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Is there a role for organic trace element supplements in transition cow health?

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Abstract

Optimal transition cow health is the key to success of the subsequent lactation, and increasing attention has been focused on management and nutritional practices that support it. Physiological stress during the transition period alters the efficiency of the immune system, making the lactating dairy cow more susceptible to infectious diseases, such as mastitis and metritis, with subsequent impairment of reproductive performance.

Trace elements have a specific role in free radical control at the cellular level and influence the anti-oxidant/free radical balance. Dietary trace elements must be available for absorption throughout the whole of the digestive process until they reach the final site of absorption in the small intestine. Negative interactions between minerals can occur and, as the intestinal environment lowers the absorption of ionic minerals, chelation technology has been developed to increase mineral bioavailability. Organic trace elements have been used in dairy cow experiments, resulting in significant improvements in udder health, lameness and reproductive performance.

Keywords: Dairy cow; Minerals; Organic; Mastitis; Lameness

Introduction

The modern dairy cow experiences most physiological stress during the transition period when it moves from the demands of fetal growth through to calving, colostrum production and, eventually, maximal milk production. In addition to these drains on the animal's physical resources, the cow must be in a suitable physiological state to ensure repair of any tissue damaged during calving, and to maintain resistance to disease challenges.

Physiological stress during the transition period decreases the efficiency of the immune system, and when the immune response is overwhelmed by pathogen challenge this may lead to the establishment of infectious disease such as mastitis and metritis. As parturition approaches, the functional capacity of neutrophils, in terms of their phagocytic and cytostatic abilities, is impaired, reducing the cow's ability to resist disease challenge (Kehrli et al., 1989; Mehrzad et al., 2002).

Minerals have a special role in ensuring efficient growth, reproduction and immunocompetence in animals. It is generally considered that uncontrolled oxidation reactions may impair the animal's immune status (Spears, 2000). Furthermore, evidence suggests that herds have increased risks of metritis, mastitis, locomotion problems or diarrhoea in calves when zinc (Zn) or copper (Cu) status are either marginal or deficient (Enjalbert et al., 2006). The important anti-oxidant/pro-oxidant balance can be upset by feeding suboptimal diets or through poor nutrient intakes, and may be restored by dietary supplementation. The most important way to balance oxidative damage and anti-oxidant defence in dairy cows is to optimize the dietary intake of anti-oxidant minerals.

Dairy cow feeds typically contain a range of different compounds that possess anti-oxidant activities, many of which are minerals or are mineral-dependent. The key trace elements involved in animal feed are Zn, Cu, selenium (Se),

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iron (Fe) and manganese (Mn) (Surai, 2002; Surai and Dvorska, 2002).

Selenium (Se)

Selenium is an essential component of a range of selenoproteins, including glutathione peroxidase, thioredoxin reductase and iodothyronine deiodinase. In mammals, 25 selenoproteins have been identified to date (Rotruck et al., 1973; Berry et al., 1991; Deagen et al., 1991), but the role of many of these proteins remains unknown. Selenium can be found in raw feed materials in varying quantities, but many of them are deficient in the element, especially when sourced from countries with low Se soils, such as UK, Finland, Sweden, Denmark, and Norway.

There are two major sources of Se for animals: (1) Se naturally originating from plants, in the form of selenoamino acids, including selenomethionine and selenocysteine; (2) inorganic Se in the form of selenate or selenite. Even if the physiological requirement for Se is low in an animal, if this is not met, the anti-oxidant system is compromised, with subsequent detrimental consequences in terms of animal health (Spears, 2000). Excessive levels of Se are associated with toxicity, so administration of the appropriate dose is important.

Zinc (Zn)

Zn is the second most abundant trace element in mammals and birds, and forms a structural component of over 300 enzymes, where it may also be key to catalytic and regulatory activity. It plays an important role in anti-oxidant defence as an integral part of the essential enzyme superoxide dismutase (SOD) (Underwood, 1999; National Research Council, 2001). Zn is also involved in hormone secretion and function (somatomedin-c, osteocalcin, testosterone, thyroid hormones, insulin, and growth hormone). Other roles of Zn include (1) keratin generation and epithelial tissue integrity; (2) bone metabolism as Zn is an essential component of the calcified matrix; (3) nucleic acid synthesis and cell division; (4) protein synthesis; (5) as a catalytic, structural and regulatory ion for enzymes and transcription factors and participates in the metabolism of carbohydrates, lipids and proteins; (6) sexual development and spermatogenesis; (7) immune function, and (8) appetite control via the central nervous system.

