed and (or) water can increase Cu and Zn depletion from the animal.

Trace Mineral Antagonists: Many element-element interactions have been documented (for an in depth review of potential element-element interactions see Puls, 1994). These include Zn-Fe, Cu-Fe, Cu-sulfur (S), Cu-molybdenum (Mo) and Cu-Mo-S interactions and interactions between elements and other dietary components. Peres et al. (2001) used perfused jejunal loops of normal rats to characterize the effects of the Fe:Zn ratio in the diet on mineral absorption. When the Fe:Zn ratio in the diet was held below 2:1, no detrimental effects on absorption were observed. However, once concentrations were increased to yield a ratio between 2:1 and 5:1, Zn absorption was decreased. Similar effects have also been seen for Cu absorption, with depressed Cu uptake in the presence of excess Fe (Phillippo et al., 1987).

The best known of mineral interactions that can cause a reduction in Cu absorption and utilization is the Cu-Mo-S interaction. However, even Mo or S alone can have antagonistic effects on Cu absorption. Suttle (1974) reported that plasma Cu concentrations were reduced in sheep with increasing concentrations of dietary S from either an organic (methionine) or inorganic (Na₂SO₄) form. In another experiment, Suttle (1975) demonstrated that hypocupraemic ewes fed Cu at a rate of 6 mg Cu/kg of diet DM, with additional S or Mo, exhibited slower repletion rates than sheep fed no Mo or S. However, when both Mo and S were fed together, Cu absorption and retention was drastically reduced. Current research would support these findings and suggest that in addition to independent Cu-S and Cu-Mo interactions, there is a three way Cu-S-Mo interaction that renders these elements unavailable for absorption and/or metabolism due to the formation of thiomolybdates (Suttle, 1991).

Ward (1978) also investigated the independent effect of Mo on Cu absorption and concluded that elevated Mo intake reduces Cu availability and can lead to a physiological Cu deficiency. This was attributed to a Cu-Mo complex which forms in the rumen that cannot be broken down and absorbed. Based on this and previous experiments, it appears that the ratio of the antagonistic elements seems to
be more important than the actual amounts. Miltimore and Mason (1971) reported that if Cu:Mo ratios fall below 2:1, Cu deficiency can be produced. Huisingh et al. (1973) further concluded, in their attempt to produce a working model of the effects of S and Mo on Cu absorption, that both S (in the form of sulfate or S-containing amino acids) and Mo reduce Cu absorption due to the formation of insoluble complexes. They also noted that S and Mo interact independently and suggested that they may share a common transport mechanism.

Mineral to mineral interactions are not the only possible inhibitors of mineral absorption. Other dietary components can also inhibit or enhance the amount of mineral that is absorbed. Protein, as might be expected from the discussion involving S-containing amino acids, is an example of a dietary component that can affect mineral metabolism. Snedeker and Greger (1983) reported that high protein diets significantly increase apparent Zn retention. In contrast, diets high in S-containing amino acids have been shown to decrease Cu absorption, most likely due to the formation of insoluble Cu-S and potentially Cu-S-Mo complexes (Robbins and Baker, 1980).

In his review, O’Dell (1984) also noted the potential for carbohydrate source to affect Cu absorption. This is attributed to phytate as well as oxalate concentrations in the diet. Fiber can also act as a mineral trap due to its relatively large negative charge that serves to bind the positively charged divalent metal cations rendering them unavailable for absorption (van der Aar et al., 1983).

Age: Animals have also been shown to have varying mineral needs depending on their age. Trace mineral requirements have been reported to vary with age of dairy cattle (NRC, 2001). Wegner et al. (1972) reported that dairy cattle in their second to fifth lactations had higher serum Zn concentrations than either first lactation or bred heifers. This change in mineral needs over time is most obvious in young growing animals.

Evaluating Trace Mineral Status

To determine an animal’s trace mineral status or to diagnose a trace mineral deficiency or toxicity, blood is commonly used due to ease of collection (Bull, 1980). However, trace mineral-dependent enzymes (e.g., ceruloplasmin, a Cu-dependent enzyme with activity proportional to Cu concentration) have also been analyzed to determine trace mineral status since collection is easy, and possible trace mineral contamination can be avoided (Bull, 1980). The most reliable method of diagnosing a mineral deficiency is to monitor an animal’s response to the supplementation of a particular trace mineral (McDowell, 1992) by monitoring health and/or production after supplementation, since conventional indices of trace mineral status (blood or liver concentrations) are only approximate measurements (Suttle, 1994). However,
due to the significant cost and time constraints of such experiments, the analysis of animal tissue(s) for trace mineral concentration is the most ideal indicator of trace mineral status (McDowell, 1992).

