A new choice for using copper in pig feeds – part 2

CoRouge, the red source of cuprous oxide, newly authorised in the EU, was introduced in a previous issue (International Pig Topics, Volume 32, Number 7). This monovalent source of copper is characterised by superior technological properties but also by some specific chemical properties differentiating it from other feed grade sources of copper.

by Valérie Kromm and Stéphane Durosoy, Animine, France. www.animine.eu

High bioavailability and improved animal performance have been shown in university studies.

Highest copper concentration

As the copper content is the highest in CoRouge (75%), it offers many advantages for the feed industry:

- Less space in premixes.
- Less warehousing.
- Less transportation.

Like other metallic compounds, copper compounds are highly regulated feed additives. They are classified as hazardous chemicals according to the Regulations on Classification, Labelling and Packaging (CLP). The new CLP classification of copper based products shall apply from 1st March 2018 (Table 1).

The highest Cu concentration in CoRouge is of special interest for premix manufacturers who are concerned by Seveso III Directive.

Replacing other Cu sources by CoRouge gives an opportunity to decrease the quantity of stored products which are classified as dangerous for the environment.

This is even more critical with the current replacement of ethoxyquin, recently banned, by classified synthetic antioxidants.

Lower contamination levels in heavy metals

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 the contribution to contamination in the feed. Table 2 illustrates this advantage with the example of lead.

Non-water soluble copper source

There are many advantages in favour of non-water soluble compounds, under the condition that they are adequately solubilised in the proximal part of the digestive tract for intestinal uptake. Copper sulphate is well known for its hygroscopicity.

Metal sulphates are water soluble compounds and, as such, they can create negative interactions in the premix and in the gut. In the early 2000s, it had already been shown that metal oxides were less aggressive on vitamin stability when mixed in vitamin/mineral premixes.

Since then, vitamin manufacturers have improved their stability so that they are less sensitive to negative effects from other compounds and from storage conditions.

However, a recent 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 sulphate, even at a mild temperature of 25°C (Fig. 1).

Attention given to vitamin stability in premixes and feeds is even more critical after the ban of ethoxyquin, and especially when vitamins levels are reduced due to extremely high prices or product shortage.

Less 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

Table 1. CLP pictograms of copper compounds.

Chemical form	CAS Number	Corresponding CLP pictograms
Copper(I) oxide (CoRouge)	1317-39-1	
Copper sulphate pentahydrate	7758-99-8	
Dicopper chloride trihydroxide (TBCC)	1332-65-6	
Copper carbonate	1184-64-1	
Copper chelate of amino acids Copper chelate of glycine Copper chelate of hydroxy analogue of methionine	No chemical formula	To be determined

Table 2. Lead concentration in feed grade copper sources. *Benchmark at 100%.

	Copper concentration (%)	Maximum authorised Pb concentration (ppm)	Relative contribution to lead content in the feed (%)
Copper sulphate, pentahydrate*	25	100	100
Copper chelate of amino acids	15	100	170
Copper bilysinate	15	100	170
Copper chelate of hydroxy analogue of methionine	18	100	139
Copper chelate of glycine	25	100	100
Dicopper chloride trihydroxide	55	100	45
Copper carbonate	55	200	90
Copper(I) oxide (CoRouge)	75	200	66

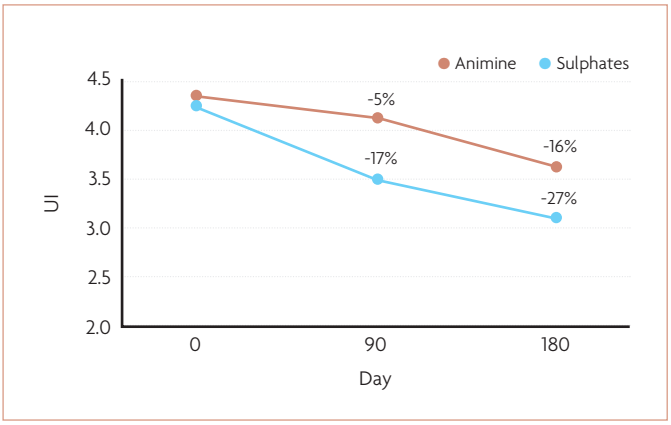


Fig. 1. Vitamin A stability in a piglet premix.

