INTERACTIONS AMONG THE TRACE MINERALS

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RESUMO

INTERAÇÕES ENTRE OS MINERAIS-TRAÇO

Embora existam pelo menos 50 interações conhecidas entre 27 elementos, muitas delas são de pouca importância prática para os criadores. Os animais que consomem dietas completas em sistemas de confinamento não deveriam apresentar problemas metabólicos resultantes de interação entre minerais, exceto em casos de acidentes de suplementação, ou por contaminação ou por erros na mistura dos ingredientes. Os ruminantes sob pastejo estão mais sujeitos aos sinais de intoxicação ou de deficiência, causados por interações entre minerais. Os problemas comuns como a interação do molibdênio, cobre e enxofre são bem conhecidos e apresentam uma extensa documentação em termos de pesquisa. No entanto, o conhecimento de um problema e sua aplicação prática nem sempre são recíprocos. O consumo de quantidades necessárias de um determinado suplemento mineral não pode ser assegurado a todos os indivíduos de um rebanho em pastejo e, conseqüentemente, os problemas advindos de interações são ainda observados em condições de campo. A ênfase corrente na literatura científica sobre produção animal nos Estados Unidos no tocante a interações minerais-traço tem levado em conta o efeito da enzima fitase e o fósforo orgânico na utilização do ferro, zinco e cobre. Experimentos que investigam a interação entre cobre e molibdênio têm sido também relatados nos últimos anos. É provável que, futuramente, a maior parte das pesquisas com minerais esteja direcionada para as funções metabólicas de elementos, com auxílio de técnicas da biologia molecular, em detrimento de ensaios de alimentação com animais. Presume-se que os ensaios simples de alimentação que unicamente avaliam crescimento e conversão alimentar vão se tornar atividades superadas.

PALAVRAS-CHAVE: Minerais-traço, alimentação, rebanho.

SUMMARY

Although there are at least fifty interactions known among twenty-seven elements, many are of little practical importance to livestock producers. Animals consuming complete diets in confinement systems should not experience metabolic problems resulting from common mineral interactions except in the case of accidental over supplementation through contamination or errors in mixing at the feed mill. Grazing ruminants are more prone to signs of toxicosis or deficiency resulting from mineral interactions. The common problems such as the molybdenum, copper, and sulfur interrelationship are widely known and have extensive research documentation; however, knowledge concerning a problem and the practical application thereof are not always mutual. Consumption of needed quantities of mineral supplements cannot be guaranteed by every individual within a grazing herd of livestock and, consequently, problems arising from interactions are still observed under field conditions.

The current emphasis in the scientific livestock production literature in the U.S. regarding trace mineral interactions has concerned the effect of phytase enzyme and organic phosphorus on utilization of iron, zinc and copper. Experiments investigating the interaction between copper and molybdenum were also reported during the last few years. In the future, the majority of mineral research will probably center around the metabolic roles of the elements making use of numerous molecular biology techniques rather than feeding trials with animals. Simple feeding trials reporting only growth and feed conversion will probably become a thing of the past.

KEY WORDS: Trace minerals, feeding, livestock

INTRODUCTION

Animal nutritionists would probably agree that all dietary nutrients are interrelated to some degree and that there is an optimal concentration for each nutrient in relation to the levels of all others to obtain the most efficient desired animal response. The requirement for optimal nutrient concentrations is important both within the intestinal tract and at the cellular level. Nutrient requirements are sometimes expressed as the mean requeriments for various classes of animals so that nutritionists sometimes include a margin of safety during times of stressful conditions. However, we need to keep in mind that life is a dynamic, complex process and consequently basic nutrient requirements are constantly shifting, especially within a growing animal or a female that is reproducing. Although there may be one ideal amount of each nutrient under each particular set of physiological and enviromental circumstances, apparently there is a certain range of overlapping dietary concentrations within which any individual nutrient can vary and animal performance will not be influenced detectably.

