IMPORTANT TRACE MINERAL SUPPLEMENTATION IN RUMINANTS

Dr Clinton Austin

Introduction

Collectively speaking, minerals make up less than 5 % of the animal body[1], however their functional importance in various physiological and metabolic functions is considerable. Trace mineral nutrition supports immunity, growth and reproduction in livestock[2], and available forage, water and ingested soil are the primary source of such minerals.

Although a mineral rich country, many parts of South Africa ironically find the soil and herbage deficient in certain important minerals such as copper, zinc, manganese and selenium[1], resulting in the need for trace mineral supplementation in South African livestock.

Mineral supplements available on the South African market come in different forms including premixes, free choice loose mineral mixes, mineral salt blocks, oral drenches and injectable preparations amongst others. Although all the above-mentioned methods of supplementation are widely accepted and practised, injectable supplements and the minerals they contain will be discussed here.

The function of minerals

Broadly speaking, the function of minerals can be divided into four main categories[3]:

1. Physiological functions which include the minerals that occur in body fluids and tissues, such as electrolytes, and are involved in regulating acid-base balance, blood pressure and transmission of nerve signals amongst others.
2. Structural functions such as the formation of the bones and teeth.
3. Regulatory functions where certain minerals are involved in regulating cell division, signal transduction and the production of hormones.
4. Catalytic functions where minerals act as catalysts in certain enzyme and hormone systems or form specific components of metalloenzymes.

The above broad functions can all be deemed essential to homoeostasis as well as optimal health and wellbeing. In any ruminant production system, these functions will underpin the three pillars of successful livestock farming: production, reproduction and immunity.

Trace minerals support many functions related to growth and immunity[2] and since growth, milk production and disease incidence (directly related to immunity) have a direct influence on profitability, it would be logical to infer that trace mineral nutrition management is essential in any dairy or calf/lamb growing operation. Trace mineral imbalances require the animal to compensate metabolically which may result in depressed performance resulting from reduced forage intake, lowered immunity, poor feed conversion and lower daily gains[4].

One of the most significant factors affecting profitability in ruminants is reproductive efficiency[5] and a number of trace minerals are vital in ensuring optimal reproductive performance. Fertility is affected by nutrition in that specific nutrients are required for development of oocytes and spermatozoa, ovulation, fertilization, survival of the embryo and pregnancy establishment[6]. Fertility is also indirectly affected by its impact on hormones and other nutrient sensitive metabolites that are required for these processes. Even marginal or subclinical deficiencies of certain minerals can impair reproductive efficiency significantly. Minerals important in reproduction include copper, manganese, zinc, selenium and chromium[5,7,8].

Copper

Copper has for a long time been of known importance for ruminant production[9,10] and is strongly influenced by dietary factors and other minerals including zinc, molybdenum and sulphur. Copper is important in the formation of metalloenzymes such as super-oxide dismutase, lysyl oxidase, ceruloplasmin and cytochrome oxidase amongst others[10], making copper critical in bodily functions such as cellular respiration, neurotransmitter function, free radical defence, tissue synthesis as well as cardiac and blood vessel integrity[11].

Low copper levels, or hypocuprosis, are often associated with female reproductive disorders, commonly resulting in embryonic loss and pre-natal mortality[12]. Symptoms of deficiency usually occur post-natally in cattle and in-utero in sheep[7], and although low copper levels in forage alone does not appear to have a significant effect on fertility, when the copper deficiency is combined with high molybdenum levels, cow fertility is adversely affected[13].

Copper is essential for development of the central nervous system of the embryonic lamb and studies have shown a high correlation between maternal and foetal copper levels[7]. Lesions due to copper deficiency are a common finding on pastures with high molybdenum content[10] but this trend can be reversed by supplementing copper[13].

Copper also modulates host immunity by its involvement in the development and differentiation of immune cells, as well as providing anti-fungal properties at a cellular level[14]. The mechanisms are complex but copper appears to be involved in progenitor cell differentiation of monocytes, as well as being concentrated in phagosomes and providing anti-bacterial bombardment[15,16].

