Reevaluation of the Metabolic Essentiality of the Minerals* - Review -

J. W. Spears[1]
Department of Animal Science, North Carolina State University, Raleigh, NC 27695-7621, USA

ABSTRACT : Essential metabolic functions have been identified for seven macrominerals (calcium, phosphorus, magnesium, sodium, potassium, chloride, and sulfur), and eight microminerals (cobalt, copper, iodine, iron, manganese, molybdenum, selenium, and zinc). Major functions for each of these minerals are summarized. Considerable research suggests that chromium is also essential and that it functions by facilitating insulin activity. Studies are reviewed which indicate that chromium supplementation of animal diets may: 1) increase glucose removal from blood, 2) reduce carcass fat and increase lean in nonruminants, 3) alter egg cholesterol content, and 4) enhance immunity and disease resistance in ruminants. A number of other minerals including nickel, boron, vanadium, arsenic, silicon, lithum, and lead have been reported to be essential, but specific metabolic functions have not been defined for any of these elements. Limited research in poultry suggests that boron may be of practical significance in some instances. (*Asian-Aus. J. Anim. Sci. 1999. Vol. 12, No. 6 : 1002-1008*)

Key Words : Minerals, Macrominerals, Microminerals, Chromium, Boron

INTRODUCTION

Minerals are required for the normal functioning of essentially all biochemical processes in the body. An essential mineral can be defined as one that is required to support adequate growth, reproduction and health throughout the life cycle, when all other nutrients are optimal (O'Dell and Sunde, 1997). Based on identification of one or more metabolic functions, at least 15 minerals can be classified as essential. A deficiency of each essential macro or micromineral in animals results in abnormalities that can only be corrected by supplementation of the deficient mineral. The severity of the deficiency will determine the extent and type of abnormality observed.

This paper will not attempt to cover all minerals but will be a review of selected minerals where advances have occurred in recent years.

MACROMINERALS

Seven macrominerals are required by animals. Metabolic functions of the macrominerals are summarized in table 1.

Phosphorus deficiency in ruminants grazing forage continues to be a major problem in many countries (McDowell, 1997). However, in areas of intensive animal production environmental concerns have grown regarding excretion of phosphorus in animal waste. Much of the phosphorus in cereal grains and other feedstuffs of plant origin are in the form of phytate phosphorus. In ruminant animals, phytase, produced by microorganisms in the rumen, hydrolyzes phytate, releasing phosphorus in an available form. However, phytate phosphorus is of very low bioavailability in nonruminants. Considerable research has indicated that addition of microbial phytase to nonruminant diets increases bioavailability of phosphorus (Jongbloed and Lenis, 1992). Use of phytase in diets reduces the need for supplemental phosphorus, and therefore, greatly reduces the excretion of phosphorus in waste.

Many of the functions of sodium, potassium, and chloride are interrelated. Research has indicated that formulating diets for a given cation-anion or electrolyte balance [milliequivalents (mEq) Na+K-Cl] may optimize animal performance. Body weight gain was maximized in chicks fed diets containing an electrolyte balance of 25 mEq/100 g of diet (Mongin, 1981). In growing and finishing swine, fed in high ambient temperature, increasing electrolyte balance from 2.5 up to 40 mEq/100 g of diet resulted in a linear improvement in gain and feed intake (Haydon et al., 1990). Increasing electrolyte balance in sow diets from 13 to 25 mEq/100 g of diet tended to improve 21-day pig weights (Dove and Haydon, 1994). Based on studies with feedlot cattle, the optimal electrolyte balance in growing and finishing diets is between 15 and 30 mEq/100 g of diet (Ross et al., 1994a, b). Electrolyte balance has been extensively studied in dry and lactating dairy cows, and a number of responses have been observed (Block, 1994).

