Which copper source for my feed?

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VALÉRIE KROMM and JENNIFER MAURIN* present dicopper oxide – an innovative source of copper.

CoRouge is unique – it is the only red source of copper(II) oxide authorized by EFSA in the European Commission. This monovalent source of copper is characterized by superior technological properties but also by some specific chemical properties (due to its different oxidation status, as monovalent) differentiating it from all other feed grade source of copper. High bioavailability and improved animal performance have been demonstrated in many university studies.

Highest copper concentration

The high copper concentration in CoRouge is of special interest for premix manufacturers who are concerned by the Seveso III Directive. Replacing other copper sources by CoRouge gives an opportunity to decrease the quantity of stored products which are classified as dangerous for the environment.

Lower heavy metal contamination

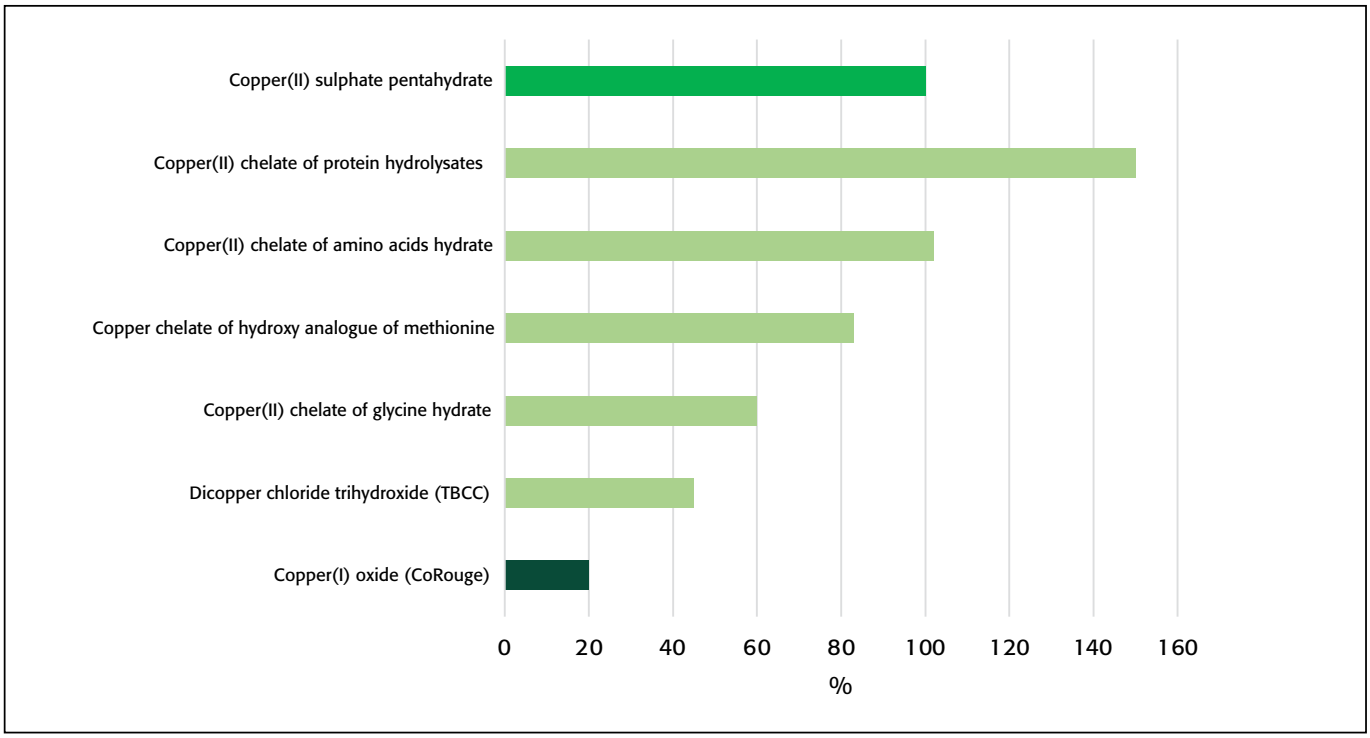
All copper feed grade sources must comply with stringent regulation on undesirable substances. Heavy metals and dioxins are the most critical risks for the feed and food chain. The higher the copper concentration, the lower is the contribution to contamination in the feed. Figure 1 illustrates this advantage with the example of arsenic, based on homogenized European regulation.