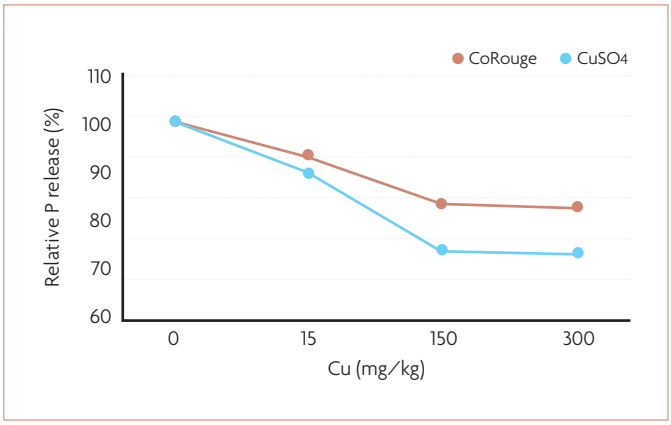


Fig. 2. Effect of copper on P release.

or supplemented phytase will be impaired. This negative interaction will be severe in such conditions:

- By the supplementation of high dosages of trace minerals.
- By the supplementation of readily soluble sources like sulphates.
- When supplemented phytase is slow acting.

Phytic acid has a strong affinity to bind with di 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 (Fig. 2).

Direct intestinal absorption

Active absorption of copper involves various intestinal transporters, the most important one being CTR1. Copper absorption depends on its oxidation state. Uptake of copper by CTR1 is possible only with the monovalent form of the copper ion, the cuprous form Cu^+. However, other copper sources authorised in animal nutrition include copper ions in the divalent form, i.e. the cupric form $Cu2^+$.

Consequently, some membrane proteins are needed to reduce $Cu2^+$ into Cu^+; currently, these proteins are not fully identified, but the main hypothesis refers to Steap proteins, like Steap2, also identified as $Fe3^+$ reductase.

A monovalent form of copper supplied from CoRouge will be directly absorbable, thus less prone to interferences (Fig. 3).

High bioavailability

In recent years, EFSA Journal has published several Opinions on the bioavailability of copper compounds. In 2008, it was concluded that copper chelate of hydroxy analogue of methionine had a bioavailability comparable to copper sulphate.

In 2013, no evidence was confirmed that the bioavailability of copper chelate of amino acids would be higher than copper sulphate. In 2014, an equivalent bioavailability was shown between copper bilysinate and copper sulphate.

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.

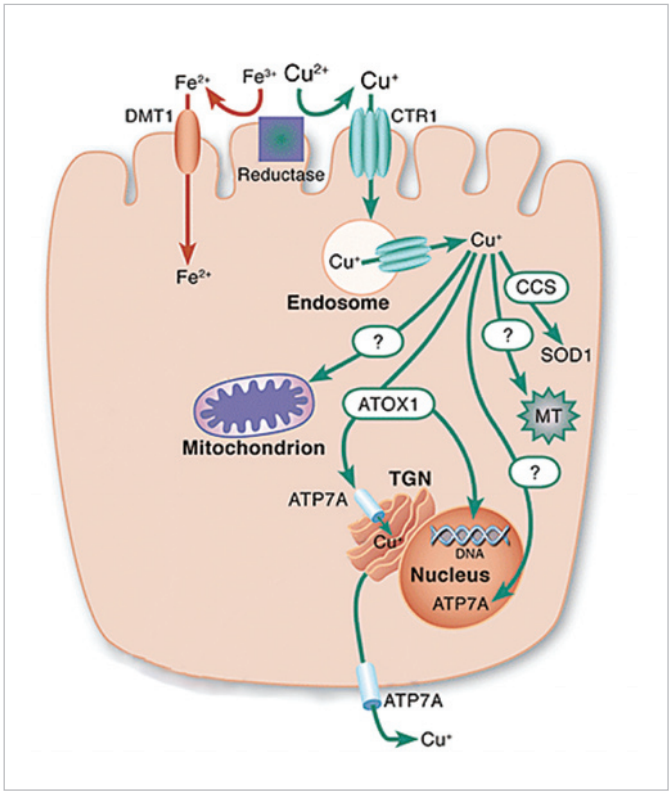
This has been realised at the University of Florida under the supervision of Dr Jamie Collins. Measured with liver concentration and serum ceruloplasmin activity, the copper status of rats was equivalent between copper sulphate and CoRouge.

The high bioavailability of dicopper oxide has also been demonstrated 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 sulphate or CoRouge (Fig. 4).

