# Reviews on the mineral provision in ruminants (XII): ZINC METABOLISM AND REQUIREMENTS IN RUMINANTS

A.M. van den Top

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# PREFACE

In the Netherlands the ´Handleiding Mineralenonderzoek bij rundvee in de praktijk´[1] is a well-known publication that has been used already for decades as a guide to trace and treat mineral disorders in cattle. The fifth edition of this guidebook was published in 1996. The content of this publication was largely identical to that of the fourth edition (1990). Therefore the (independent) committee that is responsible for the contents of the guidebook (the 'Commissie Onderzoek Minerale Voeding'[2], COMV) decided in 2000 that a thorough revision was desired.
The committee was of the opinion that, if possible, the available scientific literature should be summarized and evaluated once again. Furthermore, attention should be paid to the mineral provision of categories of cattle other than dairy cattle, as well as to that of sheep and goats. Finally, the basic principles for the calculation of the mineral requirements should be described in a transparent way.

The intended revision was made possible as the Dutch 'Ministerie van Landbouw, Natuur en Voedselkwaliteit' (LNV), the 'Productschap Diervoeder' and the 'Productschap Zuivel'[3] were willing to subsidize this extensive and ambitious project.
The COMV decided to execute the project as follows.

- External experts, invited by the COMV, should summarize and evaluate the relevant literature in a so-called 'basal document' (with two exceptions to be written in English).
- Subsequently, these documents should be critically evaluated by the COMV.
- These basal documents should then be used to write and arrange the several chapters of the revised 'Handleiding'.

The revised 'Handleiding' is available (in the Dutch language) since October 2005, under the title 'Handleiding mineralenvoorziening rundvee, schapen en geiten.'[4] This book is published by the 'Centraal Veevoederbureau' (CVB; Central Bureau for Livestock Feeding) in Lelystad, as was also the case for the previous edition.

The COMV was of the opinion that the valuable basal documents, that became available during the course of this project, should be published too. By doing so everyone has the possibility to trace the basis for the text of the revised 'Handleiding'. The CVB was gladly willing to issue these documents as CVB Documentation reports. In connection with this the authors and the members of the COMV have disclaimed all rights and have assigned them to the Productschap Diervoeder, of which the CVB is one of the services.
For an overview of the CVB Documentation Reports that will appear in this context, you are referred to an Annex in the back of this report.
For the preparation of the present report on the Zinc provision in ruminants the COMV expresses its gratitude to the author, dr. A.M. van den Top.

Utrecht/Lelystad, November 2005.

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| Professor dr. ir. A.C. Beynen | Dr. M.C. Blok |
| Chair of the COMV | Secretary of the COMV and Head of the CVB |

*The author, Dr. A.M. van den Top, expresses his thanks to the COMV, especially prof. dr. A. Th. van 't Klooster and dr. M.C. Blok, for critically reading the manuscript and their advice.*

1 Guidebook on mineral research for cattle in practice.
2 Committee for research on mineral nutrition
3 The Ministry for Agriculture, Nature and Food quality, the Product Board Animal Feed and the Dutch Dairy Board, respectively.
4 Guidebook mineral provision cattle, sheep and goats.

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# CONTENT

## LIST OF ABBREVIATIONS

| Abbreviation | Unit | Description |
|---|---|---|
| BW | kg | Body weight |
| DM | | Dry matter |
| DMI | kg | Dry matter intake |
| MT | | Metallothionein |
| ZnLys | | Zn lysine |
| ZnMet | | Zn methionine |
| ZnGly | | Zn glycine |

# 1 FUNCTIONS OF ZINC IN THE BODY

Zinc is essential for normal appetite, proper gene expression and fertility. The mechanism underlying the effect of Zn on appetite remains obscure. Its function in gene expression ("Zn-finger" domains in DNA-binding proteins) influences many processes in the body, including cell replication. Defects in cell replication may affect growth of bones, skin, hair and hooves, as well as immune function. Moreover, Zn is a component of metalloenzymes such as carbonic anhydrase, Cu-Zn superoxide dismutase, alkaline phosphatase, carboxypeptidase, alcohol dehydrogenase, and RNA polymerase. Besides this, Zn is a component of thymuline and is involved in the regulation of calmodulin, protein kinase C, thyroid hormone binding and the synthesis of inositol phosphate and prostaglandin [98;132].

# 2 DISTRIBUTION OF ZINC IN THE BODY AND ZINC KINETICS

Muscle tissue is the main Zn pool (± 65%). Approximately 25% is present in the bones. The remaining ± 10% is mainly present in the gastrointestinal tract (no details given) and in the skin. Besides these metabolically active pools, in sheep approximately the same amount as in the whole body is present in the fleece [132]. No data are available on the chemical forms in which Zn occurs in tissues.

As Zn-deficient ruminants develop clinical symptoms rapidly (see paragraph 7), apparently no substantial mobilizable Zn reserve is present in the body. On the other hand, significant amounts of Zn may be mobilized from muscle and bone tissues [132]. Failure of fine-tuned homeostasis is further demonstrated by the extreme Zn accretion in tissues of Zn-loaded animals (e.g. 2220 ppm (DM) in pancreas of calves after feeding a ration 634 ppm from ZnO for 21 days [123;132].

In the systemic blood, approximately 10-20% of Zn is present in plasma. Approximately 2/3 is bound to albumin, de remnant is mainly bound to alfa$_2$-macroglobulin. The latter part is tightly bound [16]. The non-plasma Zn is mainly bound to carbonic anhydrase in the erythrocytes and present in the erythrocyte membrane [21]. Low blood Zn concentrations are associated with increased susceptibility to hemolysis. Possibly Zn stabilizes the erythrocyte membrane after peroxidative damage has occurred. However, the exact nature of this protective function remains unclear [11].

Zinc uptake from the intestine in ruminants occurs nearly exclusively in the small intestine. Uptake capacity is similar for all parts of the small intestine [44;45]. Only approximately 2% of the total Zn absorption occurs from the large intestine [45].

In an *in vitro* experiment with brush border membrane vesicles from rats Zn uptake by the intestinal mucosa appeared to be saturable, indicating for active, carrier-mediated transport and/or facilitated diffusion. Besides this, passive diffusion into the intestinal cells and paracellular movement may be also involved in Zn transport from the intestinal lumen [75;129].

Zinc deficiency increases the maximal rate of absorption ($V_{max}$) of the active transport, although $K_m$ (the Zn-concentration at which the rate of absorption is half of $V_{max}$) remains constant [75]. In order to maintain Zn homeostasis when excess dietary Zn (238-638 ppm) is fed, the calf decreases its Zn absorption rather than that it increases its endogenous (faecal) Zn excretion after uptake of the excess Zn [87]. Changes in metallothionein (MT) synthesis are probably involved in changes in Zn absorption. When dietary Zn supply changes, both increases and decreases in Zn absorption occur within a week [132].

After uptake in the portal blood, Zn is mainly transported bound to albumin and transferrin. Thus, low blood albumin concentrations hamper blood Zn transport and Zn uptake from intestinal cells into the blood and, subsequently, Zn absorption from the intestinal lumen [64].

During the first days after a single oral dose of $^{65}$Zn, the liver is the main Zn-retaining organ in

goats and calves (9-11% of dose) [82]. At uptake by the liver MT synthesis is induced [76]. The liver Zn can subsequently be released, probably bound to albumin and amino acids [21].

# 3 ZINC ABSORPTION AND METABOLISM

## 3.1 General

The apparent Zn absorption decreases with age. This decrease is related to the Zn content of the ration. Calves consuming a Zn-deficient ration (2 ppm Zn during 7 days), did not show differences in Zn absorption between ± 2½ en 4½ month of age [85]. Apparently, the decrease in apparent Zn absorption is not caused by a decreased Zn absorption capacity. When similar calves were fed a ration containing 38 ppm Zn (the same ration supplemented with ZnO), the percentages excreted $^{65}Zn$ were 49.3 (2½ month) and 86.6 (4½ month), respectively. On the same ration with 6 ppm Zn calves of 3-4 months of age showed an apparent absorption of 83 % [82]. At Zn levels of 200, 500, 700 and 1000 ppm (DM) apparent Zn absorptions in preruminant calves were 36, 34, 26 en 22%, respectively [56]. Extreme high Zn accumulations in kidney (2498 ppm (DM) and liver (3647 ppm (DM) occurred at the 1000 ppm (DM) ration. Thus, when the Zn content of the ration increases, apparent absorption can decrease substantially, although retention can be considerable. Similar observations were made in lactating dairy cows. Apparent Zn absorption was high (± 57%) when dietary Zn concentrations were low (6 ppm Zn (DM)) and decreased exponentially with increasing dietary Zn concentrations. At concentrations of ± 100 ppm Zn (DM) a plateau was attained (± 43%), and apparent Zn absorption only slightly decreased further (to ± 40%) when dietary Zn concentrations increased up to 436 ppm (DM) [67].
True Zn availability is reported to be 12-58%[5] [98] or 70%[6], except for the non-ruminant calf, for which the estimated value is 50-85% [132].

## 3.2 Differences in zinc metabolism due to different zinc sources

In ruminant nutrition both inorganic ($ZnSO_4$, ZnO, $ZnCl_2$, $ZnCO_3$) and organic Zn sources (Zn-lysine (ZnLys), Zn-methionine (ZnMet), Zn-glycine (ZnGly), Zn proteinates and polysaccharide complexes) are used. ZnLys and ZnMet are Zn chelates ($Zn^{2+}$) of lysine and methionine, respectively. The Zn content is 10%, the lysine and methionine contents are 25% and 20%, respectively (C. Rapp, Zinpro Corp.). The exact nature of the other organic complexes is not clear.

### 3.2.1 Cattle

Although plasma Zn is thought to be one of the best parameters of Zn status (see paragraph 6), in literature reports several other parameters have been employed to judge the effect of different Zn sources. As several enzymes and immune functions depend on Zn [132], alkaline phosphatase (a Zn-dependent enzyme) and immunological parameters such as cell-mediated immunity and antibody titers have been used. The value of such parameters is questionable. However, as literature data on differences between Zn sources are limited, results from experiments employing “alternative” Zn status parameters are included as well.
Chirase et al. [18] carried out an experiment with crossbred feedlot steers (260 kg BW) to compare the bioavailability of Zn from ZnO and ZnMet. In order to reveal differences in immune function between animals fed different Zn sources both groups were challenged with infectious bovine rhinotracheitis virus. The diets contained either 96 ppm Zn (control group; maize-cottonseed-based), 163 ppm (ZnO added), or 171 ppm (ZnMet added). Each group consisted of 11 animals. Although the decrease in DMI due to the virus challenge tended to

[5] The 58%-value was observed when an adult cow was adapted to a low-Zn diet (6 ppm Zn as fed) without inhibitors and a value of 22% was reported when adult cattle were fed a diet containing 28 ppm Zn (as fed). The Zn content of the ration yielding the 12%-value was not clear.

[6] Probably estimated using the isotope dilution method [128]

be more rapid in the ZnO steers than in the control or ZnMet steers, no significant difference in DMI, rectal temperature, BW change or serum mineral concentrations between the animals fed ZnO or ZnMet could be observed. This is in agreement with the results of a similar experiment of the same authors [19]. When adding 225 mg Zn/animal/day from either ZnO or ZnMet to the ration (maize-cottonseed hulls-based; 5.9-6.7 ppm Cu (DM) and 72.1-74.1 ppm Zn (DM)) of Angus steer calves (280 kg BW), no difference between the two Zn sources for plasma Zn concentrations were observed, although DMI tended to be higher in the ZnMet group. Using Hereford x Simmental heifers (271 kg BW) receiving a maize silage-based ration (23.1 ppm Zn) supplemented with 25 ppm Zn from either ZnO or ZnMet, Spears [119] could not observe significant differences in growth or serum alkaline phosphatase activities between the two sources. The same investigators [120] found similar results using Angus and Angus x Hereford steers (214 kg BW) on a cottonseed hulls-maize-soybean meal-based diet (26.4 ppm Zn) supplemented with 25 ppm Zn from either ZnMet or ZnO and vaccinated against bovine herpes virus-1 and para-influenza 3. Although antibody titers against bovine herpes virus-1 tended to be higher for steers receiving supplemental ZnMet, no significant effect of Zn source on DMI or antibody titers could be observed. During Zn repletion of Zn deficient Hereford x Angus calves (209 kg BW), Engle et al. [31] found no difference in final BW, plasma or liver Zn concentrations between added $ZnSO_4$, ZnMet and ZnLys (23 ppm (DM)) to a hay-maize silage-alfalfa-based diet containing 17 ppm Zn. Only cell-mediated immunity against phytohemagglutinin was lower for ZnLys. Rojas et al. [109] could not observe any significant difference between ZnMet, $ZnSO_4$, and ZnO (360 mg supplemental Zn/animal/day) when fed to yearling Limousin and Angus heifers consuming hay-based diets (20-26 ppm Zn (DM)).

In young Holstein heifer calves (6 weeks of age), Kincaid et al. [63] observed higher serum Zn concentrations (24.9 vs. 19.5 µM) when 300 ppm Zn was added as ZnMet + ZnLys[7] (50% each, weight basis; total Zn concentration 400 ppm (DM)) compared with 300 ppm fed as ZnO (total Zn concentration 340 ppm (DM)). The basal ration (maize-barley-soybean meal-alfalfa based) contained 65 ppm Zn (DM). In male Holstein calves (9 weeks old, 67 kg BW) fed a diet containing 20 ppm Zn and supplemented with 20 mg Zn/kg BW from either $ZnCl_2$, $ZnSO_4$, ZnO or $ZnCO_3$, no significant differences were observed in plasma Zn concentrations 24 h after dosing [62].

