

# Zinc and copper as feed additives, growth factors or unwanted environmental factors

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## ABSTRACT

Zinc (Zn) and copper (Cu) are essential nutrients. However, the functions and interplay between these two minerals remain to be fully understood, especially in the feeding of piglets, where Cu is used as a "growth promoter". The process of weaning imposes a lot of changes in the dietary conditions which may contribute to the weaning problems. Besides being heavy metals, Cu and Zn are required in the functioning of the young pig. Thus, further studies of the basic functions and interplay between Cu and Zn in relation to environmental aspects are needed.

KEY WORDS: zinc, copper, young pigs, feed additives, nutrition, environment

## INTRODUCTION

Zinc (Zn) and copper (Cu) have structural or catalytic roles in many metallo-proteins that function as enzymes. Zn in particular participates in several enzymes which are of great importance for growth and development. Zn is deeply involved in the metabolism of DNA and protein, and as such is very important in cell differentiation and cell replication. As a result, the Zn requirement is greatest in fast-growing animals, and the effects of Zn deficiency are most harmful in foetuses and young animals, where cell differentiation and replication are highest (Apgar, 1985;

Keen and Hurley, 1987). Furthermore, Zn is important for the functioning of the immune system (Keen and Gerschwin, 1990). Cu is substantially involved in processes concerning iron utilisation and synthesis of connective tissue (Prohaska, 1988). Consequently, Zn and Cu are essential nutrients and both are classified within the group of trace minerals.

### COPPER AS A GROWTH FACTOR

Since the inclusion of large amounts of Cu results in an increase in daily gain and feed conversion ratio, Cu has been used as a "growth promoter" in pig production for several decades. However, the mechanisms behind the growth stimulating effect remain a matter of controversy. It has long been hypothesised that Cu exerts a growth-limiting effect on the intestinal microflora, thus leaving more nutrients available for absorption to the pig. However, Fuller et al. (1960), reported no apparent differences between the microflora in Cu supplemented and non-supplemented pigs. In contrast, Kirchgessner et al. (1976) found that addition of dietary Cu increased protein utilisation, probably through activation of pepsin. Later it was hypothesised that Cu supplementation exerts an effect on the villus structure and thus decreases the turnover of the intestinal cells, possibly through an interaction (Shurson et al., 1990; Radecki et al., 1992). This would likewise result in more nutrients becoming available for absorption.

Recently, it has been claimed that the growth promoting effect is a systemic effect within the body rather than an antimicrobial effect in the intestinal tract (Zhou et al., 1994 a,b). Although the growth-promoting effect is not valid under all conditions, the greatest effect of Cu addition is generally recorded in young pigs. Thus Cu addition has been restricted to feeds for young pigs from weaning (Table 1).

TABLE I  
Recommended and allowed dietary levels of copper (Cu) and zinc (Zn) in Denmark

	Recommended		Allowed <sup>1</sup>	
	Cu	Zn	Cu	Zn
mg/kg diet:				
piglets	6	100	175 <sup>2</sup>	250
growing-finishing pigs	6	100	35	250
sows	6	100	35	250

