COPPER METABOLISM

1. The unknown consequence of SARA

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Copper (Cu) is an essential trace element in ruminants as it is co-factor in 300 enzymes including lysyl oxidase, tyrosinase and cytochrome c oxidase. Copper deficiency in ruminants is characterised by depression of the immune function, cardiac failure, loss of hair pigmentation, reduced reproduction and production performances, and also bone fragility.

Unlike monogastric, ruminants have a very poor homeostatic control of copper. Indeed, cattle developed a special mechanism of storage of Cu excess in the liver by reducing its excretion in the bile which make them very sensitive to Cu with a small margin between deficiency and toxicity.

Please refer to former article in International Dairy Topics volume 19.1, 2020: "Copper in Ruminants beware of going from deficiency to toxicity".

The antagonists and its consequences

Copper deprivation occurs due to either a primary or secondary deficiency. The primary deficiency is the 'classic' form, in which low levels of Cu are supplied in the diet and it does not meet animal requirements, but this scenario is most unlikely to happen.

However, secondary deficiency happens even at the proper level of Cu supplementation. In fact, in the rumen, molybdenum (Mo) and sulfur (S) interact together, forming complexes called thiomolybdates (TM) with high affinity to Cu making it less bioavailable for the animal.

The nomenclature follows the level of S chelation: mono (TM-1), di (TM-2), tri (TM-3) or tetra (TM-4) – thiomolybdate, the latter being the most stable and having the highest affinity with Cu. Due to the presence of these antagonists, Cu absorption in adult cattle does not exceed 7%, while it is up to 70% in calves.

Interaction with S and Mo is most widely recognised, however, there are also interactions with iron (Fe), zinc (Zn) and manganese (Mn). To guarantee Cu absorption regardless of antagonist's presence, there is a tendency to supplement Cu above nutritional requirements leading to chronic copper poisoning (CCP) in cattle and especially in intensive dairy herds.

The increasing number of lethal cases reported by veterinarians showed that this silent intoxication is spreading in dairy herds. There is a need to develop strategies to monitor Cu status in dairy herds and to raise awareness of copper toxicity among farmers. Recent research indicates that Cu already accumulates in the liver of cows at dietary levels recommended by the industry, and that cattle could be less tolerant to copper than previously thought.

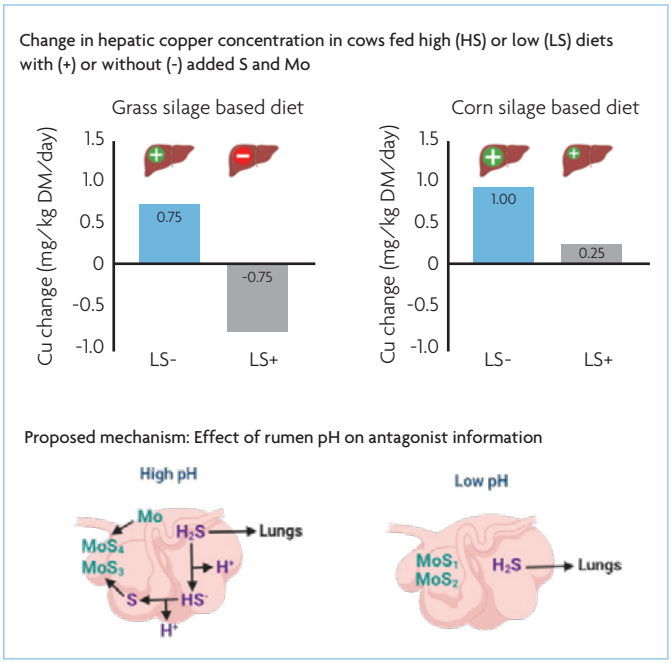

Fig. 1. Suggested mechanism of the effect of the diet on copper metabolism adapted from the study of McCaughern et al. (2020).

High starch diets: another factor affecting Cu metabolism?

It is well known that starch is a rapidly fermentable carbohydrate which can decrease rumen pH via the production of organic acids particularly when the buffering capacity of the rumen is exceeded. There are many studies regarding the effect of dietary starch on milk yield, fat and protein content.

However, few data are available on the effect of dietary starch content on Cu metabolism in lactating dairy cows. This lack of understanding of the effect of dietary factors on Cu metabolism may lead to unnecessary over-supplementation of this element in dairy rations.

