



Adequate Trace Mineral Nutrition Critical For Optimum Reproductive Performance

Introduction

Reproductive efficiency is critical to the profitability of all dairy operations. Each additional day required for a cow to conceive, after 90 days of lactation, costs between \$0.50 and \$4.00 (US\$) per day (22). Improving reproductive efficiency can be difficult as it is influenced by many factors including plane of nutrition, rate of weight gain, level of stress and level of milk production. Improving zinc, manganese, copper and cobalt nutrition of dairy cattle is part of an effective program to improve reproductive performance, as these trace minerals play vital roles in reproduction (Table 1).

The objective of this paper is to review the role of trace minerals in fertility of dairy cattle. In addition, it will address the indirect effects of mastitis, immune function and laminitis on reproduction.

Trace Mineral Function

Zinc. Zinc is an essential component of over 200 enzyme systems of which the metabolic actions include carbohydrate and energy metabolism, protein synthesis, nucleic acid metabolism, epithelial tissue integrity, cell repair and division, and vitamin A and E transport and utilization (14). In addition, zinc plays a major role in the immune system and certain reproductive hormones (14).

Zinc is known to be essential for proper sexual maturity, reproductive capacity, and more specifically, onset of estrus (25). Zinc has a critical role in the repair and maintenance of the uterine lining following parturition, speeding return to normal reproductive function and estrus (25). In bulls, a zinc deficiency results in poor semen quality and reduced testicular size and libido (20, 29, 39). Zinc has also been shown to increase plasma beta carotene levels (58). Increased plasma beta carotene has been directly correlated to improved conception rates and embryonic development.

Improved zinc status also improves fertility by reducing lameness, resulting in cows more willing to show heat and improved mobility and performance of bulls. Inadequate zinc supplementation results in mild to severe claw (hoof) disorders, including weak claws that are more susceptible to interdigital and digital dermatitis and foot rot (52).

The recommended dietary content of zinc for dairy cattle is typically between 18 and 73 ppm depending upon stage of the life cycle and dry matter intake (46). Copper, cadmium, calcium and iron reduce zinc absorption and interfere with zinc metabolism (52).

Manganese. In general, manganese is an activator of enzyme systems in the metabolism of carbohydrates, fats, proteins and nucleic acids (52). It is also essential for normal brain function, and plays a role in collagen formation, bone growth, urea formation, synthesis of fatty acids and cholesterol and digestion of protein (30, 33).

Manganese appears to have a vital role in reproduction. It is necessary for cholesterol synthesis (33), which in turn is required for synthesis of the steroids, estrogen, progesterone and testosterone. Insufficient steroid production results in decreased circulating concentrations of these reproductive hormones resulting in abnormal sperm in males and irregular estrus cycles in females (8). The corpus luteum has a high manganese content and may be affected by level of manganese supplementation. Also, vaginal manganese concentrations are higher in cycling than in anoestrous ruminants (41). A deficiency in manganese may be associated with suppression of estrus, cystic ovaries and reduced conception rate (52).

Table 1. Impact of Trace Mineral Deficiency on Ruminant Reproduction

Minerals	DIRECT	INDIRECT
Zinc	<ul style="list-style-type: none"> -reduced conception rate -atrophy in male reproductive tissue and glands - increase in retained placentas - inhibition of spermatozoa maturation 	<ul style="list-style-type: none"> - mild to severe claw (hoof) problems - suboptimal skeletal growth and weight gain - poor feed utilization and efficiency - low quality milk and high somatic cell count - slow wound healing and rough hair coat
Manganese	<ul style="list-style-type: none"> - suppression of estrus or silent heats - inhibited male libido and reduction of spermatozoa - delayed ovulation - increased incidence of abortion - delayed opening of the vaginal orifice - light birth weights with infant mortality - reduction of conception rate 	<ul style="list-style-type: none"> - poor skeletal development - weak and poor condition of legs and joints
Copper	<ul style="list-style-type: none"> - inhibited conception - early embryonic death - increase in retained placentas - subestrus - necrosis of the placenta - central nervous system abnormalities in the offspring 	<ul style="list-style-type: none"> - retarded growth - poor haircoat, reddish in color - skeletal changes - anemia
Cobalt	<ul style="list-style-type: none"> - reduced fertility - increased calf mortality - depressed milk and colostrum yield and quality 	<ul style="list-style-type: none"> - depressed appetite - poor fiber digestion - weight loss - poor growth
Selenium	<ul style="list-style-type: none"> - decreased fetal development and early calf mortality - decreased milk and colostrum quality and volume - decreased spermatogenesis - embryonic degeneration and fetal resorption - retained placentas and poor uterine involution 	<ul style="list-style-type: none"> - decreased mobility with claw (hoof) problems - reduced vitamin E metabolism and immune status - poor conception - poor growth and hair coat

The manganese requirement of weaned dairy cattle typically ranges between 13 and 22 ppm depending upon stage of the life cycle and dry matter intake (46). Levels of manganese considered adequate for growth in ruminants have been known to be associated with anoestrous, subestrus and reduced conception rates (17). By feeding manganese at increased levels, researchers have been able to minimize these problems. Dietary excesses of calcium and potassium increase manganese requirements due to increased fecal losses (41). Iron, magnesium, phosphorus and cobalt also reduce the availability of manganese (52).

Copper. Copper is a necessary component of a number of enzymes including superoxide dismutase, lysyl oxidase and thiol oxidase (15, 51). These enzymes function to eliminate free radicals that increase tissue susceptibility to bacterial infections, increase structural strength and elasticity of connective tissues and blood vessels and increase strength of horn such as in the claw (hoof), minimizing lameness (15, 51).

Reproductive problems that relate to copper deficiency manifest themselves in inhibited conception even though estrus may be normal. Symptoms of a copper deficiency include early embryonic deaths,

resorption of the embryo, increased retained placentas and necrosis of the placenta (41, 52). Weak and silent heats have been reported. Kappel et al. (32) reported dairy cows with higher serum copper levels had significantly less days to first service, fewer services per conception and fewer days open. Proper copper supplementation of the sire is needed for production of quality semen (52).

The copper requirement of dairy cattle typically ranges between 9 and 16 ppm, depending upon stage of the life cycle and dry matter intake (46). However, copper's availability is greatly diminished by sulfur and molybdenum as they form insoluble complexes in the rumen that render copper unavailable to the animal (51). Zinc and iron also reduce the availability of copper to the animal (52). Montana State research (66) indicates that supplementing zinc and copper in a ratio between 3 and 5:1 results in the best utilization of dietary copper. Producers utilizing by-products (i.e. corn gluten products, etc.) need to be aware of possible antagonists and adjust their copper levels appropriately.

Cobalt. Cobalt is needed for proper vitamin B₁₂ synthesis. Maintaining adequate vitamin B₁₂ status benefits both the dam and offspring. When adequate, sufficient amounts of vitamin B₁₂ cross the placenta and are present in colostrum (41). Milk, and colostrum in particular, contain high levels of vitamin B₁₂. Consequently, lactation depletes cobalt and vitamin B₁₂. Vitamin B₁₂ is required for the conversion of propionate to glucose and for folic acid metabolism (30).

Depletion of cobalt and vitamin B₁₂ at parturition causes depressed milk production and colostrum yield and quality (52). Reduced fertility and sub-optimal conditioning of the offspring are noted in a cobalt deficiency. Inadequate cobalt levels in the diet have been correlated with increased early calf mortality (52). A cobalt deficiency ultimately results in a vitamin B₁₂ deficiency.

Research has also shown that ketosis may be partially alleviated with cobalt. Dairy cows will respond to proper additions of cobalt to the diet with decreased occurrence of ketosis. In general, ruminants will tend to respond with better appetites and improved fiber digestion. These improvements appear to be enhanced during periods of reduced feed intake due to heat stress, poor fiber quality and by-product feeding.

The required dietary content of cobalt for dairy is 0.11 ppm (46). Manganese, zinc, iodine and monensin may reduce cobalt availability (52).

Iodine. Iodine is required for the synthesis of the thyroid hormone, thyroxin, which regulates the rate of metabolism (46). Prior to regulation of the feeding rate of ethylenediamine dihydriodide (EDDI), many producers fed iodine compounds to cattle in excess of the nutritional requirement to prevent foot rot (40).

Signs of a subclinical iodine deficiency in breeding females include suppressed estrus, abortions, stillbirths, increased frequency of retained placentas and extended gestation periods (28, 52). Calves born to cows that are marginally deficient in iodine are weak and may be hairless (52). Furthermore, animals that have a subclinical iodine deficiency will also have increased incidence of foot rot and respiratory disease due to suppressed immune responses (52). One notable characteristic of a clinical iodine deficiency is an enlargement of the thyroid gland, often termed a goiter (28).

The iodine requirement for dairy cattle typically ranges between 0.27 and 0.88 ppm (46). Soybean, rapeseed and canola increase the iodine requirement of the animal as they contain goitrogenic compounds that reduce the availability of iodine (52). High dietary nitrate also inhibits uptake of iodine by the animal (52).

Iron. Iron is a necessary component of hemoglobin and myoglobin for oxygen transport and cellular use (30). An iron deficiency is rare in adult cattle, but calves are frequently iron deficient, especially if fed milk replacer containing no supplemental iron or whole milk for extended periods of time (46).

