USE OF COPPER PROTEINATES AND COPPER LYSINE
IN ANIMAL FEEDING PROGRAMS

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Introduction

Copper (Cu) deficiencies are the result of either very low levels of copper in feedstuffs or because of other factors which affect the bioavailability of dietary copper. Baker and Ammerman (1995), in reviewing dietary factors which influence the bioavailability of copper, include metal-ion interactions, chelating agents, and compounds such as ascorbic acid, sugars and starches, and some amino acids as factors influencing copper. Frequently, nutritionists add high levels (30 to 40 ppm) of copper to the diet to assure that interfering substances can be negated or because they have observed improvements in animal performance. However, there is also the danger that the added copper can adversely affect other minerals or result in toxicity in some instances. A possible alternative is to use an organic form of copper which might not be affected by other elements.

While our initial interest in Cu at the University of Kentucky was to determine why copper deficiencies are reported on many beef and dairy farms even though copper is supplemented, we have moved to studying bioavailability of different forms, interactions, and also studying immune response.

Bioavailability Studies

Our initial studies (Xin et al. 1991) confirmed that copper oxide had a very low bioavailability as has been shown in studies with swine (Cromwell et al., 1989) and poultry (Baker et al., 1991). One of the main reasons for copper deficiency on cattle farms is the use of copper oxide as the source of copper supplementation. Even though research would suggest copper oxide is not the preferred source of Cu, many companies still include it as a source of Cu. The situation is further aggravated with many trace mineral mixes and especially trace mineralized salts by the low inclusion rate of copper oxide in these supplements. It is not unusual to have an inclusion rate that would amount to only adding 2 to 4 ppm Cu to the total diet. A number of supplements using the sulfate form use an inclusion rate which is probably not optimum.

The first trial in which we included copper proteinate (Bioplex Cu) was a field study (Clark et al., 1993) with a beef herd which had some obvious copper deficiency symptoms. The herd had been fed a mineral supplement containing relatively low levels of copper oxide. Low serum Cu levels, a low calving rate, and some haircoat color changes were
observed in the herd. A comparison of copper sulfate, copper oxide, and copper proteinate was initiated just prior to breeding season. Liver samples at the end of the trial indicated a very low bioavailability of copper oxide when compared with sulfate. In addition, the liver samples indicated a higher bioavailability for the proteinate as compared with copper sulfate. The percent of cows calving was increased to acceptable levels by the inclusion of either the sulfate or proteinate form of Cu. This, plus observations by the farmer led us to having an interest in the organic forms of copper.

Rat Studies

In order to understand what is being influenced at the absorption site and in the metabolism of Cu, several trials with rats as the experimental animals have been conducted. These trials each included 72 animals per trial which allowed us to incorporate more treatments and measure interaction of trace elements. Two mechanisms have been described for Cu absorption. The primary system for inorganic Cu is an active transport system which has interactions with zinc and iron. A diffusion system is also operational but is generally considered as having a minor role. Homeostatic mechanisms regulate the rate of absorption and may help to protect many animals from toxic levels of Cu when Cu is fed at very high levels.

Table 1. Effect of copper source on Cu and Zn content of tissues.

<table>
<thead>
<tr>
<th>Cu Source</th>
<th>Cu So₄</th>
<th>Cu P</th>
<th>Cu L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cu content (mg/g dry tissue)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td>11.5\textsuperscript{a}</td>
<td>12.6\textsuperscript{a}</td>
<td>12.0\textsuperscript{ab}</td>
</tr>
<tr>
<td>Spleen</td>
<td>4.7\textsuperscript{a}</td>
<td>5.0\textsuperscript{b}</td>
<td>5.1\textsuperscript{b}</td>
</tr>
<tr>
<td>Kidney</td>
<td>29.3</td>
<td>29.9</td>
<td>29.5</td>
</tr>
<tr>
<td>Zn content (mg/g dry tissue)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td>89\textsuperscript{a}</td>
<td>93\textsuperscript{b}</td>
<td>90\textsuperscript{ab}</td>
</tr>
<tr>
<td>Spleen</td>
<td>85</td>
<td>87</td>
<td>87</td>
</tr>
<tr>
<td>Kidney</td>
<td>109</td>
<td>113</td>
<td>111</td>
</tr>
</tbody>
</table>

\textsuperscript{ab} Means without a common superscript differ (P<0.05).

The first two trials as published by Du et al., 1996, were designed to compare Cu from sulfate, proteinate and lysine forms with their interaction from either zinc sulfate or iron sulfate. Table 1 illustrates the differences found in the trials. The increased Cu content of liver samples indicate a higher bioavailability for the organic forms of Cu. The surprising increase in liver zinc when the proteinate was fed would suggest that the normal
effect of reduced uptake of zinc when copper absorption is increased does not occur when the organic form is fed.