Zinc

Zinc is notable because it is involved in a large number of biological process including cell proliferation, immune function as well as management of free radicals[17]. Zinc has an important function in skin and claw integrity due to its role in the formation of keratin[18]; it is not stored in the body and a constant supply is required to prevent deficiencies, which may lead to conditions such as parakeratosis, slowed growth, lethargy and reduced immunity to disease[19].

Zinc has long been recognized as essential in normal reproductive functioning in males and females[12]. It plays an important role in the transcription of hyaluronic acid, which in turn makes up an essential component of the cumulus-oocyte complex in mammalian follicles[17]. Zinc is also essential for the formation of superoxide dismutase, an enzyme responsible for protecting cells (including oocytes) from damage caused by free radicals. Zinc deficient lambs show decreased spermatogenesis in lambs due to atrophy of the seminiferous tubules[12], while zinc deficient calves were found to have significantly smaller testes.

Zinc functions as a modulator in the immune system[20] and this function is highly dependent on the availability of zinc. The immune system is very proliferative and particularly susceptible to zinc deficiency, which affects the survival, proliferation and differentiation of cells involved in both innate and adaptive immunity, including monocytes, polymorphonucleocytes, as well as natural killer-T- and B-cells. In the innate immune system, insufficient zinc levels lead to a decrease in chemotaxis by polymorphonucleocytes[21], as well as a decrease in phagocytosis[22]. In the adaptive immune system, many cytokine dependent functions of T-cells are regulated by zinc and insufficient zinc levels may lead to thymic atrophy and subsequent T-cell lymphopaenia[23].

Manganese and Cobalt

Manganese is involved in many of the same processes as copper and zinc, while cobalt is essential for the production of vitamin B12 or cobalamin[4], an important component of enzymes used in metabolic reactions.

In gestating ruminants, manganese deficiency adversely affects the developing embryo[7] and impacts on normal development of epiphyseal cartilage in the foetus. In 2003 McDowell demonstrated reduced conception rates in cattle and sheep fed manganese deficient diets[24] and male lambs receiving inadequate manganese demonstrated reduced testicular growth[25].

Chromium

Chromium plays an important role in enhancing the effect of insulin which affects daily nutrient metabolism. It has also been shown to enhance antibody reactions to vaccines in cattle fed supplemental chromium[26]. Both factors will contribute strongly towards optimal production.

Chromium plays a role in optimal fertility by improving immune function, reducing tissue mobilization as well as reducing levels of non-esterified fatty acids. The incidence of retained placenta is often higher in immune-impaired cows[27], which will negatively impact measures of fertility. Chromium also plays a vital role in insulin metabolism[8] and there is evidence that this metabolic hormone plays a role in ovarian follicular development as well as the release of luteinizing hormone, through its role in glucose metabolism.

The effects of chromium on the immune system has been difficult to elucidate, with the results of numerous studies being rather inconsistent[28]. In 2003, Faldyna *et al.* demonstrated an enhanced antibody response in cattle injected with a *Clostridium tetani* vaccine[26], but it is postulated that the effect of chromium on immunity is more indirect through its effect of reducing serum concentrations of cortisol, a well-known immune suppressant[29].

Selenium

Selenium status of the animal influences growth rates because of its involvement in the metabolism of thyroid hormones[30]; a deficiency of selenium causes a decrease in the blood triiodothyronine (T3) to tetraiodothyronine (T4) ratio, slowing down growth due to the relative decrease in T3.

Selenium deficiencies in ruminants have been associated with higher incidence of reduced fertility, retained placentas, mastitis and metritis[30]. In human males, selenium deficiency is also known to inhibit normal testosterone and spermatozoan synthesis[31], whilst also reducing spermatozoan motility[32]. Along with zinc and cobalt, selenium supplementation has been shown to improve sperm motility, percentage of live sperm and sperm membrane integrity in lambs[33,34].