Minerals are much more likely to interact than other nutrients due to their lability and tendency to form chemical bonds. Certain of the nutrient interrelationships are more crucial to producers and, thus, have been recognized and become the subject of research by animal nutritionists. Others which are less critical, either economically or under practical feeding conditions, may not have been recognized yet and/or deemed unimportant in practical terms and therefore have stimulated very little investigation.

MECHANISMS OF INTERACTIONS

The term “interaction” is defined by O’Dell (1997) as “interrelationships among mineral elements as revealed by physiological or biochemical consequences”. There are two major classes of interactions, positive or synergistic, and negative or antagonistic. Georgievskii (1982) described 16 synergistic interactions among 15 of the required mineral elements. There may be a direct interaction between elements in structural processes such as the necessity for copper along with iron for hemoglobin formation, the interaction of manganese with zinc in the proper conformational shape of RNA molecules in the liver, or the roles of calcium and phosphorus together in the formation of bone hydroxyapatite. Interactions can also occur as the result of simultaneous participation of elements at the active center of enzymes, such as iron and molybdenum in xanthine oxidase or copper and iron in cytochrome oxidase. Some enzyme systems may be activated by more than one ion interchangeably, for example, magnesium or manganese in pyruvate carboxylase. Elements may react with others through functions of the endocrine organs, expressing their effect on the metabolism of other minerals. Iodine is needed for formation of the hormone thyroxine which will increase metabolic processes and, consequently, drive the positive rate of retention for elements such as magnesium and potassium in the body.

Antagonistic interactions are often expressed as a mutual inhibition of absorption from the intestinal tract. These negative relationships are more plentiful in nature. Georgievskii (1982) listed 26 antagonistic interactions among 15 of the required elements. These phenomena tend to be easier to identify experimentally as well as in practice because typical signs of deficiency for one mineral will result if either the concentration of the conflicting element is high enough or length of feeding period is long enough. Ideally, antagonistic effects are overcome by higher concentrations of the inhibited ion. For example, elevated dietary calcium can induce a deficiency of zinc in swine, especially if there is a borderline deficiency of zinc from the use of plant proteins in the diet. Some of these antagonistic interactions may have beneficial effects from the standpoint of practical nutrition. The amount of molybdenum in the diet can be increased to counteract toxic effects of copper in sheep.

There are several ways in which antagonistic relationships can occur within the gastrointestinal tract. The simplest involves a chemical reaction forming an insoluble complex between minerals such as copper and sulfur to form copper sulfide or a mineral and another dietary component such as zinc combined with phytic acid to form phytate. Mineral elements can also be adsorbed onto the surface of colloidal particles, as are manganese and iron onto the surface of magnesium or aluminum salts. Competition between minerals such as cobalt and iron for carriers in the intestinal wall has also been observed. Finally, some ions, incluing boron and lead have inhibitory effects on processes such as oxidative phosphorylation in the intestinal wall or on the activity of some enzymes which interfere with the breakdown of feed ingredients and liberation of inorganic ions for absorption.

On the cellular level there can also be antagonistic processes resulting in formation of insoluble complexes like the formation of copper thiomolybdates from copper, molybdenum and sulfur. There can be a competition among ions for the active centers in enzyme systems as occurs with magnesium and manganese in alkaline phosphatase. Competition for binding sites on carrier proteins in blood has been observed with zinc competing with iron for the transport protein, transferrin. Antagonistic effects have been reported whereby one ion will activate an enzyme and another will cause inhibition as with magnesium and calcium with ATPase. Minerals may also work in competition by activating enzyme systems with opposite effects. Copper activates ascorbate oxidase which oxidizes ascorbic acid versus activation by zinc and manganese of lactonases which promote synthesis of the vitamin.

Mineral interactions may be multiple as in the case of copper-molybdenum-sulfur or one-on-one as observed with molybdenum and tungsten. Interactions may be one-way, such as the negative effect of zinc on copper, in which the reverse effect is not observed. Reciprocal interrelationships are also found in which both elements influence the metabolism of the other. The negative interactions which exist between zinc and iron would be an example.