**Copper:** Substantial storage of Cu in the liver is possible (NRC, 1996), and therefore analysis of liver for Cu concentration is considered the best method of classifying Cu status and to document changes in Cu status (Henken et al., 1993). However, determination of Cu status via the analysis of Cu-dependent enzymes including ceruloplasmin and SOD is also common. Analysis of serum Cu concentrations to estimate mineral status is done, but the minimum liver Cu concentration necessary to maintain normal plasma Cu concentrations in ruminants is approximately 40 mg Cu/kg (Underwood, 1977), making serum evaluation a less valuable method to classify Cu status, particularly if cattle are sub-clinically deficient. Analysis of blood samples alone for diagnosis of Cu status can be misleading, and therefore should be accompanied by liver and forage analyses for Cu concentration (Corah and Arthington, 1993).

**Zinc:** Using plasma Zn concentration as a method of classifying Zn status may be inaccurate if cattle are not truly Zn deficient (Hambidge et al., 1986). In sheep, less than 0.5% of total body Zn is in the blood, of which over 80% is in the red blood cells used primarily for carbonic anhydrase activity (Hambidge et al., 1986). However, the analysis of liver tissue for Zn concentration to predict Zn status may not be the best indicator either (McDowell, 1992), since soft tissue Zn concentration varies little with Zn status. Zinc concentrations in plasma and bone have been shown to reflect Zn-deficient diets (Baker and Ammerman, 1995). Severe Zn deficiency can be diagnosed easily due to the observation of obvious clinical symptoms; however, since sensitive methods to analyze Zn status are not available, diagnosis of sub-clinical Zn deficiency can be difficult (McDowell, 1992). As with any trace mineral, observation of production responses (such as feed intake or growth with Zn, specifically) due to supplementation is the best way to diagnose a deficiency (Miller, 1970). Plasma Zn is the most commonly used method to evaluate Zn status (McDowell, 1992); however, using a combination of plasma and forage Zn concentrations may be more acceptable, particularly if large numbers of ruminants are being evaluated (McDowell, 1992). However, in cases when Zn deficiency was severe, changes in Zn concentration in the liver and blood were limited (Miller, 1970).

**Manganese:** In ruminants, the liver contains Mn (Hidiroglou, 1979); however, liver Mn concentration does not respond substantially to Mn supplementation, even at extreme dietary concentrations (Underwood and Suttle, 1999; Miller, 1979). When dietary Mn concentration was increased 130- to 140-fold, only a fourfold increase in liver Mn was detected (Ivan and Hidiroglou, 1980; Watson et al., 1973). However, when the distribution of Mn was evaluated in sheep, concentrations were highest in the liver, which were greater than the pancreas and kidney (Underwood and Suttle, 1999). The ability of the liver to store Mn for long periods of time is thought to be limited (Hidiroglou, 1979). Bone can store a large amount of Mn; however, a small increase in Mn across the entire skeletal system could be unnoticed (possibly undetectable with modern laboratory techniques), even if a substantial change in the
total amount of stored Mn occurred (Underwood and Suttle, 1999). Although using blood is easy for evaluating Mn status, blood Mn concentrations decline slowly only at extremely low Mn intakes (Hidiroglou, 1979). The best indicator of Mn status may involve the use of a compartmental model, which evaluates Mn concentrations in several tissues (i.e., liver, kidney, and bone) to determine Mn status (Henry et al., 1992).

**Selenium and chromium:** For several animal species, Se concentrations in liver, adequately portray Se status (McDowell, 1992). Furthermore, tissue activity of glutathione peroxidase (a Se dependent enzyme) is a relatively good status indicator of Se, because tissue (i.e., liver tissue) and plasma glutathione peroxidase activity increase or decrease rapidly during Se depletion or repletion (McDowell, 1992). However, glutathione peroxidase activity does not reveal the overall Se status within the tissue. Blood Se concentrations indicate current Se status but are difficult to use to determine Se storage in the body. Chromium status of an animal is difficult to determine because an established requirement for the amount of Cr in the diet for optimal cattle performance is unclear due to lack of literature pertaining to Cr, as indicated by the Beef and Dairy National Research Council (NRC, 1996; NRC, 2001).

**Summary**

The interactions between trace minerals, animal production and disease resistance are extremely complex. Many factors can affect an animal’s response to trace mineral supplementation such as the duration and concentration of trace mineral supplementation, physiological status of an animal (pregnant vs. open), the absence or presence of dietary antagonists, environmental factors and the influence of stress on trace mineral metabolism. Breed differences in trace mineral metabolism have also been documented (Wiener et al., 1978; Gooneratne, et al., 1994; Ward et al., 1995: Du et al., 1996; Mullis et al., 1997). Furthermore, research has indicated that different breeds of cattle respond differently to the same immune challenge (Schultz et al., 1971; Blecha et al., 1984; Engle et al., 1999). This may, in part, be related to differences in trace mineral metabolism between different breeds of cattle. Moreover, future research is needed to further investigate the mechanisms by which trace minerals are absorbed and metabolized. A better understanding of trace mineral absorption and metabolism will allow for a better prediction of how trace minerals may interact at the gut and metabolic levels.

**Literature Cited**


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