Iron supplementation is usually not needed in ruminant diets due to the high iron content of many feedstuffs and soil contamination of many feedstuffs that are ingested by cattle. Cadmium, cobalt, copper, manganese, phosphorus and zinc all reduce absorption and utilization of iron by cattle (52). Excess iron increases the risk of infection because it enhances bacterial growth (19). The iron requirement for weaned dairy cattle typically range between 13 and 43 ppm (46).

Chromium. Chromium potentiates insulin action, resulting in increased uptake of glucose and amino acids by cells in the body (57). A chromium deficiency in lactating cows may result in increased incidence of ketosis and decreased milk production (52). Improved energy balance in early lactation may improve reproduction.

Selenium. Prior to 1957, the nutritional significance of selenium was related to its toxicity (41). Today, selenium is recognized as an essential element that defends the body against oxidative stress.

Marginally selenium deficient animals will abort, or calves will be weak and unable to stand or suckle (52). Research indicates that selenium supplementation reduces the incidence of retained placentas, cystic ovaries, mastitis and metritis (52). In addition, cattle that maintain adequate blood selenium levels have reduced incidence of abortions, stillbirths and periparturient recumbency. (41, 52). Compromised selenium status has also been associated with poor uterine involution, and weak or silent heats. In males, selenium supplementation has been shown to increase semen quality (52).

Symptoms of a chronic selenium toxicity include lameness, sore feet, deformed claws and loss of hair from the tail (52). In pregnant animals, selenium toxicity will produce abortions, stillborns and weak and lethargic calves as selenium accumulates in the fetus at the expense of the cow (52).

Cadmium, copper, mercury, lead, zinc and sulfur can induce a selenium deficiency (52). Dietary calcium levels greater than 0.8% reduce selenium absorption (52). The selenium requirement of dairy cattle is 0.3 ppm (46).

Inorganic Trace Minerals vs. Complexed Trace Minerals

As noted above, the bioavailability of trace minerals fed to dairy cattle is dependent not only upon the source of trace minerals but also upon amounts of other trace and macro minerals in the diet. Elements such as calcium, iron and sulfur can reduce the availability of trace minerals. Some minerals compete for absorption or form insoluble complexes in the rumen and intestine rendering the trace mineral unavailable to the animal.

Attempting to increase trace mineral status of the animal by feeding higher levels of inorganic trace minerals may decrease the availability of other trace minerals in the diet, increase the toxicity risk, and increase excretion of those trace minerals into the environment. Furthermore, trace mineral content of animal waste is becoming a concern and could potentially be regulated in the future. Thus interest has increased in feeding complexed trace minerals to increase trace mineral status and animal performance.

Direct Effects of Complexed Trace Minerals on Reproduction

Research has shown that improving zinc status by feeding *complexed zinc* improves reproduction. Research conducted at the University of Tennessee (9) indicated that feeding an additional 800 mg of zinc (400 mg from Zinpro *complexed zinc* and 400 mg from zinc sulfate) to late gestation cows, which were already receiving a diet containing 100 ppm of zinc, resulted in better reproductive performance postcalving. Cows fed the additional zinc prepartum had fewer days to first estrus, less udder edema when cows were fed diets high in iron and tended to have fewer days to first service. Graham et al. (24) found that feeding additional zinc in the form of *complexed zinc* improved health status of dairy cows. Incidence of mastitis, stillborns, spontaneous abortions and lameness were reduced in cows supplemented with Zinpro *complexed zinc* (Table 2).

Table 2. Effect of Zinc Supplementation on Estimated Risk For Abortion and Other Disorders (24)

Disease/Event Category	Odds Ratio ^a of Control ^b Cows Being More Likely to Have the Disorder vs. Cows Fed Complexed Zinc ^c
Mastitis	1.67 x more likely
Calf Deaths at Birth	2.32 x more likely
Culled	1.29 x more likely
Abortions	2.30 x more likely
Lameness	2.10 x more likely

^a Cross product ratio indicating likelihood of having the problem

^b Control = methionine

^c ZINPRO[®] zinc methionine

Spears (59) reported that beef cows supplemented with *complexed zinc and manganese* rather than zinc and manganese oxide had a 15.7% improvement in pregnancy rate when artificially inseminated (Table 3). At the end of the 80 day breeding period that included first AI, then natural bull service, there were 3.1% more cows pregnant in the Zinpro *complexed zinc and manganese* group than in the zinc and manganese oxide group. Spears noted that if the goal is to reduce days open and maintain maximum economic potential, then feeding more bioavailable trace mineral sources needs to be a management consideration (59).

Table 3. Effect of Zinc and Manganese Source on Pregnancy Rate of Cows Bred AI (59)

	Cows/ Treatment	ZnO, MnO	Complexed Zn ^a , Complexed Mn ^b	% Improvement
AI Period – 45 Days				
Year 1	22	61.9	52.9	
Year 2	20	52.9	73.9	
Average		57.4	65.9	14.8
Year 3	27	55.5	65.4	
Overall Average		56.8	65.7	15.7

^a ZINPRO[®] zinc methionine

^b MANPRO[®] manganese methionine

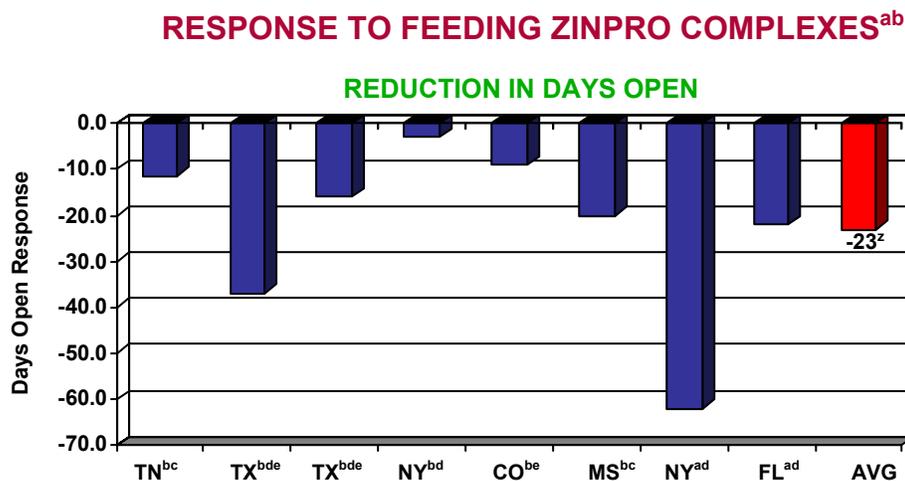
In another study at North Carolina State, replacing inorganic trace minerals with Zinpro *complexes* has been shown to improve uterine health (53). Feeding cows *complexed zinc, copper and cobalt*, both before and after calving reduced incidences of uterine infections by 54.2% (53).

A study conducted at the University of Tennessee indicates that feeding a combination of Zinpro *complexed zinc, manganese, copper and cobalt* three weeks precalving numerically reduced incidence of retained placentas by almost 38% (61). If the cows did retain the placenta, *complexes* supplemented precalving helped alleviate the negative effect retained placentas have on cows returning to normal ovarian function as evidenced in the reduction in days to first estrus, days to first luteal activity and days open (61). Similar results were observed in another study in which feeding *complexes* prior to calving reduced incidence of retained placentas, cystic ovaries and mastitis/metritis (49).

Research at the University of Tennessee also indicates that feeding a combination of Zinpro *complexes* in the postcalving period also helps alleviate the negative effects retained placentas have on reproduction (10). Small numeric responses on reproduction were observed when cows that did not retain the placenta were fed *complexes*. However, when placentas were retained, cows fed *complexes* showed estrus 37 days sooner, first luteal activity 11.8 days earlier and first corpus luteum 5.4 days earlier than cows that did not receive *complexes* (10). Overall, feeding Zinpro *complexes* reduced days to first estrus. Results from these studies indicate that cows fed *complexed* trace minerals were better able to respond to stress such as retained placentas, as evidenced by the quicker return to normal ovarian activity.

In a summary of 11 separate studies, feeding Zinpro *complexes* reduced days open by 23 days (Figure 1) and reduced services per conception by 0.3 services (2, 10, 35, 36, 37, 49, 62, 63). It should be noted that the control diets fed in most of these studies exceeded NRC requirements (46) for these trace minerals, in some cases by several-fold.

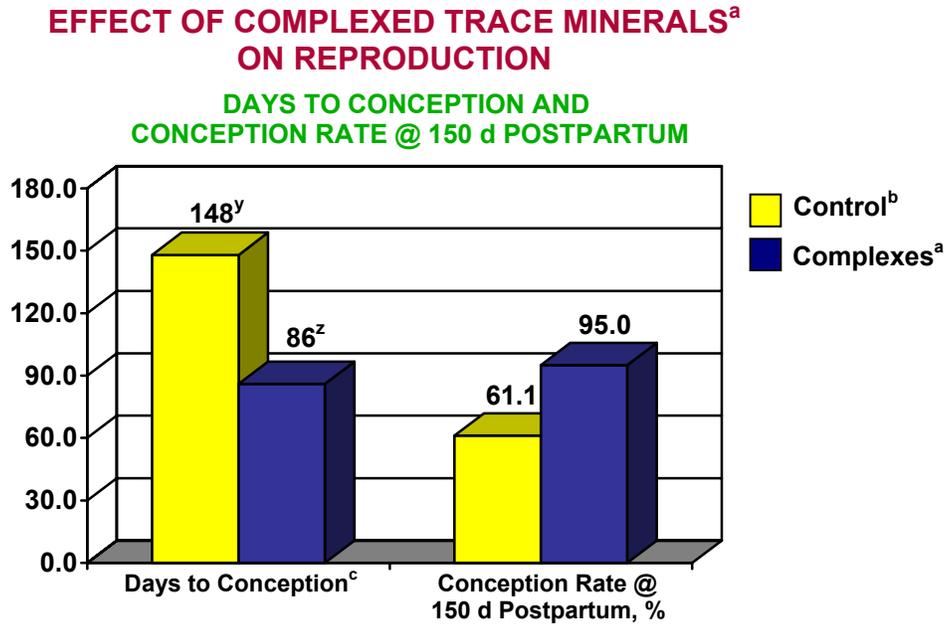
Figure 1.



