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Review

Chromium in Livestock Nutrition: A Review

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In the last two decades livestock nutritionists have been dealing not only with how to improve production efficiency, but also how to improve the nutritional profile of livestock and livestock products. Recently there has been considerable research interest in the utilization of chromium in livestock feed. Beneficial effects of chromium in human health are well documented and include a role in the maintenance of normal blood and sugar cholesterol levels. Chromium is a naturally occurring heavy metal commonly found in the trivalent state (Cr^{3+}) and the hexavalent state (Cr^{4+}). The hexavalent state compounds have been implicated in occupational carcinogen among workers in chrome plating, stainless steel and pigment industries. This paper looks at the nutritional benefits of chromium in the diet of livestock. Studies have shown that chromium is involved in glucose metabolism where it plays a vital role in the auto amplification mechanisms of insulin signaling. Chromium has also been shown to improve immune function. Chromium alters immune response by immunostimulatory or immunosuppressive processes as shown by its effects on T and B lymphocytes, macrophages, cytokine production and immune responses that may induce hypersensitivity reactions. Chromium has been shown to have positive effects on egg production, egg quality and egg cholesterol levels in laying hens. Chromium has also been shown to play a key role in lipid, protein and nucleic acid metabolism in livestock. In ruminants, chromium positively affects milk production in cows and has a profound effect on calf growth. In swine, chromium has been shown to have a positive effect on growth and carcass composition. Organic sources of chromium have been found to be highly bioavailable. Generally, chromium supplementation has been shown to alleviate the negative effects of stress by improving the performance and health of livestock leading to better farm profitability.

Keywords: Trivalent chromium, glucose, lipid, protein and nucleic acid metabolism, immune response and immune function, egg production, egg cholesterol levels, milk production, calf growth, carcass composition, stress alleviation.

INTRODUCTION

Interest in chromium as an essential nutrient for livestock in manipulating growth performance and improving carcass composition has been reported as early in the 1960s. Chromium was first reported as an essential mineral in rats (Schwartz and Mertz, 1959) and was demonstrated as an essential mineral for humans (Jeejebhoy *et al.*, 1977). The

major focus of chromium research was on the association between chromium and diabetes mellitus.

Chromium stands 21st in abundance among the minerals of the earth's crust. Theoretically, chromium may occur in all oxidation states from -2 to +6, however, it is often found in the trivalent and hexavalent forms. Trivalent chromium (Cr^{3+}) is the most stable oxidation state in which chromium is found in living organisms and is considered to be a highly safe form of chromium (Lindeman, 1996). Hexavalent chromium is mostly of industrial origin and is usually associated with chromium toxicity. Studies by Davis and Vincent (1997) have shown that the primary role of chromium in metabolism is in the area of enhancing glucose uptake by living tissues. It has also been shown that chromium activates certain enzymes and stabilizes proteins and nucleic acids (Anderson, 1994). Chromium supplementation reduces the negative effects of environmental stress (Sahin *et al*., 2001; Mowat, 1994; Lien *et al*., 1999). Chromium, as an integral component of the glucose tolerance factor (GTF), helps control appetite, hypoglycemia and protein uptake and plays a protective role against heart disease and diabetes (Mertz, 1993). NRC (1997) recommends supplemental dietary chromium for animals undergoing environmental stress. NRC (1995) has recommended 300µg chromium per kg of the diet for laboratory animals.

Chromium is usually not considered as an essential trace mineral for poultry; however studies (Sands and Smith, 1999) have provided evidence that suggests a nutritional and physiological role of chromium as a micronutrient in poultry nutrition. The beneficial effects of chromium can be observed more efficiently under environmental, dietary and hormonal stress. NRC (1989) has recommended an intake of 50-200ppb of trivalent chromium for adult humans. Currently there are no NRC recommendations for chromium in poultry diets (NRC, 1994). In ruminants, supplementation of chromium is recommended during heat stress periods, early lactation and during infections. A level of 4-5mg/head/day of supplemental chromium during the last three weeks pre-partum and 5-6 mg/head/day of supplemental chromium during the first few weeks post-partum may suffice. However there is emerging evidence to suggest that pigs and poultry may have a dietary requirement for chromium that exceeds that found in corn-soya meal diets. Recent findings on the positive effects of chromium supplementation for pigs on carcass quality and on reproductive parameters have been quite impressive. Published research (Uyanik, *et al*., 2002; Toghyani, *et al*., 2012; Rao, *et al*., 2012) has shown the beneficial effects of chromium supplementation in the diets of poultry on carcass traits, immune responses, oxidative parameters and reduction of heat stress.

Sources of Trivalent Chromium

The major organic sources of chromium include chromium propionate, chromium picolinate, chromium nicotinate and high chromium yeast. Organic source of chromium is over ten times more bio-available than inorganic sources (Lyons, 1994). Comparative studies of Cr^{3+} picolinate and niacin-bound Cr^{3+}, which are two very popular dietary supplements, reveal that Cr^{3+} picolinate produces significantly more oxidative stress and DNA damage Research findings have implicated the toxicity of chromium picolinate in renal impairment, skin blisters, pustules, anemia, hemolysis, tissue edema, liver dysfunction, neuronal cell injury, enhanced production of hydroxyl radicals, chromosomal aberration and DNA damage (Bagchi, *et al*., 2002). Studies have also shown that chromium picolinate can be mutagenic and a picolinic acid moiety has been shown to be responsible for a clastogenic effect of picolinic acid in the absence of chromium (Steams, *et al*., 1995). