Copper Antagonists in Cattle Nutrition

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Primary and Secondary Deficiencies

Mineral deficiencies may be classified as a primary or a secondary deficiency depending on the characteristics of their development.

1. Primary mineral deficiencies are the result of the consumption of feeds that are naturally low in one or more minerals. These deficiencies usually require an extended period of time for their development, often a year or more. The lack of supplemental mineral is a common characteristic of primary mineral deficiencies, as they occur rarely under normal well-managed cattle production systems.

2. Secondary mineral deficiencies are by far the most common of the two. Secondary deficiencies are derived from the consumption of one or more mineral antagonists that interfere with the normal metabolism of another mineral. A simple mineral evaluation of a feedstuff may suggest that adequate trace mineral concentrations are present; however, the presence of a mineral antagonist will decrease the availability of a mineral, potentially leading to a deficiency.

The potential interactions between various minerals are numerous (Figure 1). A clear delineation between each mineral-mineral antagonism is impossible given our current understanding. Further, ruminant and non-ruminant animals metabolize trace minerals differently, suggesting that potential antagonisms will also vary. The stage of an animal's production will also influence how trace minerals are metabolized and the potential influence of existing antagonists.

The data summarized in this report will specifically focus on copper (Cu) antagonists in cattle. The importance of Cu nutrition in cattle is recognized and the influence of multiple antagonists has been widely studied. Following phosphorus, Cu is often the second most limiting mineral nutrient in grazing cattle metabolism.

Historical reference to Cu deficiency in Florida has been common. In fact, the first reported case of Cu deficiency in cattle was reported in 1931 by researchers at the University of Florida. Copper deficiency is almost always linked to a secondary deficiency condition related to one or more Cu antagonists. The commonly recognized Cu antagonists include the following: 1) iron (Fe), 2) molybdenum (Mo), and 3) sulfur (S).
Confounding Research Designs. Research investigating the influence of Cu nutrition on cattle health and performance has often depended upon the experimental feeding of one or more antagonists to induce a Cu deficiency. This methodology creates confounding in the experimental design causing the investigator difficulty in separating outcomes between Cu deficiency and the potential direct effect of the antagonists. An example of this procedure relates to a common technique used in our laboratory as well as others, in which Mo and S are supplemented to cattle diets to induce a secondary Cu deficiency. It is difficult to separate the outcomes of this design between complications associated with the induced Cu deficiency or the direct effect of feeding high levels of Mo and S. This report provides an overview of the impact of Fe, Mo, and S on the antagonism of Cu nutrition in cattle. As described above, the reader should keep in mind that these outcomes may be related to low Cu status or the direct influence of the mineral antagonist.

Iron, Molybdenum, and Sulfur Antagonism

Iron Antagonisms. Iron is the second most common trace metal in the earth. Fe is found in nearly all sources of cattle feed, including water. A considerable amount of Fe may also be digested through the intake of soil during grazing, as well as the soil contamination of harvested forages. Indeed, with the exception of young animals, Fe deficiency is rare in healthy cattle reared under modern agricultural conditions. The more likely contribution of Fe to cattle is its ability to antagonize other trace minerals, notably Cu and zinc. The maximum tolerable concentration for Fe in cattle diets is 1000 ppm; however, dietary concentrations of 250 to 500 ppm have been linked to Cu deficiency (Beef NRC, 1996). The antagonistic role of Fe in Cu nutrition is not well
understood. One explanation relates to the potential disassociation of ferrous sulfide complexes in the low pH of the abomasum. Under this scenario, sulfide may be able to react with Cu, forming insoluble Cu-sulfide complexes (Suttle et al., 1984). Reductions in the performance of dairy cattle in New Zealand have been linked to Cu deficiency as a result of the consumption of high-Fe forages (Campbell et al., 1974).

**Molybdenum Antagonism.** Molybdenum is an essential trace element required by all animals; nevertheless, reports of Mo deficiency are rarely recorded. In contrast, the antagonistic impact of Mo on Cu metabolism has been recognized for many years. Typically, Mo exerts its influence on Cu through the association with S in the formation of ruminal thiomolybdates (discussed below). However, strong evidence exists which shows that decreased animal performance can be related to Mo toxicity independent of decreased Cu availability. Heifers consuming supplemental Mo (dietary concentration = 5 ppm) have been shown to exhibit signs of Cu deficiency, whereas, heifers supplemented with Fe and at the same Cu status had no signs of Cu deficiency. In these studies, the signs of Cu deficiency included reduced growth and feed efficiency (Phillippo et al., 1987a) and infertility (Phillippo et al., 1987b). In another study (Gengelbach et al., 1997), calves provided diets with supplemental Mo had a lower rate of gain compared to Fe-supplemented calves. Both groups of calves had an equivalent extent of Cu depletion compared to Cu-supplemented control calves. These results suggest that some conditions, which are linked to Cu deficiency, might be more accurately described as a toxicity of the antagonist (i.e. Mo toxicity).

**Sulfur Antagonism.** Sulfur is found naturally in nearly all feedstuffs. The form of S varies widely from inorganic salts to organic S-containing amino acids. Recently, more evidence has been derived from commercial cow/calf production systems in Florida suggesting that S may be a primary contributor to secondary Cu deficiencies. The relationship between S, Mo, and Cu has been widely investigated in grazing ruminants. Although Mo is an essential component in this antagonism, it will seldom affect tissue Cu stores when S levels are limiting. Provided adequate dietary S, Mo combines with Cu to form an insoluble complex in the rumen, rendering Cu unavailable for absorption. We have found that a dietary concentration of S of 0.35% (total S) is sufficient for this antagonism to become a concern. The current beef cattle NRC (1996) suggests a maximum tolerable concentration of dietary S of 0.40%.

**Sulfur in Fertilizer.** Ammonium sulfate is a widely available source of fertilizer nitrogen. In recent years consideration to S deficiency in Florida bahiagrass has arisen. In the past, fertilizer impurities provided pasture forages with supplemental S. With the refinement of modern fertilizer manufacturing processes, S contamination is uncommon. Therefore, the effect of S fertilization on bahiagrass yield and quality and the effect of added forage S on cow mineral metabolism is an important issue deserving of investigation.

Dr. Jack Rechcigl (UF-IFAS) reported on a 3-year study investigating the effect of ammonium sulfate fertilization on bahiagrass yield and quality at a site in south-central
Florida. His results showed a 25% increase in bahiagrass yield when pastures were provided with 77 lb of S per acre. In this study, bahiagrass fertilized with ammonium nitrate contained approximately 0.10% S. The application of S via ammonium sulfate increased forage S concentrations to 0.23 and 0.30% for applications of 77 and 155 lb of S per acre, respectively. (DM basis?)

More recently the effect of ammonium sulfate versus ammonium nitrate at common nitrogen rates (60 lb per acre) was investigated over three consecutive growing seasons on bahiagrass pastures near LaBelle, FL (1998 – 2000). In this study, the application of S increased bahiagrass yield only in 1999, but produced a substantial increase in plant S concentration each year, which averaged 0.50% (DM basis) over the three-year study. Cows from the LaBelle, FL pastures fertilized with ammonium sulfate had lower liver Cu concentrations at the end of the grazing season compared to those on pastures receiving no fertilizer or ammonium nitrate (Figure 2). Liver Cu concentrations greater than 125 ppm are considered adequate, 75 to 125 ppm are marginal, and less than 75 ppm are deficient. A random collection of 12 liver samples at the start of the study revealed an initial Cu concentration of 68.0 ppm (dry basis). These results suggest that the cows were Cu deficient when they initially entered the study. Cows in each pasture were provided with free-choice access to a balanced salt-based trace mineral supplement containing 0.25% Cu from Cu sulfate. The most likely explanation for the low liver Cu concentrations in cows grazing ammonium sulfate-fertilized pastures is high forage S concentrations. The 3-year average S concentration for forage samples collected on ammonium sulfate-treated pastures was 0.50%. Even though the maximum dietary S threshold was exceeded in cattle grazing ammonium sulfate pastures, no reduction in cow gain or signs of clinical distress were noted. The

Figure 2. Effect of pasture fertilizer source on liver copper levels in grazing beef cows.
only indicator of S toxicity in this study was the failure of cows on ammonium sulfate-
fertilized pastures to respond to Cu supplementation.

A concurrent cattle study was conducted using pregnant heifers grazing
ammonium sulfate-fertilized pastures from the same LaBelle, FL ranch location. Heifers
were initially Cu deficient (54 ppm liver Cu). Over 83 d, heifers experienced a marked
linear increase (1.91 ppm per day) in liver Cu concentration when removed from their
pastures and offered a control diet, which provided 123 mg of Cu per day. These data
suggest that the cattle were able to rapidly respond to Cu supplementation once the
dietary antagonism of S was removed.

**Thiomolybdate Formation (S and Mo).** Sulfur and Mo interfere with Cu
metabolism through the formation of ruminal complexes called thiomolybdates.
Thiomolybdates can impact Cu nutrition in ruminants by two means: 1) irreversibly bind
Cu in the gut, thereby preventing absorption, and 2) post-absorption systemic depletion
of Cu from tissue sites (Mason, 1990). The formation of thiomolybdates is directly
dependent upon available dietary S, and S intake is a major factor influencing the
sensitivity of ruminants to Mo (Mason, 1981). Dietary S must first be reduced to sulfide
before it can interact with Mo to form thiomolybdates (Mason, 1986). Sulfur may also
decrease Cu availability independent of Mo. In a series of experiments by Suttle (1974)
the addition of both organic and inorganic S to the diets of Cu-deficient sheep
decreased the rate and extent of Cu repletion. These responses were attributed to the
formation of insoluble Cu sulfide complexes in the gut. Their data suggested that an
increase of dietary S from 0.10 to 0.40% of the total diet may result in a 50% increase in
the overall dietary Cu requirement. The antagonistic effect of Mo and S on the overall
Cu requirement of cattle is an important consideration. Numerous equations have been
derived to aid in the determination of appropriate Cu levels in cattle feeds when
antagonists are present. Although these tools are at times helpful, the complex mineral-
to-mineral interactions, shown in Figure 1, preclude nutritionists from fully understanding
these relationships. Using equations derived from ARC (1980), Dr. Gordon Carstens
(Texas A&M University) prepared a hypothetical data set which illustrates the impact of
dietary Mo and S on the efficiency of Cu absorption (Figure 3).

**High S Water.** Excessive dietary S is often associated with a neurological
disease in feedlot cattle called polioencephalomalacia (Jeffrey et al., 1994; McAllister et
al., 1997). Sulfur concentrations greater than 0.40% of diet DM may be toxic to cattle
(Kandylis, 1984; NRC, 1996). Total dietary S is a combination of inputs from forage,
supplement, water, mineral, and ingested soil. Depending on the region of the world, as
well as many other influencing factors, each of these have the potential to contribute a
substantial amount of S to the total diet. Excessive S from water is one of the most
troubling sources to overcome. Unlike fertilizer or supplement, a simple change in
management cannot alter the problem. A water’s odor is not a good indication of the S
content. Often people will characterize water with a “sulfur smell” as having a high-S
concentration. In reality, the odor we smell is hydrogen sulfide, which has volatilized off
the water. The human nose can detect the smell of hydrogen sulfide in the parts per
billion concentration. In many cases, these levels may be too low to contribute substantially to the S level in the total diet. Water tests should be conducted that provide a total S analysis. This will include the sulfates, which are much more important for the contribution to total dietary S.

Figure 3. Impact of forage Mo and S levels on absorption of Cu

A study by Weeth and Hunter (1971) found that beef heifers consuming water that contained 5,000 ppm S had reduced feed and water intake and an associated loss of body weight. At this high level, the water contributes about 200 g of S daily to the total diet. This would be comparable to cattle consuming a diet containing more than 1.75% S, which is extremely high. As well, S from water sources may be more available to participate in ruminal antagonisms compared to S found in other feedstuffs, suggesting that high-S water may affect cattle through pathways related to mineral nutrition as well as general palatability.

Supplemental Feeds and S. Energy and protein supplements also contribute to the total dietary S intake. Typically, high-S concentrations are most closely associated with high-protein supplements, due to the contribution of S in S-containing amino acids. In contrast, liquid sugarcane molasses is considered an energy source that is rather low in protein, but is relatively high in S (0.70 to 1.0% S). Recent research from our program has illustrated the effect of S, derived from cane molasses supplements, on Cu metabolism in grazing heifers. In the southeast and other regions of the US, the use of molasses-based supplemental feeds is common. Recently we have evaluated the absorption efficiency of supplemental Cu provided in corn- versus molasses-based supplements (Arthington and Pate, 2002). Our results indicate that the S concentration
present in cane molasses may interfere with normal Cu absorption in cattle. In these studies, heifers receiving supplemental Cu through corn experienced a 46% increase in liver Cu concentration compared to a 9% decrease in heifers receiving supplemental Cu through a molasses supplement. In a following experiment a third treatment was included that provided Cu in a corn-based supplement, but also fortified with S at a level equal to the amount obtained by the molasses supplement. Increases in liver Cu concentrations were different for each treatment (155, 87, and 13 ppm for heifers fed corn, corn+S, and molasses supplements, respectively (Figure 4).

In both experiments, liver concentrations of Zn, Mn, and Fe were not affected by supplement type, suggesting that each of these elements were absorbed with similar efficiency when delivered in corn- and molasses-based supplements. In contrast, Mo tended ($P = 0.06$ and $0.10$ for Experiments 1 and 2, respectively) to accumulate in the liver of heifers fed molasses-based supplements. This response was likely due to the higher amount of Mo provided by molasses- compared to corn-based supplements (3.2 vs. 1.3 mg daily for molasses- and corn-based supplements, respectively).

In both experiments, liver Cu accumulation was reduced when provided in molasses-based supplements. This response was most likely the result of reduced Cu absorption due to the formation of ruminal thiomolybdates. In the current study, the inclusion of added dietary S to a corn-based supplement resulted in the partial, but not full, inhibition of Cu realized with the molasses-based supplement (Figure 4). This partial inhibitory response may be the result of the rumen’s inability to fully reduce the supplemental S provided in the corn supplement + S treatment. Dietary S must first be reduced to sulfide before it may interact with Mo to form thiomolybdates (Mason, 1986). Another explanation may be related to a lack of Mo in the corn-based supplement to fully participate with S for the formation of thiomolybdate.

Activity of the Cu-transport enzyme, ceruloplasmin, was reduced in molasses-supplemented heifers in both studies (27.8 and 20.5 mg/100 mL for corn- and molasses-based supplements in Experiment 1, and 28.9, 24.5, and 20.8 mg/100 ml for corn-, corn + S, and molasses-based supplements in Experiment 2, respectively; SEM = 1.10 and 1.09). This response was also likely a result of thiomolybdate formation in molasses-supplemented heifers, as reduced ceruloplasmin activity has been shown in both sheep (Mason, 1986) and cattle (Lannon and Mason, 1986) infused with thiomolybdate.

These results provide further insight on the effect of molasses-derived S on Cu nutrition in beef cattle. In further studies (Arthington et al. J. Anim. Sci., In Press), the use of organic Cu supplements were found to not be an effective alternative to CuSO_4 for improving the availability of Cu in molasses supplements. Despite these findings, cattle from the current study and our previous studies were not considered Cu deficient at any date of sample collection. It is likely that most beef cattle are provided molasses only during defined periods of winter supplementation. Although these data suggest that Cu absorption may be compromised during this time, these cattle likely replenish tissue Cu reserves during the summer months when molasses is not consumed. This
standard management scenario suggests that the contribution of S in molasses-based feeds may contribute very little to the overall mineral nutrition of cattle.

Figure 4. Effect of S content of supplemental feeds on liver Cu accumulation in beef heifers

References


Please add references ARC, 1980 and NRC, 1996.