In beef heifers (ration consisting of grass (38 mg Zn/kg) and maize/wheat), no differences between diets supplemented with 360 mg of Zn from either Zn sulphate or a Zn amino acid complex on gain, serum Zn concentrations or total and differential white blood cell counts could be demonstrated [59].

### 3.2.2 Sheep

Rojas et al. [108] fed diets (maize, cottonseed hulls, soybean meal; 16-20 ppm Zn) supplemented with 360 mg/day from either ZnMet, ZnLys, $ZnSO_4$ or ZnO for 3 weeks to sheep. Thereafter, the supplements were withdrawn for 4 weeks (reason not given) and then the supplements were resumed for another week. At the end of the experiment, the ZnLys-treated animals had the highest serum Zn values compared with all but the $ZnSO_4$-treated animals. ZnLys caused the highest accumulation and the highest metallothionein concentrations in kidney, liver and pancreas. No differences were observed between the sources in Zn concentrations in bone (marrow), cornea, skin, hooves or muscles. In sheep consuming a ration (maize/cottonseed hulls/soybean meal) containing 44 ppm Zn and supplemented with 1400 ppm Zn from either reagent grade $ZnSO_4.7H_2O$, reagent grade $ZnCO_3$, ZnO or metallic Zn, relative bioavailability estimates[8] using pancreas, liver and kidney Zn concentrations were 100, 106, 106 and 76, respectively [111]. Metallic Zn produced significantly lower concentrations than all other sources. Tissue concentrations

[7] Zinpro 100 and Lyzin 100, Zinpro Corp.

[8] Multiple linear regression slope ratios of $\log_{10}$ transformed accumulation of Zn in pancreas, liver and kidney on dietary Zn concentrations.

were not significantly different between the other sources. In a second experiment (64 ppm Zn in the basal ration), 1400 ppm additional Zn from either feed grade sulphate (2 sources) or ZnO (2 sources) bioavailability estimates were 100, 86, 87 and 79, respectively. No significant differences in tissue concentrations between these sources were observed.
Ewes fed hay (12 ppm Zn) supplemented with 140 mg Zn from either a Zn-amino acid complex (Availa-Zn 100®, Zinpro Corp.[9]) or $ZnSO_4$ during 56 days had higher faecal Zn excretion when the Zn-complex was fed (238 vs. 220 ppm for Zn-complex and sulphate, respectively) [49]. However, growth was not different, whereas liver Zn concentrations tended to be higher (P = 0.06) in the Zn-complex group, even when the initial liver Zn concentrations were included into the statistical analysis as a co-variable (139 vs. 128 ppm for Zn-complex and sulphate groups, respectively). The reason for the conflicting results (higher faecal Zn and higher liver Zn concentrations in the Zn-complex group) is not clear.
Cao et al. [13a] carried out an experiment with lambs fed a ration[10] with 1400 ppm added Zn from either $ZnSO_4.7H_2O$, Zn proteinate, Zn amino acid chelate or ZnMet[11]. They found significantly higher Zn concentrations in lambs receiving Zn proteinate as compared with $ZnSO_4.7H_2O$, whereas the other sources showed similar bioavailabilities as the sulphate.

### 3.2.3 Goats

In an experiment with 40 Angora goats consuming a diet (cottonseed hulls, maize, soybean meal + 45 mg CuO) supplemented with 120 mg Zn from either ZnMet or ZnO, average daily gain (62.9 vs. 50.5 g/day) and staple length (10.5 vs. 9.5 cm) were better in ZnMet-fed goats than in ZnO-fed goats [104]. However, as no methionine-supplemented control group was included in the experimental design and Zn was probably fed beyond requirements, the observed differences could theoretically also relate to the supplemented methionine. No significant effects were recorded as to feed intake, mohair yield or diameter or plasma Zn and Cu levels.

### 3.2.4 Discussion and conclusions

Results of Zn bioavailability trials in ruminants are summarized in Table 1.

**Table1 Summarized results of bioavailability trials with different Zn sources for ruminants**

| Ref. | Category | Sources used | Response criteria | Bioavailability |
|---|---|---|---|---|
| [18] | Beef steers | ZnO, ZnMet | Performance, serum Zn | ZnO = ZnMet |
| [19] | Beef calves | ZnO, ZnMet | Performance, plasma Zn | ZnO = ZnMet (DMI tended to be higher for ZnMet) |
| [119] | Beef heifers | ZnO, ZnMet | Performance | ZnO = ZnMet |
| [120] | Beef steers | ZnO, ZnMet | Performance, serum Zn, neutralizing antibody titers | ZnO = ZnMet |
| [31] | Beef calves | $ZnSO_4$, ZnMet, ZnLys | Performance, plasma Zn, liver Zn, skin swelling after PHA(1) injection | $ZnSO_4$ = ZnMet = ZnLys (PHA immunity(1) of ZnLys < $ZnSO_4$, ZnMet) |
| [109] | Beef heifers | ZnO, ZnMet, $ZnSO_4$ | Serum Zn, erythrocyte Zn, tissue Zn(2) | ZnO = ZnMet = $ZnSO_4$ |
| [63] | Dairy calves | ZnO, ZnMet + ZnLys | Performance, liver Zn, thymidine uptake by lymphocytes | ZnO < ZnMet |
| [62] | Dairy calves | $ZnCl_2$, $ZnSO_4$, ZnO, $ZnCO_3$ | Plasma Zn | No differences between sources (plasma Zn) |

9 4.00% Zn ($Zn^{2+}$); 8.03% amino acids.
10 Maize/soybean meal/hay ration containing 58 ppm Zn (DM).
11 No more information on product names available; it is not clear whether 1400 ppm Zn was added to the ration DM or on as fed basis.

| Ref. | Category | Sources used | Response criteria | Bioavailability |
|---|---|---|---|---|
| [59] | Heifers | $ZnSO_4$, Zn amino acid complex | Performance, serum Zn, white blood cell counts and differentiation, cell-mediated immunity | No differences (gain, serum Zn, total/differential white blood cell count) |
| [75a] | Beef steers | $ZnSO_4$, Zn amino acid complex [3], Zn polysaccharide complex [4] | Performance, intestinal and subcutaneous fat thickness, serum Zn concentration | No significant differences between sources |
| [61a] | Fattening bulls | ZnO, Zn proteinate [5], Zn polysaccharide [6] | Performance, meat quality, metabolic profile, Zn concentration in serum, liver, bone, hair and claws, claw quality | No significant differences between sources, except improvements in macroscopic claw quality for both organic Zn sources |
| [121b] | Steers | $ZnSO_4$, ZnMet, ZnGly | DMI, serum and liver Zn, apparent Zn absorption, Zn retention | Liver Zn was higher in the ZnGly than in both other groups; other parameters were not different between the groups |
| [110a] | Beef heifers | $ZnSO_4$, Zn polysaccharide [4] | Performance, morbidity after stress and IBR challenge, humoral repsonse after vaccination with ovalbumin | No significant differences, except improved humoral response after ovalbumin vaccination |
| [90a] | Steers | $ZnSO_4$, Zn proteinate [7] | Performance, serum and liver Zn concentrations | No significant differences between sources |
| [138a] | Calves | $ZnSO_4$, Zn proteinate [8] | Performance, liver and plasma Zn, plasma alkaline phosphatase | During some stages of the experiment, $ZnSO_4$ > Zn proteinate group (liver Zn) [9] |
| [121a] | Steers | ZnO, 2 different Zn proteinates | Performance, meat quality, immune response | Performance tended to be higher in Zn proteinate groups than in ZnO group; no differences for other parameters |
| [108] | Sheep | ZnMet, ZnLys, $ZnSO_4$, ZnO | Serum Zn, pancreas Zn, tissue Zn(2) and MT | ZnLys > ZnMet, ZnO (serum Zn)<br>ZnLys > other sources (liver, kidney, pancreas Zn/MT)<br>no differences (Zn in bone, cornea, skin, hooves, muscles) |
| [111] | Sheep | $ZnSO_4$, $ZnCO_3$,ZnO,Zn $ZnSO_4$,ZnO | Pancreas, liver and kidney Zn, liver MT | Zn < other sources (pancreas, kidney, liver Zn)<br>no significant differences (pancreas, kidney, liver Zn) |
| [49] | Ewes | Zn-amino acid complex, $ZnSO_4$ | Performance, faecal Zn, liver Zn, serum AP | Zn-complex < $ZnSO_4$ (faecal excretion)<br>no difference (growth, liver Zn) |
| [13a] | Wether lambs | $ZnSO_4.7H_2O$, Zn proteinate, Zn amino acid chelate, ZnMet | Zn in liver, kidney and pancreas, liver metallothionein | Zn proteinate > other sources [10] |
| [104] | Fibre-goats | ZnMet, ZnO | Performance, mohair production and quality. Plasma Zn | ZnMet > ZnO (growth, mohair staple length)<br>ZnMet = ZnO (DMI, mohair yield/diameter, plasma Zn) |

(1) Cell-mediated immunity against phytohemagglutinin (PHA); MT = metallothionein; AP = alkaline phosphatase;

(2) Zn concentrations in bone, cornea, skin, hoof, hair, kidney, liver and muscle;

(3) AvailaZn, Eden Prairie;

(4) ZnSQM, Quali Tech;

(5) Bioplex Zn, Alltech;

(6) Carbosan, Quali Tech;

(7) DuCoa (no more information);

(8) Chelated Minerals Corp.;

(9) Only when a dose of 500 ppm (DM) was administered, plasma, duodenal, liver and kidney Zn was higher in the Zn proteinate group than in the $ZnSO_4$ group;

(10) The only level tested was 1400 ppm added Zn to a ration containing 58 ppm Zn (DM)

In summary, nearly all experimental evidence does not show any difference in bioavailability between $ZnSO_4$, ZnO, ZnMet, or ZnLys for cattle. Only in two out of 16 experiments a mixture of ZnMet and ZnLys or Zn proteinate seemed to have a somewhat higher bioavailability, but this was only the case when 340-400 ppm Zn or 500 ppm Zn (DM) was fed. These levels substantially exceed allowed EU levels[12] (120 ppm [58]) and may be detrimental in milk-fed calves (> 200 ppm [56]). Results from this experiment are, therefore, of no practical importance.
For sheep and goats, evidence is very scarce. The reported results for sheep point into the direction of ZnLys being the best available source, whereas metallic Zn is a poorly available source. In one experiment [13a], Zn proteinate was shown to significantly increase tissue Zn concentrations as compared with Zn sulphate. However, the only Zn level tested was as high as 1400 ppm additional Zn. Therefore, as these results are of no practical importance, the same remarks as mentioned above for cattle apply to this experiment. No differences exist between the other anorganic Zn sources mentioned. For goats, no clear result is reported.
Finally, in the majority of the experiments the Zn levels used substantially exceeded Zn requirements. It is not clear as to what extent results from these experiments can be applied to differences between sources when fed at or below requirements. Therefore, in practice there is no (dis)advantage of one specific Zn source for use in ruminant nutrition, and the cheapest and most convenient source may be used.

## 3.3 Interactions influencing zinc absorption

### 3.3.1 Interactions of zinc and iron

#### *3.3.1.1 Cattle and sheep*

Experimental evidence on the influence of dietary Fe on Zn metabolism in ruminants is not unequivocal. Selected results of trials are given in Table 2.

#### *3.3.1.2 Goats*

No experimental evidence is available on effects of dietary Fe additions on Zn metabolism in goats.

#### *3.3.1.3 Conclusion*

Although the Fe levels used in all experiments are thought to be more or less comparable with those of “available” Fe (for interactions) occurring in practice (e.g. from contamination of feeds with soil) [51], effects of additional Fe on Zn metabolism are often minor. Deteriorations of performance as observed in some experiments are not necessarily caused by alterations in Zn metabolism. Therefore, under practical conditions the influence of Fe on Zn metabolism in cattle and sheep will be largely unimportant, unless the Fe content of the ration roughly exceeds 1000-1500 ppm (DM). Then, one should be aware of a slightly lower Zn status of the animal. Until more information is available, this is assumed to be also the case for goats.

[12] Commission Regulation No 1334/2003/EC.

**Table 2 Selected results of experiments on the influence of Fe on Zn metabolism in ruminants.**

| Ref. | Category | Feed Zn | Feed total Fe | | Fe-source | Observations | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | DMI | ADG | F/G | Liver Zn | kidney Zn |
| | | ppm | | | | kg | | | ppm (DM) | |
| [126] | beef calves | 50 (added) | 77 | | $FeSO_4$ | 7.11 | 0.81 | 8.74 | 118 | 87 |
| | | | 477 | | | 6.46 | 0.63 | 10.19 | 134 | 90 |
| | | | 1677 | | | 5.41 D | 0.39 D | 13.80 D | 98 D | 81 D |
| | * spleen, heart and muscle Zn content ND | | | | | | | | | |
| [125] | steer calves | 50 (added) | 100 | | $FeSO_4$ | 7.63 | 1.00 | 7.63 | 145 | 96 |
| | | | 1000 | | | 5.84 | 0.74 D | 7.89 | 118 D | 92 |
| | * lowest spleen Zn content at 1000 ppm Fe<br>* heart and muscle Zn content ND<br>* no Fe x P interaction (2.3 and 4.6 g total P/kg) | | | | | | | | | |
| [124] | wether lambs | 50 (added) | 0 | added | | 0.55 a | -0.005 | | 178 | 236 |
| | | | 1600 | | $FeSO_4$ | 0.55 a | -0.011 | | 166 | 188 |
| | | | 0 | | | 0.56 a | 0.0 | | 120 | 181 |
| | | | 1600 | | Fe citrate | 0.56 a | -0.109 | | 147 | 136 |
| | * spleen, heart and muscle Zn content ND | | | | | | | | | |
| [32;40] | lambs | ? | 250 | (DM of concentrate) | $FeSO_4.7H_2O$ | 0.97 | 0.32 | 3.0 | 163 | 109 |
| | | | 1000 | | | 0.89 | 0.22 | 4.0 | 141 | 93 |
| | | | 1750 | | | 0.73 D | 0.18 D | 4.0 | 129 | 88 D |
| | * brain, spleen, liver, muscle, rib and wool Zn content ND | | | | | | | | | |
| [110] | wether lambs | 30 (added) | 40 | DM | Ferric citrate | 1.38 | 0.19 | 7.6 | 90 | 99 |
| | | | 800 | | | 1.06 D | 0.13 D | 8.1 | 105 | 90 D |
| | * liver and (heart) muscle ND<br>* no Fe x P or Fe x Al interaction on Zn metabolism (1.7 or 4.2 g P/kg DM; 168 or 1618 ppm Al (DM) | | | | | | | | | |

D = significant difference between highest and lowest dietary Fe levels ($p < 0.05$);
ND = no significant difference due to dietary Fe level; a = kg feed as fed; animals were pair-fed.