<sup>1</sup> total dietary content

<sup>2</sup> until 17 weeks of age

## ZINC AS A GROWTH FACTOR

Inclusion of high amounts of Zn (about 2.500 ppm Zn as zinc oxide) in diets fed to piglets for two weeks after weaning has an inhibitory effect on the incidence and severity of unspecific post-weaning scouring and/or daily gain (Poulsen, 1989, 1995; Hahn and Baker, 1993). The functional evidence behind this beneficial effect remains to be demonstrated, but the above-mentioned effects on growth and diarrhoea were coincident with an increase in Zn concentration in plasma. A decrease in plasma Zn is seen in connection with *E. coli* infections in chickens (Butler and Curtin, 1973) and in pigs challenged with endotoxin (Chesters and Will, 1981). Furthermore, Zn retention is reduced in young pigs with intestinal infections (Whitenack et al., 1978). These findings suggest that piglets fed too little dietary Zn may be more susceptible to infections. In addition, it should be noted that negative Zn balance is seen in humans with intestinal infections, probably caused by massive secretory loss into the intestine (Prasad, 1985). Usually, endogenous Zn is secreted via the pancreatic juice (Sternlieb, 1988). However, compared with the daily intake of Zn, the secretion of Zn in pancreatic juice is low (Jensen et al., 1998). Zn is also secreted into the intestinal lumen from the intestinal cells and is also lost with discharged intestinal cells (Cousins, 1985). The urinary excretion of Zn is normally very low (Poulsen and Larsen, 1995). The labile Zn pool in the pig body is small (Larvor, 1983), and thus a constant dietary supply is necessary. In humans, Zn deficiency can cause non-thriving and diarrhoea (Golden and Golden, 1985). Frequently, cases of human non-specific diarrhoea are improved with Zn therapy (McClain et al., 1988). In pigs, failure to thrive is one of the first symptoms of Zn deficiency, yet diarrhoea is also recorded (Brink et al., 1959). These reports emphasise that Zn is indeed an essential nutrient, and demonstrate the importance of a sufficient dietary supply of Zn to young pigs. But more specific knowledge is still required.

Until now, little attention has been ascribed to define the absolute digestibility (availability) of Zn in the different inorganic and organic sources used for dietary supplementation. However, the apparent digestibility of Zn in zinc oxide has been shown to be as low as 20% (Poulsen and Larsen, 1995). Furthermore, studies have revealed differences in the relative availability when different sources are compared with a standard source (Wedekind and Baker, 1990; Wedekind et al., 1992).

## INTERACTIONS BETWEEN Zn AND Cu

Interactions between Zn and Cu have been demonstrated. In the intestinal tract, the metabolism of the two trace elements is closely coupled to thionein (Cousins, 1985). Zn and maybe also Cu can induce the synthesis of this protein in the intes-

tinal cells. As a result, thionein binds Zn and Cu by forming metallothionein. Apparently, Zn is superior in inducing the synthesis of thionein, whereas the affinity of thionein is greater for Cu than for Zn (Cousins, 1985). Zn seems to play the more active and Cu the more passive role (Davis and Mertz, 1987). From the intestinal cells, Zn and Cu may be transferred to the portal vein, or Zn and Cu may be secreted into the intestinal lumen or lost by discharge of the intestinal cells.

When Cu is added to pig diets at growth promoting levels, the interactions between Zn and Cu may cause problems, i.e. it can result in Zn deficiency, which needs to be rectified by Zn supplementation. Furthermore, the dietary Cu level seems to affect the outcome of inclusion of high amounts of Zn (as zinc oxide) in the diets for newly weaned piglets (Poulsen, 1995). By the above-mentioned intestinal antagonistic interaction, high dietary inclusion of Zn may also result in Cu deficiency (Davis and Mertz, 1987). However, these aspects need further clarification.

#### EXCLUSIVELY ESSENTIAL GROWTH FACTORS ?

As already mentioned, there is still controversy in the defining and understanding of the function of Cu when it is used as a "growth promoter". In addition, recent studies have revealed positive effects following the inclusion of Zn (as zinc oxide) in diets for newly weaned piglets. Therefore, heavy Cu and/or Zn supplementation of pig diets is clearly still a matter of complexity and of concern. Firstly, it may cause problems with interactions, especially the antagonistic interactions, which will often require readjustments of the dietary need for the interacting mineral(s). Secondly, chronic poisoning has been reported in sheep grazing herbage dressed with liquid manure from pigs fed Cu-supplemented diets (Davis and Mertz, 1987); therefore such pig manure is potentially toxic to sheep. Thirdly, the heavy inclusion of Cu and/or Zn may pose environmental problems, because the dietary Cu and/or Zn will be concentrated in the pig wastes and later spread on the arable land. This may result in substantial increases in the soil content of these minerals.