Non-water soluble copper source

There are many advantages in favor of non-water-soluble compounds, under the condition that they are enough solubilized in the proximal part of the digestive tract for intestinal uptake. Copper sulfate is well known for its hygroscopicity. Sulfates and certain chelated trace minerals are water soluble compounds and can create negative interactions in the premix and in the gut.

Already in the early 2000's, it had been shown that metal oxides were less aggressive on vitamin stability when mixed in vitamin and

Figure 1: Relative contribution to arsenic in the feed.



mineral premixes. Since, vitamin manufacturers have improved their stability so that they are less sensitive to negative effects from other compounds and from storage conditions. However, a study showed that vitamin A is 12% less degraded in a typical premix for piglet feeds when mixed with Animine products (potentiated zinc oxide HiZox and CoRouge) than with zinc and copper sulfate.

Attention given to vitamins stability in premixes and feeds is even more critical when vitamins levels are reduced due to extremely high prices or product shortage.

Reduced antagonism with phytase

Minerals like calcium, zinc, copper and iron may bind to phytic acid, thus lowering its solubility in the digestive tract. If such antagonists rapidly chelate phytate after ingestion, then its hydrolysis by endogenous or supplemented phytase will be impaired. This negative interaction will be severe in following conditions:

- supplementation of high dosages of trace minerals,
- supplementation of soluble sources like sulfates or chelates
- supplementation of phytase form slowly acting.

Phytic acid has a strong affinity to bind with divalent and trivalent forms of minerals. At the difference with other copper compounds, dicopper oxide is a monovalent form of metal. With a non-water soluble and monovalent source of copper, CoRouge is less likely to negatively interact with the release of phytic phosphorous. This has been shown in an *in vitro* study performed by the University of Barcelona (Spain).

Direct intestinal absorption

Active absorption of copper involves various intestinal transporters, the most important one being named CTR1. Copper absorption depends on its oxidation state. Uptake of copper by CTR1 is possible only with the monovalent form of the copper ion. However, most of copper sources authorized and used in animal nutrition include copper ions in the divalent form.

Consequently, some enterocytes membrane proteins have to reduce $Copper^{2+}$ into $Copper^{+}$. These proteins are not fully identified yet but the main hypothesis refers to Steap proteins, like Steap2, also identified as Fe^{3+} reductase. A monovalent form of copper supplied from CoRouge

Figure 2: Vitamin A stability in a piglet premix.