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

Fig. 3. Copper uptake in the enterocyte.



Growth performance of piglets

The growth promoting effect of copper supplementation on weaned piglets is well documented, but its mode of action is not yet fully elucidated. Copper is known for its antibacterial action and this remains the most assumed effect on intestinal health. Ionic form may play a role, as antibacterial activity of Cu^+ ions has been shown stronger compared to $Cu2^+$ ions.

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 of Wageningen University. The first experiment tested different copper doses, from 15-160mg/kg supplied as copper sulphate.

Dose response

A dose-response effect was confirmed for growth performance: average daily gain (ADG) increased as Cu dose increased ($p<0.01$), while feed conversion ratio decreased ($p<0.01$).

Piglet weights were improved by 2.8kg after 40 days of supplementation: it is very unlikely that most 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, received two wheat/barley/maize based diets, a prestarter (17% CP) for two weeks followed by a starter diet (15%) for three weeks.

There were no medicated zinc

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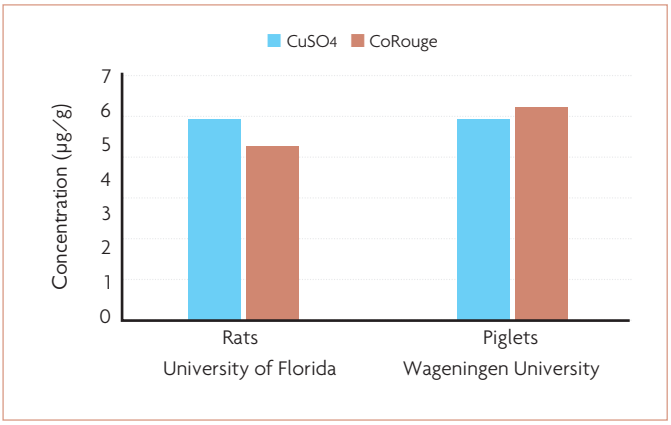

Fig. 4. Copper concentration in liver.

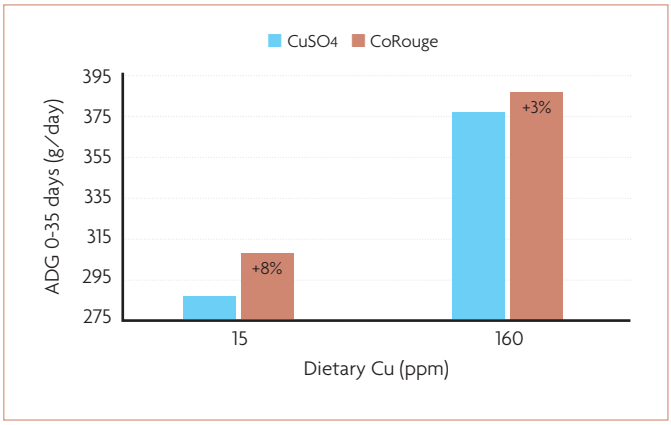

Fig. 5. Effect of copper on piglet weight gain (Wageningen University).

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oxide or antibiotics in the feeds. The experiment compared different doses of copper, supplied either with copper sulphate 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 160mg/kg of copper in comparison to 15mg/kg. Piglets which received 160mg/kg Cu from CoRouge achieved even higher final BW at 21.4kg, resulting from improved feed intake and feed conversion ratio.

To conclude, the beneficial effect of high Cu dose on piglet weight gain is still exceptional, and this effect is maximised with CoRouge (Fig. 5).

If in the future, European authorities decide for a drastic decrease in Cu supplementation in piglet diets, growth performance would be significantly impaired.

However, at 15mg/kg Cu, piglets fed CoRouge would gain 800g more BW in comparison to copper sulphate after five weeks of supplementation.

Conclusion

Copper is an essential nutrient for livestock animals, but it is also under scrutiny by the authorities due to its possible effect on environmental accumulation and the development of microbial resistance.

The feed industry is forced to improve its current practices in order to find a compromise between animal performance and sustainability.

Despite widespread usage for decades, the modes of action and dose responses of copper supplementation are still being debated.

New doses and sources of phytase raise new questions on interactions with macro and microminerals.

With the authorisation of di-copper oxide (CoRouge), nutritionists have a unique opportunity to utilise this innovative source of copper and to accompany regulatory changes in the European Union. ■

References are available from the author on request