More and more recent studies demonstrated that feeding high starch diets in dairy herds increases Cu reserves. 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 be 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 TM-4 formed at lower

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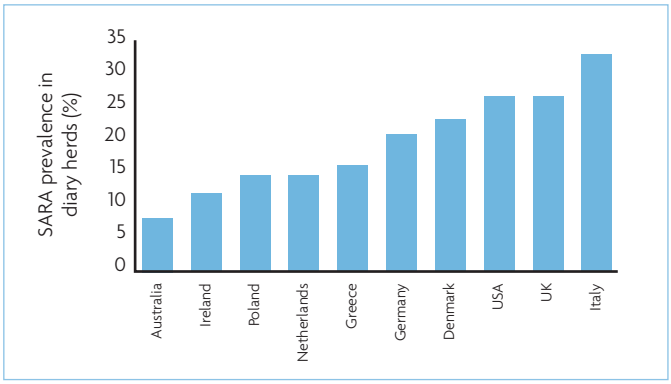
Fig. 2. Prevalence of sub-acute rumen acidosis in dairy herds. Rumen pH lower than 5.5.



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pH values. 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 inhalation. In fact, in the rumen, S-containing amino acids and/or inorganic sulfates are reduced to hydrogen sulfide (H2 S) by sulfur reducing bacteria and excreted into the ruminal fluid. Some of H2S produced disassociates to form bisulfide (HS-) in the fluid, while the remaining H2S migrates to the gas cap of the rumen.

This reaction is pH-dependent, whereby at a rumen pH of 5.5, approximately 5% of H2S will disassociate to HS-, whereas at a pH of 7.0, approximately 50% will disassociate to HS-.

The more H2S is formed the less S is available for TM formation (see Fig. 1). Sulfide in the rumen fluid is subsequently free to form an insoluble Cu sulfide compound which is suggested to reduce Cu availability.

Reasons for these differences in Cu absorption and metabolism highlight the need to take these factors into account when calculating appropriate Cu supplementation levels for lactating dairy cows.

Is sub-acute rumen acidosis a real problem worldwide?

Acidosis remains a major challenge for dairy and beef cattle production worldwide. Especially sub-acute rumen acidosis (SARA), because of its difficulty to get diagnosed.

The lack of accurate diagnostic test, combined with the variable nature of rumen pH has contributed to this vagueness on diagnosis criteria. SARA was defined as a rumen pH reduction from 5.5 to 5.0 for 111 to 180 minutes per 24 h. Prevalence of SARA was studied in different countries (Fig. 2). On average, the range of SARA prevalence in dairy herds was from 8% in Australia to 33% in Italy.

The huge variation of SARA prevalence is due to its multifactorial origin. SARA could be caused by the consumption of diets high in readily fermentable carbohydrates and low in effective fibre which lead to produce organic acids that exceed the buffering capacity of the rumen.

The evidence shows that the ruminal microbiota plays a substantial role in SARA, with cellulolytic bacteria decreasing and acid-tolerant bacteria such as Streptococcus and Lactobacillus spp. increasing.

There are others factor also affecting SARA incidence, like the days in milk, especially cows in early lactation and cows at the peak of dry matter intake.

Also, the farm feeding management can affect SARA incidence. The more understood consequences of SARA such as rumenitis, milk fat depression, laminitis, and liver abscesses affect animal production and health. This is why this pathology has a big impact in farm profitability and animal welfare. But as was mentioned before, there are other consequences less known of SARA, like the influence on Cu bioavailability and potential toxicity.

The right source of copper could help with preventing copper toxicity

Choosing the appropriate copper source to supplement is also of importance. Indeed, selecting copper sources with known physicochemical characteristics and dissolution kinetics is key to prevent formation of the TM- Cu complexes in the rumen. Copper(I) oxide (CoRouge), recently authorised in the market, combines high bioavailability with a 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 S, Mo and Fe levels in the diet. Increasing the quantity of Cu supplemented in bovine diets leads to copper chronic poisoning. The risk of copper toxicity is higher in intensive dairy herds. Some good practices should be taken into account to prevent this metabolic disorder.

Thus, special attention should be paid to the basal diet as it is important to know the initial Cu and its antagonist's concentration. Moreover, diets with high starch levels are more likely to induce Cu toxicity. Finally, it is important to use bioavailable Cu sources to avoid insoluble complex formation in the rumen. ■

This article is a first part of a series on copper in ruminants.