



## Roles of Minerals in the Bovine Claw

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### Introduction

The trace minerals zinc, copper, manganese, Cobalt and selenium are components of a wide variety of enzymes and proteins that support metabolism, growth, production, and reproduction and have important roles in protein synthesis, vitamin metabolism, formation of connective tissue, and immune function (Miller et al., 1988; Cousins, 1996). The supply of these trace minerals affects several aspects of cattle performance and health, such as claw integrity and immune functions (Miller et al., 1988; Smart and Cymbaluk, 1997; NRC, 2001).

Trace mineral supplements are being added to dairy cattle rations to prevent mineral deficiencies, and supplementation has traditionally been provided in the form of inorganic salts. When these inorganic salts dissociate in the reticulo-rumen, omasum, and abomasum, the trace minerals can form indigestible compounds with other feed components which renders them unavailable for absorption in the intestines. Organic trace mineral supplements that are both stable in the digestive tract and available for intestinal absorption have the potential to be more available to the cow than inorganic supplements. Amino acid complexes of trace minerals are more bioavailable (Wedekind et al., 1992; Paripatananont and Lovell, 1995) and are better retained by the body (Nockels et al., 1993) than inorganic sources of trace minerals. Clinical responses to improved bioavailability and retention of Zn, Mn, and Cu AA complexes and improved claw integrity have been demonstrated (Moore et al., 1989). Improvements in claw integrity have been demonstrated when Co glucoheptonate and AA complexes of Zn, Mn, and Cu (OTM) replaced sulfate trace minerals.

The objective of this paper is to gather and summarize researches related to zinc (Zn), copper (Cu), manganese (Mn), cobalt (Co) and selenium (Se) on claw integrity. After a brief summary of the functions of these nutrients, specific attention will be paid to the effect of trace minerals on claw integrity.

### Roles of Zinc, Copper, Manganese, Selenium and Cobalt in Hoof production and integrity

#### Zinc

Zinc is widely distributed throughout the body as a component of metalloenzymes and metalloproteins (Vallee and Falchuk, 1993). Zinc finger proteins play an integral role in regulating gene expression, consequently impacting a wide variety of body functions including cell division, growth, hormone production, metabolism, appetite control, and immune function (Predieri *et al.*, 2003; Vallee and Falchuk, 1993). Zinc has a catalytic, coactive, or structural role in a wide variety of enzymes that regulate many physiological processes including metabolism, growth, and immune function (Vallee and Falchuk, 1993). Because Zn is required for production of protective keratins in the hoof, one area of recent attention has been evaluating the role Zn plays in maintaining structural integrity and health of the hoof (Tomlinson *et al.*, 2004, 2008). Zinc has been identified as a key mineral in the processes of keratinization (Smart and Cymbaluk, 1997; Mulling *et al.*, 1999; Mulling, 2000b). Zn has a role in 3 key functions in the keratinization process-catalytic, structural, and regulatory (Cousins, 1996).

Catalytic roles are found in enzymes such as RNA nucleotide transferases, RNA polymerase, alkaline phosphatase, carboxypeptidase, alcohol dehydrogenase, and the carbonic anhydrases (Cousins, 1996; NRC, 2001). These catalytic enzymes are Zn metalloenzymes and are dependent upon Zn as an activator, and thus an integral component in the differentiation of keratinocytes.

Zinc also plays a key role in the formation of the structural proteins during the keratinization process. Zinc-finger proteins are involved in functions requiring protein-to-protein interactions, most of which are thought to affect cellular differentiation or proliferation (Cousins, 1996). It is postulated that insufficient Zn status may decrease the formation of Zn-finger proteins and thus the formation of keratin filaments needed in the developing keratinocyte.

The third key role of Zn in differentiating cells, including differentiating keratinocytes, is regulatory.

Zinc regulates calmodulin, protein kinase C, thyroid hormone binding, and inositol phosphate synthesis (NRC, 2001). Calmodulin is responsible for binding Ca<sup>2+</sup> and carrying it into the cytosol of the cell when activated. This is important in the final step of the developing keratinocyte because calcium activates epidermal transglutaminase.

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Protein kinase C (which is also calcium dependent) is responsible for phosphorylation of proteins, thus adding available energy to the differentiation process.

Mulling reported that organic Zn has an important role in the activation and regulation of keratin Protein production by horn tissue explants.

