Copper in Ruminants

Best Practices to Master the Supplementation

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Why Copper is essential for ruminants?

Copper (Cu) is an essential element to all living beings as it plays an important role in many biological processes. It is a co-factor of several important enzymes including lysyl oxidase, tyrosinase and cytochrome c oxidase. These important enzymes are required mainly for the synthesis of erythrocytes, myelin, keratin and collagen but also for effective immune and anti-oxidant responses. Nevertheless, Cu is the most common trace element deficiency in ruminants, characterised by a loss of hair pigmentation (particularly around the eyes), mucosal atrophy, depression of the immune function, bone fragility, cardiac failure and reduced reproduction and production performances.

Why copper metabolism is different in ruminants?

Unlike monogastric, ruminants have very poor homeostatic control of Cu. Indeed, cattle developed a special mechanism of storage of Cu excess in the liver by reducing its excretion in the bile which makes them very sensitive to Cu. Ensuring adequate Cu supplementation in ruminants is challenging for nutritionists because of the complexity of copper metabolism with a very small margin between deficiency and toxicity.

Copper deficiency occurs due to either a primary or a secondary deficiency. The primary deficiency is mainly associated with low Cu diets (<4 ppm) but this scenario is most unlikely to happen. However, secondary deficiency happens even at the right level of Cu supplementation. The three-way interaction between Cu, molybdenum and sulphur (Cu-Mo-S) in the rumen makes ruminants, particularly cattle, very susceptible to suffering from secondary copper deficiency. In fact, in the rumen, Mo and S interact together, forming complexes called thiomolybdates (TM) with high affinity to Cu making it less bioavailable for the animal. To guarantee Cu absorption, regardless of the antagonist's presence, there is a tendency to supplement Cu above nutritional requirements leading to chronic copper poisoning (CCP) in cattle and especially in dairy herds.

Chronic copper poisoning is mainly due to the slow accumulation of small quantities of Cu in the liver during a long period of time. Identifying CCP is not an easy task to do, as in the first stage, there are no changes in blood Cu and only evaluating liver concentration is relevant. An increase in blood Cu is only seen as a second stage when the liver is overloaded and it is released into the bloodstream. This causes acute toxicity with animals often dying within 24-48 hours. A growing number of lethal cases reported by veterinarians showed that such silent intoxication is spreading in dairy herds. A study was conducted in the UK to survey liver copper concentration within the UK dairy and beef herds using 510 abattoir cull cow samples. This study demonstrated that over 50 % of the liver samples analysed were above usual values of copper (Table 1). Moreover, 40 % of the female dairy cattle had liver copper concentrations above the AHVLA (Animal Health and Veterinary Laboratories Agency reference) range of 8000 mmol/kg DM. For all these reasons, there is a real need to set up strategies to monitor herd Cu status and amplify the awareness of farmers for CCP.

How to prevent copper toxicity in cattle?

Precision mineral feeding

Knowing the mineral composition of forages and the basal diet is fundamental to ensuring precision mineral supplementation and thus preventing CCP in ruminants. Indeed, minerals in the basal diet are often not investigated because they are not a priority when formulating the diet and also because of the high cost and long process of the mineral fraction analysis. Animine developed a portable analytical

Table 1: Numerical distribution of liver copper concentration by NuVetNa (School of Veterinary Medicine and Science, University of Nottingham) category of bulls, beef cows, Holstein-Friesian (HF) dairy and other dairy cows (Kendall et al., 2015)

NUVetNA category	Liver copper µmol/kg DM	HF dairy cows	Other Dairy Cows	Beef Cow	Bull	Total
Deficient	281-1404	30	6	42	5	83
Normal	1405-11237	294	18	30	7	349
High	11238-14046	34	2	3	1	40
Toxic	14047-44952	31	4	2	1	38
Total		389	30	77	14	**510**
Above AHVLA reference range	>8000	149 (38.9%)	12 (40.0%)	13 (16.9%)	3 (21.4%)	177 (34.7)

tool for animal nutrition, able to evaluate mineral fractions in forages with a rapid and affordable method. This portable XRF analyzer (X-ray fluorescence spectrometry) allows users to obtain instantly high precision and immediate results to help nutritionists optimise mineral supplementation and thus make an adequate Cu supply.

Beware of higher risk of copper toxicity in high starch diets

Recent studies have highlighted that feeding high starch diets in dairy herds is likely to increase Cu reserves. Indeed, when cows are fed additional S and Mo in a grass silage-based versus a corn silage-based diet, there is a greater decrease in hepatic Cu concentration. It is suggested that this may have been due to the potential effect of rumen pH on S metabolism and TM formation. Indeed, TM formation is highly pH dependent in the rumen, with a greater proportion of Tetra TM formed at lower pH values which has a high affinity to Cu. Corn silage is higher in starch than other forages such as grass or alfalfa silage, and its inclusion is often associated with a decrease in rumen pH. Lower rumen pH means greater loss of Hydrogen Sulfide (H2S) by eructation and exhalation. The more H2S is formed the less S is available for TM formation (see Figure. 1). Reasons for these differences in Cu absorption and metabolism as a result of dietary starch concentration or reticular pH are unclear and require further investigation, but highlight the need to take these factors into account when calculating appropriate Cu supplementation levels for lactating dairy cows.