Copper (Cu)

Cu is a component of a range of physiologically important metalloenzymes and takes part in (1) anti-oxidant defence as an integral part of SOD; (2) cellular respiration; (3) cardiac function; (4) bone formation; (5) carbohydrate and lipid metabolism; (6) immune function; (7) connective tissue development; (8) tissue keratinisation, and (9) myelination of the spinal cord.

Table 1
Main Cu-containing enzymes (National Research Council, 2001)

Enzyme	Role
Cytochrome oxidase	Electron transport during aerobic respiration
Lysyl oxidase	Formation of desmosine cross links in collagen and elastin
Ceruloplasmin	Iron absorption and transport for haemoglobin synthesis
Tyrosinase	Melanin production
Superoxide dismutase	Anti-oxidant in cells, role in phagocytic cell function

The main Cu-containing enzymes are shown in Table 1. Inorganic Cu, in certain valency states, has a strong pro-oxidant effect, and (if not bound to proteins), can stimulate lipid peroxidation in feed or the intestinal tract (Surai et al., 2003).

Iron (Fe)

Fe performs a vital role in many biochemical reactions, including (1) anti-oxidant defence as an essential component of catalase; (2) energy and protein metabolism; (3) as a haem respiratory carrier; (4) oxidation–reduction reactions, and (5) in the electron transport system. Reduced Fe is also a catalyst for lipid peroxidation and radical formation, thus having a strong pro-oxidant effect (Halliwell, 1987).

The role of Fe in the immune response was first recognized in the late 1960s and an insufficient supply has long been known to cause anaemia in deficient animals due to failure to produce haemoglobin. Fe deficiency is rare in adult cattle as their requirement is low and Fe is ubiquitous in the environment, but it is more frequent in calves as milk Fe content is low (Underwood, 1999).

In dairy cattle, plasma Fe concentration is decreased during the acute phase response to immunological challenges as are Zn concentrations (Kushner, 1982), whereas plasma Cu concentration may increase (Hayes, 1994). These ion changes reflect changes in cation binding of plasma proteins, and more importantly, alterations in cellular uptake mechanisms. During mastitis, increased secretion of binding proteins such as lactoferrin in milk decreases the amount of available Fe and thus reduces the availability of the divalent Fe for Gram-negative bacterial growth (Todhunter et al., 1990).

Manganese (Mn)

Mn plays an important role in body metabolism as an essential part of a range of enzymes that are involved in (1) anti-oxidant protection as an integral part of SOD; (2) bone growth and egg-shell formation; (3) carbohydrate and lipid metabolism; (4) immune and nervous function, and (5) reproduction.

Trace elements and immunity

From this brief outline of trace element function, it can be clearly seen that they are all relevant to immune function, primarily via antioxidative processes. The comprehensive range of mineral-dependent anti-oxidant enzymes that can be synthesized in the body are able to deal effectively with free radicals, but require a supply of feed-derived mineral co-factors to do so. For example, Se is an essential part of a family of enzymes called glutathione peroxidases (GSH-Px) and thioredoxin reductases (Rotruck et al., 1973; Berry et al., 1991). Zn, Cu and Mn are integral parts of SOD, and Fe is an essential part of catalase. When these metals are delivered via feed in sufficient amounts, the body is able to synthesize adequate anti-oxidant enzymes. In contrast, deficiency or excess of these elements results in oxidative stress, leading to potential damage of tissue, biological molecules and membranes.

An increase in oxidative reactions within the cell, or at the cell membrane, produces free-radicals or activated molecules with the potential to inhibit cellular functions, damage membranes, and even to result in the destruction of the cell. These free radicals can be denoted as $O2^{\bullet}$, $O^{\bullet}$, $OH^{\bullet}$, $NO^{\bullet}$. Oxidation–reduction reactions occur in the body under normal metabolic processes, but when the reactions become uncontrolled, the end products of oxidation (i.e., free radicals) accumulate, and tissue damage occurs. In an effort to protect itself, the cell prevents the accumulation of free radicals by the action of several anti-oxidants present in the body (Table 2).

Various factors facilitate the accumulation of free radicals, but common stressors (heat stress, high physiological demands) increase both the cell's metabolic rate and the accumulation of free radicals (Bernabucci et al., 2002; Lohrke et al., 2005). If the anti-oxidants that prevent the accumulation of free radicals are absent, or present at suboptimal levels within the cell, or not available at the precise place within the cell where free radicals are formed, damage can occur. Cows that are under stress at calving, challenged by a high infective load or experiencing the peak demands of lactation have a heavier loading of free radicals (Bernabucci et al., 2002) and therefore require a greater supply of anti-oxidants.