Supplementing cattle diets with Zn has been shown by to improve claw integrity by reducing the incidence of foot rot, heel cracks, interdigital dermatitis, and laminitis resulting in improved locomotion. The level or form of supplemental Zn did not have an effect on locomotion scores during the 14-wk study (Moore et al.1988). Zn deficiency can cause parakeratosis and hyperkeratosis in the epidermis of the hoof (Stern et al. 1998) and,if the nutrient is interrupted, formation of inferior horn of the cow's feet can result, causing claw disorders and subsequently lameness. Zinc has been identified as one of the key minerals in the processes of keratinization (Tomlinson et al., 2004) and greater concentrations of Zn are found in the harder keratin of the hoof wall compared with the softer keratin in the heel (Baggott et al., 1988). Also, the concentration of Zn in the hoof wall in lame animals has been reported to contain significantly less Zn compared with normal animals (Baggott et al., 1988). Level and form of supplemented Zn again resulted in no difference in hoof hardness (Griffiths et al. 2007). The duration of this study (14 wk) could have been responsible for the lack of effect on locomotion and hoof hardness, as hoof growth is accepted to be around 4.5 mm per month. A greater concentration of Zn is present in the harder keratin of the hoof wall compared with the softer keratin in the heel (Baggott et al., 1988). The interruption of nutrient supply to the keratin-forming cells could result in the formation of inferior keratin tissue, potentially causing claw disorders and subsequent lameness (Tomlinson et al., 2004).

If the bioavailability of trace minerals is increased, this could lead to improved production in the keratinized tissues of the claw, ultimately reducing lameness incidence (Tomlinson et al., 2004).

### Copper

Copper functions as component of metalloenzymes that take part in reduction reactions. This metalloenzyme is involved in multiple physiological processes including respiration, carbohydrate and lipid metabolism, antioxidant activities, and collagen formation (Andrieu, 2008; NRC, 2001; Tomlinson *et al.*, 2004). One of the Cu-containing enzymes, ceruloplasmin, binds up to 95% of circulating Cu, regulates iron availability, takes part in oxidation-reduction reactions, and may regulate immune function (Healy and Tipton, 2007). Like Zn, Cu is important for keratin formation and is a component of SOD (Tomlinson *et al.*, 2004). Copper's role in the production of a healthy claw horn is related to the Cu enzyme, thiol oxidase, which strengthens claw horn through the formation of disulfide bonds between Cys residues of adjoining keratin filaments (O'Dell, 1990). This process is essential for structural strength on the cellular level, giving rigidity to the keratinized cell matrix.

Cattle suffering from a subclinical Cu deficiency are more susceptible to heel cracks, foot rot, and sole abscesses (Puls, 1984). This response may be the result of insufficient cytochrome-c oxidase activity, resulting in reduced respiration and oxidative phosphorylation and thus deficient energy supplies for differentiating keratinocytes (Linder, 1996). Heel cracks and abscesses may also be the result of insufficient Cu availability for activation of Cu/Zn SOD. Reduced activity of the Cu/ Zn SOD is expected to enhance the fragility of cell membranes because unsaturated lipids in the cell periphery are particularly vulnerable to oxidative damage (Linder, 1996). The intercellular lipids are an integral parts of the cementing substance responsible for cell-to cell adhesion (Mulling and Budras, 1998). Therefore, any nutrient deficiency that leads to the production of inferior ICS or predisposes it to excessive oxidative damage may lead to production of dyskeratotic horn tissue, with increased susceptibility to cracking and wear.

The connective tissue that suspends the distal phalanx within the claw capsule is strengthened by the Cu-dependent enzyme lysyl oxidase, which forms the cross-linkages between collagen fibers (Smart and Cymbaluk, 1997). Overloading the suspensory connective tissue of the distal phalanx compresses the corium, resulting in the development of claw lesions such as sole hemorrhages, sole ulcers, and Cu is instrumental in the activation of enzymes.