- ^a Availa[®]4: Availa[®]Zn zinc amino acid complex, Availa[®]Mn manganese amino acid complex, Availa[®]Cu copper amino acid complex and COPRO[®]cobalt glucoheptonate
- ^b 4-Plex[®]: ZINPRO[®] zinc methionine, MANPRO[®] manganese methionine, CuPLEX[®] copper lysine and COPRO cobalt glucoheptonate
- ^c Diet that contained Zinpro complexes supplied an additional 360 mg Zn/hd/d, 200 mg Mn/hd/d, 125 mg Cu/hd/d and 12 or 25 mg Co/hd/d
- ^d Diets contained similar concentrations of Zn, Mn, Cu and Co
- ^e Diets supplied 360 mg Zn/hd/d from ZINPRO zinc methionine
- ^z Treatment effect ($P \leq 0.01$)

High Milk Production and Reproduction Results – Miner Institute Researchers at the Miner Institute observed a significant improvement in reproductive performance when cows were supplemented with Zinpro *complexes* vs. slightly higher level of trace minerals provided from inorganic sources (63; Figure 2). In the study, high producing cows averaging almost 45 litres/day were fed diets fortified with zinc, manganese, copper and cobalt at levels several times higher than the requirement (46). Cows fed Availa[®]4 had fewer days to conception and at 150 days post calving, 95% of cows fed Availa-4 were pregnant versus 61.1% of cows fed the inorganic trace mineral diet (38). Availa-4 cows also produced numerically more milk solids (protein plus fat) than control cows (63).

Figure 2.



^a Availa[®] 4: supplied per head/per day: 360 mg Zn from Availa[®]Zn zinc amino acid complex, 200 mg Mn from Availa[®]Mn manganese amino acid complex, 125 mg Cu from Availa[®]Cu copper amino acid complex and 12 mg Co from COPRO[®] cobalt glucoheptonate

^b All Zn, Mn, Cu and Co supplied by inorganics, 30% from sulfates and 70% from oxides

^c No voluntary waiting period observed

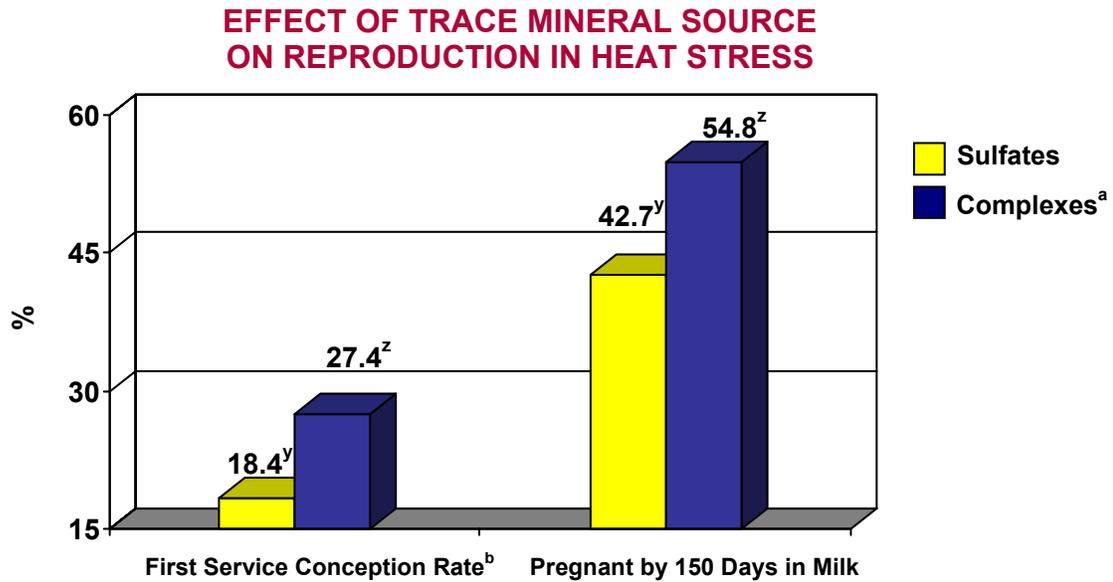
^{y,z} Means lacking a common superscript letter differ (P<0.05)

Uchida et al., 2001, Anim. Feed Sci. Technol. 93(3-4):193

Heat Stress and Reproduction Results – Florida Research Hot and humid environments are associated with poor reproductive performance in dairy cattle. Recent research conducted in a high producing dairy herd in Florida again demonstrated that supplementation with Zinpro *complexes* improves reproductive performance even under heat stress conditions such as those found in Florida. In the study, cows fed Availa-4 produced more milk and milk solids than cows fed similar levels of inorganic trace minerals (2). In addition to higher milk production, cows fed Availa-4 tended to have a 32.8% increase in first service conception rates, 22.1% more cows pregnant by 150 days in milk, and 22 fewer days open (2; Figure 3).

Pasture Based Dairying and Reproduction – NZ Research High input, high milk production dairying systems demonstrate significant benefits from supplementation with Zinpro *complexes*. Recent research conducted on a pasture based dairy system in NZ confirmed that similar responses can be expected in low input dairy systems as those recorded in high input confinement systems. Cows supplemented with Availa-4 produced significantly more milk protein and fat, had less mastitis and had improved reproductive performance as indicated by less reliance on hormone therapy (CIDR) to induce estrus (26; Figure 4 and 5).

Figure 3.

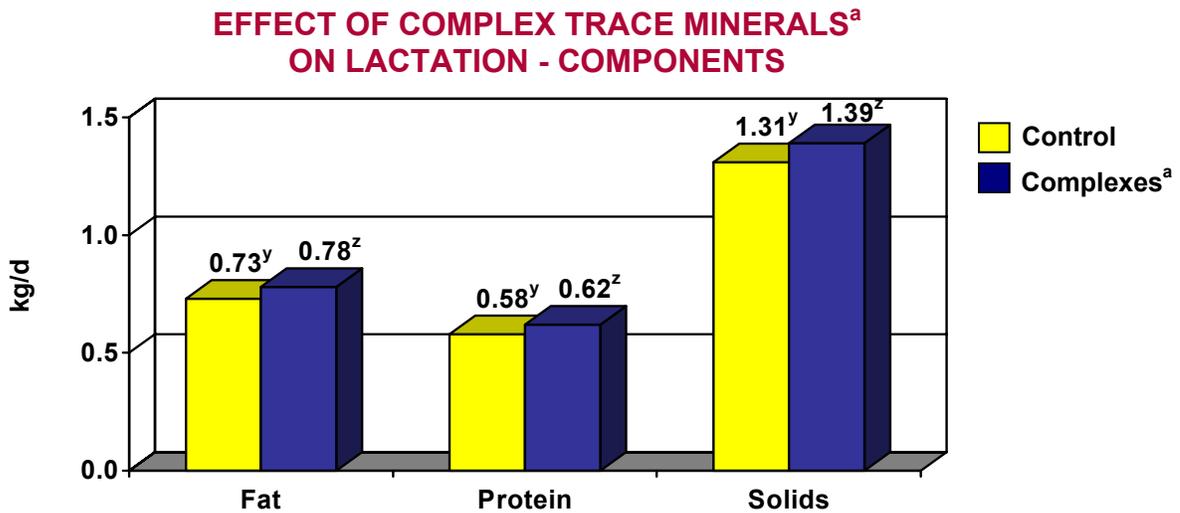


^a Availa[®] 4: supplied per head/per day: 360 mg Zn from Availa[®] Zn zinc amino acid complex, 200 mg Mn from Availa[®] Mn manganese amino acid complex, 125 mg Cu from Availa[®] Cu copper amino acid complex and 12 mg Co from COPRO[®] cobalt glucoheptonate

^b Total number of cows pregnant to first service divided by total number of cows eligible to be bred

^{yz} Within a category, means lacking a common superscript letter differ (P<0.15)
Ballantine, 2001

Figure 4.