Calculations have been made, based on the maximum allowed pig density in Denmark and on standard values of feed intake, dietary mineral content and mineral retention, of the amounts of Cu spread per hectare (ha) of arable land, for different scenarios (Table 2). Furthermore, it was calculated how many years of manure application will pass until the upper soil quality criteria is reached in a standard soil (Larsen et al., 1996). The critical value for soil Cu content is laid down by the Danish Environmental Protection Agency for sludge and is based on the EU Directive 86/278/EØF (Larsen et al., 1996). It is assumed in the calculations that the Cu contribution per ha originates exclusively from pig manure, and that

TABLE 2

Calculated copper (Cu) content and accumulation in the soil at different hypothetical cases

	A <sup>1</sup>	B <sup>1</sup>	C <sup>1</sup>	D <sup>1</sup>
Growing- finishing pigs, 30-100 kg:				
dietary intake, g/pig	2.0	14.4	17.3	33.6
retained in the body, g/pig	0.1	0.1	0.1	0.1
excreted by urine and faeces, g/pig	1.9	14.3	17.2	33.5
g Cu/51 pigs/ha/year	100	730	875	1700
removal with crop, g/ha/year <sup>2</sup>	30	30	30	30
accumulation, g/ha/year	70	700	845	1670
number of years to reach 40 mg Cu/kg soil <sup>3</sup>	1300	130	110	50
Year sow incl.22 piglets, to 30 kg:				
dietary intake, g/unit	22.9	193.6	80.5	
retained in the body, g/unit	1.4	1.4	1.4	
excreted by urine and faeces, g/unit	21.5	192.2	79.1	
g Cu/4.5 year sow, incl.22 piglets	100	865	355	
removal with crop, g/ha/year <sup>2</sup>	30	30	30	
accumulation, g/ha/year	70	835	325	
number of years to reach 40 mg. Cu/kg soil <sup>3</sup>	1300	110	280	

<sup>1</sup> A: 10 mg Cu/kg (normal content in feed without Cu addition) for all categories

B: at maximum allowed Cu addition for all categories

C: if 90 mg Cu/kg for piglets, 90 mg Cu/kg for slaughter pigs during the entire period, and 10 mg Cu/kg for sows

D: if 175 mg Cu/kg for slaughter pigs during the entire growth period

<sup>2</sup> wheat<sup>3</sup> calculated on the basis of a 20 cm deep ploughing and a specific gravity of 1.5, i.e. in case of an addition of 3 kg Cu/ha, the Cu content will increase by 1 mg/kg (dry soil). The natural soil content is estimated at 10 mg/kg (Magid,1997)

the amount taken away by a standard crop (wheat) approximates 30 g per ha. Table 2 shows that when Cu is used as a "growth promoter" at allowed Danish (and EU) levels, it will only take about 110 years, before the Cu content in the soil reaches the given critical value. When Cu supplementation is used from weaning until slaughter, which is not allowed in Denmark (or in the EU), the critical value will be reached within 50 years. In evaluating the risk of heavy metal accumulation and pollution of the soil, it is important to be aware of the fact that it takes much longer to get rid of the accumulated amounts than it takes to reach the critical values.

Some values on the corresponding Zn accumulation in some hypothetical cases are shown in Table 3. It is obvious that the Zn situation is not as critical as the Cu case. However, Zn accumulation may become a problem, especially in cases where the maximum allowed dietary Zn content is used in practice.

TABLE 3

Calculated zinc (Zn) content and accumulation in the soil at different hypothetical cases

	A <sup>1</sup>	B <sup>1</sup>	C <sup>1</sup>	D <sup>1</sup>
Growing- finishing pigs, 30-100 kg:				
dietary intake, g/pig	19.2	48.1		
retained in the body, g/pig	1.4	1.4		
excreted by urine and faeces, g/pig	17.8	46.7		
g Zn/51 pigs/ha/year	910	2380		
removal with crop, g/ha/year <sup>2</sup>	200	200		
accumulation, g/ha/year	710	2180		
number of years to reach 1000 mg Zn/kg soil <sup>3</sup>	380	125		
Year sow incl. 22 piglets, to 30 kg:				
dietary intake, g/unit	208.4	522.2	736.4	1017
retained in the body, g/unit	14.4	14.4	14.4	14.4
excreted by urine and faeces, g/unit	194.0	507.8	722	1002.8
g Zn/4.5 year sow (incl. 22 piglets)	875	2290	3250	4510
removal with crop, g/ha/year <sup>2</sup>	200	200	200	200
accumulation, g/ha/year	675	2090	3050	4310
number of years to reach 100 mg Zn/kg soil <sup>3</sup>	340	110	75	55