Mastering mineralisation in calves and heifers

When feeding young calves, we are actually feeding monogastric as their rumen are not completely developed yet which means that they are less exposed to the impact of the antagonists' effects in the rumen. Indeed, they readily absorb Cu without any depletion factors and even if their feed intake at birth is low, they are efficient absorbers of this mineral. The CCP is particularly acute with pre-ruminant calves. In fact, when calves consume more Cu than they need, the excess is stored in the liver and builds up over time. Previous studies demonstrated that eventual liver toxicosis can lead to the premature breakdown of red blood cells (hemolysis), anaemia, jaundice, and even death. In the absence of cases of clinical toxicity, heifers begin with very high initial hepatic Cu concentrations and may lead to altered liver function which is translated into reduced conception rate and milk yield.

The right source of copper

Choosing the appropriate Cu source to supplement in the feed is also of importance. Indeed, the physicochemical characteristics and dissolution kinetics are key to preventing the formation of the TM-Cu complexes in the rumen. Copper(I) oxide (CoRouge), recently authorised in the market, combines high bioavailability with low solubility at rumen pH. This innovative source of copper will help to restrict the need for higher copper dosages in ruminant diets and to preserve animal productivity, health and welfare.

Conclusion

Copper bioavailability for ruminants is mainly determined by sulphur, molybdenum and iron levels in the diet. Increasing the quantity of copper supplemented in bovine diets leads to copper chronic toxicity. Some good practices should be adopted to prevent this metabolic disorder. Thus, special attention should be paid to the basal diet as it is important to know the initial copper and its antagonists' concentration. Moreover, feeding diets with high starch levels is more likely to induce copper toxicity in intensive dairy herds. Calves and heifers fed with high levels of copper have initial high liver copper concentration which will lead to reduced fertility and production performance later as dairy cows. Finally, it is important to use bioavailable copper sources to avoid insoluble complex formation in the rumen.

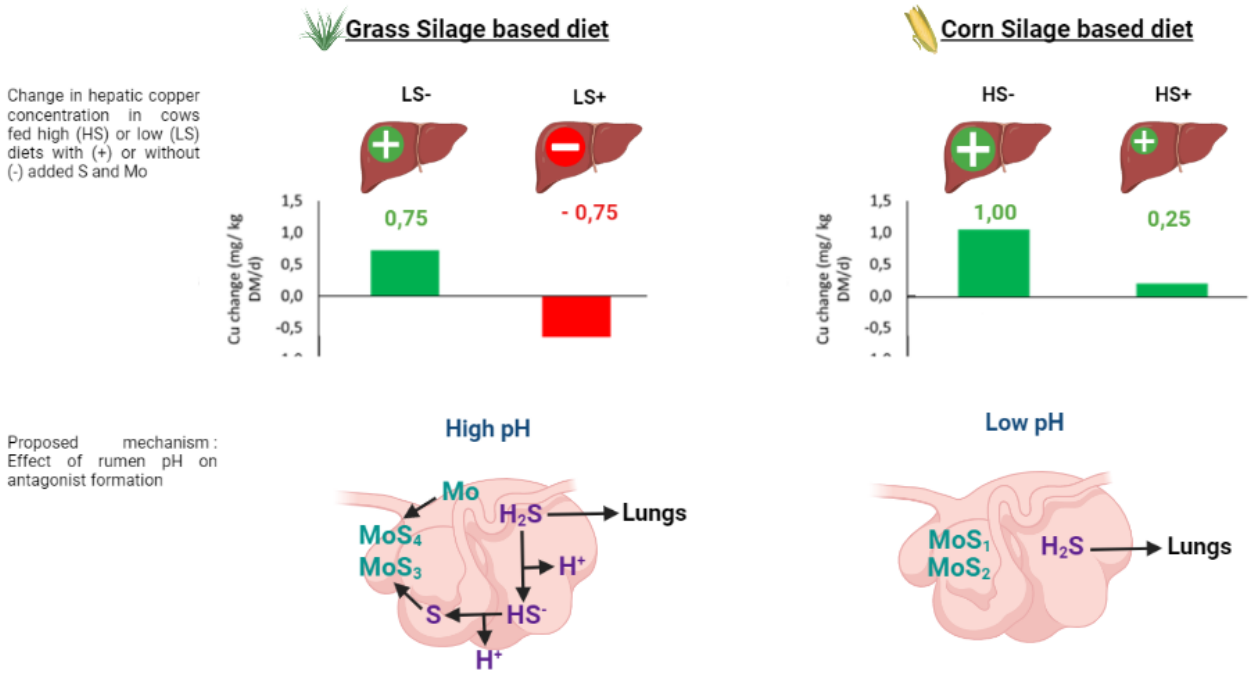

Figure 1: Suggested mechanism of the effect of the diet on copper metabolism adapted from the study of McCaughern et al. (2020)