MICROMINERALS

One or more metabolic functions have been

[1] Address reprint request to J. W. Spears. Tel: 919-515-4008 or 2763, Fax: 919-515-4463. E-mail: jerry.Spears@ncsu.edu.
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Table 1. Important metabolic functions of macrominerals

Mineral	Functions
Calcium	Bone mineralization
	Metabolic regulation (cell signaling)
	Blood clotting
	Muscle contraction
	Transmission of nerve impulses
Phosphorus	Bone mineralization
	Component of RNA and DNA
	Component of high energy compounds (ATP, etc.)
	Regulation of key regulatory enzymes
	Component of phospholipids
Magnesium	Cofactor for over 300 enzymes
	Component of bone
	Involved in neuromuscular activity
Sodium	Regulation of osmotic pressure
	Nerve conduction
	Active transport of nutrients
	Regulation of acid-base balance
	Muscle contraction
	Control of water balance
Chloride	Regulation of osmotic pressure
	Regulation of acid-base balance
	Control of water balance
	Formation of HCl in gastric juice
Potassium	Regulation of acid-base balance
	Regulation of osmotic pressure
	Muscle contraction
	Nerve impulse transmission
	Control of water balance
Sulfur	Component of sulfur amino acids
	Component of thiamin and biotin
	Component of sulfated mucopolysaccharides
	Involved in detoxication reactions

Table 2. Important metabolic functions of microminerals

Mineral	Function(s)
Cobalt	· Component of vitamin B_{12}
Copper	· Component of numerous enzymes (lysyl oxidase, ceruloplasmin, tyrosinase, cytochrome oxidase, superoxide dismutase, etc.)
Iodine	· Component of thyroid hormones (thyroxine, triiodothyronine)
Iron	· Oxygen transport and storage (hemoglobin, myoglobin)
	· Electron transport
	· Component of numerous enzymes (catalase, tryptophan 5-monoxygenase, phenylalanine 4-monoxygenase, aconitase, etc.)
Manganese	· Enzyme component (pyruvate carboxylase, arginase, mitochondrial superoxide dismutase)
	· Enzyme activator (glycosyl transferases)
Molybdenum	· Enzyme component (xanthine oxidase, sulfite oxidase, aldehyde oxidase
Selenium	· Enzyme component (glutathione peroxidase, type 1 iodothyronine deiodinase)
Zinc	· Component of over 70 enzymes (alcohol dehydrogenase, DNA polymerase, RNA polymerase, carbonic anhydrase, carboxypeptidase A & B, pyruvate dehydrogenase, etc.)
	· Gene expression
	· Membrane stability

described for copper, cobalt, iodine, iron, manganese, molybdenum, selenium, and zinc (table 2). An array of evidence also suggest that chromium is an essential minerals (Offenbacher et al., 1997) and chromium will be discussed in more detail in a subsequent section. A number of other minerals including nickel, vanadium, arsenic, boron, silicon, lithium, and lead have been reported to be essential, based on the occurrence of deficiency signs in animals fed experimental diets low in these minerals. However, a specific metabolic function in animals has not been identified for any of these minerals. Microbial functions have been identified for nickel and these may affect performance of ruminants via effects on rumen fermentation. Nickel is required for the enzyme urease produced by ureolytic bacteria (Spears, 1984) and for factor F_{430}, a coenzyme, found in methanogenic bacteria (Oscar and Spears, 1989).

In recent years, the importance of certain trace minerals in immune function has become increasingly evident. Selenium, copper, zinc, cobalt, and iron have been shown to alter various components of the immune system (Suttle and Jones, 1989). Reduced disease resistance has been observed in animals deficient in selenium (Stable and Spears, 1993; Larsen et al., 1997), copper (Suttle and Jones, 1989), and cobalt (MacPherson et al., 1989). Recent studies have indicated that dietary chromium may affect immunity and disease resistance (see chromium section).

Zinc has been found to be a component of over 70 enzymes present in mammalian tissues. However, it has been difficult to explain many of the signs of severe zinc deficiency based on reduced activity of zinc requiring enzymes (Bettger and O'Dell, 1981). Recent research has indicated that zinc is involved in gene expression and a number of transcriptional regulators have been shown to contain zinc (Chesters, 1997). Alterations in gene expression can explain reduced growth and many of the abnormalities seen in zinc deficiency.

Glutathione peroxidase was identified as the first known selenium metalloenzyme in 1973 (Rotruck et

al., 1973). This enzyme catalyzes the reduction of hydrogen peroxide and lipid hydroperoxides, thus preventing oxidative damage to body tissues. A second selenometalloenzyme, type 1 iodothyronine-5-deiodinase, was recently identified (Arthur et al., 1990). This enzyme catalyzes the deiodination of thyroxine (T_4) to the more metabolically active triiodothyronine (T_3) in tissues. Arthur et al. (1988) reported that selenium-deficient cattle had increased T_4 and decreased T_3 concentrations in plasma relative to selenium-supplemented cattle. Depressed activity of iodothyronine-5'-deiodinase may explain the unthriftiness and poor growth sometimes observed in selenium deficiency (Wichtel et al., 1996).

Chromium

Early studies by Schwartz and Mertz (1959) indicated that chromium was an essential component of a glucose tolerance factor that corrected impaired glucose metabolism in rats fed certain diets. Later research showed that chromium functioned as a potentiator of insulin action (Offenbacher et al., 1997).

Chromium bioavailability from most feedstuffs is extremely low. However, until recently, practical diets fed to domestic animals were assumed to provide sufficient chromium to meet animal requirements. In the past six years a number of published reports have indicated that chromium supplementation of diets can affect animal metabolism and production criteria as well as the composition of animal products produced. A review of animal studies with chromium was published recently (NRC, 1997).

The addition of chromium picolinate to diets of ruminating calves (Bunting et al., 1994) and growing pigs (Amoikon et al., 1995), increased glucose clearance rate following intravenous glucose administration (table 3). In both of these studies, chromium supplementation also increased glucose removal from blood following intravenous administration of insulin.

Table 3. Effect of chromium picolinate on glucose clearance after intravenous glucose challenge in calves and pigs[a]

	Treatment	
	Control	Chromium picolinate[e]
Glucose clearance rate, %/min		
Calves[b]	1.98[d]	2.66[e]
Pigs[c]	4.98[d]	6.54[e]

[a] Chromium was added to provide 370 and 200 ppb of supplemental chromium in calves and pigs, respectively.
[b] From Bunting et al. (1994).
[c] From Amoikon et al. (1995).
[d,e] Mean in a row with unlike superscripts differ ($p<0.05$).

Research in nonruminants has indicated that chromium supplementation in the form of chromium picolinate may increase carcass lean and decrease carcass fat. Page et al. (1993) reported that the addition of 100 to 800 ppb of chromium, from chromium picolinate, reduced backfat, and increased longissimus muscle area and percentage of muscling in growing-finishing pigs (table 4). Dressing percentage also tended to be improved by chromium. Other studies also have indicated reduced backfat in growing-finishing pigs fed supplemental chromium (Lindemann et al., 1995; Min et al., 1997). Mooney and Cromwell (1995) reported that supplementing 200 ppb of chromium (from chromium picolinate) to growing-finishing pig diets increased accretion of protein and reduced accretion of fat.

Table 4. Effect of chromium picolinate on carcass traits in growing-finishing pigs[a]

	Supplemental chromium[b] (ppb)				
	0	100	200	400	800
10th rib fat, cm[c]	3.15	2.34	2.63	2.20	2.46
Longissimus muscle area, cm[c]	34.0	40.4	39.9	41.7	40.3
Percentage of muscling[c]	51.7	56.1	54.7	57.4	56.2
Dressing percentage[d]	65.9	66.4	67.4	68.1	68.0

[a] From Page et al. (1993).
[b] Supplemented as chromium picolinate.
[c] Quadratic effect of chromium ($p<0.01$).
[d] Quadratic effect of chromium ($p<0.09$).