Table 2
Antioxidants present in body tissues (Markesbery et al., 2001)

Enzymatic	Non-enzymatic
Cu–Zn superoxide dismutase	Ascorbic acid
Mn superoxide dismutase	Carotenoids
Catalase	Ceruloplasmin
Glutathione peroxidase	Uric acid
Glutathione reductase	Bilirubin
	Melatonin
	Isoflavone
	Methionine
	α-Tocopherol

Effective supplementation

Basic deficiencies in trace elements have been traditionally addressed by supplementation with inorganic salts, such as copper sulfates, zinc oxide or sodium selenite. Dairy nutritionists, who are aware of the low availability of inorganic forms, commonly use higher quantities of these elements in an attempt to guarantee uptake of the required amounts from the gut. However, a growing awareness of the environmental impact caused by undigested mineral compounds, such as those excreted by animals, has led to numerous research studies examining viable alternatives, with the focus on identifying ways to increase trace elements uptake at the intestinal level.

Negative interactions between ingested metal ions and certain dietary factors have been documented over the years. It is well known that polyphenols and certain sugars and fibre sources are implicated as metal binders that can hinder absorption of ions from the gastrointestinal tract (McDonald et al., 1996). Mutual antagonism between metal ions, such as Fe, Mn and cobalt (Co), can also occur at the absorption level, due to competition for common uptake mechanisms (National Research Council, 2001). The absorption of dietary Cu is reduced by the presence of sulfur (S) and molybdenum (Mo) in the diet. Sources of S can be converted to sulfide in the rumen, leading to formation of copper sulfide precipitates rendering the Cu unavailable for absorption (Bird, 1970). Sulfur and Mo also interact together in the rumen and form tetrathiomolybdate in the solid phase of the ruminal digesta. Tetrathiomolybdate binds Cu to form a highly insoluble complex that renders the Cu unavailable for absorption (Allen and Gawthorne, 1987).

Some of the greatest losses are encountered by those metal ions that are prone to 'hydroxy-polymerization' reactions (Fig. 1). This is a particular concern for the 'hydrolytic metals' such as aluminium (Al), Mn, Zn, Cu and Fe. These metals are readily acid-soluble, but upon alkalization in the small intestine, their associated water molecules rapidly loose protons, to form hydroxy-metals. This reaction can lead to widespread polymerization of the hydroxy-metal species and, ultimately, to precipitation, which renders the metal unavailable for uptake (Whitehead et al., 1996).

Additionally, during digestion, the luminal nutrients that are propelled towards the villi of the small intestine first encounter an 'unstirred water layer' followed by a mucosally-adherent mucus layer, through which they must

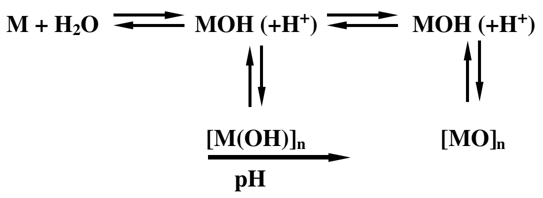

Fig. 1. Hydroxy-polymerization of hydrolytic metal ions as a function of pH.