The results of the trials with both zinc and iron suggest that the mechanism of absorption of the organic forms may be due to a different absorption system other than an active transport system. This concept has been proposed by Lowe (1996) in a study utilizing radioisotope techniques to study zinc absorption in dogs. He compared zinc in a proteinate/chelate form with zinc oxide and concluded that the organic zinc is absorbed more efficiently by a different mechanism than that of inorganic zinc. In addition he suggests a different transport mechanism for the organic form after it enters the blood. His study supports our rat studies and expands the data to zinc proteinate.

A later study (Shi et al., 1995) with rats studied the interaction of Cu proteinate and Cu sulfate with either iron oxide, iron sulfate or iron proteinate. This was our first trial in which both minerals were supplemented in an organic form. The results (Table 2) showed a higher bioavailability for organic forms and a decline of the interference which would normally be expected when a high level of iron is fed. The data supports the recommendation to feed proteinates when an interference from a high level of iron is present.

### Table 2. Comparison of copper sulfate and proteinate when diet is supplemented with iron as the oxide, sulfate and proteinate forms.

<table>
<thead>
<tr>
<th>Cu Source</th>
<th>Fe Source</th>
<th>Cu SO₄</th>
<th>Cu P</th>
<th>Fe₂O₃</th>
<th>Fe SO₄</th>
<th>Fe P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cu content (mg/g DM)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td>10.8ᵃ</td>
<td>11.7ᵇ</td>
<td>10.9ᵃ</td>
<td>10.9ᵃ</td>
<td>11.9ᵇ</td>
<td></td>
</tr>
<tr>
<td>Kidney</td>
<td>20.3</td>
<td>20.4</td>
<td>21.5ᵇ</td>
<td>18.7ᵃ</td>
<td>20.8ᵇ</td>
<td></td>
</tr>
<tr>
<td>Fe content (mg/g DM)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td>550</td>
<td>557</td>
<td>470ᵃ</td>
<td>610ᵇ</td>
<td>580ᵇ</td>
<td></td>
</tr>
<tr>
<td>Kidney</td>
<td>208</td>
<td>190</td>
<td>204</td>
<td>201</td>
<td>192</td>
<td></td>
</tr>
</tbody>
</table>

Means from source without a comma superscript differ (P< 0.05).

### Cattle Studies

The initial study (Xin et al., 1991) demonstrated that marginally Cu deficient steers had a reduced ability to kill *S. Aureus*, one of the primary mastitis organisms. This has led to additional studies by Harmon (Harmon et al., 1994a and b) on the importance of Cu in immune response and susceptibility of dairy cows to mastitis. These studies also support the proposal that optimum immune response has a higher requirement for copper
than growth and performance. The data also demonstrate that a high incidence of mastitis at calving time can be caused by inadequate Cu as well as by other minerals which are known to influence immune response.

It has been suggested that both reproductive performance and immune response are optimized by higher levels of dietary copper than for growth or animal performance. Since many of our requirements were established before the recognition that resistance to disease was an important function of many of our trace elements, we may need to reevaluate some of our trace mineral requirements. The establishment of the principal of a higher requirement for immune response than for growth has been demonstrated in a basic study with rats. (Nelson et al., 1992).

**Copper Toxicity**

Rather than trying other approaches to copper problems such as using a proteinate, a number of nutritionists has formulated diets containing 40-50 ppm of Cu. While this level is well below the maximum tolerable level of 100 ppm as stated by the National Research Council (1980), it has led to some death losses in a number of Jersey herds. The combination of high levels of copper together with the feeding of whole cottonseed has caused copper toxicity as clearly shown by toxic levels of Cu in the liver. We (Du et al., 1996) have confirmed that Jerseys metabolize Cu somewhat different from Holsteins and probably metabolize iron differently. While we have not established a safe upper limit for Cu, we would recommend that those formulating Jersey diets be very careful and only add what is needed. It would be a very unusual situation which would call for more than 20 ppm. We would suggest that an alternative to high levels of Cu would be to try an organic form of Cu. It should also be remembered that high levels of Cu can also affect the use and absorption of other minerals.

**Conclusions**

1. Copper deficiencies occur not only because of low levels of dietary copper but are frequently caused by interferences from high level of molybdenum and sulfur, iron, zinc, and other compounds. Adjustments from the NRC recommended levels are sometimes needed due to these interactions.

2. Supplemental copper must provide copper in a form which has a high bioavailability. Copper oxide is not recommended but is still widely used in livestock diets.

3. Errors made in supplementing copper include both inadequate amounts as well as excessive amounts which can be especially dangerous with Jersey cattle.
4. Organic forms of copper are recommended when interferences with iron and zinc are possible. High iron levels in feeds as well as in water are frequently observed on dairy farms.

5. Organic forms, since they are metabolized somewhat differently than inorganic forms, may be beneficial in herds that appear to have copper related problems, such as reduced immune response or reproductive problems.

References


