Zinc supplementation to cover nutritional requirements: Focus on bone P

The first article in this series (Monteiro and Minetto, 2023) highlighted the impact of zinc supplementation on bone zinc, noting that the dissolution kinetics of zinc sources influence zinc bio-availability. This second article focuses on the impact of zinc on bone phosphorus.

BY DR. ALESSANDRA RIGO MONTEIRO, ANIMINE

The most significant organic phosphorus (P) source in broiler diets is phytate-P. However, non-ruminant animals have limited capacity to utilise phytate-P due to a lack of endogenous enzymes capable of breaking down phytate. Consequently, exogenous phytases are commonly added to broiler feed to enhance phytate breakdown and protect inorganic phosphorus deposits. Maximising phytase efficacy is crucial to this process. *In vitro* studies have shown that the source and amount of zinc (Zn) may be influencing factors. Since phytate is negatively charged, it can form complexes with divalent cations, such as Zn. This complex formation may reduce the availability of phytate to phytase enzymes.

A recent review by Philippi and others investigated the *in vivo* effects of Zn supplementation on bone mineralisation *(Table 1)*. The effects of Zn on phosphorus-related traits are varied. Some studies report an increase in tibia ash, while others show a reduction. It is also evident that zinc studies often use bone ash as an indicator of mineralisation but few measure bone phosphorus directly. This led to the interest in looking at the possible impact of Zn on P metabolism in bone.

Phosphorus metabolism in bone in relation to zinc

The physiological mechanisms controlling phosphorus levels in the body involve various processes *(Figure 1)*. Serum phosphate levels increase due to the release of parathyroid hormone (PTH) which reduces calcium and phosphorus excretion in the kidneys, enhances phosphorus absorption in the small intestine and releases phosphate from bone. Elevated serum phosphate levels provide negative feedback on PTH release, prompting the parathyroid glands to increase calcitonin secretion.

Calcitonin increases phosphate excretion in the kidneys, inhibits phosphorus absorption in the small intestine and decreases bone resorption. PTH plays a crucial role in ensuring proper phosphorus metabolism. Several studies have demonstrated that zinc deficiency causes an increase in serum PTH concentration due to an inability to maintain calcium homeostasis, resulting in bone fragility. Similarly, Yamaguchi and others found that zinc inhibits PTH-stimulated osteoclast-like cell formation. Another hormone with a significant role in phosphorus regulation is fibroblast growth factor 23 (FGF-23), produced by bone cells. FGF-23 acts on the kidneys to induce phosphaturia, impairing the capacity to re-absorb phosphate from the glomerular filtrate, leading to urinary phosphate wasting. This hormone controls phosphorus levels and stimulates bone formation. Evidence suggests that certain minerals, such as