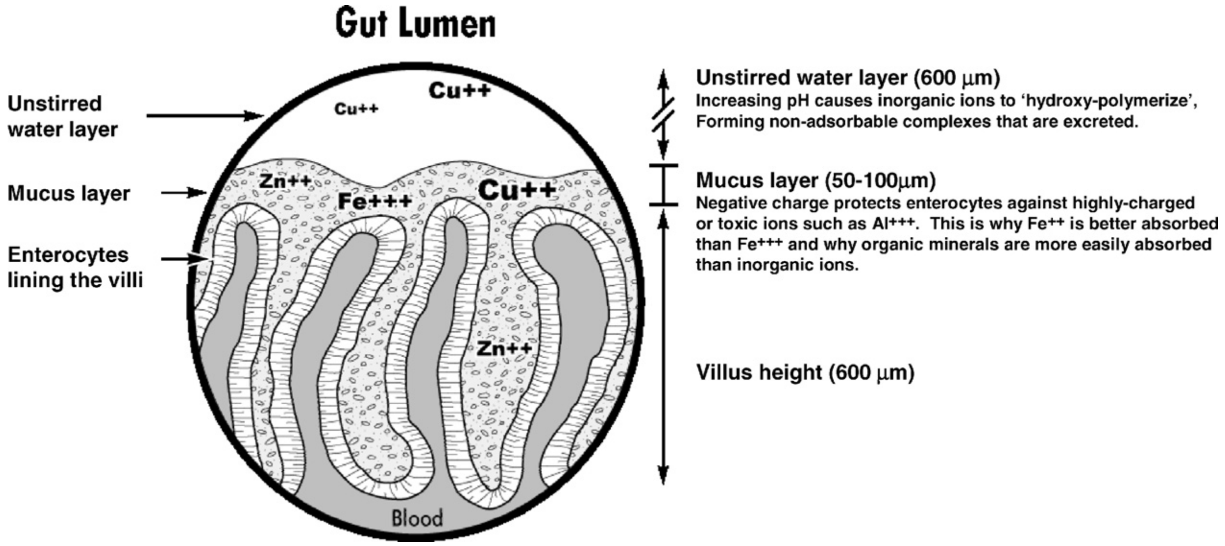

Fig. 2. The unstirred water and mucus layer between the lumen and enterocytes (Power, 2006).

pass in order to be absorbed (Fig. 2). The pH environment of the unstirred water layer causes the inorganic ions to hydroxy-polymerize (Whitehead et al., 1996), while the negatively charged mucus layer has a high affinity and capacity for metal cation binding, both actions which can reduce absorption (Guth and von Engelhardt, 1989).

One of the first attempts at complexation used ethylenediaminetetraacetic (EDTA), which linked transition metal ions via nitrogen atoms and four oxygen atoms. However, this did not result in a better zootechnical performance (Stansbury et al., 1990) and different ligands, such as partially hydrolyzed protein, amino acids or polysaccharides, were subsequently used for chelation.

The term 'chelate' derives from the Greek word '*chele*', meaning 'a crab claw'. This refers to the chelate structure that involve ligands bound to the metal ion via two or more donor atoms in structures called heterocyclic rings that contain the metal atom. Chelation technology allows the presentation of trace elements in an electrically neutral form, thus avoiding the previously described events to hinder trace element uptake at the intestinal level.

An understanding the complexity of the intestine microclimate and its regulation makes it clear that it is not necessarily absorption itself, but also the interactions occurring during transport from intestinal lumen to enterocyte membrane that is the key to enhancing the bioavailability of essential trace elements.

Trace element nutrition and dairy cow health

Adequate trace element nutrition has a significant influence on infertility, lameness and udder health in lactating dairy cows. These conditions have a significant detrimental impact on profitability. For instance, the cost of mastitis in UK dairy herds was reported to vary from £149[1] for a mild case to £1709 for a fatal case, with an average value of £177 (Esslemont and Kossaibati, 2002).

Udder health

Suboptimal udder health affects somatic cell counts (SCC) and milk yield, as well as the incidence of clinical mastitis. High SCC is detrimental for milk producers because of the milk losses encountered with the treatment cost forming a secondary, although important component. Schroeder (1997) estimated that 65.8% of total costs associated with mastitis cases were due to milk losses, while 22.7% were associated with replacement costs. Elevated SCC can reduce milk production from 2.6% for counts between 50,000 and 100,000 cells/mL for a first lactation cow, up to 13.3% for SCC > 80,000 cells/mL for a second lactation animal (Jahnke, 2004).

Both environmental and host factors are important in mastitis. The balance between the environmental pathogen load and animal resistance determines whether or not invasion of the udder will result in mastitis. A certain level of immune surveillance in the form of macrophages is constantly present in the healthy mammary gland. Following invasion of mammary tissue by pathogens, an initial neutrophil response occurs, which, if unsuccessful in overcoming the infection, may result in the establishment of clinical mastitis.

The end of the teat is in constant contact with the external environment and offers a first line of defence to pathogens, so farm management strategies that limit teat exposure to external pathogens are beneficial for udder health. For instance, practices that prevent the dairy cow lying on the bedding soon after milking allow the teat canal sphincter muscle to contract, decreasing the risk of internal exposure to pathogens present in the bedding (Hogan and Smith, 1996).

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[1] £1 = approx. €1.32, US$ 1.97, as at 22 February 2008.