Feeding broilers chromium picolinate for six weeks altered carcass composition (Kim et al., 1996). Carcass protein was increased in broilers supplemented with 100 to 400 ppb of chromium but not in those fed 600 or 800 ppb of chromium (table 5). Percent fat in carcass was lower while percent ash was higher in chicks supplemented with chromium. Consistent with the observed reductions in carcass fat, adipose tissue obtained from chicks (Kim et al., 1996) and pigs (Min et al., 1997) fed supplemental chromium had a higher *in vitro* rate of lipolysis than tissue from control animals. *In vitro* lipogenic activity was lower in adipose tissue from chicks (Kim et al., 1996) and tended to be lower in adipose tissue of pigs (Min et al., 1997) supplemented with chromium picolinate. The mechanism whereby chromium increases carcass protein and reduces fat is unclear. The increased protein accretion could relate to the ability of chromium to enhance insulin activity. However, increased insulin activity also would be expected to increase fat deposition.

Table 5. Carcass composition of broiler chicks fed varying levels of dietary chromium[a]

	Supplemental chromium[b] (ppb)					
	0	100	200	400	600	800
Crude protein, %	43.1	43.9	44.1	44.5	40.4	42.1
Ether extract, %	50.3	44.4	43.9	43.4	47.8	48.1
Crude ash, %	5.7	7.2	6.4	7.0	7.0	6.4

[a] From Kim et al. (1996).
[b] Supplemented as chromium picolinate.

There is less evidence that dietary chromium affects carcass composition in ruminants. Lambs fed 250 ppb of supplemental chromium from chromium picolinate had 18% less fat over the 10th rib than controls (Kitchalong et al., 1995). However, chromium picolinate supplementation to provide 500 or 1000 ppb of chromium did not affect backfat or carcass composition in feedlot lambs (Olsen et al., 1996). Similarity, feeding steers 200 ppb of chromium in the form of high chromium yeast did not affect carcass characteristics or protein and fat content of rib sections (Chang et al., 1992).

Supplementing Single Comb White Leghorn hen diets with 800 ppb of chromium (from chromium picolinate) reduced serum and egg yolk cholesterol concentrations (table 6; Lien et al., 1996). Egg yolk cholesterol tended to be reduced by lower levels (200 or 400 ppb) of chromium. Egg production was not affected by treatment but chromium supplementation tended to reduce egg weights slightly. In brown layers of the Shaver breed, chromium picolinate supplementation did not affect egg production, egg weight or crude protein and ether extract content of eggs (Kim et al., 1997).

Table 6. Effect of chromium supplementation on egg production and serum and egg yolk cholesterol[a]

Item	Supplemental chromium[b] (ppb)			
	0	200	400	800
Egg production, %	81.2	79.4	81.4	79.0
Egg weight, g	68.5[c]	60.6[d]	66.0[f]	64.5[cd]
Yolk cholesterol, mg/g	23.1[c]	19.9[c]	16.5[cd]	15.3[d]
Serum cholesterol, mg/dl	122.8[c]	125.2[c]	114.3[c]	75.4[d]

[a] From Lein et al. (1996).
[b] Supplemented as chromium picolinate.
[cd] Mean in a row with unlike superscripts differ ($p<0.05$).

Growth and feed efficiency responses to chromium supplementation have been highly variable. Page et al. (1993) found that the addition of 200 ppb of chromium increased gain in one of three experiments with growing-finishing pigs. Mooney and Cromwell (1995) reported improved gain in growing-finishing pigs supplemented with 200 ppb of chromium from chromium picolinate. A number of chromium sources including chromium chloride, chromium nicotinic acid complex, and chromium picolinate tended to increase gain and feed intake in nursery pigs (van Heugten and Spears, 1997). In nursery pigs injected with lipopolysaccharide to induce stress, chromium supplementation did not improve performance (van Heugten and Spears, 1997). Feed efficiency of broilers was improved by the addition of 200 ppb of chromium from chromium picolinate (Kim et al., 1995).