Selenium is notable for its role in the formation of various leukocytes including Natural Killer cells, Helper T-cells and Cytotoxic T-cells[30]. This becomes important in the incidence of diseases commonly problematic in dairy animals such as mastitis, where the functioning of phagocytic and cytotoxic cells is of primary importance. Selenium supplementation has also been shown to induce a higher level of IgG antibodies in dam serum and colostrum[35], which resulted in higher serum IgG levels in the calf.

Supplementation

Malnutrition and mineral deficiencies in particular have long been recognized as a cause of poor performance and disease in production animals[7,36,37], both of which have a detrimental effect on the profitability of a farming enterprise. Ensuring optimal trace mineral levels in production animals has been shown to support **production**[2,28,38], **reproduction**[17,39] and **immunity**[26,40,41] in ruminants.

It stands to reason that increasing the mineral status of an animal when biological needs are increased, such as growing or breeding, would be advantageous[39] – this can be achieved by giving supplements. However, supplementation requires considerable amounts of planning and expert knowledge, as simply supplementing excess amounts of all necessary minerals will not lead to optimal production and may even be deleterious. This is because interactions between various minerals can affect their relative levels in the body, particularly in ruminants[10,42]. These same minerals, many of which are co-factors in enzymes controlling free radicals in the body, may become pro-oxidants when consumed or administered in excess.

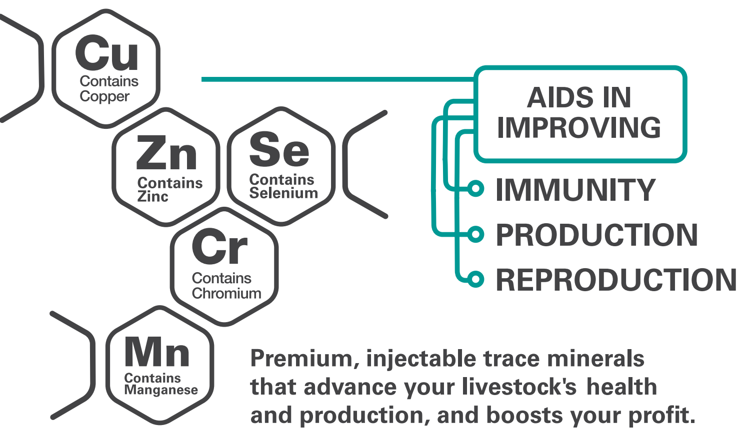
Injecting trace minerals into ruminants is advantageous compared to oral dosing in that the gastrointestinal tract is bypassed, thereby avoiding antagonists and competition for absorption[43]. Injecting trace minerals also provides a targeted and specified dose of minerals to individual animals[2,39], eliminating the variability in voluntary intake in cattle provided access to free choice minerals[44].

Commercially available injectable trace mineral supplements for cattle and sheep vary in content but generally contain various combinations of zinc, manganese, copper, chromium and selenium, the benefits of which were discussed earlier.

Mineral interactions and safety

Daily mineral requirements for cattle are widely published and available, but it must be stressed that these are minimum required concentrations in feed. Injectable mineral supplements should not be considered a replacement for good quality feed, but rather as a "top-up" designed to boost mineral levels during times of stress or additional need.

Although it is possible to cause toxicity by over-dosing certain minerals, the levels of these mineral within well-known and commercially available injectable supplements are far below the Maximum Tolerance Levels (MTL) stated in Table 1.



Interactions between minerals must also be taken into account, as many minerals are able to positively or negatively affect levels of other minerals[10,42]. A common example is the relationship between copper, molybdenum and sulphur discussed earlier in this article. When using mineral supplements, it is important to consider any mineral excesses which may occur naturally in a specific area; this is because if animals have high levels of a specific mineral, supplementation may push levels to toxic levels.

Table 1: Maximum tolerance levels allowed in supplementation of cattle and sheep[45]

Element	Maximum Tolerance Levels in Cattle (mg/kg)
Copper	40
Chromium (soluble)	100
Manganese	2 000
Selenium	5
Zinc	500

Conclusion

Trace mineral supplementation is essential in many areas to support optimal levels of production in ruminants. Symptoms of deficiencies are not often obvious, frequently manifesting as insidious, non-specific signs related to decreased production, negatively affected fertility and disease occurrence (immunity).