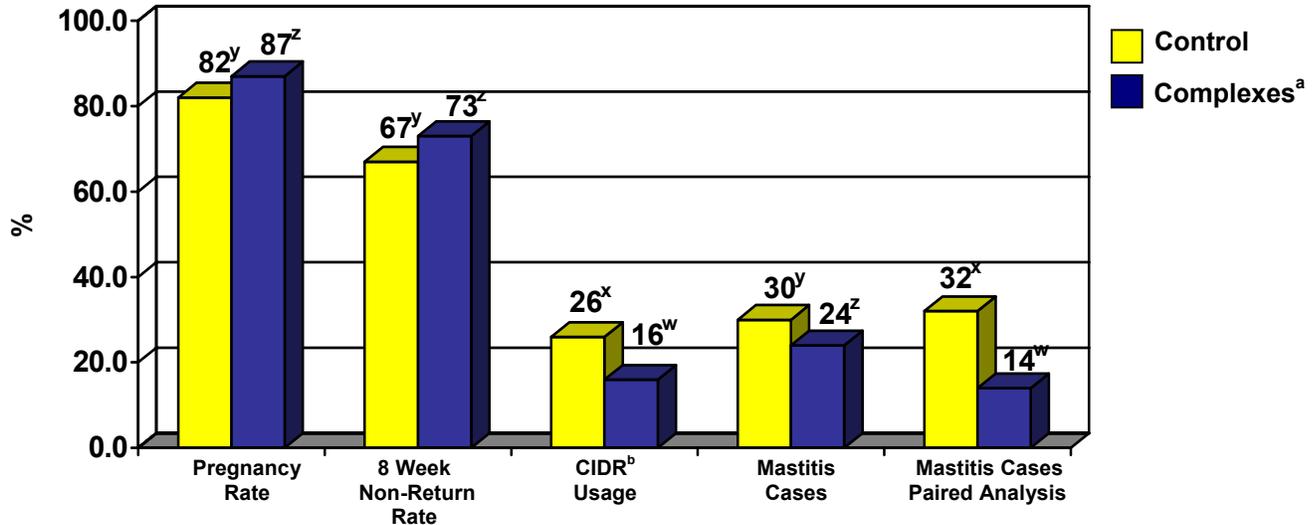


^a Availa-4 was fed 45 d prior to calving through 230 d postpartum and supplied: 360 mg Zn from Availa[®] Zn zinc amino acid complex, 200 mg Mn from Availa[®] Mn manganese amino acid complex, 125 mg Cu from Availa[®] Cu copper amino acid complex and 12 mg Co from COPRO[®] cobalt glucoheptonate

^{yz} Means lacking a common superscript letter differ (P<0.05)

Figure 5.

EFFECT OF COMPLEX TRACE MINERALS^a ON REPRODUCTION AND MASTITIS



- ^a Availa-4 was fed 45 d prior to calving through 230 d postpartum and supplied: 360 mg Zn from Availa[®]Zn zinc amino acid complex, 200 mg Mn from Availa[®]Mn manganese amino acid complex, 125 mg Cu from Availa[®]Cu copper amino acid complex and 12 mg Co from COPRO[®]cobalt glucoheptonate
- ^b Controlled internal drug releasing (progesterone secreting vaginal implant given to non-cycling cows)
- ^{wx} Means lacking a common superscript letter differ (P<0.01)
- ^{yz} Means lacking a common superscript letter differ (P<0.15)

Reproduction and Laminitis

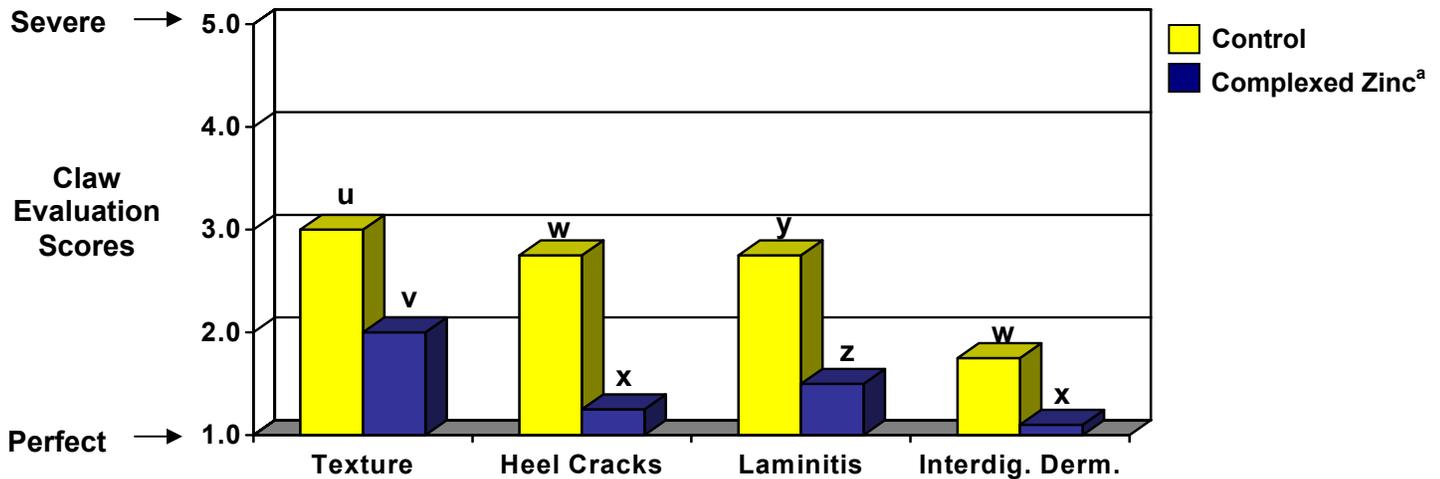
Lame cows tend to have lower dry matter intake, milk production and extended days open as a result of the laminitic insult. Lameness in bulls has the potential for loss of use in two general areas (12). First, lameness results in bulls failing to follow, mount and serve cows. Secondly, lameness can result in testicular degeneration, and thus poor semen quality (12). Lameness in cows also affects fertility. Cornell research indicates that lame cows have 28 more days open (27). British studies reported that cows lame between 36 and 70 days postpartum had 17 days more to first service and 30 days more open.

It is theorized that zinc improves claw (hoof) integrity by speeding wound healing, increasing rate of epithelial tissue repair and maintaining cellular integrity. Zinc is also required for the synthesis and maturation of keratin (55). On dairies with high incidence of foot problems, feeding 2 or 3 grams per day of zinc sulfate for 70 days reduced claw disorders (64). In contrast, sheep fed rations supplemented with zinc sulfate for six months did not show a reduction in claw problems (16). The lack of a consistent response to feeding zinc in the form of zinc sulfate can be attributed to antagonists present in the diet reducing the bioavailability of zinc from zinc sulfate. *Complexed* sources of zinc have proven to be more bioavailable than zinc from inorganic sources in part because the absorption of complexed trace minerals is only minimally affected by antagonists (65).

Feeding *complexed zinc* has been shown to reduce incidence of claw disorders in sheep and cattle. In a year long study conducted at Illinois State University, cows fed an additional 200 mg/d of zinc from Zinpro *complexed zinc* had fewer cases of foot rot, heel cracks, interdigital dermatitis and laminitis than control cows (42; Figure 6).

Figure 6.

EFFECTS OF COMPLEXED ZINC^a ON CLAW EVALUATION SCORES



^a ZINPRO[®] zinc methionine

^{uv} Means lacking a common superscript letter differ (P<0.01)

^{wx} Within a category, means lacking a common superscript letter differ (P<0.05)

^{yz} Means lacking a common superscript letter differ (P<0.10)

Scoring; 1-5 (1 = Perfect, 2 = Good, 3 = Fair, 4 = Poor, 5 = Severe)

Moore et al., 1989; Trans. Ill. Acad. Sci., 82:99

Complexed zinc also improved claw quality of crossbred steers grazing native grass (7). Of cattle receiving 216 mg per day of zinc from *Zinpro complexed zinc*, 2.45% had foot rot while 5.38% of cattle not receiving complexed zinc had foot rot (7). The reduction in foot rot may have partially contributed to the higher average daily gain for cattle fed *complexed zinc* (1.27 kg vs. 1.23 kg), (7).

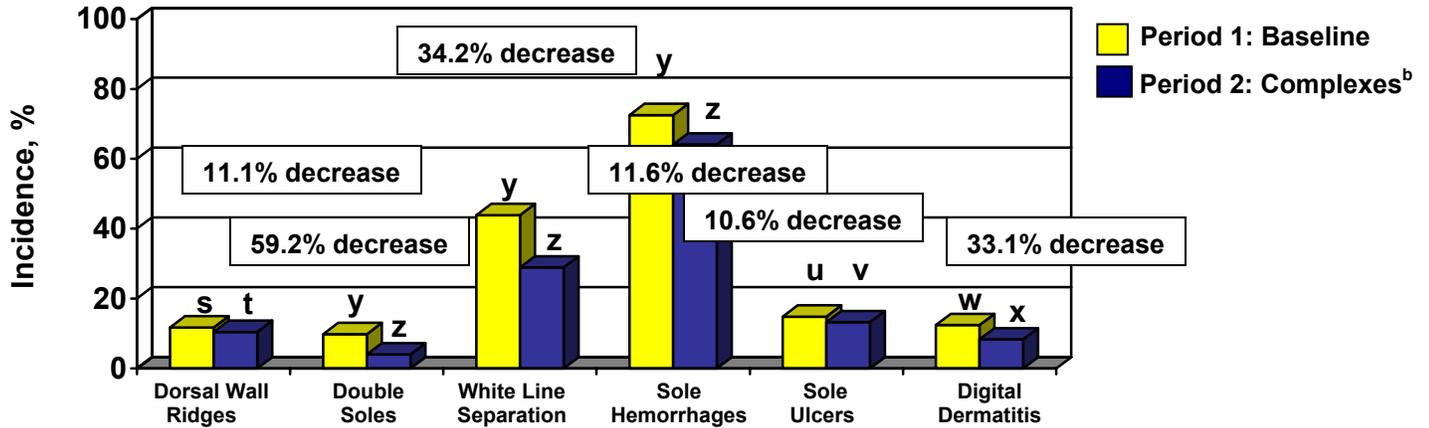
Sheep fed 80 mg per day of *complexed zinc* had a reduction in mean lesion scores per foot (4). Feet were scored for lesions on a scale of 0 to 3, with 0 being no lesions and 3 being under-mining of the wall (4). Sheep fed *complexed zinc* had a 43% improvement in foot lesion scores, while control sheep had no change in foot lesion scores from start to finish of the trial (4).