One popular theory of mineral interactions based on chemical and physical properties of the elements was proposed by Hill and Matrone (1970). Ions with similar ionic size or electron configurations of their outer orbitals are likely to interact competitively. Most of the recognized essential trace elements are in the first transition series in the Periodic Table and have unfilled 3*d* orbitals. Elements in the second and third series have unfilled 4*d* and 5*d* orbitals, respectively. Molybdenum and tungsten both have similar chemical properties and tungsten does, indeed, interfere with the function of molybdenum as might be expected. Unfortunamentely, this system is far from foolproof and has provided researchers with many surprises in the past.

INTERACTION EXPERIMENTS

The elucidation of mineral interrelationships represents an increasingly complex research problem for nutritionists. One of the first relationships of nutritional significance between minerals was that observed between calcium and phosphorus. Considerable research has been conducted with these minerals since there is a major interaction between them which is quite evident under either laboratory or practical feeding considerations. In addition, without dietary supplementation phosphorus is very often a limiting nutrient and there are more known functions for this element in normal cell metabolism than any other mineral. The commercial availability of phytase enzyme form genetically-engineered microorganisms has placed the study of the interaction between calcium and phosphorus back on the forefront of current mineral research. Phytase included in diets for swine and poultry allows these species to make use of a portion of organic phosphorus in dietary ingredientes and, thus, decrease the amount of supplemental inorganic phosphorus needed. Research on energy-enhancing benefit of phytase for his M. S. research back in 1972 (Miles and Nelson, 1974). However, environmental concerns of eutrophication coupled with advances in molecular biology so that the enzyme can be produced more economically by *Aspergillus niger* have renewed research in this area of mineral metabolism.

Although interactions among elements comprise a fascinating area of study for scientists, they are almost equally as frustrating. It is not too difficult to study the interaction between calcium and phosphorus, but it becomes increasingly complicated when we recognize that magnesium is related to the two elements and also iron to phosphorus, copper to iron, molybdenum to copper, sulfur to both copper and molybdenum and so forth. In 1965, Ammerman reported 28 known interactions among 16 mineral elements. In 1979, Miller expanded this list to include 39 interactions among 22 elements (Ammerman and Henry, 1982). Recently, O'Dell and Sunde (1997) included at least 52 interactions among 27 elements. A human nutrition text on micronutrients listed 70 total interactions among 15 essential mineral elements and 11 vitamins (Berdanier, 1998). Of that total, 37 were mineral – mineral interactions.

A primary way in which mineral interrelationships are studied is through the use of a factorial arrangement of dietary treatments. As can be seen in Table 1, the number of treatments involved soon becomes unmanageable as the number of mineral elements or other nutrient factors is increased. With only two dietary levels for each of seven nutrient factors, 128 treatments would be required in an individual experiment. The number of pens required to study interactions is also given based on a minimum of three pens per treatment. An experiment with three factors would require 24 pens, while that with four factors would require 48 pens. Those numbers can easily be accommodated with two Petersime brooders for work with chicks, but would become more difficult with ruminants. According to statisticians, ideally, there should be at least as many replications of a single treatment as there are dietary treatments in an experimental design. Following this regimen would require 64 pens or cages to conduct a 2 x 2 x 2 factorial arrangement, not the 24 indicated in Table 1.

Perhaps even more limiting than the number of treatments and replicates required is the difficulty of making meaningful interpretations of experimental results as the number of nutrients is increased. The use of fractional factorial arrangement of treatments can reduce the total number of complexity of the interpretation of results. These difficulties in conducting experiments on the interaction of nutrients undoubtedly explain the observation that seldom are more than two or three minerals studied within an experiment and that these studies are generally conducted with poultry or laboratory animals.