<sup>1</sup> A: 100 mg zn/kg (normal recommended content) for all categories

B: at maximum allowed Zn addition for all categories

C: if 2500 mg Zn/kg for piglets for two weeks after weaning and then 100 mg/kg and mg Zn/kg for sows

D: if 2500 mg Zn/kg for piglets for two weeks after weaning and then 250 mg/kg, and 250 mg Zn/kg for sows

<sup>2</sup> wheat<sup>3</sup> calculated on the basis of a 20 cm deep ploughing and a specific gravity of 1.5, i.e. in case of an addition of 3 kg Zn/ha, the Zn content will increase by 1 mg/kg (dry soil). The natural soil content is estimated at 25 mg/kg (Magid, 1997)

## CONCLUSIONS

Summing up, Zn and Cu are essential nutrients, and also nutrients that play a special and very important role in young, newly-weaned piglets. However, the specific functions and interplay between the two minerals remain to be fully understood. The process of early weaning imposes a lot of changes in the dietary and the housing conditions. These changes contribute to the problems frequently seen after weaning (diarrhoea, reduced growth etc.). Evidently, the supply of both Zn and Cu is crucial to the functioning of the young pig. Nevertheless, there is a lack in the understanding of the role of these trace elements, especially in the young pig.

How then should we feed the young pig so that we fulfil its need for Zn and Cu and at the same time pay regard to the environmental aspects? Bearing this in mind, several points have to be addressed:

- the basic function of Cu in young pigs
- the basic function of Zn in young pigs
- the interactions between Zn and Cu and their functional consequences
- the availability of the dietary intrinsic Zn and Cu content and of the Zn and Cu sources used for dietary supplementation
- the specific physiologic need of Zn and Cu in terms of available amounts.

Finally, it might be important and necessary in the future to relate the young piglet's need for Cu and especially Zn to daily amounts per pig instead of per kg diet. This will enable us to focus more directly on the specific process of weaning and the possibilities to reduce the post weaning problems, i.e. diarrhoea and failure to thrive, by dietary means. Obviously, there is a great need for further research in this specific field.

#### REFERENCES

- Apgar J., 1985. Zinc and reproduction. *Ann. Rev. Nutr.* 5, 43-68
- Brink M.F., Becker, D.E., Terrill, S.W., Jensen A.H., 1959. Zinc toxicity in the weanling pig. *J. Anim. Sci.* 18, 836-842
- Butler E.J., Curtin M.J., 1973. The effects of *Escherichia coli* endotoxin and ACTH on the plasma zinc concentration in the fowl. *Res. Vet. Sci.* 15, 363-367
- Chesters J.K., Will M., 1981. Measurement of zinc flux through plasma in normal and endotoxin-stressed pigs and the effects of zinc supplementation during stress. *Brit. J. Nutr.* 46, 119-130
- Cousins R.J., 1985. Absorption, transport, and hepatic metabolism of copper and zinc: Special reference to metallothionein and ceruloplasmin. *Physiol. Rev.* 65, 238-309
- Davis G.K., Mertz W., 1987. Copper. In: W. Mertz (Editor). Trace elements in human and animal nutrition. 5th Edition. Vol. 1, pp. 301-364
- Golden B.E., Golden M.H.N., 1985. Zinc, sodium and potassium losses in the diarrhoeas of malnutrition and zinc deficiency. Trace Elements in Man and Animals TEMA 5. In: C.F. Mills, I. Bremner, J.K. Chesters (Editors). Proceedings of the 5th International Symposium on Trace Elements in Man and Animals, pp. 228-232
- Hahn J.D., Baker D.H., 1993. Growth and plasma zinc responses of young pigs fed pharmacologic levels of zinc oxide. *J. Anim. Sci.* 71, 3020-3024
- Jensen M.S., Gabert V.M., Larsen T., 1998. Pancreatic secretion of zinc and carboxypeptidase A and B in growing pigs. *Reprod. Nutr. Dévelop.* (submitted)
- Keen C.L., Hurley L.S., 1987. Effects of zinc deficiency on prenatal and postnatal development. *Neuro Toxicol.* 8, 379-388
- Keen C.L., Gershwin M.E., 1990. Zinc deficiency and immune function. *Ann. Rev. Nutr.* 10, 415-431
- Kirchgessner M., Beyer M.G., Steinhart H., 1976. Activation of pepsin (EC 3.4.4.1) by heavy-metal ions including contribution to the mode of action of copper sulphate in pig nutrition. *Brit. J. Nutr.* 36, 15-23