### Manganese

The Mn-dependent enzymes, galactotransferase and glycosyl transferase, are required for the formation of proteoglycans (Miller et al., 1988), which are components of synovial fluid, cartilage, and loose connective tissues (Murray et al., 1993). Animals suffering from a Mn deficiency will exhibit skeletal abnormalities, crooked legs, and shortening of tendons, as noted by knuckling over of feet (NRC, 2001).The fibrocartilaginous insertions in the claw wall and sole and insertion areas of the ligaments and tendons are currently being investigated to determine if

failure of these components is a contributing factor to breakdown of the suspensory apparatus of the distal phalanx (Westerfield et al., 2004).

Manganese also plays a role in the activation of other critical enzyme systems, such as pyruvate carboxylase, an enzyme that catalyzes the first step of carbohydrate synthesis. This process is responsible for gluconeogenesis and the production of cellular energy, an essential component in the production of quality horn tissue (Keen and Zidenberg-Cherr, 1996). Similar to Cu/Zn SOD, Mn plays a role in the activation of Mn superoxide white line separation

### **Cobalt**

Although Co appears to have a lesser role in maintaining claw integrity, vitamin B12 deficiency has been shown to increase the risk of lameness (Smart and Cymbaluk, 1997).

### **Selenium**

Selenium functions as a component of at least 25 different selenoproteins (Andrieu, 2008). In these proteins, sulfur (S) is replaced with Se, which allows the proteins to donate hydrogen and take part in reduction reactions. Selenoproteins include the enzyme iodothyronine deiodinase which is important in regulating metabolism and glutathione peroxidase and thioredoxin reductase which are important components of antioxidant and immune systems (Andrieu, 2008; NRC, 2001). Selenium is a constituent of the enzyme glutathione peroxidase. Glutathione peroxidase plays a role in protecting both the intra- and extra-cellular lipid membranes against oxidative damage. This way Se may contribute to the protection and maintenance of physiological function of the lipid-rich ICS. Excessive supplementation of Se may be damaging to developing keratinocytes.

Due to the diversity of proteins and enzymes containing Zn, Cu, Mn, and Se, these trace minerals are essential for a wide variety of physiological processes regulating growth, production, reproduction, and health. Deficiencies in these nutrients consequently lead to reduced performance, and dairy cattle diets are formulated with trace mineral supplements to prevent deficiencies (Miller, 1981; NRC, 2001). However, chemical composition of trace mineral supplements varies, and research is showing that some supplements are better available to support animal productivity and health than others.

### **Combinations of trace minerals**

There are significant interactions between trace minerals, and hence it is imperative that nutritionists formulate rations to maintain an appropriate balance of trace minerals in order to maximize animal performance. Research has demonstrated that supplying a combination of complexed trace minerals is more beneficial to claw integrity than supplying a sole complexed trace mineral because of synergistic effects. A 2-yr study conducted on 5 commercial dairy herds in Central New York indicated that cows fed 360 mg of complexed Zn, 200 mg of complexed Mn, 125 mg of complexed Cu, and 25 mg of complexed Co resulted in better claw integrity than cows fed only 360 mg of complexed Zn or no complexed trace minerals (Nocek et al., 2000). Supplementation of the diet with a combination of complexed trace minerals reduced the incidence of double soles, white line separation, digital dermatitis; sole hemorrhages, and ultimately, sole ulcerations (Nocek et al., 2000). In addition, 300 cows on a large commercial dairy in Florida were fed a combination of complexed Zn, Mn, Cu, and Co to evaluate claw health (Ballantine et al., 2002). Cows fed complexed trace minerals tended to have fewer incidents ( $P \leq 0.15$ ) of claw disorders than cows fed inorganic trace minerals at 75 d postpartum (23.6 vs. 34.1%) and numerically lower incidence at 250 d postpartum (10.0 vs. 17.7%). Feeding complexed trace minerals reduced incidents ( $P \leq 0.05$ ) of white line disease at 75 (9.5 vs. 14.6%) and 250 d postpartum (4.9 vs. 8.8%). Feeding complexed trace minerals during the late dry period and during early lactation tended to improve claw lesion scores and thus was associated with improved claw health and integrity.

### **Conclusion**

Calcium, Zn, Cu, Mn and Selenium play important roles in the production and maintenance of healthy keratinized tissues. Increasing the bioavailability of trace minerals, especially Zn, Cu, and Mn, improves their utilization and thus contributes to an improved integrity of keratinized tissues, such as skin and claw. Integrity of claw horn is one prerequisite for claw health, which in turn is the prerequisite for overall animal well being, productivity, and potential profitability.

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