It is important to seek expert advice when designing a supplementation program, which considers management practises, type of enterprise, species, as well as regional or local mineral levels in water, soil and herbage. Frequency of supplementation should also be carefully considered, taking into account therapeutic versus strategic supplementation at critical times in the production cycle, in order to ensure that financial benefit accrues from use of any particular supplement.

References

1. Boyazoglu PA. *Animal Nutrition: Concepts and Applications*. Van Schaik; 1997.
2. Arthington JD, Moriel P, Martins PGMA, Lamb GC, Havenga LJ. Effects of trace mineral injections on measures of performance and trace mineral status of pre- and postweaned beef calves. *J Anim Sci*. 2014;92(6):2630-2640. doi:10.2527/jas.2013-7164
3. Underwood EJ. *The Mineral Nutrition of Livestock*. CABI; 1999.
4. Paterson JA, Engle TE. Trace mineral nutrition in beef cattle. In: *Nutrition Conference Sponsored by University of Tennessee*. ; 2005.
5. Spears JW. Trace minerals and reproduction in ruminants. *Salt Inst Newsl*. Published online 2014.
6. Robinson JJ, Ashworth CJ, Rooke JA, Mitchell LM, McEvoy TG. Nutrition and fertility in ruminant livestock. *Anim Feed Sci Technol*. 2006;126(3):259-276. doi:10.1016/j.anifeedsci.2005.08.006

7. Hidiroglou M, Knipfel JE. Maternal-fetal relationships of copper, manganese, and sulfur in ruminants. A review. *J Dairy Sci.* 1981;64(8):1637-1647.

8. Kafilzadeh F, Shabankareh HK, Targhibi MR. Effect of Chromium Supplementation on Productive and Reproductive Performances and Some Metabolic Parameters in Late Gestation and Early Lactation of Dairy Cows. *Biol Trace Elem Res.* 2012;149(1):42-49. doi:10.1007/s12011-012-9390-0

9. Ammerman CB. Recent Developments in Cobalt and Copper in Ruminant Nutrition: A Review. *J Dairy Sci.* 1970;53(8):1097-1107. doi:10.3168/jds.S0022-0302(70)86353-6

10. Suttle NF. The interactions between copper, molybdenum, and sulphur in ruminant nutrition. *Annu Rev Nutr.* 1991;11:121-140. doi:10.1146/annurev.nu.11.070191.001005

11. Riaz, M, Muhammad G. Copper deficiency in ruminants in Pakistan. *Matrix Sci Medica.* 2018;2(1):18-21. doi:10.26480/msm.01.2018.18.21

12. Hidiroglou M. Trace Element Deficiencies and Fertility in Ruminants: A Review. *J Dairy Sci.* 1979;62(8):1195-1206. doi:10.3168/jds.S0022-0302(79)83400-1

13. Phillippo M, Humphries WR, Lawrence CB, Price J. Investigation of the effect of copper status and therapy on fertility in beef suckler herds. *J Agric Sci.* 1982;99(2):359-364. doi:10.1017/S0021859600030148

14. Li C, Li Y, Ding C. The Role of Copper Homeostasis at the Host-Pathogen Axis: From Bacteria to Fungi. *Int J Mol Sci.* 2019;20(1):175. doi:10.3390/ijms20010175

15. Khera D, Sharma B, Singh K. Copper deficiency as a cause of neutropenia in a case of coeliac disease. *Case Rep.* 2016;2016. doi:10.1136/bcr-2016-214874

16. Wagner D, Maser J, Lai B, *et al.* Elemental Analysis of *Mycobacterium avium-*, *Mycobacterium tuberculosis-*, and *Mycobacterium smegmatis-*Containing Phagosomes Indicates Pathogen-Induced Microenvironments within the Host Cell's Endosomal System. *J Immunol.* 2005;174(3):1491-1500. doi:10.4049/jimmunol.174.3.1491

