Getting the balance right: the underestimated weight of dietary calcium

The macronutrient calcium (Ca) is mostly known for its crucial role in bone mineralisation and bone strength. Containing 99% of the body Ca reserves, the skeleton is the major storage site for Ca. Besides maintaining skeletal integrity, Ca is important for muscle contraction, neuronal transmission, intracellular signalling and many other functions (see Fig. 1).

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In the gut, dietary Ca is absorbed by active transcellular transport via different transporters and by passive paracellular transport (Fig. 2). Which pathway dominates at a given time depends on age, intestinal site, Ca requirement and dietary Ca content.

Ca concentration in the cytoplasm of cells is up to 10,000 times lower than extracellular Ca concentrations and high intracellular Ca levels are cytotoxic.

In combination with the sensitive nature of the role of Ca, for example in heart function, a close control of Ca levels is essential.

Serum Ca is therefore kept in a narrow range and Ca homeostasis in the circulation is monitored by the Ca-sensing receptors located in the parathyroid and the kidneys.

These receptors are highly sensitive and detect and react to minute deviations from the normal serum Ca.

Such deviations trigger a reaction to re-establish Ca homeostasis which involves the kidney, the gut, and the skeleton.

The key players in this dance are parathyroid hormone (PTH) and 1,25-dihydroxycholecalciferol ($1,25(OH)_2D_3$).

Vitamin D_3 metabolism and Ca homeostasis

$1,25(OH)_2D_3$ is the metabolically active form of vitamin D_3. It is produced by two hydroxylation steps from vitamin D_3.

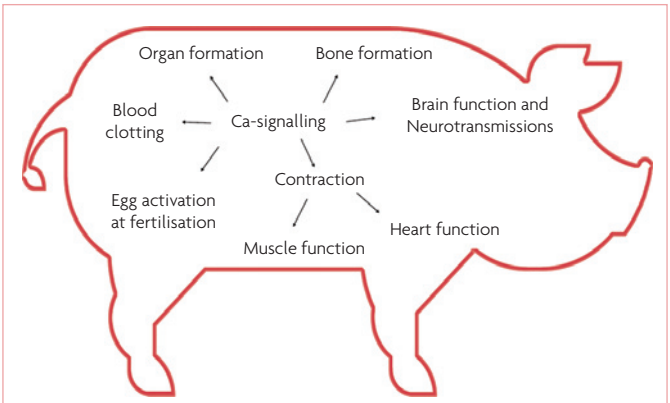

Fig. 1. Involvement of calcium in selected developmental processes and physiological functions (adapted from Rajagopal and Ponnusamy, 2017).

The enzyme 25-hydroxylase is responsible for the first step which takes place in the liver and converts vitamin D_3 to its main circulating form, 25-hydroxy-vitamin D_3 ($25(OH)D_3$). The second step is orchestrated predominantly in the kidneys by 1alpha-hydroxylase.

The activity of the 1alpha-hydroxylase is controlled by PTH, serum Ca and $1,25(OH)_2D_3$ itself, thus linking the vitamin D metabolism to the Ca-metabolism. Basically, a decreasing serum Ca level increases PTH secretion.

This increases serum $1,25(OH)_2D_3$ concentrations, which in turn increases intestinal Ca absorption, reduces urinary Ca excretion and increases Ca mobilisation from bone until serum Ca is restored. If serum Ca level is increasing, secretion of calcitonin is elevated, which reduces PTH. This consequently reduces $1,25(OH)_2D_3$ and Ca absorption from the gut.

At the same time urinary Ca excretion and Ca deposition into the bone are increased, returning serum Ca to its steady state (see Fig. 3), .

Consequences of too little and too much calcium

The effects of Ca deficiency have been known for a long time as the consequences are easily visible such as, for example, deformed bones due to rickets or 'downer cows' due to postpartum hypocalcaemia at onset of lactation. Subclinical Ca deficiencies are more difficult to detect as they normally do not affect growth performance.

Lack of Ca is especially critical for skeletal integrity in growing animals. The effects of Ca depletion are more pronounced in grower than in finisher pigs. Adverse effects of low Ca diets on bones of grower pigs are already visible within a month. However, supplementation of high Ca levels in the finisher diet after low Ca in the grower diet leads to compensatory bone mineralisation.

In the case of Ca, the saying 'the more the better' does not apply. At a certain point additional dietary Ca

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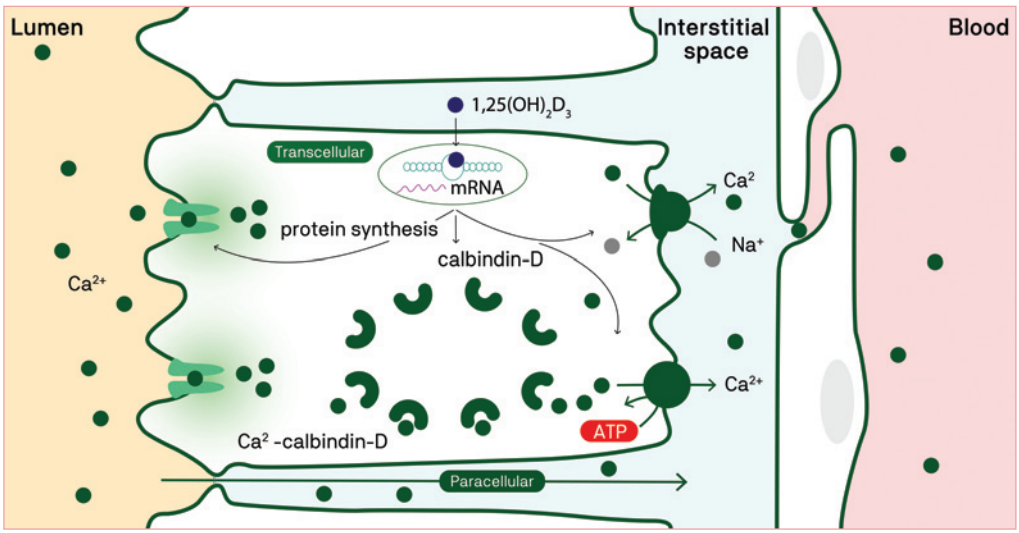
Fig. 2. Mechanism of epithelial Ca^{2+} transport. Epithelia can absorb Ca^{2+} by paracellular and transcellular transport. Passive and paracellular Ca^{2+} transport takes place across the tight junctions and is driven by the electrochemical gradient for Ca^{2+} (green arrow). Simplified and adapted from Hoenderop et al. (2005)



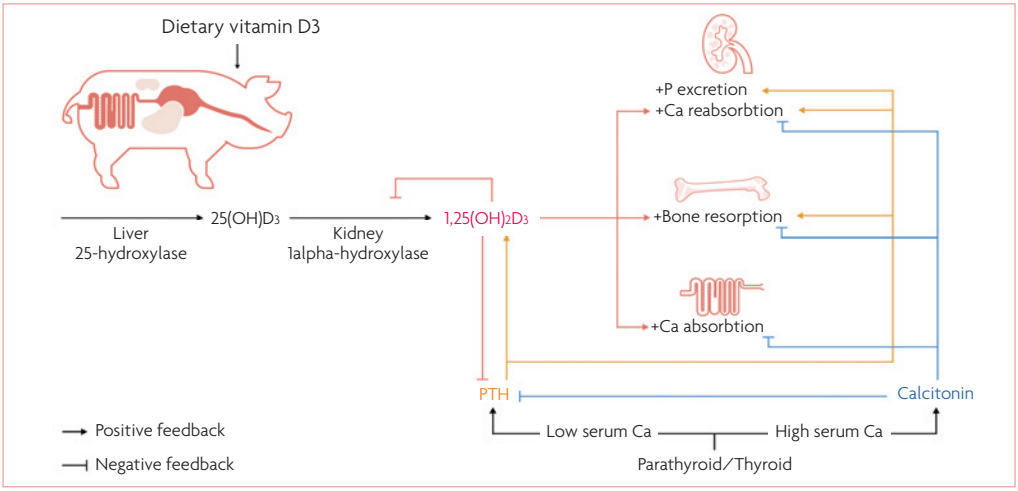


Fig. 3. Regulation of Ca homeostasis. Low serum Ca triggers excretion of parathyroid hormone (PTH), while calcitonin is excreted at high serum Ca.