Dietary chromium also may affect reproductive performance in swine. Gilts fed 200 ppb of chromium (from picolinate) throughout growth and gestation had larger litters than controls (Lindemann et al., 1995). Litter weights also were heavier for chromium-supplemented sows at birth and at 21 days of age.

Considerable research has indicated that chromium can affect immune response and disease resistance in cattle. Dietary chromium effects on humoral immunity have been evaluated by measuring specific antibody production following administration of either a foreign protein or a vaccine. Dairy cows supplemented with 500 ppb of chromium, from an amino acid chelate, had greater primary and secondary antibody responses to ovalbumin than control cows (Burton et al., 1993). In calves that had been stressed, due to shipping and feed restriction, chromium supplementation from high chromium yeast increased primary but not secondary antibody responses to human red blood cells (Moonsie-Shageer and Mowat, 1993). In contrast, Kegley et al. (1997) reported that chromium supplementation from a chromium nicotinic acid complex did not affect antibody response to porcine red blood cell immunization in stressed cattle. Similarly, in young calves fed milk diets neither chromium chloride or chromium nicotinic acid complex enhanced specific antibody responses to porcine red blood cells (Kegley et al., 1996). Supplemental chromium, as an amino acid chelate, increased antibody titers to bovine rhinotracheitis virus but not to parainfluenza virus type 3 following immunization using a commercial vaccine (Burton et al., 1994).

Studies have investigated the effect of dietary chromium on cell mediated immunity by measuring the ability of isolated lymphocytes to proliferate in response to mitogen stimulation. Lymphocytes isolated from dairy cows supplemented with a chromium amino acid chelate, from 6 weeks prepartum through 16 weeks postpartum, had increased blastogenic responses to concanavalin A stimulation (Burton et al., 1993). In stressed calves, chromium supplementation, from an amino acid chelate, increased concanavalin A induced

lymphocyte blastogenesis in calves showing signs of morbidity but not in calves with normal body temperature and no visual signs of sickness (Chang et al., 1994). Other studies in cattle have reported no effect of chromium supplementation on mitogen stimulated lymphocyte blastogenesis (Kegley and Spears, 1995; Kegley et al., 1996; Arthington et al., 1997).

Effects of chromium on cell mediated immunity have also been evaluated *in vivo* by measuring inflammatory responses following percutaneous application of dinitrochlorobenzene or intradermal injection of phytohemagglutinin (PHA). In stressed calves that had been sensitized to dinitrochlorobenzene, chromium supplementation did not affect responses to dinitrochlorobenzene application (Moonsie-Shageer and Mowat, 1993; Kegley et al., 1997). Supplementation of either chromium chloride or a chromium nicotinic acid complex increased inflammatory responses to intradermal injection of PHA in young calves fed milk (Kegley et al., 1996).

Studies with cattle that had been stressed due to shipping indicate that chromium supplementation may alleviate effects of stress on animal performance and health. Incidence of respiratory disease is frequently high in stressed calves. Chromium supplementation of stressed calves has reduced morbidity following shipping (Mowat et al., 1993; Moonsie-Shageer and Mowat, 1993). Table 7 shows results of a study by Mowat et al. (1993). Supplementing stressed steers with a high chromium yeast or a chromium amino acid chelate reduced morbidity and improved feed efficiency during a 35-day period following shipping and marketing. Wright et al. (1994) reported no effect of chromium supplementation on morbidity but chromium-supplemented calves that required treatment had fewer relapses than control calves during a 28-day period following shipping. Chromium addition to diets of stressed calves has also improved or at least tended to improve rate of body weight gain in some studies (Moonsie-shageer and Mowat, 1993; Wright et al., 1994). Chromium picolinate supplementation of dairy cows during the last 9 weeks of pregnancy reduced incidence of retained placenta after parturition from 56 to 16% (Vallalobos-F et al., 1997).