In addition to zinc, manganese, copper and cobalt play important roles in maintenance of claw integrity (55). Copper plays an important role in keratin maturation and formation of connective tissue. Manganese plays an integral role in maintaining foot and leg condition (41). In addition, increased claw problems are observed in a cobalt deficiency due to decreased protein synthesis.

Research conducted in Central New York indicated that feeding *Zinpro complexed zinc, manganese, copper and cobalt* resulted in fewer claw disorders than feeding no organic trace minerals or only *complexed zinc* (50). Supplementation of the diet with *complexes* reduced the incidence (P<0.05) of double soles, white line separation, sole hemorrhages and ultimately, sole ulceration (50). Supplementation with *complexes* also reduced the incidence (P<0.05) of digital dermatitis (50). Incidence of dorsal wall ridges tended to be reduced (P<0.15) by complexed trace minerals (50). The addition of *Zinpro complexes* to diets of lactating dairy cows improved claw condition compared to feeding no complexed trace minerals or only *Zinpro complexed zinc* (50; Figure 7).

Figure 7.

EFFECT OF COMPLEXED TRACE MINERALS^a ON INCIDENCE OF CLAW DISORDERS



^a 4-Plex[®]: ZINPRO[®] zinc methionine, MANPRO[®] manganese methionine, CuPLEX[®] copper lysine and COPRO[®] cobalt glucoheptonate

^b In period 2, cows were fed 14 g/hd/d of 4-Plex to supply 360 mg Zn from ZINPRO zinc methionine, 200 mg Mn from MANPRO[®] manganese methionine, 125 mg Cu from CuPLEX copper lysine and 25 mg Co from COPRO[®] cobalt glucoheptonate

st LSM means lacking a common superscript letter differ (P<0.15)

^{uv} LSM means lacking a common superscript letter differ (P<0.05)

^{wx} LSM means lacking a common superscript letter differ (P<0.01)

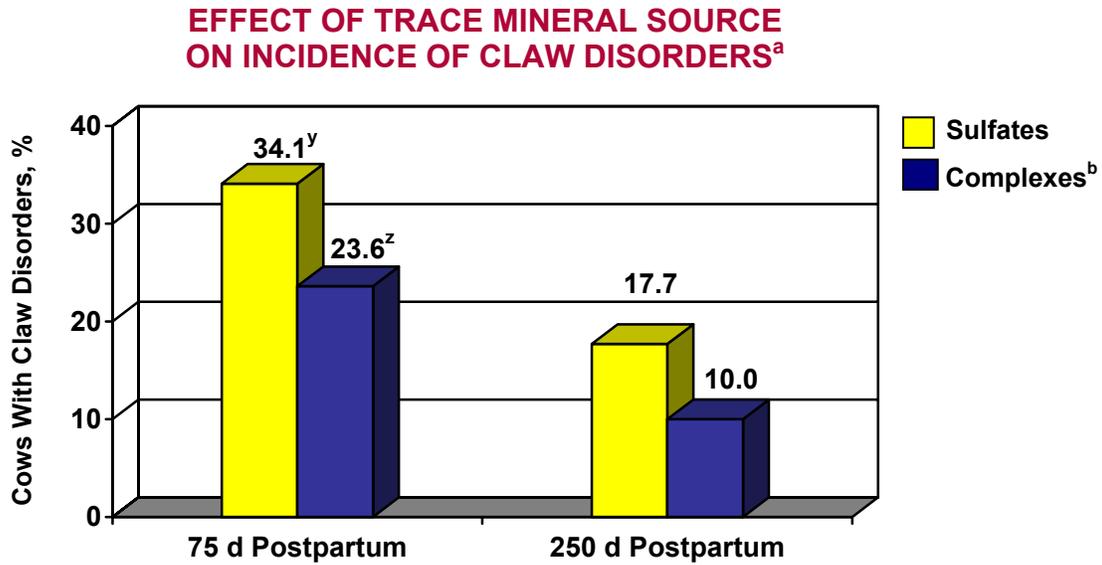
^{yz} LSM means lacking a common superscript letter differ (P<0.001)

Nocek et al., J.Dairy Sci., 2000, 83:1553

Similarly, Florida researchers found that replacing inorganic zinc, manganese, copper and cobalt with similar amounts of these trace minerals from Zinpro *complexes* resulted in reductions in total claw lesions (2). Feeding Availa-4 tended to reduce the incidence of foot rot and white line disease (2). If cows did exhibit a claw lesion such as white line disease, heel erosion or sole ulcers, Availa-4 supplementation reduced the severity of the lesion. (2; Figure 8 and 9).

An interesting footnote to this study is that source of trace mineral had no effect on trace mineral content of the liver. Levels of zinc, manganese and copper in the liver were above levels considered to be adequate and were similar both statistically and numerically for both Availa-4 and sulfate groups. However, cows fed Availa-4 had not only improved feet but also better reproduction and milk production (2). These results indicate that trace mineral content of liver may only be useful to identify deficiencies, not ability of trace mineral source to impact animal performance.

Figure 8.

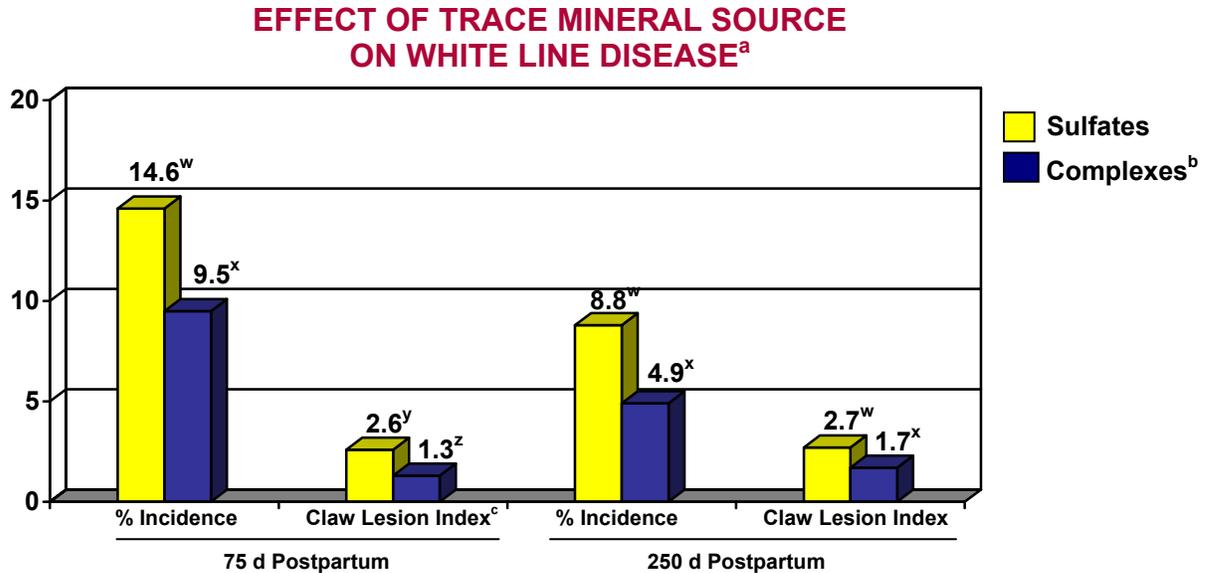


^a Means were covariately adjusted using data collected prior to treatment administration

^b Availa[®]4 supplied daily 360 mg Zn from Availa[®]Zn zinc amino acid complex, 200 mg Mn from Availa[®]Mn manganese amino acid complex, 125 mg Cu from Availa[®]Cu copper amino acid complex and 12 mg Co from COPRO[®] cobalt glucoheptonate

^{yz} Means lacking a common superscript letter differ ($P \leq 0.15$)
Ballantine, 2001

Figure 9.