A survey of mineral research published in the *Journal of Dairy Science, Journal of Animal Science, Poultry Science* and the *Journal of Nutrition* was reported by Ammerman and Henry (1982) for the years 1954, 1964, and 1981 and this early review was updated to include 1998 as shown in Table 2. Invention of the atomic absorption spectrophotometer by Walsh in 1955, allowing simple, rapid determination of cations, heralded a meteoric rise in mineral research as seen

TABLE 1. Dietary treatments required to study interactions using a factorial arrangement with two levels of each factor.

Dietary factors	Treatments required	Pens required at 3/treatment
2	4	12
3	8	24
4	16	48
5	32	96
6	64	192
7	128	

TABLE 2. Survey of mineral papers reported in four years[a]

	Year			
	1954[b]	1964[b]	1981[b]	1998
Total number	40	80	116	59
One factor, %	66	66	75	91
Two factors, %	21	21	22	9
Three or four factors, %	13	13	3	0
Phytase papers	0	0	0	5
Cell culture papers	0	0	0	8

(a) *Journal of Dairy Science, Journal of Animal Science, Poultry Science* and *Journal of Nutrition.*
(b) Ammerman and Henry (1982).

by a doubling of the number of research papers between 1954 and 1964. The total numbers of papers continued to increase in 1981, but declined sharply in 1998. Does this mean that mineral research has become less important to the animal industry? Perhaps so, although it is also likely that mineral work is now reported in specialty publications such as *Biological Trace Mineral Research* or journals more specific to the feed industry such as *Animal Feed Science and Technology.* In either case, the trend showing very limited work with more than two dietary factors continues even more strongly today despite newer statistical computer programs available to help interpret data. The percentage of experiments including two mineral elements as dietary treatments dropped from 21% in 1954 to 9% in 1998, while those making use of three or four elements decreased from 13% to zero (Table 2). Five papers using phytase enzyme as a dietary factor and, indirectly, dietary phosphorus are also reported as a separate category which was not included in the percentages calculated. A very noticeable change in mineral research comes in the form of experiments making use of cell cultures rather than animal feeding trials. The eight papers of this nature found in 1998 were all in the *Journal of Nutrition.* Government regulations now mandate alternative research methods to animal experimentation, essencially involving work conducted at public universities, be used whenever possible and we will continue to see many advances in this area.

TRACE MINERAL INTERRELATIONSHIPS

Despite the fact that numerous mineral interactions have been documented in the literature during the last half century, livestock producers making use of confinement production systems in the U.S. should not encounter practical problems when feeding complete diets. The National Research Council made allowances for the common mineral interrelationships when estimating the nutrient requirements for all species. The use of a new ingredient which has not been adequately characterized or a mixing error at the feed mill would be the most likely scenarios to precipitate mineral-related problems in a confinement production system. Accidental contamination of feed ingredients has also occurred when grain was transported in a contaminated railroad car or truck.

Mineral interactions may become a more practical consideration with grazing ruminants. It is not difficult to formulate mineral supplements to compliment available forages; however, there is no guarantee that every individual within a given herd will consume a sufficient quantity of a supplement to assure optimal performance. Thus, signs of mineral deficiencies may appear despite our knowledge to prevent their occurrence. Various economical, political and sociological factors may make mineral interactions and resulting deficiencies more of a practical problem overseas. We’ve known that iodine supplementation will prevent goiter for almost one hundred years, yet 220 million people worldwide are still afflicted with this condition. In 1990, the World Health Organization estimated that 1 billion people in developing countries were at risk of iodine deficiency disorders.

Currently in the U.S., perhaps the most likely place to encounter inefficient performance or health problems in livestock caused by mineral interactions would be in the case of the horse. Many horse owners do not have a livestock-related background or education. Tradition and hearsay, rather than science, seem to determine the diet of many performance horses. Owners will often spend exorbitant sums for various supplemental nutritional products based on testimonials from other horse owners, but without any scientific evidence of efficacy or safety. Presently, the Internet has allowed these recommendations to be publicized on a world-wide basis, greatly bolstering sales of these products. The desire to improve scores during competitive events often outweighs common sense. Adding “farm chemistry”, ie, “if a little is good, more is better”, to the desire to win can be a dangerous combination resulting in poor health, crippling injuries and occasional death of the animal from imbalances and over supplementation on the part of well-meaning horse owners. For example, a friend recently asked about an expensive mineral supplement which she was feeding her Morgan gelding. There was nothing wrong with this supplement from the standpoint of formulation. However, rather than following the label instructions to add a tablespoon to the feed daily, this individual was hanging a bucket of the highly palatable, grain-based product on the fence and allowing free-choice access. When it was pointed out that all minerals were potentially toxic at high levels, the answer was a simple, “I didn’t know that, they’re supposed to be good for you!!”.

The rising interest in promoting better health and living through “health foods”, nutritional supplements, and nutraceuticals for the human population may very well also lead to more mineral interaction problems and nutrient deficiencies in the future. For example, dental caries resulting from fluoride deficiency is on the rise in the children of healh-conscious families who have been consuming “healthier” bottled water rather than their local fluoridated water supply.

The trace mineral manufacturing business is adjunctly, a mineral recovery industry making use of many byproducts. Tribasic copper chloride recovered from metal etchings has been shown to be a highly available source of copper and has some beneficial physical characteristics making it a safe, effective substitute for copper sulfate in animal diets. Some of the byproducts of the galvanizing industry include zinc-iron and iron-zinc compounds. These products may contain 20% iron, but only 10 – 14% zinc. When used as a source of zinc in a feed formula, a limit should be put on the total concentration of iron because this element will also be present in many dicalcium phosphates and can potentiate a problem with iron toxicosis. In addition, it has been reported that use of iron sulfate as a flocculating agent in the offal and meat meal industry can add significant amounts of iron to diets using these ingredients. It is preferable to have a complete mineral analysis of any new ingredient used at the feed mill, rather than a quick check on calcium and phosphorus. Adequate quality control of mineral products is also essential for mineral supplement manufactures. There have been cases in which a compound thought to be zinc sulfate was purchased, but was in actuality zinc metal mixed with iron sulfate. Chemical analysis would have detected zinc and sulfur, but the product is essentially worthless as a suplemental source of zinc for animals. The same can be said about organic mineral sources. Most of these products sold in the U.S. come from reputable companies and are manufactured in accordance with strict AAFCO guidelines, resulting in highly available sources of trace elements. It would not be difficult, however, to mix meat meal with copper oxide to make an “organic” product which will assay a correct concentration of copper and nitrogen, but is essentially worthless as a source of copper. It could require x-ray diffraction and polarographic or gel chromotographic methods to detect some of these fraudulent products, rather than atomic spectroscopy generally used in mineral analysis.

COBALT

There has been relatively little research done on cobalt as this element is incorporated into the vitamin B12 molecule to exert a metabolic function. However, iron and cobalt mutually inhibit the absorption of each other, apparently due to a shared intestinal carrier system (Thomson et al., 1971).

COPPER

Copper is affected negatively by excess dietary zinc and iron, as well as the copper-molybdenum-sulfur inteaction. Early studies with rats demonstrated that high dietary zinc induced signs of copper deficiency (Smith and Larson, 1946; vanReen, 1953; Magee and Matone, 1960). Effects were reversed by supplementation with copper. High dietary concentrations of zinc will induce synthesis of metallothinein protein in the intestinal cells to protect the animal against zinc toxicosis. Copper has a higher affinity for the protein than zinc and it was speculated originally to cause a secondary copper deficiency. However Reeves et al. (1993) did not find a positive correlation between the amount of zinc-induced metallothionein and concentration of copper in intestinal mucosa of rats. Similar effects on copper transport were reported using high zinc concentrations in human cell culture media (Reeves et al., 1996). Adverse effects on copper metabolism have also been observed in chicks when copper was limiting and zinc was supplemented at concentrations slightly above the dietary requirement (O'Dell, 1967). Excess dietary zinc in sheep decreased feed intake and daily gain which was restored with additional copper supplementation (Rosa et al., 1986). A similar effect was also observed in that experiment on liver and serum copper concentrations. Wellington et al. (1998) reported a 59% decrease in liver copper in heifers given 612 mg/day zinc for 90 days.