### 3.3.2 Interactions of zinc and cadmium

#### *3.3.2.1 Cattle*

In bull calves (average 76 kg BW), the addition of 350 ppm Cd as $CdCl_2$ to a glucose/maize starch/whey diet containing either 4 or 44 ppm of Zn (extra Zn from ZnO, Cd content not given) significantly decreased apparent Zn absorption (significant difference between percentage of a dose $^{65}Zn$ excreted in faeces) and $^{65}Zn$ retention in tissues (heart, lung, liver, spleen, kidney, testicles, scrotum, muscle and skin in Zn-deficient calves). The effect was not different for the two Zn levels. Urinary Zn excretion was not influenced by Cd treatment [102]. Similar results on $^{65}Zn$ absorption were obtained in another experiment with calves, although tissue Zn levels were hardly affected [106]. On the contrary, liver and kidney Zn levels were higher in calves supplemented with either 640 or 2560 ppm Cd, whereas spleen, testis, hair and skin Zn levels were not affected [103]. No data on Zn metabolism were given from the groups receiving either 40 or 160 ppm Cd. Selected results are given in Table 3.

#### *3.3.2.2 Sheep*

When Cd (0, 5, 15, 30 or 60 ppm) was added to the diet (0.2 ppm Cd, 32 ppm Zn) of ram lambs, liver and kidney Zn concentrations were significantly increased in the highest Cd-groups when compared with the control group [29]. The experiment lasted for 191 days. In contrast, dietary Cd loading did not affect ewe plasma and liver Zn, whereas their lambs showed lower plasma and liver Zn concentrations [88]. Lambs were fed the same diet as the ewes. The experiment was started at 13-14 weeks of pregnancy and terminated at 7.5-8 weeks *post partum*. The diets consisted of dried grass cubes. Selected results are given in Table 3.

#### *3.3.2.3 Goats*

Under the same experimental conditions as mentioned for calves [102], 350 ppm Cd significantly decreased apparent Zn absorption and $^{65}$Zn retention in tissues (muscle, tibia and skin in goats fed adequate Zn), whereas urinary Zn output was not influenced by Cd treatment. In another experiment, goats fed a semi-synthetic diet containing 75 ppm Cd (ration composition and Cd-level of control group not given) for up to 15 months, 50 percent of the Cd-loaded goats aborted, whereas none of the normally born kids was viable [6]. Zinc concentrations in kidneys, liver and milk of the dams, as well as liver Zn concentrations in the kids were significantly increased in the Cd-loaded group compared with the control group. Milk Zn contents were 37 and 19 mg/kg for control and Cd-loaded goats, respectively. This difference was significant. Selected results are given in Table 3.
In an experiment with pregnant goats fed 0 or 500 ppm additional Cd for 10 months, Zn content of lambs and milk of these animals was not influenced by Cd addition [5]. Zinc contents of lambs and milk were 69 vs. 65 and 33 vs. 36 ppm for 0- and 500 ppm Cd-supplemented animals, respectively.

#### *3.3.2.4 Conclusion*

Although significant influences of Cd addition on Zn metabolism have been reported (Table 3), these results are conflicting. In calves and goats, Cd decreased the ($^{65}$)Zn retention in the liver, whereas in lambs and calves stable (non-radioactive) Zn concentrations were highest in the Cd-treated groups. Labile (radioactive) Zn has been suggested to be most affected by dietary Cd additions [106]. As yet, this phenomenon cannot be explained. Moreover, in all experiments except two with sheep [29;88] the Cd concentrations applied extremely exceed those normally found in herbage under practical conditions (0.1-0.8 ppm (DM)) and even in Cd-contaminated areas (1-21 ppm (DM))[88]. Therefore, results from experiments employing Cd levels as high as 350 ppm added Cd are of no practical relevance. In conclusion, the scarce, conflicting data preclude quantification of the effect of Cd on Zn metabolism in ruminants.

**Table 3 Selected results of experiments on the influence of Cd on Zn metabolism in ruminants**

| Ref. | Category | Zn | Cd (added) | | Faecal Zn | Liver Zn | Kidney Zn |
|---|---|---|---|---|---|---|---|
| | | ppm in feed | | | % of dose $^{65}$Zn [a] | | |
| [102] | dairy bull calves | 4.0 | 0 | | - | 3.34 | 1.59 |
| | | | 350 | | - | 1.59 | 0.58 |
| | | 44.0 | 0 | | ± 30 [b] | 5.19 | 2.56 |
| | | | 350 | | ± 90 [b] | 1.58 D | 0.56 D |
| [102] | male goats | 4.0 | 0 | | ± 32 [b] | 17.68 | 8.45 |
| | | | 350 | | ± 38 [b] | 9.96 | 6.02 |
| | | 44.0 | 0 | | ± 28 [b] | 21.33 | 11.92 |
| | | | 350 | | ± 45 [b] | 18.10 | 9.21 |
| [6] | female goats | | | | | ppm Zn (DM) | |
| | | ? | 0 | | | 44 [e] | 17 [e] |
| | | | 75 | | | 118 [e] D | 66 [e] D |
| | matching kids | ? | 0 | | | 67 [e] | 20 [e] |
| | | | 75 | | | 26 [e] D | 17 [e] |
| [106] | dairy bull calves | 8.5 | 0 | | ± 40 [c] | 122 | 79 |
| | | | 350 | | ± 75 [c] | 166 | 89 |
| [103] | dairy bull calves | 27 (DM) | 0 | 0.3 | | 88 | 59 |
| | | | 640 | | | 169 | 110 |
| | | | 2560 | | | 166 | 125 |
| [29] | ram lambs | 32 | added | total | | | |
| | | | 0 | 0.2 | 125 | 112 | |
| | | | 5 | | 141 | 150 | |
| | | | 15 | | 167 | 209 D | |
| | | | 30 | | 188 D | 255 D | |
| | | | 60 | | 208 D | 251 D | |
| [88] | ewes [d] | 37 | | | | | Plasma Zn (µM) |
| | | | 0 | 0.7 | | 109 | |
| | | | 2.8 | 3.5 | | 106 | |
| | | | 6.4 | 7.1 | | 107 | |
| | | | 11.6 | 12.3 | | 114 | |
| | matching lambs [d] | | 0 | 0.7 | | 135 | 16.5 |
| | | | 2.8 | 3.5 | | 96 | 15.7 |
| | | | 6.4 | 7.1 | | 103 | 14.8 |
| | | | 11.6 | 12.3 | | 94 D | 11.5 D |

[a] = excreted in faeces or retained / kg of fresh tissue;
[b] = accumulated percentage of a given dose of $^{65}$Zn excreted into faeces by day 12 after oral dosing (values depicted only in a graph);
[c] = accumulated percentage of a given dose of $^{65}$Zn excreted into faeces by day 7 after oral dosing (values depicted only in a graph);
[d] = values at the end of the experiment (7.5-8 weeks p.p.);
[e] = calculated values supposing DM content of liver = 28% and of kidney = 20%; D = significantly different from values of control group not receiving extra Cd.

### 3.3.3 Interactions of zinc and copper

#### *3.3.3.1 Cattle*

In preruminant calves fed a milk substitute ration (48 ppm Zn) containing graded Cu levels of 10-1000 ppm (DM) liver Zn concentrations significantly decreased, whereas faecal Zn excretion increased [54;55]. Selected results are given in Table 4.

**Table 4 Selected results of an experiment on the influence of Cu on Zn metabolism in preruminant calves**

| Parameter | Dietary Cu (ppm (DM)) | | | | |
|---|---|---|---|---|---|
| | 10 | 50 | 200 | 500 | 1000 |
| Faecal Zn excretion (% of intake) | 59.8 | 57.7 | 62.1 | 67.3 | 70.4 D |
| Liver Zn (ppm (DM)) | 262 | 189 D | 170 D | 167 D | 139 D |

D = significantly different from 10 ppm Cu level

When 8 or 16 ppm Cu (from either Cu lysine or $CuSO_4$) was supplemented to the ration of beef heifers, no significant influence on plasma and liver Zn concentrations due to Cu level was observed [105]. The basal maize/soybean meal/cottonseed hulls-ration contained 5.1 ppm Cu and 30 ppm added Zn. It is not clear as to what extent the lack of Cu-effect on Zn metabolism is related to the deficient basal Cu level [132]. In dairy cows, no effect of increasing the daily Cu intake from ± 300 to 550-850 mg on milk Zn concentrations could be demonstrated [114]. Copper was added as $CuSO_4.5H_2O$. Daily DMI was 15-16 kg, so Cu contents of the rations were approximately 19 and 35-55 ppm for control and Cu-supplemented groups, respectively.

*3.3.3.2 Sheep*

In wethers (6-9 months of age) given 5.1 mg of additional Cu (as $CuSO_4.5H_2O$) on 5 days/week, no effect on liver Zn concentrations was observed [27]. The basal ration consisted of lucerne, lupine and grains and contained 5 ppm Cu and 48 ppm Zn. Again, it is not clear as to what extent the lack of Cu-effect on Zn metabolism is related to the deficient basal Cu level [132]. After 28 weeks, liver Zn concentrations were 118 and 114 ppm (DM) for the low- and high Cu groups, respectively.

*3.3.3.3 Goats*

No information is available on any influence of dietary Cu on Zn metabolism in goats.

*3.3.3.4 Conclusion*

As discussed by Jongbloed et al [58], for Dutch cattle current practical levels of Cu in feeds are 4-8 (roughages) and 27-32 ppm (DM) (concentrates) and of Zn in feeds are 34-48 (roughages) and 78-85 ppm (DM) (concentrates). Thus, as Cu levels applied in the experiments with ruminating animals mentioned above resemble practical levels, results indicate that Cu-Zn antagonism is not of practical importance for cattle [132]. In Dutch veal calf rations, Cu concentrations range from 0.3-17 ppm [136]. Although liver Zn concentrations were already reduced in calves fed 50 ppm Cu (DM), no Cu levels in between have been tested. Thus, the importance of dietary Cu for the Zn metabolism of the non-ruminating (veal) calf cannot be judged. This is even more evident for the 1000 ppm Cu (DM) level increasing faecal Zn excretion in preruminant calves.
Until more information is available, the above considerations are supposed to be valid for goats either.

3.3.4 Interactions of zinc and phytate

*3.3.4.1 Non-ruminant animals*

Phytate can affect the bioavailability of several minerals and trace elements [60]. In an experiment with veal calves, the control group was fed milk replacer as the sole feed (124 ppm Zn (DM)), whereas in the experimental ration part of the milk replacer was replaced by soy protein (142 ppm Zn (DM)) [139]. After 26 weeks feeding, both plasma and hepatic Zn concentrations were significantly reduced in the experimental group as compared with the control group. Performance was slightly worse in the experimental group. As soy protein is

rich in phytate, it was hypothesized that dietary phytate from the soy protein hampered Zn absorption. This was proven by adding either phytase (100 mg Natuphos®/kg of diet), 175 ppm Zn, 175 ppm Zn + 100 mg Natuphos®/kg of diet or no supplement (control group) to a milk replacer diet (soy protein instead of milk powder) [28]. Plasma Zn values were 38, 38, 80 and 26 µM, whereas liver Zn concentrations were 589, 552, 1257 and 256 ppm (DM) (phytase, Zn, phytase+Zn and control group, respectively).

No data are available as to the influence of phytate in the ration of non-ruminant lambs and kids.

#### *3.3.4.2 Ruminating animals*

As the ruminal flora of ruminating animals produces phytase, no negative effect of phytate on Zn bioavailability in ruminants may occur. As yet, no experimental results on this subject are available (H. Valk, personal communication).

### 3.3.5 Interactions of zinc and lead

#### *3.3.5.1 Cattle*

In dairy calves (86 kg BW; 10.5 weeks of age) fed maize/soybean meal/grass diets either without (control) or with additional 500 or 1500 ppm Pb for 7 weeks, Zn metabolism was partly influenced [137]. Lead was supplied as $PbSO_4$. In the 1500 ppm Pb group, Zn absorption was slightly reduced when compared with the control group. Seven days after oral dosing of $^{65}Zn$ [13] ± 80% of dose was excreted via the faeces in the unsupplemented control group, compared with ±70% in the 1500 ppm Pb group. Tissue stable Zn concentrations were significantly reduced in pancreas, heart and testicle, whereas intestinal tissue Zn, blood Zn and cellular distribution of Zn in liver and kidney were not significantly altered.
Male calves (1 month of age) given either 4.1 mg Pb/kg BW (as Pb acetate) or no Pb supplement did not show significant differences in blood Zn concentrations between the groups [100]. The ration consisted of whole milk and/or calf starter and green fodder. Detailed data on ration composition were not given. After 28 days on experiment, blood Zn concentrations were 61.7 and 71.3 µM for control and Pb-loaded animals, respectively. In the Pb-loaded calves, blood Zn values significantly increased during the experiment (time effect, initial blood Zn concentration was 60.9 µM).