^a Means were covariately adjusted using data collected prior to treatment administration

^b Availa[®]4 supplied daily 360 mg Zn from Availa[®]Zn zinc amino acid complex, 200 mg Mn from Availa[®]Mn manganese amino acid complex, 125 mg Cu from Availa[®]Cu copper amino acid complex and 12 mg Co from COPRO[®] cobalt glucoheptonate

^c Calculated for only cows with at least one zone afflicted with the stated disorder; Calculated by multiplying the number of zones afflicted by the average lesion score; Lesions were scored on a scale of 1, no pain to 3, severe pain

^{wx} Within a category, means lacking a common superscript letter differ ($P \leq 0.15$)

^{yz} Means lacking a common superscript letter differ ($P < 0.05$)
Ballantine, 2001

Interaction of Mastitis and Reproduction Function

Mastitis has been implicated in decreasing reproductive performance of dairy cows. Moore et al. (43) reported a negative correlation between clinical mastitis and reproduction due to altered interestrus intervals and decreased luteal phase length in cows with clinical mastitis caused by Gram-negative pathogens. Cullor (18) suggested that endotoxin might induce luteolysis and influence conception and early embryonic survival by release of inflammatory mediators. Moore and O'Connor (44) hypothesized that Gram-negative mastitis pathogens may stimulate production of prostaglandin $F_{2\alpha}$ which subsequently would cause luteal regression. Barker (3) reported clinical mastitis in the first 150 days in milk has a highly negative effect on services per conception, days to conception, breeding period, and days to first service. University of Florida researchers reported a 2.7 time higher risk of abortion in cows with clinical mastitis in the first 45 days of lactation (54).

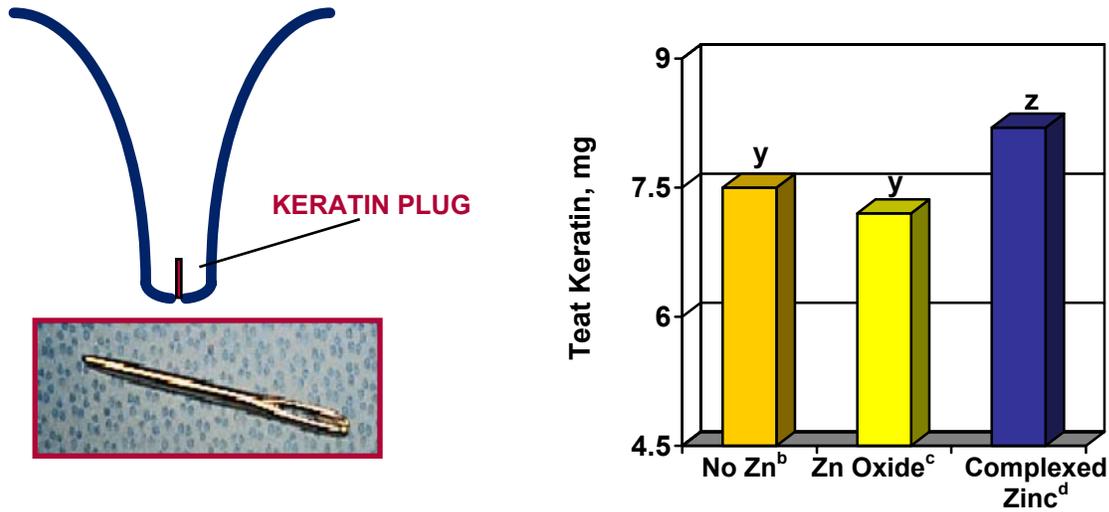
There are several plausible means by which increasing zinc status improves udder health. Zinc is important in maintenance of health and integrity of epithelial tissue, such as skin (teats) and mammary tissue, due to its role in cell division and protein synthesis (13). An additional mode of action for zinc reducing SCC is related to zinc's role in keratin formation. Zinc is required for the incorporation of cysteine into keratin (45). The keratin lining of the teat canal entraps bacteria and prevents their upward movement into the mammary gland (16, 47, 48). Approximately 40% of the keratin lining in teat canals of Holstein dairy cattle is removed during the milking process, thus requiring continuous regeneration. Capuco et al. (11) estimated that approximately 1.3 mg of keratin must be regenerated during the inter-milking period.

Zinc deficiencies have been shown to reduce cellular and humoral immune responses (13). Reduced immune function, resulting from a zinc deficiency, is attributed to decreased cell mediated immune response and natural killer cell activity, atrophy of the spleen and thymus, and decreased T-dependent and independent antibody-mediated responses (67).

Results from a study conducted at the University of Missouri lends credence to the theory that reduced SCC is due to increased keratin synthesis and improved immune function (31). The researchers (31) initially collected more keratin from teat canals of cows fed a combination of Zinpro *complexed zinc* and zinc oxide than cows fed an equivalent amount of zinc in the form of zinc oxide (Figure 10 and Table 4). However, due to the time required to regenerate keratin, there was no difference in amount of keratin collected from cows at subsequent collection time points (31). When cows in this same study were challenged with *E. coli*, cows fed *complexed zinc* recovered more quickly from the bout with *E. coli* mastitis than cows fed zinc oxide, as evidenced in numerically higher milk production and dry matter intake for cows fed *complexed zinc* (31; Table 4). Prior to the bacterial infection, cows fed *complexed zinc* produced a similar level of milk as cows fed zinc oxide, but tended to produce milk with a lower SCC (31; Table 4).

Figure 10.

EFFECT OF ZINC SOURCE ON TEAT KERATIN^a PRODUCTION



- ^a Keratin collected from front quarter at time zero, no difference at other timepoints
- ^b No added zinc, 30 ppm zinc
- ^c 800 mg of added zinc from zinc oxide
- ^d 400 mg of added zinc from ZINPRO[®] zinc methionine, 400 mg from zinc oxide
- ^{yz} Bars with uncommon superscripts differ (P<0.10)
Jones and Spain, 1996

Table 4. Effect of Zinc Source on Milk Production and DMI Before and After *E. coli* Challenge and Keratin Production In the Teat Canal (31)^a

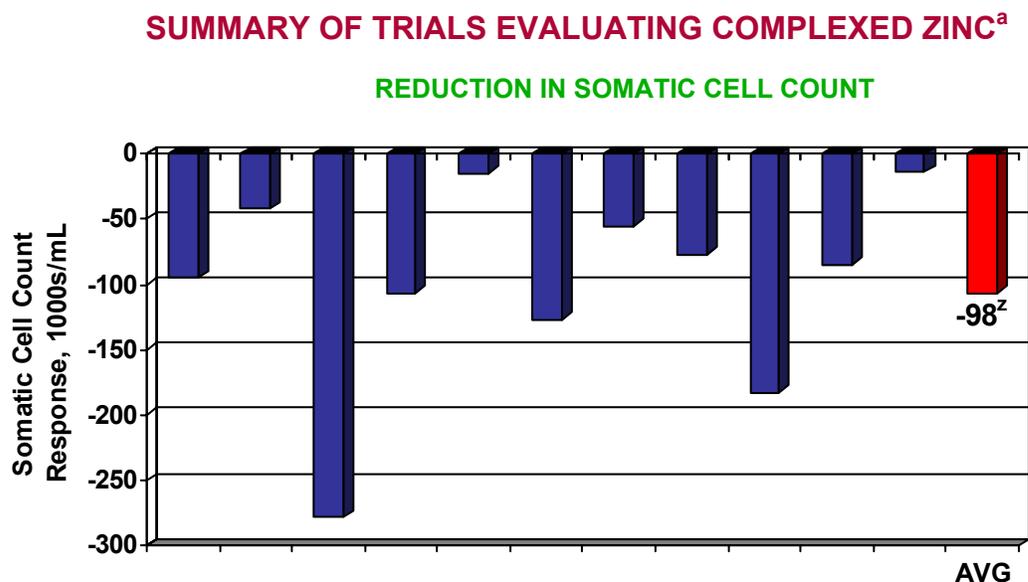
Item	No Zinc Added ^a	Zinc Oxide ^b	Complexed Zinc ^c
Before <i>E. coli</i> challenge			
DMI, kg/d	17.5	18.6	18.6
Milk, kg/d	26.7	27.1	27.2
SCC day 80, 1000s/mL	228	131	46
Amount of keratin collected			
Keratin, front quarter, mg ^d	7.5 ^y	7.2 ^y	8.2^z
Keratin, rear quarter, mg ^d	8.1	6.9	7.5
After <i>E. coli</i> challenge			
DMI, kg/d	13.3	14.3	15.1
Milk, kg/d	17.0	14.9	17.3

- ^a Basal diet contained 30.4 ppm Zn
- ^b Supplied 800 mg Zn/hd/d of added zinc from zinc oxide
- ^c Supplied 400 mg Zn/hd/d of added zinc from ZINPRO[®] zinc methionine, 400 mg Zn/hd/d from zinc oxide
- ^d Data presented from keratin collection at time zero; No difference in amount collected from other time points
- ^{yz} Means lacking a common superscript letter differ (P<0.10)

Complexed Trace Minerals and SCC Reduction

Increasing the zinc status of lactating dairy cattle by feeding Zinpro *complexed zinc* has been shown to reduce somatic cell counts (SCC). In a summary of 12 trials, cows receiving *complexed zinc* produced milk with a 33% reduction in SCC (an average of 98,000 less SCC), (1, 23, 31, 34, 42, 56, 58, 60; Figure 11).

Figure 11.



^a ZINPRO[®] zinc methionine
^z Treatment effect ($P \leq 0.001$)

Copper plays an important role in immune function. In mice, a copper deficiency has been shown to impair both humoral and cell-mediated immunity (51). Research has shown that increasing copper status by feeding *complexed copper* improves udder health. In a study conducted at Texas A&M, copper depleted beef cows fed 40 and 80 ppm of copper from *complexed copper* had lower SCC levels in colostrum than copper depleted beef cows fed 0 and 20 ppm of *complexed copper* (565,000 and 379,000 vs. 1,746,000 and 1,628,000, respectively; (5)). It should be noted that routinely supplementing 40 and 80 ppm of copper is not recommended. However this study does illustrate that if cows do not have adequate copper status at calving, they are more prone to mastitis.