Figure 2 – Studies on the effect of zinc on phosphorus deposition in bone

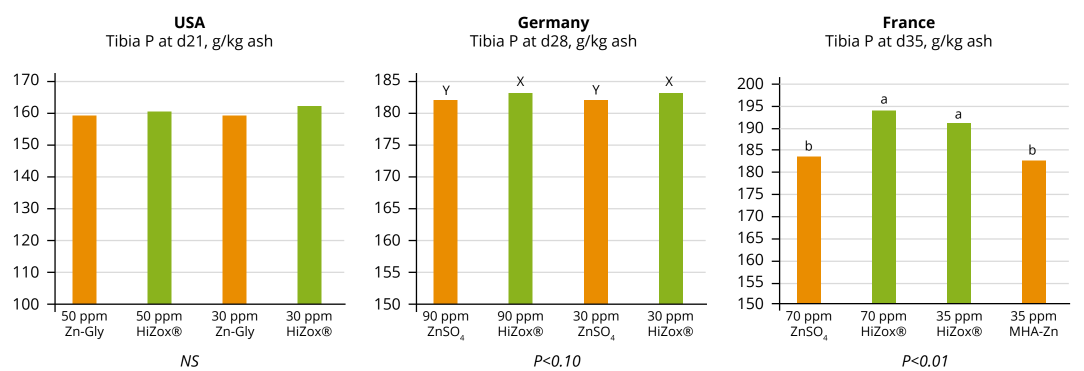
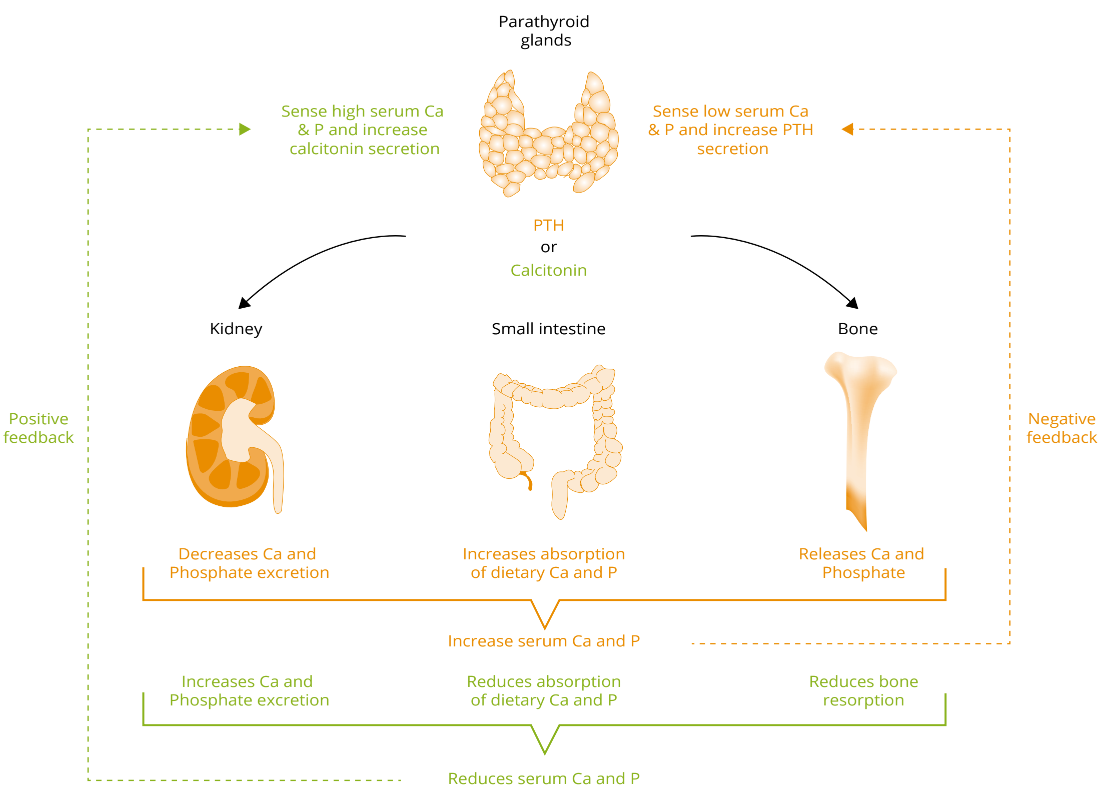


Figure 1 – Ca and P homeostasis



iron and zinc, impact FGF-23 levels, possibly through a direct effect on bone cell FGF-23 production. However, the specific mechanisms remain to be identified.

Effect of zinc on phosphorus deposition in bone

Animine conducted three studies on broilers in France, Germany and the USA, using diets with 750 FTU/kg of phytase. The efficacy of a potentiated Zn source (PZn; HiZox, Animine) was compared to different Zn sources. The studies were structured as follows:

- Study 1 (University of Georgia, USA): Involved 288 Ross 308 male broilers 1-21 days old. The four treatments included a basal diet (29 mg/kg native Zn) supplemented with either 30 or 50 mg/kg Zn from a chelated source (Zn-Gly) or PZn.
- Study 2 (University of Hohenheim, Germany): Involved 320 Ross 308 male broilers 1-28 days old. The four treatments included a basal diet (33 mg/kg native Zn) supplemented with either 30 or 90 mg/kg Zn from $ZnSO_4$ or PZn.
- Study 3 (Field trial, France): Involved 2,880 Ross 308 male broilers from 1 to 35 days old. The four treatments included a basal diet (35 mg/kg native Zn) supplemented with 70 mg/kg Zn from $ZnSO_4$ or PZn, and 35 mg/kg Zn supplemented from a chelated source (MHA-Zn) or PZn.

At the end of each trial tibia samples were collected to determine mineral concentration.

In Study 1 (USA), although not statistically significant, birds fed with either 30 or 50 mg/kg Zn from PZn showed a numerically higher phosphorus content in bones (2% on average) compared to those fed with Zn-Gly chelate. Conversely, in Study 2 (Germany) the treatments with either 30 or 90 mg/kg Zn from PZn tended to increase phosphorus content (1% on average) in the tibia compared to those receiving $ZnSO_4$.
In Study 3 (France), broilers fed with PZn containing 35 mg/kg or 70 mg/kg Zn, exhibited higher phosphorus deposition (5% on average) in the tibia compared to those receiving 70 mg/kg

Table 1 – In vivo effects of Zn supplementation on bone mineralisation.

Reference	Duration	Native Zn	Supplemented Zn level	Zn source	Phytase	Tibia ash
	(days)	(mg/kg)	(mg/kg)			(FTU/kg)
Mohanna and others, 1999	5 -> 21	31	14, 35	$ZnSO_4$	0, 800	↑, g
Augspurger and others, 2004	8 -> 20	~33	75 (+800)	ZnO (+$ZnCl_2$)	0, 500	↓, %
Ao and others, 2007	1 -> 21	25	0, 2, 4, 6, 16, 32	Zn chelate	0, 500	↑, mg
Schlegel and others, 2010	2 -> 21	38	0, 15	$ZnSO_4$, Zn chelate	0, 500	NS, g/kg DM
Attia and others, 2019	1 -> 56	26	0, 30	ZnO	0, 500	↓, %

Zn from ZnSO4 or 35 mg/kg Zn from MHA-Zn chelate. These findings suggest that HiZox supplementation may enhance phosphorus deposition in broiler bones more effectively than other zinc sources.

Potentiating factors

Several hypotheses can be put forward to explain the potential mechanisms by which zinc influences phosphorus deposition in bones:

- Dissolution kinetics of zinc sources:
  Complex formation with InsP6-P: Fast-dissolving zinc sources can form complexes with inositol hexakisphosphate (InsP6-P), commonly known as phytate, which may impair phytase efficiency. Reduced phytase efficiency can lead to decreased phosphorus availability for deposition in bones.
- Bio-availability of zinc sources:
  Enhanced hormonal regulation: More bio-available zinc can better support the physiological processes that regulate phosphorus metabolism. High bio-availability of zinc may help achieve optimal levels of PTH and FGF-23.

PTH: Zinc supports calcium homeostasis which is crucial for maintaining proper PTH function. Adequate zinc levels help maintain calcium balance, reducing PTH secretion and subsequently promoting phosphorus deposition in bones.
FGF-23: Zinc may directly or indirectly influence the production of FGF23 by bone cells. Optimal zinc levels could enhance FGF-23 function, promoting better phosphorus metabolism and deposition in bones.

- Zinc-phosphorus interactions in bone cells:
  Bone cell function: Zinc is essential for the proper functioning of osteoblasts (bone-forming cells) and osteoclasts (bone-resorbing cells). Adequate Zn levels support bone mineralisation processes, potentially leading to improved phosphorus deposition.

Understanding these mechanisms can help optimise dietary formulations and supplementation strategies to enhance phosphorus deposition in broiler bones, improving bone health and growth.

Impact of zinc source

Zinc sources could impact the bone deposition of phosphorus. This effect could be related to the dissolution kinetics of zinc sources, their bio-availability, or both. The results suggested that HiZox, a potentiated source of zinc oxide, may offer a more effective solution for improving bone health in broilers.