Supplementation of swine with 123 ppm zinc in a diet containing 14 ppm copper decreased absorption of copper from 4.0 to 1.8 mg/day (Adeola et al., 1995). In the same experiment, addition of 1.500 units/kg diet of microbial phytase also increased absorption of copper from 2.4 mg/day. In broiler chicks, supplementing the diet with 600 units phytase/kg increased serum copper concentration, but decreased retention of copper when the diet contained 9 ppm copper (Sebastian et al., 1996). Phytase at 600 units/kg did not improve copper utilization from either soybean meal or cottonseed meal for chicks (Aoyagi and Baker, 1995).

A high concentration of dietary iron in the presence of required amounts of copper and zinc caused a slight depression in daily gain of sheep and this effect was greatly exacerbated rather than ameliorated by high dietary copper. The combination of both elements caused a zinc deficiency complicated by copper toxicosis (Rosa et al, 1986). Hepatic copper and iron concentrations were greatly elevated with essentially no change in liver zinc. Addition of high dietary zinc improved daily again and greatly reduced liver copper and iron levels. Addition of 600 ppm iron to a copper-deficient diet for calves did not further decrease plasma copper or ceruloplasmin (Gengelbach et al., 1997). Crowe and Morgan (1996) reported elevated liver and brain iron concentrations when copper was simultaneously supplemented to rats along with added iron.

An interaction of major importance in ruminant animals is that among copper, molybdenum and sulfur. In 1954, Dick indicated that inorganic sulfate was important in the copper-molybdenum. Suttle (1973) reported that either the inorganic or organic form of sulfur was effective and total dietary sulfur was the appropriate value to consider in calculations. Molybdenum becomes less dependent upon sulfur for its adverse effect as the level of dietary molybdenum increases. Sulfur also exerts an independent effect on copper absorption through the formation of insoluble copper sulfide, CuS, in the rumen and other sections of the gastrointestinal tract. A combination of dietary molybdenum and endogenous sulfide in the rumen results in formation of tetrathiomolybdate or oxythiomolybdates, which react with copper to form insoluble complexes (Mason et al., 1980). A recent study made use of this three-way interaction to reduce ruminal hydrogen sulfide associated with polioencephalomalacia (Loneragan et al., 1998). These authors reported that liver copper was depressed with addition of 100 ppm added dietary molybdenum, but 30% of the animals still had dangerously elevated concentrations of hydrogen sulfide. Intravenous injection of tetrathiomolybdate will also impair copper utilization (Gooneratne et al., 1981) and has been used as a treatment and prophylactic for copper toxicosis.

A dietary ratio of Cu:Mo has been proposed to prevent copper deficiency or molybdenum toxicosis. Militmore and Mason (1971) suggested a ratio greater than 2:1 to prevent copper deficiency in cattle. Alloway (1973) indicated a Cu:Mo ratio nearer 4:1 was necessary to prevent copper deficiency signs in sheep. In an experiment concerning various immune factors, heifers were supplemented at a Cu:Mo ratio of 0.4:1 with sulfur at 0.3% (Arthington et al., 1996). Liver copper, plasma copper, and ceruloplasmin concentrations were all significantly decreased by about 75 days on the study. Gengelbach et al. (1997) also studied the relationship of copper deficiency with immune function in cattle. Supplementation of a basal diet containing 4.5 ppm copper, 0.3% sulfur and 1.5 ppm molybdenum with 5 ppm molybdenum, decreased plasma copper, ceruloplasmin, and Cu, Zn-superoxide dismutase activity compared to calves supplemented with 10 ppm copper. In a study with feedlot steers given a basal diet containing approximately 5 ppm copper and 1 ppm molybdenum, supplementation with 5 ppm molybdenum decreased plasma copper and ceruloplasmin concentrations. This effect was overcome with addition of 5 ppm copper (Ward and Spears, 1997). However, liver copper concentrations decreased despite the added dietary copper.