- Larsen M.M., Bak J., Scott-Fordsman J., 1996. Monitoring af tungmetaller i danske dyrkningsog naturjorder. Prøvetagningen 1992/93. Faglig rapport Nr.157, Danmarks Miljøundersøgelser
- Larvor P., 1983. The pools of cellular nutrients: Minerals. In: P.M. Riis (Editor). Dynamic biochemistry of animal production. World Anim. Sci. A3, 281-317
- Magid J., 1997. [Heavy metals and soil quality]. Tidsskrift for Landøkonomi 2, 77-80
- McClain C.J., Adams L., Shedlofsky S., 1988. Zinc and the gastrointestinal system. In: A. Prasad (Editor). Essential and toxic trace elements in human health and disease. Alan R. Liss, Inc., New York, pp. 55-73
- Poulsen H.D., 1989. Zinc oxide for weaned pigs. Proceedings of the 40th Annual Meeting of the European Association for Animal Production, Dublin, Ireland, Vol. 2, pp. 265-266
- Poulsen H.D., 1995. Zinc oxide for weanling piglets. Acta Agric. Scand., Sect. A. Anim. Sci. 45, 159-167
- Poulsen H.D., Larsen T., 1995. Zinc excretion and retention in growing pigs fed increasing levels of zinc oxide. Livest. Prod. Sci. 43, 235-242
- Prasad A.S., 1985. Clinical manifestations of zinc deficiency. Ann. Rev. Nutr. 5, 341-363
- Prohaska J.R., 1988. Biochemical functions of copper in animals. In: A.S. Prasad (Editor). Essential and toxic trace elements in human health and disease. Alan R. Liss, Inc., New York, pp. 105-124
- Radecki S.V., Ku P.K., Bennink M.R., 1992. Effects of dietary copper on intestinal mucosa enzyme activity, morphology and turnover rates in weanling pigs. J. Anim. Sci. 70, 1424-1431
- Shurson G.C., Ku P.K., Waxler G.L., Yokoyama M.T., Miller E.R., 1990. Physiological relationships between microbiological status and dietary copper levels in the pig. J. Anim. Sci. 68, 1061-1071
- Sternlieb I., 1988. Copper and zinc. In: I.M. Arias, W.B. Jakoby, H. Popper, D. Schachter, D.A. Shafritz (Editors). The liver: biology and pathobiology. Raven Press, Ltd., New York, pp. 525-533
- Wedekind K.J., Baker D.H., 1990. Zinc bioavailability in feed-grade sources of zinc. J. Anim. Sci. 68, 684-689
- Wedekind K.J., Hortin A.E., Baker D.H., 1992. Methodology for assessing zinc bioavailability: Efficacy estimates for zinc-methionine, zinc sulphate, and zinc oxide. J. Anim. Sci. 70, 178-187
- Whitenack D.L., Whitehair C.K., Miller E.R., 1978. Influence of enteric infection on zinc utilization and clinical signs and lesions of zinc deficiency in young swine. Amer. J. Vet. Res. 39, 1447-1454
- Zhou W., Kornegay E.T., Laar van H., Swinkels J.W.G.M., Wong E.A., Lindeman M.D., 1994a. The role of feed consumption and feed efficiency in copper-stimulated growth. J. Anim. Sci. 72, 2385-2394
- Zhou W., Kornegay E.T., Lindeman M.D., Swinkels J.W.G.M., Welten M.K., Wong E.A., 1994b. Stimulation of growth by intravenous injection of copper in weanling pigs. J. Anim. Sci. 72, 2395-2403