#### *3.3.5.2 Sheep and goats*

No data on the influence of Pb on Zn metabolism in small ruminants are available.

#### *3.3.5.3 Conclusion*

Practical levels of Pb in forage downstream a lead smelter are reported to be 163-212 ppm compared with 5 ppm before the start of the smelter [30]. Assuming a DM content of fresh grass of 16% [15], these concentrations are 1019-1325 and 31 ppm Pb (DM), respectively. The former value is in accordance with others (500-1000 ppm (DM)) in Pb-contaminated areas [47]. As plants do not take up Pb, it is present as a contamination on the surface of the plant. However, Pb-contaminated plants cannot be easily cleaned with water [47]. Data from the dairy calf experiment [137] are, therefore, applicable to heavily contaminated areas. At levels in this order of magnitude, Pb has some influence on Zn metabolism. However, at the much lower Pb levels used in the other experiment [100] (assessed to be 100-150 ppm (DM)), no significant effect could be observed. Normal values for Pb-concentrations in herbage are < 10 ppm (DM), whereas these values can increase up to 300 ppm (DM) in the vicinity of highways [47]. Thus, although Pb-concentrations in feed >15 ppm (DM) are considered to be toxic for ruminants [47], under practical circumstances (except in

[13] Via gelatine capsules.

contaminated areas) the influence of Pb on Zn metabolism in cattle may be irrelevant. Unless proven otherwise, this is assumed to be also valid for small ruminants.

### 3.3.6 Interactions of zinc, aluminium and phosphorus

#### *3.3.6.1 Cattle*

Growing beef steers (226 kg BW) fed additional Al for 84 days (basal diet: maize/soybean meal/cottonseed hulls; 100 ppm added Zn, 210 ppm total Al[14]) showed significantly higher Zn concentrations in liver and kidney [134]. Added Al levels were 0, 300, 600 or 1200 ppm (as $AlCl_3.6H_2O$). Liver Zn concentrations were 59.3 and 81.3 ppm (DM), whereas kidney Zn concentrations were 45.0 and 57.9 ppm (DM) for groups receiving 0 and 1200 ppm additional Al, respectively. Performance was not significantly influenced. In ruminating dairy calves (72 kg BW, 64 d of age) [91], the effects of adding P and/or Al were investigated. The experimental design consisted of 4 groups: normal P/low Al; low P/low Al; normal P/high Al and low P/high Al. The basal diet (low P/low Al; maize (cobs/meal)/ beet pulp)) contained 1.3 g P, 200 mg Al and 50 mg Zn per kg DM and was supplemented with either 2.2 g P/kg[15] and/or 2000 ppm Al. The high Al versus the low Al diet (extra Al from $AlCl_3.6H_2O$) decreased apparent $^{65}$Zn absorption and increased tibia Zn concentrations, whereas DMI and growth tended to be lower and liver and kidney Zn concentrations tended to be higher in the high Al group[16]. The high P versus the low P diet significantly increased DMI and growth. Apparent $^{65}$Zn absorption tended to be higher in the low-P group, whereas tissue stable Zn levels were not different. Alterations due to the P-level may have been influenced by the increased DMI in the normal-P group. Using a similar design, the same research group found little or no effect on Zn content of tissues and $^{65}$Zn absorption of the addition of 1.4, 2.0 or 3.2 g P to a diet (maize (cobs/meal)/beet pulp/blood meal) containing 0.8 g P/kg [69]. Likewise, no differences between Zn metabolism of steer calves fed diets (maize/grass hay/soybean meal) containing either 2.3 or 4.6 g P/kg could be demonstrated [125]. Performance, tissue Zn concentrations and apparent Zn absorption were similar in both groups.
In the above experiments investigating the influence of both Al and P on Zn metabolism, hardly any Al x P interaction was observed.

#### *3.3.6.2 Sheep*

Two experiments using wether lambs were carried out investigating the influence of Al and P on tissue mineral composition [110;133]. Rations were similar (maize/soybean meal/cotton seed) and contained 1.5 or 1.7 g P/kg DM, 168 ppm Al (DM), 100 or 30 ppm added Zn (basal diet) and 3.2 or 4.2 g P/kg DM and 2168 or 1618 ppm Al (DM) and 100 or 30 ppm added Zn (experimental diet). In both experiments, additional Al (from $AlCl_3.6H_2O$) significantly depressed DMI and growth. In the first experiment [133], no effect of Al level on either liver, kidney, muscle or brain Zn concentrations could be observed. Kidney Zn levels were significantly lower in the high-P group when compared with the low-P group. In the second experiment [110], Zn concentrations were higher in the high-Al (kidney) and lower in the high-P group (kidney, spleen). Significant Al x P interactions were observed. No differences due to either Al or P were found in Zn concentrations of liver, muscle or heart tissues.

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[14] Although data on normal Al concentrations in feeds and Al requirements are scarce, sweet clover was reported to contain 139 ppm Al (DM) [35]. In the ration of young goats, 25 ppm Al (DM) seemed to be sufficient [4].

[15] From Dynafos®, a mixture of mono- and dicalciumphosphate containing 18.5% P

[16] In some tissues, high Al tended to lower Zn concentrations, but Al x P interactions yielded confusing results.

#### *3.3.6.3 Goats*

No experimental evidence is available concerning the influence of Al and/or P on Zn metabolism in goats.

#### *3.3.6.4 Conclusion*

The Al concentrations used in the experiment mentioned above substantially even exceed those found in plants from polluted areas (e.g. 237 ppm Al (DM) in sweet clover grown on fly ash [35]). Nevertheless, only minor influences on Zn metabolism have been reported. Although the employed P levels are practical, in conclusion, the practical importance of both Al and P on Zn metabolism in ruminants seems to be minor.

### 3.3.7 Interactions of zinc and calcium

#### *3.3.7.1 Cattle*

Based on field observations in cattle (fed 250-400 mg Zn/day) and the (dis)appearance of symptoms associated with Zn deficiency (itch, hair licking), a relationship between dietary Ca and required Zn levels has been suggested [42]. The equation is as follows:

required Zn level (ppm (DM)) = 15.9 x feed Ca (g/kg DM)

Thus, when dietary Ca level is 2.5 g/kg DM, dietary Zn level should be 40 ppm (DM). A total of 355 cows were investigated. The Ca levels underlying this calculations range from ± 2.5 to 9 g/kg DM, whereas the Zn levels range from ± 30-100 ppm (DM). However, no suitable observations (adjacent to the line described by the equation) were made at dietary concentrations >7 g Ca/kg DM and >100 ppm Zn (DM), whereas linearity of the relationship is not substantiated. The validity of the equation for dietary concentrations exceeding these values is questionable. Moreover, only a subjective criterion (itch, hair licking) has been used to define “sufficiency” of Zn supply. Finally, in lactating cows fed a maize/sugar beet pulp/pea/soybean meal diet (40 ppm Zn, 8 g Ca/kg), no significant effect of adding 7 g Ca/kg of diet (from limestone) on plasma Zn concentrations after an oral dose of Zn was observed [62]. Before dosing, plasma Zn levels were 12.4 and 13.2 µM for low- and high Ca groups, respectively. At 24 h after Zn dosing these levels were 16.5 and 16.2 µM, respectively.

#### *3.3.7.2 Sheep*

In pregnant ewes fed maize silage/alfalfa hay diets containing either 20 or 74 ppm Zn and/or either 2.4 or 8.0 g Ca/kg, plasma Zn concentrations were significantly lower in the high Ca group [101]. Mean plasma Zn concentrations were 11,6 and 10,4 µM for low- and high Ca groups, respectively.
Lambs fed diets (1.2 ppm Zn + extra Zn gradually declining (18, 13, 10, 5 or 0 ppm) during 20 weeks) supplemented with Ca to a total concentration of 18 g Ca/kg had lower plasma Zn concentrations than lambs on similar diets containing either 12 or 6 g Ca/kg [89]. Each Ca treatment group consisted of 6 animals. After 6 weeks on the diet containing 5 ppm supplementary Zn (total Zn 6.2 ppm), 2 animals in the 6 g Ca/kg-group had mild parakeratotic lesions, whereas all animals in the 18 g Ca/kg-group had severe parakeratosis.

#### *3.3.7.3 Goats*

No experimental data are available on the influence of Ca on Zn metabolism in goats.

#### *3.3.7.4 Conclusion*

Dietary Ca influences Zn metabolism in sheep and cattle. For goats evidence is lacking. Due to scarcity of data and uncertainties concerning the validity of the proposed equations, the effects cannot be reliably quantified.

### 3.3.8 Interactions of zinc and nickel

#### *3.3.8.1 Cattle*

In dairy calves (74 kg BW), no influence of the addition of 5 ppm Ni (as $NiCl_2.6H_2O$) to a ration (maize/cottonseed hulls) containing on average 0.5 ppm Ni on performance and Zn concentrations in liver, kidney, spleen, lung, heart and muscle could be demonstrated [121].

#### *3.3.8.2 Sheep and goats*

No data are available on any influence of Ni on Zn metabolism in small ruminants.

#### *3.3.8.3 Conclusion*

Under practical circumstances, influences of Ni on Zn metabolism in ruminants are considered to be irrelevant.

### 3.3.9 Interactions of zinc and potassium

#### *3.3.9.1 Cattle*

In a study with 120 dairy cows from four farms, increasing the K content of the ration caused a secondary Zn deficiency with lower plasma Zn levels, an increased incidence of claw lesions and infectious diseases such as mastitis and a decreased reproductive performance [12]. The K contents of the rations were 10 (control), 15, 20, 25, 30 g/kg DM. At the 25 and 30 g/kg DM levels, plasma Zn levels were significantly lower than in the control groups from the $4^{th}$ month of the lactation on two of the four farms.

#### *3.3.9.2 Sheep*

In lambs fed grass hay/soybean meal/barley diets, increasing the K content of the diets slightly decreased Zn retention [72]. At dietary K intakes of 5.6, 10.1 or 13.9 g/day, Zn retention was 43, 28 and 24 mg/day, respectively.

#### *3.3.9.3 Goats*

No suitable data are available on the interaction of K and Zn in goats.

#### *3.3.9.4 Conclusion*

The K levels applied in the experiments mentioned commonly occur in practice, and can be even higher in heavily fertilized roughage fed to cattle (BLGG, Oosterbeek, The Netherlands [112]). Thus, the K x Zn interaction may be of practical importance. However, due to lack of suitable data this remains speculative and quantification of the interaction is precluded.

## 3.4 Recycling

Although recycling of Zn after excretion via pancreatic juice, bile and intestinal wall should occur, no data on this process in ruminants are available.

## 3.5 Excretion

Excretion of Zn occurs via the faeces (contributions from bile (i.a. bound to glutathione), pancreatic juice and directly via the intestinal wall) and via the urine. Lambs (9 weeks of age) fed Zn according to NRC requirements (19-26 ppm Zn) excreted 0.10 mg Zn/24 hours via

their bile (0.17 mg Zn/L bile) [37]. In calves (dietary Zn intake 108 mg/day), Zn excretion via the bile was demonstrated to be 0.98-1.2 µg/min [130]. In calves fed milk replacer containing either 40, 200, 500, 700 or 1000 ppm Zn (DM) for 5 weeks, final bile Zn concentrations were 1.0, 1.2, 3.1, 3.0 and 6.4 mg/L, respectively [56]. The contribution of urinary excretion is considered to be minor [132]. For example, in goats (46 ppm dietary Zn), after 28 days ± 12% of an intravenous dose of $^{65}$Zn was excreted in the faeces, whereas ± 0.5% of dose was excreted via the urine [83]. In Zn-deficient goats (6 ppm Zn) these values were 9 and 0.3%, respectively. In calves on the same diets, after 12 days these values were 15 and 0.3% (46 ppm Zn) and 10 and 0.3% (6 ppm Zn), respectively. In another experiment by the same investigators [81], after 3 weeks on diets containing 33, 233 and 633 ppm Zn calves excreted 69, 81 and 82%, respectively of the dietary Zn intake via the faeces, whereas urinary Zn excretion of these animals was 1.4, 0.4 and 0.2% of dietary intake. In adult wethers on a high-Zn diet (236 ppm Zn (DM)), ± 91% of dietary Zn intake was excreted via the faeces, whereas 1.4% was excreted via the urine [68]. In mature ewes fed hay (providing 8 mg Zn/day) and intraruminally infused with a Zn sulphate solution providing either 0, 75, 150 or 225 mg Zn/day, Zn excretion via the urine was independent from dietary Zn intake (0.83 mg/day), while faecal Zn excretion increased from 20 to 251 mg/day [128]. In one dairy cow on a ration containing only 6 ppm Zn, after 19 weeks faecal Zn excretion was ± 30%, whereas urinary Zn excretion was ± 5% of the daily Zn intake [67]. Finally, pregnant cows consuming 100 mg Zn excreted 78 mg via the faeces, whereas urinary excretion was 4 mg [46].

Urinary Zn excretion in sheep was significantly increased by the addition of S to the diet (173 vs. 3 mg Zn/day when total dietary S concentration was 8.1 vs. 1.5 g/kg (DM) [39]. Moreover, in lambs urinary Zn excretion significantly increased from 2.7 to 6.5 mg/day when dietary K concentration was raised from 9.6 to 30.2 g/kg, even while daily Zn intake was slightly lower (78.3 mg) in the high K than in low K group (90.6 mg) [72]. In calves in which the pancreatic duct was ligated or cannulated the influence on faecal Zn excretion was investigated [122]. When these animals received an intravenous dose $^{65}$Zn, the $^{65}$Zn content of the faeces through a period of 7 days appeared to be ± 25% lower than in calves from a control group (no surgery or sham-operated). Apparently, the pancreatic juice is not the main excretion route for Zn. Moreover, the maximum of the $^{65}$Zn-excretion via the pancreatic juice is attained much earlier (2 hours after dosing) than that of the faeces (2 days after dosing). Through a much more extended period the contribution of the pancreatic juice to the Zn-excretion will, therefore, be even lower. In growing goats and calves (3-4 months of age) receiving diets containing either 6 or 46 ppm Zn, accumulated $^{65}$Zn excretion into the faeces at 18 days after dosing in the non Zn-deficient goats appeared to be higher than in their bovine counterparts (± 42 vs. 24%) [82]. For the Zn-deficient goats and calves, differences in faecal excretion were minor (± 23 vs. 21% for goats and calves, respectively).