Manganese also plays an important role in immune response as it removes superoxide radicals from the body (33). Superoxide radicals disrupt cellular membranes and cause cellular damage.

In a study recently completed on the South Island of New Zealand (26), cows fed a combination of *complexed zinc, manganese, copper and cobalt* had fewer mastitis cases and produced milk with a numerically lower raw SCC (Table 5).

Table 5. Effect of Zinpro Complexes^a on Milk Production, Milk Composition and SCC (26).

Measurement	Control	Complexes ^a	P=
Milk production, kg/d	16.6	17.5	0.04
Energy-corrected milk, kg/d ^b	19.1	20.2	0.01
Fat-corrected milk, kg/d ^c	19.0	20.2	0.02
Fat yield, kg/d	0.73	0.78	0.02
Protein yield, kg/d	0.58	0.62	0.01
Solids, kg/d	1.31	1.39	0.01
Fat, %	4.44	4.49	0.11
Protein, %	3.51	3.55	0.37
Solids, %	7.94	8.03	0.50
Mastitis cases, %	29.9	23.8	0.08
Mastitis cases-paired analysis, % ^d	32.1	13.6	0.01
Somatic cell count, 1000s/mL	126	110	0.22

^a Availa-4 was fed 45 d prior to calving through 230 d postpartum and supplied:
 360 mg Zn from Availa[®] Zn zinc amino acid complex, 200 mg Mn from Availa[®] Mn manganese amino acid complex,
 125 mg Cu from Availa[®] Cu copper amino acid complex and 12 mg Co from COPRO[®] cobalt glucoheptonate

^b Energy-corrected milk, 3.5% fat and 3.2% protein

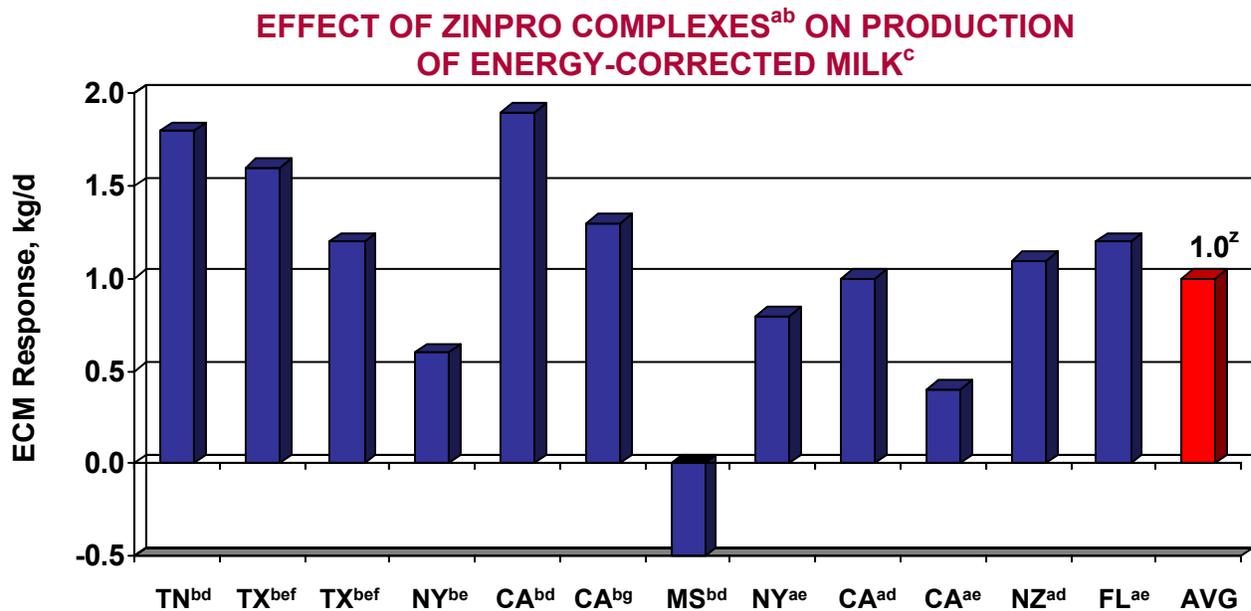
^c Fat-corrected milk, 3.5% fat

^d Data analysis only included the 162 cows assigned to treatment based upon age, calving date and previous production history

Complexed Trace Minerals and Milk Production

Numerous trials have evaluated the milk yield response to feeding either Zinpro *complexed zinc* or a combination of Zinpro *complexes* (2, 6, 10, 21, 26, 35, 36, 37, 49, 62, 63; Figure 12). The results of these studies indicate that feeding Zinpro *complexes* will result in an increase of total milk yield and total milk component yield (fat and protein). The milk response alone observed in these studies would indicate that producers would obtain a 4:1 return on their investment in supplementing Zinpro *complexes* such as Availa-4, without factoring any of the substantial benefits on reproduction, udder health and claw integrity.

Figure 12.



- ^a Availa[®] 4: Availa[®] Zn zinc amino acid complex, Availa[®] Mn manganese amino acid complex, Availa[®] Cu copper amino acid complex and COPRO[®] cobalt glucoheptonate
- ^b 4-Plex: ZINPRO[®] zinc methionine, MANPRO[®] manganese methionine, CuPLEX[®] copper lysine and COPRO cobalt glucoheptonate
- ^c Energy-corrected milk, 3.5% fat and 3.2% protein
- ^d Diet that contained Zinpro complexes supplied an additional 360 mg Zn/hd/d, 200 mg Mn/hd/d, 125 mg Cu/hd/d and 12 or 25 mg Co/hd/d
- ^e Diets contained similar concentrations of Zn, Mn, Cu and Co
- ^f Diets supplied 360 mg Zn/hd/d from ZINPRO zinc methionine
- ^g Diets supplied equivalent amounts of Zn, Mn and Cu, but the 4-Plex diet supplied an additional 13 mg Co/hd/d
- ^z Treatment effect (P<0.0001)

Developing Trace Mineral Status

Trace mineral deficiencies can have a dramatic impact on animal performance. In order to gain a better understanding of trace mineral status, body tissues (i.e. blood, liver, etc.) may be sampled. However, trace mineral content of some tissues may not be reflective of trace mineral status of the animal and may result in erroneous conclusions.

While blood is a suitable tissue to sample to assess iodine, iron (saturation of iron binding proteins) and selenium (glutathione peroxidase activity) status in cattle, it may not be an appropriate tissue to sample to assess status of other trace minerals (52; Table 6).

Liver is a better indicator of manganese and selenium status than blood (Table 6). Liver vitamin B₁₂ or a combination of serum vitamin B₁₂ and serum methylmalonic acid concentrations can be used to assess cobalt adequacy of the diet (52). Zinc concentration in liver is a better indicator of zinc status than serum or plasma zinc concentration, although zinc levels in liver are affected by bacterial infections, stress and life cycle stage (52).

Liver copper levels are a better indicator of copper status of the animal than serum copper levels. Serum copper levels are a poor indicator of copper status of the animal, as serum copper levels do not change significantly until liver copper stores are virtually depleted (52). Furthermore, copper present in serum may not be available to the animal. In situations where animals are consuming diets high in molybdenum and sulfur, one of the species of thiomolybdates that forms, MoOS₃²⁻, trithiomolybdate (TM₃), can be absorbed by the animal. The absorbed TM₃ binds to copper present in the serum, rendering it

unavailable to the animal. In addition to sampling liver to assess copper stores of the animals, sampling blood to determine ceruloplasmin levels may be prudent to determine copper availability.

Table 6. RELATIVE VALUE OF LIVER AND BLOOD IN ASSESSING TRACE MINERAL STATUS

Mineral	Blood		Liver
	Level	Enzyme/Function/Other	
Iodine	Interpret with caution	-	Not Acceptable
Iron	Interpret with caution	Erythrocytes, Iron Binding Capacity	Not Acceptable
Selenium	Interpret with caution	GSH-PX (Glutathione peroxidase)	Better than Blood
Chromium	?	Glucose Clearance, Insulin Sensitivity	?
Zinc	Interpret with caution	AP (Alkaline phosphatase), Metallothionein SOD (Superoxide dismutase),	Better than Blood
Copper	Not Acceptable, unless extremely low	Ceruloplasmin, SOD, Metallothionein	Acceptable
Manganese	Not Acceptable	-	Acceptable
Cobalt	Not Acceptable	Vitamin B ₁₂ , Methylmalonic acid	Vitamin B ₁₂ Level

Concluding Remarks

The function of trace minerals in reproduction and in overall animal performance is of considerable economic concern. While gross or major deficiencies may not be seen, lesser problems still may be serious in nature. Meeting the true trace mineral needs of the dairy cow requires knowledge of the animal's requirements. Additionally those factors that affect the availability of the needed minerals must also be considered. Adequate long-term trace mineral supplementation is required to maintain normal cellular activity, reproductive function, growth and development, and mammary and claw health. Improving overall trace mineral status by feeding highly bioavailable trace minerals, such as complexed trace minerals, is one way livestock producers can ensure that their cattle have adequate trace mineral status to help maximize health, fertility and productivity.