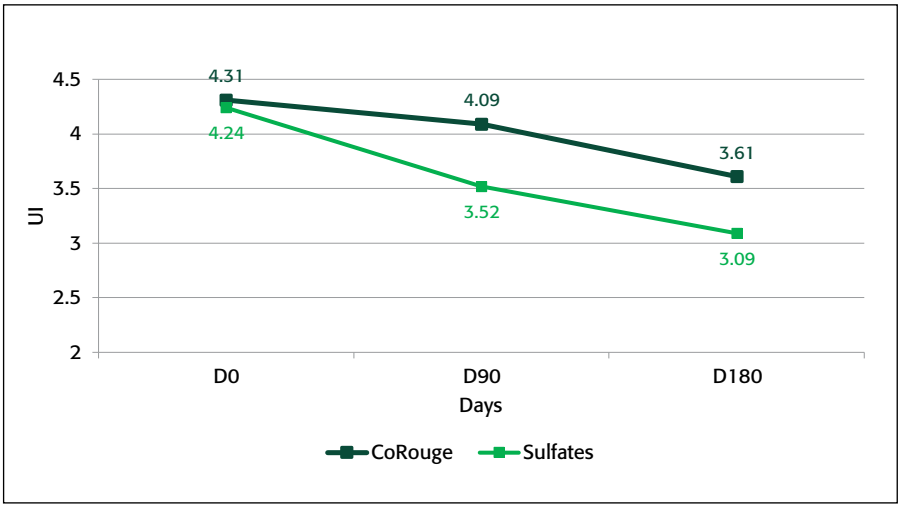
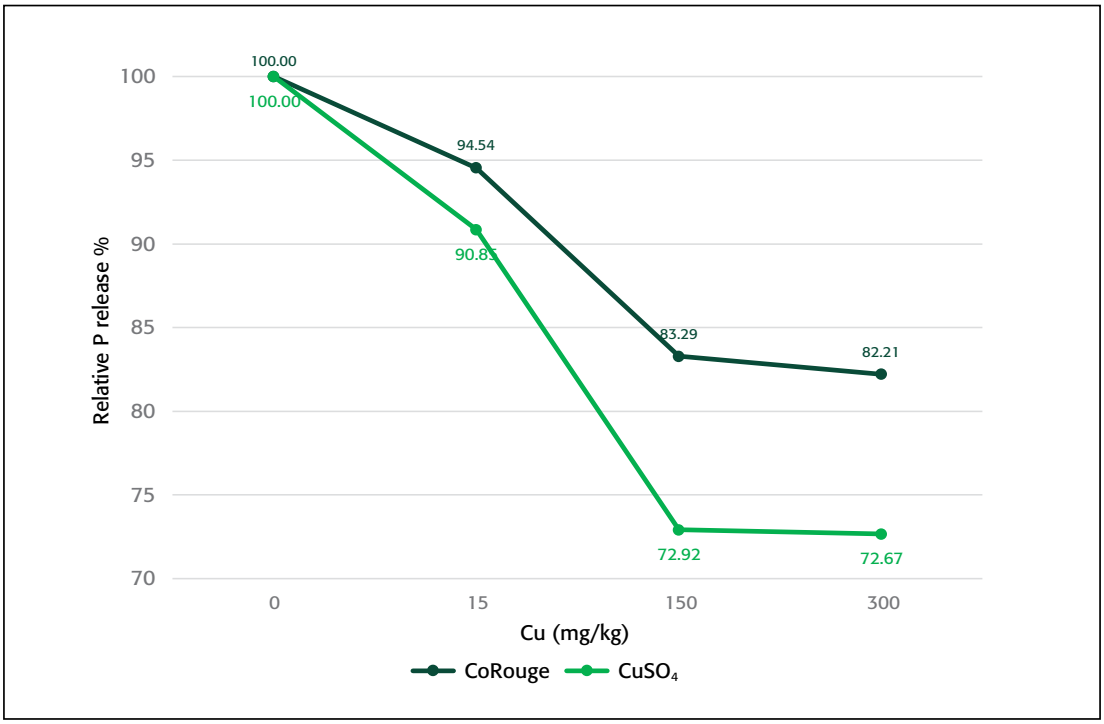


Figure 3: Effect of copper on phosphorous release.



will be directly absorbable, thus less prone to interferences.

High bioavailability

During last decades several EFSA opinions showed the non-superior bioavailability of chelated forms compared to sulfates, considered as the reference:

- In 2008, EFSA concluded that copper chelate of hydroxy analogue of methionine had a bioavailability comparable to copper sulfate.
- In 2013, EFSA confirmed that the bioavailability of copper chelate of amino acids would not be higher than copper sulfate.
- In 2014, EFSA showed an equivalent bioavailability between copper bilysinate and copper sulfate.

At the contrary, the high bioavailability of dicopper oxide in CoRouge has been verified in laboratory animals and in farm animals. In comparison to livestock, it is much easier to deplete rats in copper, and to measure how dietary sources can replete animals. Such experimental protocol is necessary when we lack sensitive biomarkers of mineral status. This has been realized at the University of Florida under the supervision of Dr Jamie Collins. Measured with liver concentration and serum ceruloplasmin activity, copper status of rats was equivalent between copper sulfate and CoRouge. The high bioavailability of dicopper oxide has been demonstrated also on piglets, when supplied at low dosages. An experiment performed at Wageningen University (Netherlands) showed that copper concentrations in plasma, liver and bile were equal when piglets were fed either copper sulfate or CoRouge.

At nutritional levels, it is confirmed that the monovalent form of copper oxide shows high bioavailability for the animals, comparable to copper sulfate or chelated compounds.

Growth performance of piglets

The growth promoting effect of copper supplementation on weaned piglets is well documented. Free forms of copper (not chelated ones) are known for their antibacterial action and this remains the most assumed effect on intestinal health.