In rats, ± 80% of the endogenous faecal Zn secretion occurs through the full length of the intestinal wall [78].

# 4 ZINC REQUIREMENTS

The Zn requirements of adult animals are determined by the endogenous (inevitable) losses and the secretion into milk. In growing and pregnant animals Zn is also deposited in growing (foetal) tissues.

## 4.1 Cattle

### 4.1.1 Dairy cattle

In dairy cows, the endogenous faecal Zn loss is assessed to be 0.033 mg/kg BW[17], whereas the urinary excretion is assessed to be 0.012 mg/kg BW. Thus, total endogenous Zn loss is calculated to be 0.045 mg/kg BW [7;98]. However, based on the fact that the 0.033 mg/kg BW estimate originated from an experiment allowing clinical deficiency symptoms to develop, a much higher direct estimate of 0.11 mg/kg BW for faecal endogenous Zn loss has been made in sheep by means of an isotope dilution technique, whereas urinary Zn loss was negligible (<0.2 mg/animal/day) [128]. This estimate was classified to be "minimal". This qualification is not further explained. As this estimate is the only direct one, this value is also used for cattle.

During gestation, the pregnant bovine uterus requires about 1.1 mg (mid stage) to 6.3-12 mg Zn/day [98;132] or 6.7-10.5 mg Zn/day [31a] from 190 days of gestation until parturition. Both the 1.1 and 6.3 mg estimates are qualified to be "minimal". Again, this qualification is not further explained. The 12 mg estimate is made employing rations containing as much as 56-78 ppm Zn (DM) [50] and is certainly not "minimal", as apparent Zn absorption decreases when dietary Zn concentrations increase [67] (see paragraph 3.1). For the last stage of pregnancy, therefore, the average of both ranges (8.9 mg Zn/day) is adopted. Growing tissues are reported to contain 16-31 mg Zn/kg. A mean value of 24 mg Zn/kg growth seems to be defendable [98;132].

Colostrum is reported to contain 12.4 [10] or even 25.8 (day 1) mg Zn/kg [116]. The Zn concentration falls sharply during the first days *post partum*. A steady state is attained approximately on day 3 [116]. The Zn content of mature milk is assessed to be (mg/kg) 2.3-5.1 [53], 3.6 [22], 3-3.8 [135], 3.9 [8], 4.2 [92], 4.3 [73] or 4.4 [107], 3.4-5.8 [98] or 4.0-4.6 [10;114]. On average, a value of 4.1 mg of Zn/kg has been chosen arbitrarily for all ruminants.

The influence of dietary Zn concentrations on milk Zn content is limited, although results do not fully agree. In one heifer fed a semi-synthetic diet containing 6 ppm Zn during 19 weeks, the final milk Zn concentration was 2.3 mg Zn/kg [116]. When 4 other cows were repleted with Zn during 13 weeks, levels > 87 ppm dietary Zn did not result in increases of milk Zn concentrations. After feeding a diet containing 130-436 ppm Zn for 9 weeks, milk Zn concentration was on average 5.5 mg/kg. In cows fed a diet containing 16.6 ppm Zn during 6 weeks, mean milk Zn concentration at the end of the experiment was 3.3 mg/kg [92]. A substantial increase of the Zn content of the feed (100 ppm Zn (DM) in basal ration; 2.2 g Zn from ZnMet added) during 22 weeks did not result in an increased Zn concentration of the milk [66]. Although the basal Zn level was already high and dietary Zn intake was approximately doubled by the ZnMet addition, final milk Zn concentrations were 2.6 (lowest Zn) and 2.8 mg/kg (highest Zn). These results do not agree with those from another study, in which lactating dairy cows consuming a forage/concentrate ration were fed either 44, 372, 692 or 1279 ppm Zn (DM) [84]. Corresponding milk Zn values were 4.2, 6.7, 8.0 and 8.4 mg/kg. Feeding dairy cows 0 or 8 g Zn from ZnO (8 cows/group) during 2 months significantly increased the milk Zn content from 3.8 to 5.1 mg/kg [8].

[17] method unclear.

The Zn content of bovine hair depends i.a. on the age, feeding and region of the body. On average, Zn content is 106 ppm (DM) [86]. For dairy cows, the Zn requirement for hair growth is neglected.

#### 4.1.2 Beef cattle

No separate calculations need to be made for the Zn requirements of beef cattle. As Zn supplementation to rations containing 17-29 ppm Zn improved gain in a minority of cases, and not when diets contained 22-32 ppm Zn, 30 ppm Zn is considered to cover beef cattle Zn needs in most cases [97].

### 4.2 Sheep

For sheep, the value for endogenous loss (0.1 mg Zn/kg BW) is assumed to be the same as for cattle. For growth, a value of 25.5 mg Zn/kg growth is reported [37a]. However, for both cattle and small ruminants arbitrarily a value of 24 mg Zn/kg growth is used. During twin pregnancy, 0.28 (mid stage) and 1.5 mg Zn/day (late stage) would be the extra Zn requirements. For wool growth, 115 mg Zn/kg fleece weight is assessed [132]. As clean wool yield is 1.0-3.8 kg/year [7], Zn need for wool growth is assessed to be 115-437 mg/year or 0.3-1.2 mg/day.
Milk Zn content is assessed to be 4.4 [20](assuming sheep milk to contain 18.3% DM [14]) or 7.2 mg Zn/kg[18] [132].

### 4.3 Goats

As no separate information is available on true Zn absorption, endogenous Zn loss or Zn content of growing tissues or pregnancy the values assumed for sheep are used.
Goat colostrum contains (mg/kg) 12.5 (day 1) to 11.8 (day 2) [10], whereas mature goat milk contains (mg/kg) 3.1 [99], 3.3 [107], 3.6 [10], 3.8 [77] or 4.9 [73]. An extremely high value of 33 mg/kg is given in reference [5]. As no data on ration composition are given, the reason for this high value is unclear and is considered to an abberating value.
The Zn content of goat hair is reported to be ± 120 ppm (40 ppm of dietary Zn) or ± 75 ppm (4 ppm of dietary Zn) [93] (breed not given). In another experiment employing Barbari goats, 43.8 ppm Zn in hair was reported [43]. However, Zn content of the ration was not given. As no information is available on the Zn content of typical fibre-producing goats (Cashmere and Angora), an intermediate value of 80 ppm Zn is adopted. As fibre production of goats has been reported to be 0.63 (Cashmere) to 3.5 (Angora) kg/year (= 3.4 to 9.6 g/day, respectively) [2], Zn requirement for fibre production ranges from 0.13-0.77 mg Zn/day. For dairy goats, no data are available on hair production, but it is supposed to be lower than that of fibre-producing goats. As Zn for fibre production in Cashmere and Angora is already small when compared with their Zn needs for other purposes, Zn requirement for hair growth in dairy goats is neglected.

### 4.4 Conclusion

The following equation can be used to calculate the required Zn concentration of ruminant rations:

[18] Any experimental evidence for this abberating high value is unclear.

$$C = \frac{100 \times ((BW \times 0.1) + (kg\ milk \times a) + (kg\ growth \times 24) + b)}{A_{Zn} \times DMI}$$

in which C = required dietary Zn concentration (ppm (DM))
BW = body weight (kg)
$A_{Zn}$ = true Zn absorption (%) (assumed to be 70%[19], except for milk-fed animals (85%))
DMI = dry matter intake (kg/day).
a = 4.1 mg/kg for all ruminants
b = amount of Zn needed for pregnancy (mg/day)
For cattle, b = 1.1 or 8.9 for mid- and late stages of gestation. For sheep and goats, b = 0.3 or 1.5 mg/day for mid- and late stages of gestation [132].

[19] The choice for a relatively high value for $A_{Zn}$ is compensated by the safety margin of 50%.

# 5 ALLOWANCES

Using the above equation (see 4.4), some examples of minimal dietary requirements and allowances (including a safety margin of 50%) have been calculated (Table 5). For more examples, see reference [132] (Tables 6 and 7). Slight differences arise from different assumptions concerning milk Zn concentrations, BW and endogenous losses.

**Table 5 Examples of calculated Zn requirements and allowances**

| Category | DMI | Requirement | Allowance | |
|---|---|---|---|---|
| | kg | mg/day | mg/day | ppm (DM) |
| Growing female cattle | | | | |
| 4 months, 850 g growth/day, 130 kg BW | 3.9 | 48 | 72 | 18.4 |
| 9 months, 700 g growth/day, 250 kg BW | 5.6 | 61 | 92 | 16.4 |
| 16 months, 625 g growth/day, 400 kg BW | 7.3 | 79 | 118 | 16.1 |
| Dairy cattle (650 kg BW) | | | | |
| Cow, dry, pregnant, 8-3 wk a.p. | 11.5 | 106 | 158 | 13.8 |
| Cow, dry, pregnant, 3-0 wk a.p. | 11.0 | 106 | 158 | 14.4 |
| Cow, lactating, 20 kg of milk | 18.5 | 210 | 314 | 17.0 |
| Cow, lactating, 40 kg of milk | 23.5 | 326 | 490 | 20.8 |
| Beef cattle, intermediate type | | | | |
| 1000 g growth/day, 100 kg BW | 3 | 49 | 73 | 24.3 |
| 1200 g growth/day, 250 kg BW | 6 | 77 | 115 | 19.2 |
| 1100 g growth/day, 500 kg BW | 9 | 109 | 164 | 18.2 |
| Veal calves | | | | |
| 1150 g growth/day, 150 kg BW | 4.5 | 61 | 91 | 20.3 |
| 1450 g growth/day, 275 kg BW | 7 | 89 | 134 | 19.1 |
| | | | | |
| Sheep (75 kg BW) | | | | |
| Growing lamb, 0.3 kg growth/day, 40 kg BW | 1.6 | 16 | 24 | 15.0 |
| Sheep, pregnant, last trimester | 1.9 | 15 | 23 | 11.8 |
| Sheep, lactating, 3 kg of milk, nursing 2 lambs | 2.6 | 29 | 44 | 16.7 |
| | | | | |
| Goats (70 kg BW) | | | | |
| Goat, pregnant, last trimester | 1.7 | 13 | 19 | 11.3 |
| Goat, lactating, 4 kg of milk | 3.2 | 33 | 50 | 15.7 |

For non-ruminating calves consuming rations rich in phytic acid, the addition of 50 ppm Zn (DM) to the ration is recommended [52]. The phrase “rich in phytic acid” is not further specified. However, as a total dietary concentration of 188 ppm Zn did not suffice to prevent deterioration of performance (and liver Zn values) at a 15% inclusion rate of soybean flour into veal calf rations [70], an allowance of 200 ppm Zn is proposed for veal calves consuming rations containing soybean products.

# 6 CRITERIA TO JUDGE ZINC STATUS

## 6.1 Ranking criteria for indicators of Zn status

When comparing different sources of Zn, bioavailability has to be related to a reference mineral source. This source has by definition a relative bioavailability of 100%. For Zn, the reference source is $ZnSO_4.H_2O$ (reagent grade) or $ZnSO_4.7H_2O$ (reagent grade). Several criteria are used to judge the effect of supplying a certain amount of Zn on the animal's mineral status. However, not all criteria are equally important. Therefore, criteria have to be ranked in order of their importance. This order may be different for the individual animal species or even category. Beside this, it is important to note that the order of importance may depend on the level of supply (below or above recommended requirements). If more criteria are available then weighing factors can be used to obtain a final score. Ranking of criteria to judge Zn status of cattle is given in Table 6.

**Table 6 Ranking of criteria to judge the effects of a certain supply of Zn on cattle performance as given by Jongbloed [57]**

| Criterion | Ranking of importance (weighing factors) | |
|---|---|---|
| | Supply | |
| | below requirements | above requirements |
| True Zn absorption | 4 | 1 |
| Tibia/bone Zn concentration | 5 | 3 |
| Pancreatic Zn concentration | No | 2 |
| Performance | 2 | No |
| Serum/plasma Zn concentration | 3 | No |
| Liver metalloproteins | No | No |
| Urinary Zn | No | No |
| Hair Zn | No | No |
| Erythrocyte Zn | No | No |
| Hair condition | No | No |
| Zn balance | No | No |

Serum Zn concentrations are normally between 12-23 µM (cattle), 11-23 µM (sheep) [127] or 6-9 µM (goats). Concentrations < 6 µM are often considered deficient [132]. However, due to stress or disease serum Zn concentrations can fall rapidly without inadequate dietary Zn supply. Liver Zn concentrations can also be used and should be 100-400 ppm (DM) [98]. More detailed marginal bands are given in reference [132] (Table 5).

## 6.2 Conclusions

For judgement of Zn status under practical circumstances, serum or plasma Zn concentrations are most appropriate. Besides this, bone Zn can be used. A review of these response parameters has been given by Delves [24].
Delves [24] arranges indicators of Zn status in approximate order of merit: plasma Zn; Zn tolerance test; plasma albumin-bound Zn; plasma alkaline phosphatase; leukocyte Zn. According to this author, the following tests are of little value: erythrocyte Zn, urinary Zn, and hair Zn. However, it has to be taken into account that this is a human study. Plasma Zn is indeed a valuable indicator of Zn status, but bone Zn may be a better indicator [58]. Plasma alkaline phosphatase is judged to be too variable (even due to totally different causes than suboptimal Zn supply) to be of value for the assessment of Zn status. Leukocyte Zn is indeed also in animals a sensitive and specific indicator of Zn status, but only in mature animals. In growing animals leukocyte Zn concentration is not affected by Zn supply [131].