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does not have further benefits. In contrast, besides taking up valuable space in the formulation, excess dietary Ca adversely affects the digestibility of other nutrients and the efficacy of feed enzymes.

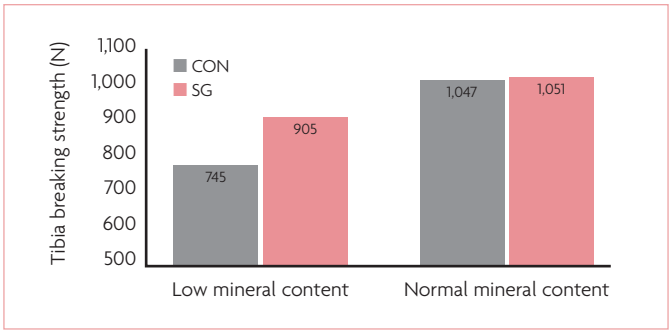
Calcium can form complexes in the intestinal lumen, 'trapping' nutrients such as minerals, amino acids, and fatty acids, thus making them unavailable for digestion. In the case of P and N, a reduced digestibility increases the excretion of these elements and thus the environmental load. Another undesired side effect of excessive dietary Ca is its buffering capacity.

Especially with the upcoming ban of therapeutic levels of zinc oxide, alternative approaches to reduce the risk of post-weaning diarrhoea are needed.

Limiting the buffering capacity by avoiding excessive dietary Ca can be one of the tools.

A reduced buffering capacity helps to maintain stomach pH. This increases the barrier function of the stomach against pathogens and increases protein digestibility. In addition, it reduces the risk of the aforementioned complex formation of Ca with other nutrients. As there is a close connection between Ca and P metabolism, the effects of suboptimal Ca content in the diet can be mitigated or exacerbated, depending on the ratio and availability of the two minerals.

Fig. 4. Tibia breaking strength in piglets five weeks after weaning that were fed a control diet (CON) or a diet supplemented with Solanum glaucophyllum (SG).



Benefits of a natural source of the bioactive form of vitamin D3

Reducing the dietary Ca content to optimise buffering capacity and to avoid antinutritive effects of Ca without compromising bone development is a fine line to walk. Efforts are made to increase the knowledge of Ca content and Ca availability of various feedstuffs.

These efforts, however, are futile if the Ca cannot be absorbed. One approach is to support the vitamin D metabolism. This can, for example, be achieved by using a natural source of the metabolically active form of vitamin D, 1,25(OH)2D3, supplied as glycosides from plant origin.

In a trial, 72 Large White piglets (28 days old, 8.1kg BW) were fed a normal (0.75% Ca, 0.35% dP) or a low mineral diet (0.50% Ca, 0.25% dP) for five weeks. The diet contained 500 FTU/kg phytase and 1,000 IU/kg of vitamin D3. The diets were either supplemented with 1µg 1,25(OH)2D3-equivalents from Solanum glaucophyllum (SG) or fed as such (CON).

At the end of the trial, tibia breaking strength in the low mineral SG diet was numerically higher than in the low mineral CON diet.

This demonstrates the beneficial impact of Solanum glaucophyllum on mineral metabolism in case of limited mineral availability.

There was no difference in tibial breaking strength between CON and SG in the normal mineral diets, indicating that the mineral content of these diets was at or above requirement. ■

References are available from the authors on request