It is generally perceived that the growth promoting effect of some additives such as copper is limited under good nutritional and management practices. However, this has not been confirmed in two recent experiments supervised by Dr Paul Bikker (Wageningen University). The first experiment tested different copper doses, from 15 to 160 mg/kg supplied as copper sulfate. A dose-response effect was confirmed for growth performance: average daily gain (ADG) increased as Copper dose increased ($p < 0.01$), while feed conversion ratio decreased ($p < 0.01$). Piglet's weights were improved by 2.8 kg after 40 days of supplementation: it is very unlikely that most of feed additives can achieve such performance

The most recent study was also performed on a high number of animals - 600 piglets, weaned at 26 days. There were no medicated zinc

Figure 4: Copper uptake in the enterocyte.

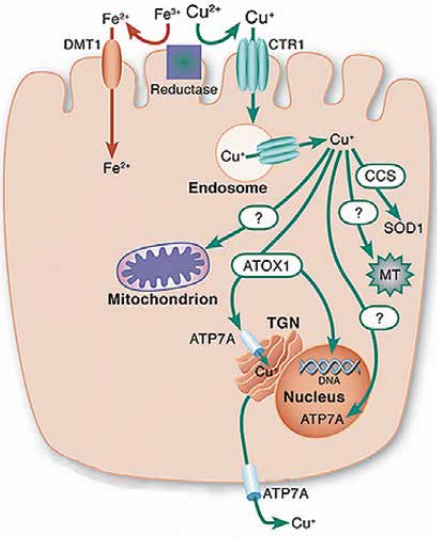
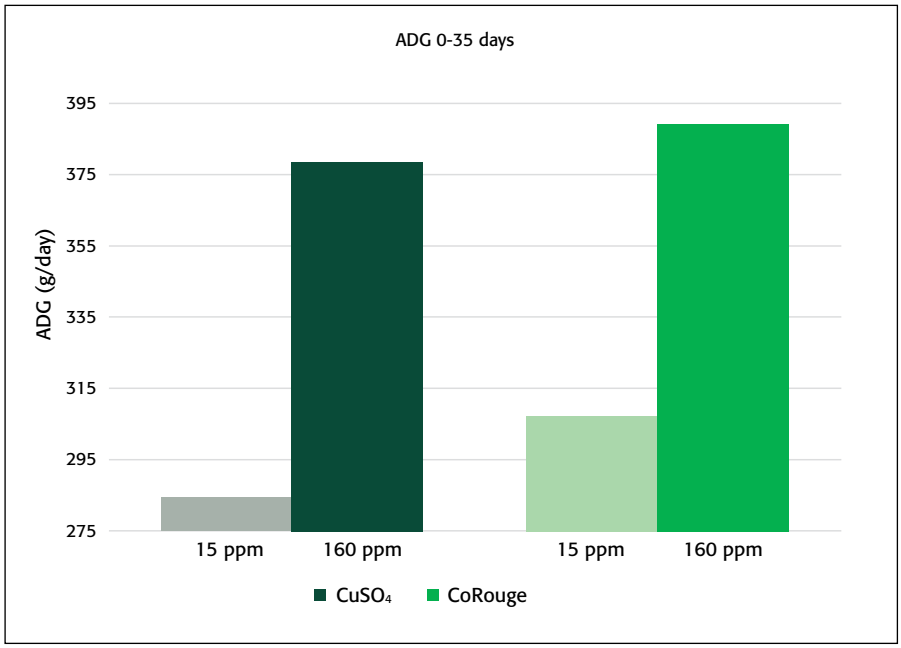


Figure 5: Effect of copper on piglet average daily weight gain (0-35 days).



Wageningen University

oxide or antibiotics in the feeds. The experiment compared different doses of copper, supplied either with copper sulfate or with CoRouge. At 14 days of supplementation, a clear dose response was already observed, with CoRouge fed piglets growing faster. After 35 days of supplementation, piglets gained 3.3kg weight when fed 160 mg/kg of copper in comparison to 15 mg/kg. Piglets which received 160 mg/kg copper from CoRouge achieved even higher final BW at 21.4 kg, resulting from improved feed intake and feed conversion ratio. To conclude, the beneficial effect of high copper dose on piglet weight gain is still exceptional, and this effect is maximized with CoRouge.

Conclusion

Copper is an essential nutrient under clear scrutiny of authorities due to its possible effect on environmental accumulation and development of microbial resistance. The feed industry, as already the case in EU, is forced to improve current practices in order to find a compromise between animal performance and sustainability. Despite widespread usage since decades, the modes of action and dose responses of copper supplementation are still debated. New doses and sources of phytase raise new questions on interactions with macro and microminerals. AF

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