References

1. Andersson, R., and L. Leon. 2000. Zinpro Corporation Technical Bulletin, TB-D-4021
2. Ballantine, H. T. 2001 Zinpro Final Report.
3. Barker, A. R., F. N. Schrick, M. J. Lewis, H.H. Dowlen, and S. P. Oliver 1998. *J. Dairy Sci.* 81:1285-1290
4. Berg, J. N. 1984. Zinpro Technical Bulletin TB O-8549
5. Branum, J. C., G. E. Carstens, E. H. McPhail, K. W. McBride and A. B. Johnson. 1998. *J. Anim. Sci.* 76(Suppl.1):43
6. Bravo, J. L. 1997. Organic trace minerals in dairy cows. MS Thesis, Instituto Tecnológico Y De Estudios Superiores De Monterrey.
7. Brazel, F. K. 1993. *J. Dairy Sci.* 76(Suppl. 2):36
8. Brown, M.A., and E. R. Casillas. 1986. *Arch. Biochem. Biophys.* 244:719-726
9. Campbell, M. H. and J. K. Miller. 1998. *J. Dairy Sci.* 81:2693
10. Campbell, M. H., J. K. Miller and F. N. Schrick. 1999. *J. Dairy Sci.* 82:1019.
11. Capuco, A. V., S. A. Bright, J. W. Pankey, D. L. Wood, R. H. Miller, and J. Bitman. *J. Dairy Sci.* 75:2126.
12. Carson, R. L. 2000. *Proc. North Amer. Vet. Conf.* pp. 3,4
13. Cook-Mills, J. M. and P. J. Fraker. 1993. Nutrition Modulation of the Immune Responses. Susanna Cunningham-Rundles, ed.
14. Cousins, R. J., and J. M. Hempe. 1990. Zinc. pp. 251-260 Present Knowledge in Nutrition. M. L. Brown, ed. International Life Sciences Institute Nutrition Foundation, Washington, D.C.
15. Cromwell, G.L. 1997. Handbook of Copper Compounds and Applications. pp. 177-202
16. Cross, R. F. and C. F. Parker. 1981. *J. Anim. Vet. Med. Assoc.* 178:704
17. Corrah, L. 1996. *Anim. Feed Sci. Tech.* 59:61-70
18. Cullor, J. S. 1990. *Proc. Natl. Mastitis Council, Inc. and Am. Assoc. Bovine Pract.* pp. 176-180
19. Dallman, P. R. 1990. Iron. pp. 251-260 in Present Knowledge in Nutrition. M. L. Brown, ed. International Life
20. Duffy, J.H., J.B. Bingley, and L.Y. Cove. 1977. *Aust. Vet. J.* 53:519-522
21. Ecthebarne, M. 2000. Zinpro Technical Bulletin, TB-D-4018
22. Fetrow, J. and T. Blanchard. 1987. Economic impact of the use of prostaglandin to induce estrus in dairy cows. *J. Am. Vet. Med. Assoc.* 190:163-169
23. Galton, D. 1989. Zinpro Technical Bulletin, TB-8911.
24. Graham, T.W., M.C. Thurmond, F.C. Mohr, C.A. Holmberg and C.L. Keen. 1992. *FASEB* 6:A16810
25. Green, L. W., A. B. Johnson, J. Paterson and R. Ansotegui. 1998. *Feedstuffs* Vol. 70, No. 34
26. Griffith, L. 2000. Zinpro Technical Bulletin, TB-D-4019.
27. Guard, C. 1997. *Proc. North American Vet. Conf*
28. Hetzel, B. S. 1990. pp. 308-313 in Present Knowledge in Nutrition. M. L. Brown, ed. International Life Sciences Institute Nutrition Foundation, Washington, D.C.
29. Hidiroglou, M. 1979. *J. Dairy Sci.* 62:1195-1206
30. Hunt, S. M. and J. L. Groff. 1990. *Advanced Nutrition and Human Metabolism.* West Publishing Co. St. Paul, MN
31. Jones, C. A. 1995. Effect of zinc source on zinc retention and animal health. M.S. Thesis. University of Missouri-Columbia
32. Kappel, L. C., R. H. Ingraham and E. B. Morgan. 1984. *Am. J. Vet. Res.* 45:346-350
33. Keen, C. L. and S. Zidenberg-Cherr. 1990. Manganese. pp. 279-286 in Present Knowledge in Nutrition. M. L. Brown ed. International Life Sciences Institute Nutrition Foundation, Washington, D.C.
34. Kellogg, D. W. 1990. *Feedstuffs.* 62:35
35. Kellogg, D. W. 1994. Zinpro Technical Bulletin. TB D-9465
36. Kellogg, D. W. 1996. Zinpro Technical Bulletin. TB-D-4003
37. Kellogg, D. W. 1996. Zinpro Technical Bulletin. TB-D-4001
38. Mandebvu, P., K. C. Uchida, C. J. Sniffen, C. S. Ballard and M. P. Carter. 2000. *J. Dairy Sci.* 83(suppl. 1):303 abstr.
39. Mass, J. 1987. *Vet Clin. N. Amer. Food Anim. Pract.* 3:633-646
40. Miller, J. K., and K. Tillapaugh. 1967. *Cornell Feed Serv.* 62:11

41. Miller, J. K., N. Ramsey, and F. C. Madsen. 1988. The Ruminant Animal. D. C. Church, ed. pp. 342-400. Prentice Hall, Englewood Cliffs, NJ
42. Moore, C. L., P. M. Walker, M. A. Jones and J. M. Webb. 1988. J. Dairy Sci. 71(suppl.1): 152. Abstr.
43. Moore, D. A., J. S. Cullor, R. H. BonDurant and W. M. Sischo. 1991. Theriogenology 36:257-265
44. Moore, D. A. and M. L. O'Connor. 1993. Proc. Natl. Mastitis Council. pp. 162-166
45. Moynahan, E. J. 1981. Acrodermatitis enterpathica and the immunological role of zinc *in* Immunodermatology ed. B. Safai and R. A. Good. Plenum Medical Book Co., N.Y., N.Y.
46. National Research Council. 2001. Nutrient Requirements of Dairy Cattle. 7th rev. ed. Natl. Acad. Sci. Washington, D.C.
47. Nickerson, S. C. 1985. The teat's role in mastitis prevention. p. 18 National Mastitis Council Annual Meeting Proceedings
48. Nickerson, S. C. 1990. Defense mechanisms of the cow. p. 157 National Mastitis Council Annual Meeting Proceedings
49. Nocek, J. E. 1994. Zinpro Technical Bulletin, TB D-9460
50. Nocek, J. E., A. B. Johnson and M.T. Socha. 2000. J. Dairy Sci. 83:1553.
51. O'Dell, B. L. 1990. pp. 261-267 Present Knowledge in Nutrition. M. L. Brown, ed. International Life Sciences Institute Nutrition Foundation, Washington, D.C.
52. Puls, R. 1994. Mineral Levels in Animal Health. Diagnostic Data. 2nd Edition. Sherpa International, Clearbrook, BC, Canada
53. Rakes, A. H., J. W. Spears, and L. W. Whitlow. 1993. Inorganic trace minerals vs. organic trace mineral complexes for dairy cows. Zinpro Final Report
54. Risco, C. A., G. A. Donovan and J. Hernandez. 1999. J. Dairy Sci. 82: 1684
55. Smart, M. and N. F. Cymbaluk. 1997. Role of nutritional supplements in bovine lameness-review of nutritional toxicities. pp. 145 to 161 Lameness in Cattle. 3rd Edition. P. R. Greenough ed. W. B. Saunders Co., Philadelphia, PA
56. Smith, M. B., H. E. Amos and M. A. Froetschel. 1999. The Professional Animal Scientist 15:268.
57. Stoecker, B. J. 1990. Chromium. pp. 287-293 in Present Knowledge in Nutrition. M. L. Brown, ed. International Life Sciences Institute Nutrition Foundation, Washington, D.C.
58. TB-D-8602. 1986. WSU Research: Zinc Methionine Increases B-Carotene, Vitamin A Levels
59. TB B-9202-A. 1992. ZINPRO[®] zinc methionine and MANPRO[®] manganese methionine utilization in Cow/Calf studies: Three year summary
60. TB-D-4002. 1997. Effect of ZINPRO[®] zinc methionine on milk production and somatic cell count in high producing dairy cows in Israel
61. TB-D-4027. 2001. 4-Plex[®] helps transition cows offset effects of oxidative stress in Tennessee study.
62. Tomlinson, J. and S. Sneed. 2001. Zinpro Technical Bulletin, TB-D-4028.
63. Uchida, K, P. Mandebvu, C. S. Ballard, C. J. Sniffen and M. P. Carter. 2001. Anim. Feed Sci. Technol. 93:191-203
64. Weaver, A.K D., E. Toussaint-Raven, J.R. Egerton, P.R. Greenough, P. N. Demertizis, D. J. Peterse and A. Modrakowski. 1978. Skara, Sweden; Veterinary Institute, p. 113
65. Wedekind, K. J., A. E. Horton and D. H. Baker. 1992. J. Anim. Sci. 70:178
66. Wellington, B. K., J. A. Patterson, C. K. Swenson, R. P. Ansotegui, P. G. Hatfield, and A. B. Johnson. 1998. Proc. West Sect. Amer. Soc. Anim. Sci. 49:323
67. Wirth, J. J., P. J. Fraker and F. Kierszenbaum. 1984. J. Nutr. 114:1826