IRON

Iron is another trace element which is adversely affected by both inorganic phosphorus and phytate. In a recent experiment with chicks, the utilization of iron in soybean meal was not improved by addition of 1,430 units/kg of phytase in iron-deficient diets (Biehl et al., 1997). Increasing dietary calcium and/or phosphorus decreased iron absorption in chicks (Sell, 1965). Excessive dietary manganese decreased hemoglobin in young lambs (Hartman et al., 1955) and young chicks (Baker and Halpin, 1991). There is a synergistic effect of copper on iron as the copper containing enzyme ceruloplasmin catalyzes the oxidation of Fe^{+2} to Fe^{+3} which is necessary for binding to transferrin to take place for transport of iron in plasma. Mobilization of iron from storage sites in mucosa and liver does not occur at a normal rate during copper deficiency with resulting anemia observed as a consequence. On the other hand, elevated dietary concentrations of copper (120 to 240 ppm) decreased liver iron concentrations in swine by 50 to 60% (Bradley et al., 1983).

There are locations in the world where iron intakes are increased due to excessively high levels in the water. Also, there are areas where an increased iron intake in the form of soil in combination with low dietary phosphorus levels may contribute to inefficient performance of grazing ruminants. The adverse effects of high dietary levels of iron can be overcome to some extent by increasing the level of dietary phosphorus. Additional phosphorus above that usually considered to be required helped to overcome the depressing effect of excess iron on both gain and feed conversion in steers given high iron (Standish et al., 1971). Supplemental phosphorus also decreased iron accumulation in the liver. High dietary iron decreased liver phosphorus, copper and zinc concentrations in that study. Addition of 0.25% phosphorus to a diet containing 0.17% phosphorus and 760 ppm added iron, decreased liver iron deposition in lambs, but kidney iron concentration was not affected (Rosa et al., 1982).

There is a mutual inhibitory interaction between iron and zinc. Part of this effect may take the form of excess zinc inhibiting absorption of copper with a resulting copper deficiency causing the iron deficiency anemia. There is also a direct inhibitory effect of zinc on cellular uptake of iron (O'Dell, 1967). Rosa et al. (1986) reported a decrease in daily gain of sheep supplemented with 1000 ppm zinc and normal dietary iron, but this depression was virtually overcome by addition of 1000 ppm iron to the diet. Little change in concentrations of either mineral in liver was reported.

MANGANESE

Non-heme iron shares a mutual inhibition pathway with manganese in rats (Thomson and Valberg, 1972), but this effect was not observed in chicks (Baker and Halpin, 1991). In addition, manganese competes with iron for binding sites on the plasma iron carrier protein transferrin, inhibiting mobilization and transport of iron (Davidsson et al., 1989). Excess dietary phosphorus, and to a lesser extent, calcium have an antagonistic effect on absorption of manganese in swine, poultry and dairy calves (Henry, 1995). Dietary phytate has also been reported to inhibit absorption of manganese (Halpin and Baker, 1986).

SELENIUM

The interrelationship between selenium and vitamin E is not within the scope of this paper, but is one of the more widely researched practical interactions in animal nutrition. The major mineral interactions with selenium of practical importance involve iodine and sulfur. Selenium can replace sulfur in amino acids such as cysteine and methionine which are then incorporated into body proteins. Selenium may be absorbed via the pathways for these amino acids. Selenium is also an integral part of the enzyme thyroxin 5'-deiodinase, which converts thyroxin (T4) to triiodothyronine (T3), the more active form of the hormone (Arthur, 1992). Selenium deficiency blocks the thyroid feedback-control system resulting in larger goiters than if iodine alone were deficient. Heifers grazing marginally selenium-deficient pastures supplemented with intraruminal selenium pellets had decreased T4 and increased T3 concentrations (Wichtel et al., 1996).