Erythrocyte Zn reflects the historical rather than the actual Zn status, whereas at least in rats and cows urinary Zn excretion is not related to dietary Zn supply [131].

# 7 DEFICIENCY

One of the earliest and most striking features of Zn deficiency is anorexia, which may provoke several other symptoms as has been demonstrated by pair-feeding experiments. Growth arrest occurred within 2 weeks and plasma Zn concentrations fell within 1 week of feeding a diet containing 1-2 ppm Zn to calves and lambs [90]. However, in an experiment with calves on a diet (albumin/glucose/fat/cellulose) containing 3.6 ppm Zn, feed intake and growth did not decrease until 4 weeks of treatment. Another early sign is excessive salivation. In calves after 6 weeks on a diet containing 5 ppm Zn and 18 g Ca/kg [89] or 3.6 ppm Zn (Ca content not given) [79] parakeratotic lesions of the skin occurred, although in lactating dairy cows the first skin lesions could be observed as early as 2 weeks after the start of a 6 ppm Zn ration [115]. Later on, the bones, as well as reproductive and immunological functions are affected. The skin is thick, hard and fissured. In calves and cows, the muzzle, neck, ears, scrotum, limbs and teats are affected. Hoof horn may be weak and infectious pododermatitis (in Dutch: “stinkpoten” in cattle, foot rot in sheep and goats) may occur more frequently. However, not in all experiments oral application of Zn was effective in preventing of healing infectious pododermatitis [23;25;26;48;74;94;118]. In sheep, parakeratotic lesions around the eyes, above the hooves and on the scrotum can be observed. Wound healing is retarded. Wool fibers lose their crimp, and thin staples and shedding of the whole fleece may occur [132].
In goats, alopecia, rough hair coats, weight loss, abnormal hoof growth, gingivitis, conjunctivitis, hypogonadism and unthriftiness have been reported [93;113;117].
Bowing of the hind legs, and stiffness and swelling of joints are signs of the impaired skeletal functions, although to some extent these may be due to anorexia. The impairment of male reproductive functions are secondary to anorexia. Hypogonadism in bull calves, reversible cessation of spermatogenesis in lambs and reduction in testicular size and loss of libido in goats have been observed on Zn-deficient diets [132]. The effects of Zn deficiency and vitamin A deficiency seem to be additive with respect to female fertility. Supplementation of both 65 ppm Zn and 1800 IU vitamin A to a starch/casein diet improved serum vitamin A and Zn levels, and also follicle quality [17]. Serum Zn and vitamin A levels were highest when both supplements were given. Feeding a diet containing 3 ppm Zn (DM) to pregnant sheep reduced lamb survival and was associated with pregnancy toxaemia due to loss of appetite in the ewe. Several symptoms such as decreased cytokine production and thymic atrophy indicate for the disturbance of immunological functions.
There is conflicting evidence as to whether or not immunopathology is secondary to anorexia [96-98;132]. On the other hand, as yet no convincing evidence is available as to beneficial effects of supplying extra Zn above requirements [58]. In Dutch-Friesian cattle, a genetic defect (trait A 46, Adema disease) substantially raising Zn requirements has been reported [13;33].

## 7.1 Direct measures in deficiency cases

### 7.1.1 Direct continuous supplementation

Zinc can be added to the ration of housed ruminants as mineral mixes incorporated in total mixed rations or concentrates. Supplementation of 50 ppm Zn (DM) from $ZnSO_4$ or ZnO is usually sufficient. For non-ruminant animals, improvement of the Zn availability of phytate-rich rations by the addition of phytase is recommended, but is as yet not admitted by EU legislation for ruminants [132].

### 7.1.2 Direct discontinuous supplementation

As recovery is usually very rapid and remarkable after oral application of Zn supplements (see 7.1.1) [79], no additional measures need to be taken. Oral drenches with Zn sulphate solutions (2 g $ZnSO_4$/week for cattle, concentration not given) are effective, but relatively expensive [71;132].

### 7.1.3 Slow release oral supplementation

Under extensive rearing conditions, heavy intraruminal pellets (e.g. providing ± 20 ppm Zn (DM) for at least 6 weeks) can be used to overcome seasonal deficiency and improve fertility in sheep.

# 8 TOXICITY

Zinc toxicity may principally arise from the use of massive amounts to combat facial eczema (see below) or the faulty use or preparation of mineral supplements. Although Zn is not very toxic, reduced feed intake and weight gain have been reported as signs of Zn toxicity. In veal calves, weight gain was reduced and polyuria and diarrhoea occurred at high Zn levels (500 ppm (DM) and higher) [56]. Moreover, Zn levels of 750 ppm can induce severe Cu deficiency and increase the incidence of abortions and stillbirths in sheep [96], whereas levels as high as 1500 and 1700 ppm (DM) can induce anorexia and pica [132]. The anorexia is probably due to decreased numbers of ruminal microorganisms, causing reductions of ruminal digestion of dietary amino acids and cellulose [1;34]. Wethers consuming 750 g of a grain/hay ration and dosed intraruminally with 2 g of Zn (from Zn sulphate, 4 weeks; 2667 ppm Zn) and subsequently with 3 g of Zn (4000 ppm Zn) showed significantly increased plasma creatinine, kidney and liver Zn concentrations when compared with control animals not given extra Zn [3]. Renal damage was further confirmed by histological investigation of the kidneys. Finally, in order to prevent facial eczema in sheep and cattle (caused by sporidesmin produced by the fungus *Pithomyces chartarum*) huge amounts (23 mg/kg BW in cattle) are applied, which induce Zn toxicosis. An intraruminal bolus releasing 0.8 g of Zn from ZnO per day for about 6 weeks has been shown not to induce Zn toxicosis but to provide prolonged protection against facial eczema [98;132].
Zn toxicity has been observed in cattle fed 900 ppm Zn [98], but the main reason to limit Zn intake is the negative effect of very high Zn levels (2000 ppm (DM)) on Cu uptake [80]. In veal calves, weight gain was reduced when dietary Zn levels were 700 ppm (DM) and over (from ZnO) [56]. The NRC suggests a maximum tolerable dietary level of 300-1000 ppm Zn for dairy cattle [98] and 500 ppm for beef cattle [97]. In sheep, 1000 ppm Zn caused reduced appetite in lambs, whereas 750 ppm Zn induced severe Cu deficiency in pregnant ewes and caused a high incidence of abortion and stillbirths [96]. For veal calves on a milk substitute ration, 100 ppm Zn is recommended as a maximum safe level [38]. According to the AFRC [2] up to 150 ppm Zn (DM) is well tolerated by goats, and even higher levels may have no adverse effects. In conclusion, Zn levels up to 100 ppm (DM; preruminant animals) or 150 ppm (DM; ruminant animals) can be considered safe.

## 8.1 Direct measures in toxicity cases

Except lowering the Zn content and increasing the roughage content of the ration [38] no direct measures are reported that can be taken in cases of Zn toxicity in ruminants. Shipping for immediate slaughter should be considered in order to minimize economic losses [38].

# 9 PREVENTION OF DEFICIENCY

## 9.1 Short-term prevention strategies

No specific short-term prevention measures except the application of intraruminal boluses [132] have been recommended.

## 9.2 Long-term prevention strategies

In the long term, Zn-containing fertilizers can be applied to increase soil and plant Zn contents. In Dutch grass silages, Zn contents range from 20-74 ppm (DM), depending on soil type. Even wider ranges have been reported from other countries (7-100 ppm (DM), whereas values of 150-1500 ppm (DM) can occur due to industrial contamination [132]. Successive cuts may contain up to 50% lower values compared to the first cuts. Legumes may contain 20-60 ppm (DM), whereas hay tends to be low in Zn (13-25 ppm (DM) [35;132]. Maize silage is reported to contain 12-45 ppm (DM) [132]. Depending on soil conditions (soil analysis each 4 years is recommended), 5-7 kg $ZnSO_4$/ha can be applied [132].

**Table 7 Inventory of Zn allowances for cattle, sheep and goats as used in some other countries (ppm (DM)).**

| | | Allowance | | | | |
|---|---|---|---|---|---|---|
| **Country** | **Ref.** | **Cattle** | **Ref.** | **Sheep** | **Ref.** | **Goat** |
| Great Britain | [58] | 30-50 | [132] | 9-27 (lamb)<br>10-12 (gestation)<br>12-18 (lactation) | [2] | 50-80 |
| USA[a,b] | [138] | 33 (300-kg heifer)<br>31 (500-kg heifer)<br>63 (650-kg cow, 40 kg of milk)<br>23 (650-kg cow, end of gestation)<br>30 (beef cattle) | [96] | 20 (growth)<br>33 breeding, lactation) | [95] | 10 |
| Germany | [36] | 40-50 (growth)<br>50 (mature) | | ? | [9] | 50-80 |
| France | [41] | 50 (45 is deficiency limit) | | | | |

[a] Allowances for cattle are expressed in mg/kg feed as fed; as DM contents of the feeds are not given, allowances cannot be calculated in ppm (DM).
[b] minimum requirements.

# LITERATURE


1 Abdel-Mageed AB, Oehme FW. A review of the biochemical roles, toxicity and interactions of zinc, copper and iron: I. Zinc. Veterinary and Human Toxicology 1990; 32: 34-39.

2 AFRC. AFRC Technical committee on responses to nutrients. Report No. 10. The nutrition of goats. Nutrition Abstracts and Reviews, B 1997; 67: 765-830.

3 Allen JG, Masters HG. Renal lesions and tissue concentrations of zinc, copper, iron and manganese in experimentally zinc intoxicated sheep. Research in Veterinary Science 1985; 39: 249-251.

4 Angelow L, Anke M, Groppel B, Glei M, Müller M. Aluminum: an essential element for goats. TEMA 1993; 8: 699-704.

5 Anke M, Hennig A, Groppel B, Lüdke H. Der Einfluß des Kadmiums auf das Wachstum, die Fortpflanzungsleistung und den Eisen-, Zink- und Kupferstoffwechsel. Effect of cadmium on growth, reproductive function and the metabolism of iron, zinc and copper. Archiv für experimentelle Veterinärmedizin 1971; 25: 799-803.

6 Anke M, Hennig A, Schneider HJ, Lüdke H, Gagern Wv, Schlegel H. The interrelations between cadmium, zinc, copper and iron in metabolism of hens, ruminants and man. TEMA 1970; 1: 317-320.

7 ARC. Trace elements. In: Agricultural Research Council (ed.), Nutrient requirements of ruminant livestock. Londen: 1980: 221-262.

8 Archibald JG. Zinc in cow's milk. Journal of Dairy Science 1944; 27: 257-261.

9 Ausschuss für Bedarfsnormen der Gesellschaft für Ernährungsphysiologie. Recommendations for the supply of energy and nutrients to goats. Frankfurt am Main: DLG Verlag; 2003.

10 Benemariya H, Robberecht H, Deelstra H. Zinc, copper, and selenium in milk and organs of cow and goat from Burundi, Africa. Science of the Total Environment 1993; 128: 83-98.

11 Bettger WJ, Fish TJ, O'Dell BL. Effects of Cu and Zn status of rats on erythrocyte stability and superoxide dismutase activity. Proceedings of the Society for Experimental Biology and Medicine 1978; 158: 279-282.

12 Bonomi A, Bonomi BM, Quarantelli A. Contenuto in potassio della razione e carenza di zinco nelle bovine da latte. Relationships between the potassium content of the feed ration and zinc deficiency in dairy cows. Obiettivi e Documenti Veterinari 2000; 21: 37-47.

13 Bosma AA, Kroneman J. Chromosome studies in cattle with hereditary zinc deficiency (lethal trait A46). Veterinary Quarterly 1979; 1: 121-125.

13a Cao J, Henry PR, Guo R, Holwerda RA, Toth JP, Littell RC, Miles RD, Ammerman CB. Chemical characteristics and relative bioavailability of supplemental organic zinc sources for poultry and ruminants. Journal of Animal Science 2000; 78: 2039-2054.

14 Casoli C, Duranti E, Morbidini L, Panella F, Vizioli V. Quantitative and compositional variations of Massese sheep milk by parity and stage of lactation. Small Ruminant Research 1989; 2: 47-62.

15 Centraal Veevoeder Bureau. Tabellenboek Veevoeding. 2002.

16 Chesters JK, Will M. Measurement of zinc flux through plasma in normal and endotoxin- stressed pigs and the effects of Zn supplementation during stress. British Journal of Nutrition 1981; 46: 119-130.

17 Chhabra A, Arora SP. Effect of Zn deficiency on serum vitamin A level, tissue enzymes and histological alterations in goats. Livestock Production Science 1985; 12: 69-77.

17a Chirase NK, Greene LW. Dietary zinc and manganese sources administered from the fetal stage onwards affect immune response of transit stressed and virus infected offspring steer calves. Animal Feed Science and Technology 2001; 93: 217-228.

18 Chirase NK, Hutcheson DP, Thompson GB. Feed intake, rectal temperature, and serum mineral concentrations of feedlot cattle fed zinc oxide or zinc methionine and challenged with infectious bovine rhinotracheitis virus. Journal of Animal Science 1991; 69: 4137-4145.

19 Chirase NK, Hutcheson DP, Thompson GB, Spears JW. Recovery rate and plasma zinc and copper concentrations of steer calves fed organic and inorganic zinc and manganese sources with or without injectable copper and challenged with infectious bovine rhinotracheitis virus. Journal of Animal Science 1994; 72: 212-219.

20 Coni E, Bocca A, Coppolelli P, Caroli S, Cavallucci C, Marinucci MT. Minor and trace element content in sheep and goat milk and dairy products. Food Chemistry 1996; 57: 253-260.