An important feature of this defence mechanism is the keratin plug lining the teat canal, which creates a physical and chemical barrier to protect the mammary gland. Keratin is thought to have three mechanistic functions: physical adsorption, adsorption of pathogens in a mesh-like matrix, and elimination, when keratin is flushed out of the canal during milking. Trial work carried out by Bitman et al. (1991) revealed that the amount of keratin at the end of the teat canal of Holsteins before milking was 1.6 times greater than after milking (3.1 mg vs. 1.9 mg). Zinc is an essential trace element involved in the catalytic, structural and regulatory processes of keratinisation and in general protein metabolism (Paulrud, 2005); consequently teat canal keratin production is dependant on Zn status (Paulrud, 2005).

Nutrition has been clearly shown to influence immune cell function in lactating dairy cows. A review published by Sordillo et al. (1997) discussed how energy and protein status, Se, vitamin E, B-carotene, Cu and Zn can enhance the function of several immune cells, including leucocytes, lymphocytes and neutrophils.

Comparison of supplementing dairy cows with inorganic or organic mineral forms

Several studies comparing inorganic trace element supplementation to Bioplex organic minerals (Alltech Biotechnology), have demonstrated a reduction in SCC and infection prevalence in dairy cattle supplemented with the organic mineral forms.

Spain (1993) reported beneficial effects of organic Zn (50% of supplemental 800 mg Zn per cow as organic Zn) on the rate of new intramammary infections. While there were no differences in SCC or milk yield when compared with zinc oxide, new infections were significantly reduced by about 50% in the organic Zn group compared to zinc oxide-supplemented animals ($P = 0.03$). The majority of new infections were caused by environmental pathogens, and feeding organic Zn may have enhanced resistance to mastitis pathogens because of improved skin integrity and keratin lining of the teat canal.

O'Donoghue and Boland (2002) supplemented lactating dairy cows with similar amounts of either inorganic or organic trace elements. Supplemental organic minerals (Bioplex copper, Bioplex zinc, Sel-Plex) provided 100 mg Cu, 300 mg Zn, and 2 mg Se per cow per day. Blood mineral status between treatment groups was not affected by treatments and initial serum values suggested that mineral status was adequate for both groups. However, cows supplemented with organic minerals had significant reductions in SCC when compared to control animals ($P < 0.05$).

In another trial, Popovic (2004) reported a reduction in SCC of dairy cows fed organic Zn when compared to cows fed a similar amount of zinc sulfate pre-partum and at the beginning of lactation. Although the herd SCC level was only 193,530 cells/mL at 10 days post-partum, there was a significant impact of organic Zn on SCC counts (158,840 cells/mL) ($P < 0.05$). These figures reached 116,440 and 62,670 cells/mL for inorganic and organic groups, respectively, at 100 days after calving ($P < 0.05$). No effect was recorded on milk yield or milk composition.

Scaletti et al. (2002) supplemented heifers pre-partum with 10 ppm copper sulfate or organic Cu, providing about 110 mg of supplemental Cu daily compared to a basal 6.5 ppm Cu in the diet. An intramammary challenge with *Escherichia coli* was then performed and the mean number of *E. coli* in milk following challenge was monitored for the following 10 days. The mean number of *E. coli* in milk increased following challenge in all groups. The *E. coli* numbers in milk (expressed as log of CFU) 24 h after the challenge were lower in the group fed organic Cu than in the control or inorganic Cu group ($P < 0.08$). The mean *E. coli* number was consistently lower for the group fed organic Cu when compared to the control group throughout the trial period. However, there was no significant difference in milk *E. coli* numbers between the control, organic and inorganic Cu groups in this experiment. Milk yield was significantly depressed 2 days after the intramammary challenge for all groups, but heifers fed organic Cu had a significantly higher milk yield at day 2 than heifers fed inorganic Cu ($P < 0.05$). This remained throughout the trial, resulting in a significantly higher milk yield recorded for the organic Cu group at days 2, 3, 4, 5, 6 and 10 after *E. coli* intramammary infusion in comparison with the heifers fed copper sulfate ($P < 0.05$), suggesting that the heifers fed organic Cu may have been more efficient at overcoming the pathogen challenge than those fed inorganic Cu.

Kinal et al. (2007) supplemented dairy cows from 6 weeks before calving until the end of lactation. The control group received Zn, Cu and Mn as sulfates, while in the treatment groups, 50% or 100% of the cow's added trace element daily supply was delivered as organic Zn, Cu and Mn. Cows receiving 100% Zn and Mn (600 and 400 mg/day, respectively) and Cu (120 mg/day) in organic form had significantly higher milk production during the first 3 months of lactation compared to the control group ($P < 0.05$), and also showed a 34% decrease in SCC (319,000, 255,000 and 212,000 cells/mL for the control group, 50% organic and 100% organic treatments, respectively).