17. Anchordoquy J, Anchordoquy J, Sirini M, Picco S, Peral-García P, Furnus C. The Importance of Having Zinc During In Vitro Maturation of Cattle Cumulus-Oocyte Complex: Role of Cumulus Cells. *Reprod Domest Anim.* 2014;49(5):865-874. doi:10.1111/rda.12385

18. Bauer Benjamin U, Rapp C, Mülling Christoph KW, Meissner J, Vogel C, Humann-Ziehank E. Influence of dietary zinc on the claw and interdigital skin of sheep. *J Trace Elem Med Biol.* 2018;50:368-376. doi:10.1016/j.jtemb.2018.07.026

19. Ianni A, Innosa D, Martino C, Grotta L, Bennato F, Martino G. Zinc supplementation of Friesian cows: Effect on chemical-nutritional composition and aromatic profile of dairy products. *J Dairy Sci.* 2019;102(4):2918-2927. doi:10.3168/jds.2018-15868

20. Bonaventura P, Benedetti G, Albarède F, Miossec P. Zinc and its role in immunity and inflammation. *Autoimmun Rev.* 2015;14(4):277-285. doi:10.1016/j.autrev.2014.11.008

21. Ibs K-H, Rink L. Zinc-Altered Immune function. *J Nutr.* 2003;133(5):1452S-1456S. doi:10.1093/jn/133.5.1452S

22. Sheikh A, Shamsuzzaman S, Ahmad SM, *et al.* Zinc Influences Innate Immune Responses in Children with Enterotoxigenic *Escherichia coli*-Induced Diarrhea. *J Nutr.* 2010;140(5):1049-1056. doi:10.3945/jn.109.111492

23. King LE, Frentzel JW, Mann JJ, Fraker PJ. Chronic Zinc Deficiency in Mice Disrupted T Cell Lymphopoiesis and Erythropoiesis While B Cell Lymphopoiesis and Myelopoiesis Were Maintained. *J Am Coll Nutr.* 2005;24(6):494-502. doi:10.1080/07315724.2005.10719495

24. McDowell LR. *Minerals in Animal and Human Nutrition.*; 2003. Accessed February 17, 2020. https://www.cabdirect.org/cabdirect/abstract/20053041640

25. Masters DG, Paynter DI, Briegel J, Baker SK, Purser DB. Influence of manganese intake on body, wool and testicular growth of young rams and on the concentration of manganese and the activity of manganese enzymes in tissues. *Aust J Agric Res.* 1988;39(3):517-524. doi:10.1071/ar9880517

26. Faldyna M, Pechova A, Krejci J. Chromium Supplementation Enhances Antibody Response to Vaccination with Tetanus Toxoid in Cattle. *J Vet Med Ser B.* 2003;50(7):326-331. doi:10.1046/j.1439-0450.2003.00680.

27. Kimura K, Goff JP, Kehrli ME, Reinhardt TA. Decreased neutrophil function as a cause of retained placenta in dairy cattle. *J Dairy Sci.* 2002;85(3):544-550. doi:10.3168/jds.S0022-0302(02)74107-6

28. Lashkari S, Habibian M, Jensen S. A Review on the Role of Chromium Supplementation in Ruminant Nutrition—Effects on Productive Performance, Blood Metabolites, Antioxidant Status, and Immunocompetence. *Biol Trace Elem Res.* 2018;186(2):305-321. doi:10.1007/s12011-018-1310-5

29. Depew CL, Bunting LD, Fernandez JM, Thompson DL, Adkinson RW. Performance and Metabolic Responses of Young Dairy Calves Fed Diets Supplemented with Chromium Tripicolinate. *J Dairy Sci.* 1998;81(11):2916-2923. doi:10.3168/jds.S0022-0302(98)75853-9

30. Mehdi Y, Dufrasne I. Selenium in Cattle: A Review. *Molecules.* 2016;21(4):545. doi:10.3390/molecules21040545

31. Rayman MP. Selenium and human health. *The Lancet.* 2012;379(9822):1256-1268. doi:10.1016/S0140-6736(11)61452-9

32. Maiorino M, Flohé L, Roveri A, Steinert P, Wissing JB, Ursini F. Selenium and reproduction. *BioFactors.* 1999;10(2-3):251-256. doi:10.1002/biof.5520100224

33. Anderson JM, Axford RFE, Ap Dewi I. The effect of selenium supplementation on fresh and frozen ram semen. In: *Proceedings of the British Society of Animal Science.* Vol 1996. Cambridge University Press; 1996:185–185.