21 Cousins RJ. Absorption, transport, and hepatic metabolism of copper and zinc: special reference to metallothionein and ceruloplasmin. Physiological Reviews 1985; 65: 238-309.

22 Cousins RJ, Smith KT. Zinc-binding properties of bovine and human milk in vitro: influence of changes in zinc content. American Journal of Clinical Nutrition 1980; 33: 1083-1087.

23 Cross RF, Parker CF. Oral administration of zinc sulfate for control of ovine foot rot. Journal of the American Veterinary Association 1981; 178: 704-705.

24 Delves HT. Assessment of trace element status. Clinics in Endocrinology and Metabolism 1985; 14: 725-761.

25 Dembinski Z, Wieckowski W. Application of zinc in cases in pododermatitis in cattle. Bulletin of the Veterinary Institute in Pulawy 1987; 30-31: 104-112.

26 Demertzis PN, Mills CF. Oral zinc therapy in the control of infectious pododermatitis in young bulls. Veterinary Record 1973; 93: 219-222.

27 Deol HS, Howell JM, Dorling PR. Effect of the ingestion of heliotrope and copper on the concentration of zinc, selenium and molybdenum in the liver of sheep. Journal of Comparative Pathology 1994; 110: 303-307.

28 Dijk TAv, Wensing T, Beynen AC, Hof JB. Supplemental phytase raises plasma and hepatic zinc concentrations in veal calves fed a milk replacer containing soy protein. Production Diseases in Farm Animals 10th International Conference1998, Utrecht, T. Wensing, ed. , Wageningen Pers, Wageningen 1998; 125.

29 Doyle JJ, Pfander WH. Interactions of cadmium with copper, iron, zinc, and manganese in ovine tissues. Journal of Nutrition 1975; 105: 599-606.

30 Dwivedi P, Swarup D, Dey S, Patra RC. Lead poisoning in cattle and buffalo near primary lead-zinc smelter in India. Veterinary and Human Toxicology 2001; 43: 93-94.

31 Engle TE, Nockels CF, Kimberling CV, Weaber DL, Johnson AB. Zinc repletion with organic or inorganic forms of zinc and protein turnover in marginally zinc-deficient calves. Journal of Animal Science 1997; 75: 3074-3081.

31a Ferrell CL, Laster DB, Prior RL. Mineral accretion during prenatal growth of cattle. Journal of Animal Science 1982; 54: 618-624.

32 Flachowsky G, Hennig A, Löhnert H-J, Grün M. Überhöhte orale Eisengaben an Schafe. 1. Mitteilung. Verdaulichkeit der Ration, Mast- und Ausschlachtungsergebnisse. Archiv für Tierernährung 1976; 26: 765-771.

33 Flagstad T. Lethal trait A46 in cattle. Intestinal zinc absorption. Nordisk Veterinaermedicin 1976; 28: 160-169.

34 Froetschel MA, Martin AC, Amos HE, Evans JJ. Effects of zinc sulfate concentration and feeding frequency on ruminal protozoal numbers, fermentation patterns and amino acid passage in steers. Journal of Animal Science 1990; 68: 2874-2884.

35 Furr AK, Parkinson TF, Heffron CL, Reid JT, Haschek WM, Gutenmann WH, Bache. Elemental content of tissues and excreta of lambs, goats, and kids fed white sweet clover growing on fly ash. Journal of Agricultural and Food Chemistry 1978; 26: 847-851.

36 GfE. Spurenelemente. In: Staudaucher W (ed.), Empfehlungen zur Energie- und Nährstoffversorgung der Milchkühe und Aufzuchtrinder. Frankfurt am Main: DLG Verlag; 2001: 89-104.

37 Gooneratne SR, Chaplin RK, Trent AM, Christensen DA. Effect of tetrathiomolybdate administration on the excretion of copper, zinc, iron and molybdenum in sheep bile. British Veterinary Journal 1989; 145: 62-72.

37a Grace ND, Watkinson JH. Se, Cu, Zn and Fe metabolism of the young lamb. Proceedings of the New Zealand Society of Animal Production 1988; 48: 257-260.

38 Graham TW, Goodger WJ, Christiansen V, Thurmond MC. Economic losses from an episode of zinc toxicosis on a California veal calf operation using a zinc sulfate-supplemented milk replacer. Journal of the American Veterinary Medical Association 1987; 190: 668-671.

39 Gralak M, Sieranska B, Krasicka B, Anke M, Meissner D, Mills CF. The effect of sulphur supplement on zinc, copper and magnesium status in growing lambs. TEMA 1993; 8: 660-661.

40 Grün M, Anke M, Hennig A, Seffner W, Partschefeld M, Flachowsky G, Groppel B. Überhöhte orale Eisengaben an Schafe. 2. Mitteilung. Der Einfluss auf den Eisen-, Kupfer-, Zink- und Mangangehalt verschiedener Organe. Excessive oral iron application to sheep. (2) The influence on the level of iron, copper, zinc and manganese in different organs. Archiv für Tierernährung 1978; 28: 341-347.

41 Gueguen L, Lamand M, Meschy F. Nutrition minérale. In: Jarrige R (ed.), Alimentation des bovins, ovins & caprins. Paris: INRA; 1988: 98-111.

42 Haaranen S. Some observations on the zinc requirement of cattle for the prevention of itch and hair licking at different calcium levels in the feed. Nordisk Veterinaermedicin 1963; 15: 536-542.

43 Haldar A, Prakash V, Duttagupta R. Zinc, manganese, chromium and nickel status in blood and hair of goat reared on grazing regimen. Indian Veterinary Journal 1998; 75: 514-516.

44 Hampton DL, Miller WJ, Blackmon DM, Gentry RP, Neathery MW, Lassiter JW, Kincaid RL, Stake PE. Zinc absorption from the small intestine in young calves. Journal of Dairy Science 1976; 59: 712-715.

45 Hampton DL, Miller WJ, Neathery MW, Kincaid RL, Blackmon DM, Gentry RP. Absorption of zinc from small and large intestine of calves. Journal of Dairy Science 1976; 59: 1963-1966.

46 Hansard SL, Mohammed AS, Turner JW. Gestation age effects upon maternal-fetal zinc utilization in the bovine. Journal of Animal Science 1968; 27: 1097-1102.

47 Hapke HJ, Prigge E. Neue Aspekte der Bleivergiftung bei Wiederkäuern New aspects of lead poisoning in ruminants. Berliner und Münchener Tierärztliche Wochenschrift 1973; 86: 410-413.

48 Hartmans J. Zinkgebrek en 'stinkpoten' bij het Nederlandse rund Zinc deficiency and infectious pododermatitis in cattle in the Netherlands. Tijdschrift voor Diergeneeskunde 1975; 100: 51-52.

49 Hatfield PG, Swenson CK, Kott RW, Ansotegui RP, Roth NJ, Robinson BL. Zinc and copper status in ewes supplemented with sulfate- and amino acid-complexed forms of zinc and copper. Journal of Animal Science 2001; 79: 261-266.

50 House WA, Bell AW. Mineral accretion in the fetus and adnexa during late gestation in Holstein cows. Journal of Dairy Science 1993; 76: 2999-3010.

51 Humphries WR, Phillippo M, Young BW, Bremner I. Influence of dietary iron and molybdenum on copper metabolism in calves. British Journal of Nutrition 1983; 49: 77-86.

52 Interdepartmental Working Party. Mineral, trace element and vitamin allowances for ruminant livestock. In: Haresign W, Cole DJA (eds.), Recent advances in Animal Nutrition. London: Butterworths; 1984: 113-142.

53 International Dairy Federation. Trace elements in milk and dairy products; Bulletin 278/1992. Brussels: IDF; 1992.

54 Jenkins KJ. Effect of copper loading of preruminant calves on intracellular distribution of hepatic copper, zinc, iron, and molybdenum. Journal of Dairy Science 1989; 72: 2346-2350.

55 Jenkins KJ, Hidiroglou M. Tolerance of the calf for excess copper in milk replacer. Journal of Dairy Science 1989; 72: 150-156.

56 Jenkins KJ, Hidiroglou M. Tolerance of the preruminant calf for excess manganese or zinc in milk replacer. Journal of Dairy Science 1991; 74: 1047-1053.

57 Jongbloed AW. Minutes of the meeting for bioavailability of mineral sources for ENFEMA on 06-03-2000. 2000; 1-7.

58 Jongbloed AW, Top AMvd, Beynen AC, Klis JDvd, Kemme PA, Valk H. Consequences of newly proposed maximum contents of copper and zinc in diets for cattle, pigs and poultry on animal performance and health. Report ID-Lelystad 2001; 2097.

59 Kegley EB, Kreider DL, Coffey KP, Silzell SA, Galloway DL. Immune response and performance of heifers supplemented with zinc from an organic and an inorganic source. Journal of Animal Science 1997; 75: 250 S1.

60 Kemme PA, Jongbloed AW, Mroz Z, Bruggencate Rt. Effect van het gehalte aan Ca en microbieel fytase in twee voeders op de Ca-, Mg- en P-benutting en op de beschikbaarheid van Zn en Cu bij groeiende varkens. Rapport ID-DLO 1995; 288: 1-42.

61 Kessler J. Mineral nutrition of goats. In: Morand-Fehr P (ed.), Goat Nutrition. Wageningen: Pudoc; 1991: 104-119.

61a Kessler J, Morel I, Dufey P-A, Gutzwiller A, Stern A, Geyer H. Effect of organic zinc sources on performance, zinc status and carcass, meat and claw quality in fattening bulls. Livestock Production Science 2003; 81: 161-171.

62 Kincaid RL. Biological availability of zinc from inorganic sources with excess dietary calcium. Journal of Dairy Science 1979; 62: 1081-1085.

63 Kincaid RL, Chew BP, Cronrath JD. Zinc oxide and amino acids as sources of dietary zinc for calves: effects on uptake and immunity. Journal of Dairy Science 1997; 80: 1381-1388.

64 Kincaid RL, Cronrath JD. Effects of dietary zinc upon tissue zinc and percent unsaturated plasma-zinc binding capacity. Journal of Dairy Science 1979; 62: 572-576.

65 Kirchgessner M, Heindl U. Investigations about the determination of the zinc requirement of calves Untersuchungen zur Ableitung des Zinkbedarfs von Aufzuchtkälbern. Journal of Animal Physiology and Animal Nutrition 1993; 70: 38-52.

66 Kirchgessner M, Paulicks BR, Hagemeister H. Zum Zinkgehalt der Kuhmilch bei Verfütterung hoher Mengen Zinkmethionat Zinc concentration in the milk of dairy cows supplemented with high levels of zinc methionine. Journal of Animal Physiology and Animal Nutrition 1994; 72: 165-167.

67 Kirchgessner M, Schwarz WA. Zum Einfluß von Zinkmangel und unterschiedlichen Zinkzulagen auf Resorption und Retention des Zinks bei Milchkühen [Effect of zinc deficiency and varying zinc supplements on resorption and retention in dairy cows]. Archiv für Tierernährung 1976; 26: 3-16.

68 Kreuzer M, Kirchgessner M. Faecal and urinary excretion of iron, copper, zinc and manganese in faunated and defaunated wethers fed semi-purified diets of different carbohydrate composition. Animal Feed Science and Technology 1990; 28: 135-143.

69 Laflamme DP, Miller WJ, Neathery MW, Gentry RP, Blackmon DM, Logner KR, Fielding AS. The effect of low to normal dietary phosphorus levels on zinc metabolism and tissue distribution in calves. Journal of Animal Science 1985; 61: 525-531.

70 Leeuwen JMv, Weide HJ. Zink, koper and ijzer in de mestkalverenvoeding. Landbouwkundig Tijdschrift 1969; 81: 22-29.

71 Legg SP, Sears L. Zinc sulphate treatment of parakeratosis in cattle. Nature 1960; 186: 1061-1062.

72 Leontowicz H, Gralak M, Kulasek G, Anke M, Meissner D, Mills CF. The effect of potassium loading on some macro and microelements balance in sheep. TEMA 8 1993; 672-673.

73 Lopez A, Collins WF, Williams HL. Essential elements, cadmium and lead in raw and pasteurized cow and goat milk. Journal of Dairy Science 1985; 68: 1878-1886.

74 Lopez JR, Montana JRG, Diez AJA, Montana FP. Failure of oral zinc supplementation to control ovine foot rot. Small Ruminant Research 1999; 31: 273-276.

75 Lönnerdal B. Intestinal absorption of zinc. In: Mills CF (ed.), Zinc in human biology. London: Springer Verlag; 1989: 33-56.

75a Malcolm-Callis KJ, Duff GC, Gunter SA, Kegley EB, Vermeire DA. Effects of supplemental zinc concentrations and source on performance, carcass characteristics, and serum values in fnishing beef steers. Journal of Animal Science 2000; 78: 2801-2808.

76 McCormick CC, Menard MP, Cousins RJ. Induction of hepatic metallothionein by feeding zinc to rats of depleted zinc status. American Journal of Physiology 1981; 240: E414-E421.

77 Meschy F. Recent progress in the assessment of mineral requirements of goats. Livestock Production Science 2000; 64: 9-14.

78 Methfessel AH, Spencer H. Zinc metabolism in the rat II. Secretion of zinc into intestine. Journal of Applied Physiology 1973; 34: 63-67.

79 Miller JK, Miller WJ. Experimental Zinc Deficiency and Recovery of Calves. Journal of Nutrition 1962; 76: 467-474.

80 Miller WJ, Amos HE, Gentry RP, Blackmon DM, Durrance RM, Crowe CT, Fielding AS, Neathery MW. Long-term feeding of high zinc sulfate diets to lactating and gestating dairy cows. Journal of Dairy Science 1989; 72: 1499-1508.