At excessive pharmacological concentrations copper and zinc (Jensen, 1975), iron, cadmium, mercury, silver, and arsenic have been reported to interfere with utilization of selenium, but these interactions are highly unlikely to be of any practical importance to the nutritionist (Henry and Ammerman, 1995).

ZINC

In the 1950s, the association between zinc deficiency and parakeratosis in swine was established (Tuker and Salmon, 1955). The phytate found in plant proteins was shown to have a profound effect on zinc absorption and a molar ratio of phytate: zinc in excess of 15 was considered a risk for deficiency of the element (Davies and Olpin, 1979). The importance of calcium (Oberleas et al., 1966) in the formation of insoluble complexes with zinc and phytate led to inclusion of this macro element in the equation. A molar ratio of (calcium x phytate): zinc in excess of 3.5 was associated with significant growth depression (Davies et al., 1985). In a more recent experiment, increasing dietary addition of calcium from 0.6 to 1.0 and 1.25 in a diet containing approximately 50 ppm zinc, decreased feed intake, body weight, and tibia zinc concentrations in broiler chicks, which were not improved by addition of 600 units phytase/kg (Sebastian et al., 1996).

Of all the required elements, zinc has been shown to form the most stable complexes with phytate at a physiological pH of 7.0 (Maddaiah et al., 1964; Maenz et al., 1996). A pH 4.0 in the media, the inhibitory potency of zinc and iron on phytase activity was decreased. Zinc absorption and retention were improved when 1,500 units phytase/kg were added to diets for swine (Adeola et al., 1995). Addition of 600 units phytase/kg to a diet for chicks containing 20 ppm zinc increased zinc concentration in toe and tibia but not liver (Yi et al., 1996). Roberson and Edwards (1994) also reported increased bone zinc concentration in chicks fed 35 ppm zinc when 600 units phytase/kg were added to the diet.

Although high dietary concentrations of zinc affect copper absorption, the reverse interaction does not occur. Rosa et al. (1986) saw no detrimental effect of performance or tissue zinc concentrations of sheep given 40 ppm Cu for 56 days in a diet containing 50 ppm zinc. Addition of 1000 ppm iron to the normal zinc diet also had a minimal effect on tissue zinc concentrations. Apgar et al. (1995) reported no change in liver or kidney zinc concentrations of swine supplemented with as much as 200 ppm added copper as either copper sulfate or copper lysine for 35 days.

OTHERS

Zinc (Hahn and Evans, 1975) and phytate (Chen et al., 1973) have been reported to decrease absorption of chromium. As mentioned previously, tungsten is a potent inhibitor of molybdenum uptake and transport which can be incorporated into molybdenum-proteins to make them nonfunctional, although the interaction has little practical importance (Johnson, 1997). It appears that nickel may share a common absorptive pathway with iron. Increasing dietary iron decreased toxicosis of nickel in chicks (Hill, 1981). Other interactions mentioned for nickel in a recent review include calcium, chromium, cobalt, copper, iodine, iron, mangesium, manganese, molybdenum, phosphorus, potassium, sodium, and zinc (Eder and Kirchgessner, 1997). The toxicity of lead may be sodium, and zinc (Eder and Kirchgessner, 1997). The toxicity of lead may be reduced by dietary inclusion of calcium, iron, magnesium and phosphorus (Reichlmayr-Lais and Kirchgessner, 1997). Calcium (Jowsey and Riggs, 1987) and magnesium (Cerklewski, 1987) decrease absorption of fluoride in the small intestine.

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