34. Kendall N, McMullen S, Green A, Rodway R. The effect of a zinc, cobalt and selenium soluble glass bolus on trace element status and semen quality of ram lambs. *Anim Reprod Sci.* 2000;62(4):277–283.

35. Hefnawy AEG, Tórtora-Pérez JL. The importance of selenium and the effects of its deficiency in animal health. *Small Rumin Res.* 2010;89(2):185-192. doi:10.1016/j.smallrumres.2009.12.042

36. McDowell LR. *Mineral Nutrition History, the Early Years.* First Edition Design Publishing; 2017. https://search.ebscohost.com/login.aspx?direct=true&db=edsebk&AN=1800389&site=eds-live&scope=site

37. Weiss WP. A 100-Year Review: From ascorbic acid to zinc—Mineral and vitamin nutrition of dairy cows. *J Dairy Sci.* 2017;100(12):10045-10060. doi:10.3168/jds.2017-12935

38. Mallaki M, Norouzian M, Khadem A. Effect of organic zinc supplementation on growth, nutrient utilization,and plasma zinc status in lambs. *Turk J Vet Anim Sci.* 2015;39:75-80. doi:10.3906/vet-1405-79

39. Stokes RS, Volk MJ, Ireland FA, Gunn PJ, Shike DW. Effect of repeated trace mineral injections on beef heifer development and reproductive performance. *J Anim Sci.* 2018;96(9):3943-3954. doi:10.1093/jas/sky253

40. Arthington JD, Havenga LJ. Effect of injectable trace minerals on the humoral immune response to multivalent vaccine administration in beef calves. *J Anim Sci.* 2012;90(6):1966-1971. doi:10.2527/jas.2011-4024

41. Teixeira AGV, Lima FS, Bicalho MLS, *et al.* Effect of an injectable trace mineral supplement containing selenium, copper, zinc, and manganese on immunity, health, and growth of dairy calves. *J Dairy Sci.* 2014;97(7):4216-4226. doi:10.3168/jds.2013-7625

42. Goff Jesse P. Invited review: Mineral absorption mechanisms, mineral interactions that affect acid–base and antioxidant status, and diet considerations to improve mineral status. *J Dairy Sci.* 2018;101(4):2763-2813. doi:10.3168/jds.2017-13112

43. Pogge D, Richter E, Drewnoski M, Hansen S. Mineral concentrations of plasma and liver after injection with a trace mineral complex differ among Angus and Simmental cattle. *J Anim Sci.* 2012;90(8):2692–2698.

44. Arthington J, Swensont C. Effects of trace mineral source and feeding method on the productivity of grazing Braford cows. *Prof Anim Sci.* 2004;20(2):155–161.

45. National Research Council. *Mineral Tolerance of Animals: Second Revised Edition, 2005.* National Academies Press; 2006. https://books.google.com/books?id=UTva4Zbh_8UC

REGISTRATION HOLDER Vetvax (Pty) Ltd. Reg. No. M2004/035302/07 | 442 Rigel Avenue South, Rigel Park, Erasmusrand, Pretoria, 0181 | Tel: +27 (0) 12 349 2772 | **www.designbio.co.za**.

MARKETED & DISTRIBUTED BY MSD Animal Health | 20 Spartan Road, Spartan, 1619, RSA. Tel: +27 (0) 11 923 9300, Fax: +27 (0) 11 392 3158 | **www.msd-animal-health.co.za**

ZA-MIC-200600007

veeVERNUF stockSENSE

MSD Animal Health