81 Miller WJ, Blackmon DM, Gentry RP, Pate FM. Effects of high but nontoxic levels of zinc in practical diets on 65Zn and zinc metabolism in Holstein calves. Journal of Nutrition 1970; 100: 893-902.

82 Miller WJ, Blackmon DM, Gentry RP, Pitts WJ, Powell GW. Absorption, excretion, and retention of orally administered zinc-65 in various tissues of zinc-deficient and normal goats and calves. Journal of Nutrition 1967; 92: 71-78.

83 Miller WJ, Blackmon DM, Powell GW, Gentry RP, Hiers JM, Jr. Effects of zinc deficiency per se and of dietary zinc level on urinary and endogenous fecal excretion of 65Zn from a single intravenous dose by ruminants. Journal of Nutrition 1966; 90: 335-341.

84 Miller WJ, Clifton CM, Fowler PR, Perkins HF. Influence of high levels of dietary zinc on zinc in milk, performance and biochemistry of lactating cows. Journal of Dairy Science 1965; 48: 450-453.

85 Miller WJ, Martin YG, Gentry RP, Blackmon DM. 65Zn and stable zinc absorption, excretion and tissue concentrations as affected by type of diet and level of zinc in normal calves. Journal of Nutrition 1968; 94: 391-401.

86 Miller WJ, Powell GW, Pitts WJ, Perkins HF. Factors affecting zinc content bovine hair. Journal of Dairy Science 1965; 48: 1091-1095.

87 Miller WJ, Wells ES, Gentry RP, Neathery MW. Endogenous zinc excretion and 65 Zn metabolism in Holstein calves fed intermediate to high but nontoxic zinc levels in practical diets. Journal of Nutrition 1971; 101: 1673-1681.

88 Mills CF, Dalgarno AC. Copper and zinc status of ewes and lambs receiving increased dietary concentrations of cadmium. Nature 1972; 239: 171-173.

89 Mills CF, Dalgarno AC. The influence of dietary calcium concentration on epidermal lesions of zinc deficiency in lambs. Proceedings of the Nutrition Society 1993; 26: 19.

90 Mills CF, Dalgarno AC, Williams RB, Quarterman J. Zinc deficiency and the zinc requirements of calves and lambs. British Journal of Nutrition 1967; 21: 751-768.

90a Mullis LA, Spears JW, McCraw RL. Effects of breed (Angus vs Simmental) and copper and zinc source on mineral status of steers fed high dietary iron. Journal of Animal Science 2003: 81: 318-322.

91 Neathery MW, Crowe NA, Miller WJ, Crowe CT, Varnadoe JL, Blackmon DM. Influence of dietary aluminum and phosphorus on zinc metabolism in dairy calves. Journal of Animal Science 1990; 68: 4326-4333.

92 Neathery MW, Miller WJ, Blackmon DM, Gentry RP. Performance and milk zinc from low-zinc intake in Holstein cows. Journal of Dairy Science 1973; 56: 212-217.

93 Neathery MW, Miller WJ, Blackmon DM, Pate FM, Gentry RP. Effects of long term zinc deficiency on feed utilization, reproductive characteristics, and hair growth in the sexually mature male goat. Journal of Dairy Science 1973; 56: 98-105.

94 Nocek JE, Johnson AB, Socha MT. Digital characteristics in commercial dairy herds fed metal-specific amino. Journal of Dairy Science 2000; 83: 1553-1572.

95 NRC. Nutrient Requirements of Goats: Angora, Dairy, and Meat Goats in Temperate and Tropical Countries. Washington: National Academy Press; 1981.

96 NRC. Nutrient Requirements of Sheep. Washington: National Academy Press; 1985.

97 NRC. Nutrient Requirements of Beef Cattle. Washington, USA: National Academy Press; 1996.

98 NRC. Nutrient Requirements of Dairy Cattle. Washington: National Academy Press; 2001.

99 Park YW. Comparison of mineral and cholesterol composition of different commercial goat milk products manufactured in USA. Small Ruminant Research 2000; 37: 115-124.

100 Patra RC, Swarup D, Dwivedi SK, Sahoo A. Trace minerals in blood of young calves during exposure to lead. Indian Journal of Animal Sciences 2001; 71: 507-510.

101 Pond WG, Wallace MH. Effect of gestation-lactation diet calcium and zinc levels and of parenteral vitamins A, D and E during gestation on ewe body weight and on lambs weight and survival. Journal of Animal Science 1986; 63: 1019-1025.

102 Powell GW, Miller WJ, Blackmon DM. Effects of dietary EDTA and cadmium on absorption, excretion and retention of orally administered 65Zn in various tissues of zinc- deficient and normal goats and calves. Journal of Nutrition 1967; 93: 203-212.

103 Powell GW, Miller WJ, Morton JD, Clifton CM. Influence of dietary cadmium level and supplemental zinc on cadmium toxicity in the bovine. Journal of Nutrition 1964; 84: 205-214.

104 Puchala R, Sahlu T, Davis JJ. Effects of zinc-methionine on performance of Angora goats. Small Ruminant Research 1999; 33: 1-8.

105 Rabiansky PA, McDowell LR, Velasquez-Pereira J, Wilkinson NS, Percival SS, Martin FG, Bates DB, Johnson AB, Batra TR, Salgado-Madriz E. Evaluating copper lysine and copper sulfate sources for heifers. Journal of Dairy Science 1999; 82: 2642-2650.

106 Roberts KR, Miller WJ, Stake PE, Gentry RP, Neathery MW. High dietary cadmium on zinc absorption and metabolism in calves fed for comparable nitrogen balances. Proceedings of the Society for Experimental Biology and Medicine 1973; 144: 906-908.

107 Rodriguez-Rodriguez EM, Sanz AM, Diaz RC. Chemometric studies of several minerals in milk. Journal of Agricultural and Food Chemistry 1999; 47: 1520-1524.

108 Rojas LX, McDowell LR, Cousins RJ, Martin FG, Wilkinson NS, Johnson AB, Velasquez JB. Relative bioavailability of two organic and two inorganic zinc sources fed to sheep. Journal of Animal Science 1995; 73: 1202-1207.

109 Rojas LX, McDowell LR, Martin FG, Wilkinson NS, Johnson AB, Njeru CA. Relative bioavailability of zinc methionine and two inorganic zinc sources fed to cattle. Trace Elements in Medical Biology 1996; 10: 205-209.

110 Rosa IV, Henry PR, Ammerman CB. Interrelationship of dietary phosphorus, aluminum and iron on performance and tissue mineral composition in lambs. Journal of Animal Science 1982; 55: 1231-1240.

110a Salyer GB, Galyean ML, Defoor PJ, Nunnery GA, Parsons CH, Rivera JD. Effects of copper and zinc source on performance and humoral immune response of newly received, lightweight beef heifers. Journal of Animal Science 2004; 82: 2467-2473.

111 Sandoval M, Henry PR, Littell RC, Cousins RJ, Ammerman CB. Estimation of the relative bioavailability of zinc from inorganic zinc sources for sheep. Animal Feed Science and Technology 1997; 66: 223-235.

112 Schonewille JT. Magnesium absorption in ruminants. Universiteit Utrecht; 1999. Thesis.

113 Schulze A, Üstdal KM. Mögliche Ursachen der Alopezie türkischer Angora-Ziegen. Berliner und Münchener Tierärztliche Wochenschrift 1975; 88: 66-73.

114 Schwarz FJ, Kirchgessner M. Kupfer- und Zinkgehalte in der Milch und im Plasma von Kühen nach hoher nutritiver Kupferdosierung. Copper and zinc contents in milk and plasma of cows after high nutritional copper supplements. Zeitschrift für Lebensmittel Untersuchung und Forschung 1978; 166: 5-8.

115 Schwarz WA, Kirchgessner M. Experimental zinc deficiency in lactating dairy cows. Veterinary Medical Review 1975; 1-2: 19-41.

116 Schwarz WA, Kirchgessner M. Veränderungen des Zinkgehaltes in der Kuhmilch bei unterschiedlicher Zinkversorgung. 14. Mitteilung. Zum Stoffwechsel des Zinks im tierischen Organismus. Zinc metabolism in animals. 14. Changes in zinc content of cow's milk with different zinc supplies. Zeitschrift für Tierphysiologie, Tierernährung und Futtermittelkunde 1975; 35: 1-8.

117 Singer LJ, Herron A, Altman N. Zinc responsive dermatopathy in goats: two field cases. Contemporary Topics in Laboratory Animal Science 2000; 39: 32-35.

118 Skerman TM. Footscald and footrot in goats. Sheep and Beef Cattle Society of the New Zealand Veterinary Association. Proceedings of the Society's 17th Seminar 2000; Waikato University: 65-69.

119 Spears JW. Zinc methionine for ruminants: relative bioavailability of zinc in lambs and effects of growth and performance of growing heifers. Journal of Animal Science 1989; 67: 835-843.

120 Spears JW, Harvey RW, Brown-TT J. Effects of zinc methionine and zinc oxide on peformance, blood characteristics, and antibody titer response to viral vaccination in stressed feeder calves. Journal of the American Veterinary Medical Association 1991; 199: 1731-1733.

121 Spears JW, Harvey RW, Samsell LJ. Effects of dietary nickel and protein on growth, nitrogen metabolism and tissue concentrations of nickel, iron, zinc, manganese and copper in calves. Journal of Nutrition 1986; 116: 1873-1882.

121a Spears JW, Kegley EB. Effect of zinc source (zinc oxide vs zinc proteinate) and level on performance, carcass characteristics, and immune response of growing and finishing steers. Journal of Animal Science 2002; 80: 2747-2752.

121b Spears JW, Schlegel P, Seal MC, Lloyd KE. Bioavailability of zinc from zinc sulfate and different organic zinc sources and their effects on ruminal volatile fatty acie proportions. Livestock Production Science 2004; 90: 211-217.

122 Stake PE, Miller WJ, Blackmon DM, Gentry RP, Neathery MW. Role of pancreas in endogenous zinc excretion in the bovine. Journal of Nutrition 1974; 104: 1279-1284.

123 Stake PE, Miller WJ, Gentry RP, Neathery MW. Zinc metabolic adaptations in calves fed a high but nontoxic zinc level for varying time periods. Journal of Animal Science 1975; 40: 132-137.

124 Standish JF, Ammerman CB. Effect of excess dietary iron as ferrous sulfate and ferric citrate on tissue mineral composition of sheep. Journal of Animal Science 1971; 33: 481-484.

125 Standish JF, Ammerman CB, Palmer AZ, Simpson CF. Influence of dietary iron and phosphorus on performance, tissue mineral composition and mineral absorption in steers. Journal of Animal Science 1971; 33: 171-178.

126 Standish JF, Ammerman CB, Simpson CF, Neal FC, Palmer AZ. Influence of graded levels of dietary iron, as ferrous sulfate, on performance and tissue mineral composition of steers. Journal of Animal Science 1969; 29: 496-503.

127 Stichting Gezondheidszorg voor dieren. Mogelijkheden voor onderzoek en normaalwaarden. 1987.

128 Suttle NF, Davies HL, Field AC. A model for zinc metabolism in sheep given a diet of hay. British Journal of Nutrition 1982; 47: 105-112.

129 Swinkels JWGM, Kornegay ET, Verstegen MWA. Biology of zinc and biological value of dietary organic zinc complexes and chelates. Nutrition Research Reviews 1994; 7: 129-149.

130 Symonds HW, Mather DL, Mallinson CB, Hughes DL. Bile flow, bile salt secretion and the excretion of iron, copper zinc and manganese in the bile of calves infected with *Fasciola hepatica*. Research in Veterinary Science 1983; 35: 69-74.

131 Top AMvd, Beynen AC, Blok MC, Jongbloed AW, Kemme PA, Verdonk J, Wensing T. Literatuuronderzoek naar nieuwe statusindicatoren voor Cu en Zn bij vleeskalveren. 2001.

132 Underwood EJ, Suttle NF. The Mineral Nutrition of Livestock, 3rd edition ed. Wallingford: CABI; 1999.

133 Valdivia R, Ammerman CB, Henry PR, Feaster JP, Wilcox CJ. Effect of dietary aluminum and phosphorus on performance, phosphorus utilization and tissue mineral composition in sheep. Journal of Animal Science 1982; 55: 402-410.

134 Valdivia R, Ammerman CB, Wilcox CJ, Henry PR. Effect of dietary aluminum on animal performance and tissue mineral levels in growing steers. Journal of Animal Science 1979; 47: 1351-1356.

135 Verheijden JHM, Schotman AJH, Miert ASJPAMv, Duin TMv. Zinc concentrations of skimmed milk and whole milk samples from healthy and mastitic cows. American Journal of Veterinary Research 1983; 44: 1637-1640.

136 Vos G, Teeuwen JJMH. Koper in levers van Nederlandse mestkalveren. RIKILT-Rapport 1986; 86.52: 1-18.

137 White FD, Neathery MW, Gentry RP, Miller WJ, Logner KR, Blackmon DM. The effects of different levels of dietary lead on zinc metabolism in dairy calves. Journal of Dairy Science 1985; 68: 1215-1225.

138 Woolf GM, Miller C, Kurian R, Jeejeebhoy KN. Diet for patients with a short bowel: high fat or high carbohydrate? Gastroenterology 1983; 84: 823-828.

138a Wright CL, Spears JW. Effect of zinc source and dietary level on zinc metabolism in Holstein calves. Journal of Dairy Science 2004; 87: 1085-1091.

139 Xu C, Wensing T, Beynen AC. The effects of dietary soybean versus skim milk protein on plasma and hepatic concentrations of zinc in veal calves. Journal of Dairy Science 1997; 80: 2156-2161.

# ANNEX: OVERVIEW OF THE SERIES OF CVB DOCUMENTATION REPORTS 'REVIEWS ON THE MINERAL PROVISION IN RUMINANTS'

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