In the same experiment, the use of organic forms of trace elements positively influenced the total immunoglobulin levels in both colostrum and blood serum of newly born calves. A significant ($P < 0.05$) increase in Zn and Cu concentrations in blood samples from cows receiving organically-bound Zn, Mn and Cu was also reported.

Lameness

In addition to its impact on animal welfare, the primary costs associated with lameness result from reduced milk yield (Hernandez et al., 2002) and decreased reproductive efficiency with lame cattle having greatly decreased first service conception rates, a higher percentages of cystic ovaries, and a much higher cull rate (Melendez and Shearer, 2002). The additive effects of lameness have led many researchers to place lameness as the third most costly disease of cattle on modern dairy farms. This cost is currently estimated at £171 for every single case of lameness (Esslemont and Kossaibati, 2002).

Lameness in dairy cows can be influenced by adequate trace element supplementation (Tomlinson et al., 2004), which can play a significant role in the production of quality hoof formation. Zn has been identified as a key mineral in the processes of keratinisation, where it is involved in three key functions of the keratinisation process – catalytic, structural, and regulatory (Cousins, 1996). When nutrient supply to keratin-forming cells is compromised or interrupted, inferior horn is produced, leading to increased susceptibility to claw disorders and lameness. Trace minerals and vitamins play important roles in production and maintenance of healthy keratinized tissues (Tomlinson et al., 2004).

Dairy cows fed additional organic Zn as zinc methionine over a 12 month period experienced fewer lameness cases, heel horn erosion, foot rot, interdigital dermatitis and laminitis with a lower incidence of sole ulcers and white line separation (Moore et al., 1988). In a trial carried out at Zurich University (Kessler et al., 2003), 54 bull calves with initial live weights of between 138 and 160 kg were fed either a control diet (no additional Zn, 35 ppm in basal feed), a diet supplemented with zinc oxide (10 ppm additional Zn as zinc oxide) or a diet supplemented with organic Zn (10 ppm additional organic Zn). The calves were slaughtered after 284 days on trial. Following claw trimming, claws were graded for hoof quality at the beginning, after 140 days and at the end of the trial. The severity of observed alterations were classified according to a scoring scheme ranging from 0 (no alteration) to 3 (severe alteration). Animals fed organic Zn had significantly less deterioration of claw quality than control bulls during the trial ($P < 0.05$).

Fertility

Infertility is one of the most significant factors influencing profitability on any dairy unit. The causes of dairy herd infertility are multi-factorial and include negative energy balance of the dairy cow around parturition. Even though some studies have recorded beneficial effects of feeding trace elements at this physiological stage, the exact role of minerals and vitamins on subsequent fertility is not yet clearly understood.

O'Donoghue and Boland (2002) carried out an experiment examining the effects of organic minerals (100 mg Cu, 300 mg Zn, 2 mg Se) fed pre-partum and during lactation on reproduction in dairy cows in comparison to a control diet. No significant results were found on time to first ovulation or conception rate to first service even though numerical improvement for both parameters was observed. Some other researchers have reported similar improvements in conception rates and days to first service when replacing inorganic sulfates of Cu, Zn or Mn and Co with organic sources (Ballentine et al., 2002) but the mode of action remains unclear.

Conclusions

The appropriate inclusion of Se, Mn, Cu and Zn in cattle diets is important for optimising the health of lactating and periparturient cows. Adequate trace mineral status may protect the cow from the adverse effects of acute inflammation caused by mastitis pathogens. Furthermore, supplementation with organic Cu and Zn and organic Se has improved udder health and lowered SCC significantly. Reducing mastitis and lowering SCC will result in economic benefits and improved health and welfare of dairy cattle. However, it must be stressed that nutritional approaches towards improving milk quality must be only implemented in association with proper mastitis management practices that reduce exposure of cattle to pathogens and limit spread of infection within the herd.

Zinc is an essential constituent for hoof keratin and has been demonstrated to play a regulatory role in its formation along with other vitamins and trace elements. Feeding organic Zn has been found to be beneficial to hoof hardness and reduced hoof deterioration.

Conflict of interest statement

Sylvie Andrieu, the author of the manuscript entitled *Is there a role for organic trace element supplements in transition cow health*? is Ruminant Technical Manager for Alltech Europe.

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