Effects of dietary chromium on physiological responses of calves to an experimental disease challenge also have been evaluated. Chromium has been supplemented for 49 to 75 days prior to disease challenge in these studies. Kegley et al. (1996) inoculated young calves, fed milk diets, intranasally, with infectious bovine rhinotracheitis virus followed by *Pasteurella hemolytica*, intratracheally, 5 days later. Calves supplemented with 400 ppb of a chromium nicotinic acid complex or inorganic chromium chloride tended to have lower body temperatures at certain time points following the viral and bacterial challenges than control calves. Supplementing calves with 400 ppb of chromium (chromium nicotinic acid complex) for 56 days prior to shipping did not affect body temperature or feed intake responses to an intranasal infectious bovine rhinotracheitis viral challenge (Kegley et al., 1997). However, chromium supplementation did increase body weight gain after the disease challenge. Rectal temperature responses were also not affected by chromium supplementation (high chromium yeast) in calves inoculated with bovine herpesvirus-1 (Arthington et al., 1997).

Table 7. Effect of chromium on morbidity and performance of stressed feeder calves[a]

Item	Treatment[b]		
	Control	Cr-yeast	Chelated-Cr
Morbidity, %	55.6	33.3	11.1
Daily gain, kg	0.62	0.71	0.70
Feed intake, kg/d	4.03	4.10	4.41
Gain/feed	0.147[c]	0.169[d]	0.157[cd]

[a] From Mowat et al. (1993).
[b] Chromium was supplied from a high chromium yeast or from an amino acid chelate.
[cd] Means in a row with unlike superscripts differ ($p<0.05$).

Boron

Boron was shown to be essential for plants in 1923 (Nielsen, 1997). More recent studies suggest that boron is also essential for animals (Nielsen, 1997). However, the function of boron is unknown.

Limited research suggests that boron may have practical significance in certain situations. The addition of 5 ppm of boron to a corn-soybean meal based diet increased body weight of male but not female broilers (table 8; Rossi et al., 1993). Tibia weight and breaking load were increased by 5 ppm of supplemental boron in both sexes. Percent ash was not significantly affected by boron. Higher levels of boron supplementation were also tested but they appeared to be less effective than the 5 ppm level.

In ovo administration of 150 $\mu\ell$ of boron into turkey embryos on day 15 of embryogenesis increased embryonic weights, tibial length, and bone ash at 26 days of embryogenesis (King et al., 1993). At hatching, boron increased bone ash but did not affect body weight. In a relatively short term study, Brown et al. (1989) found that boron supplementation increased calcium and magnesium retention in lambs.

Future studies are needed to define the metabolic role of boron and to determine if boron supplementation can affect performance or health of domestic animals.

Table 8. Effect of supplemental boron on performance and tibia characteristics of broilers to 21 days of age[a]

	Supplemental boron[b] (ppm)				
	0	5	40	80	120
Body weight, g					
Males	586[c]	647[d]	637[cd]	612[cd]	612[cd]
Females	564	579	568	547	553
Feed intake	850	884	880	846	799
Feed:gain	1.48[c]	1.44[cd]	1.46[cd]	1.46[cd]	1.37[d]
Tibia					
Weight, g	1.52[c]	1.77[d]	1.66[cd]	1.68[cd]	1.64[cd]
Breaking load, kg	9.1[c]	11.2[d]	10.1[cd]	9.7[cd]	9.7[cd]
Ash, %	45.8	46.5	46.7	47.0	47.1

[a]From Rossi et al. (1993).
[b]Supplemented as boric acid.
[cd]Means in a row with unlike superscripts differ ($p<0.05$).

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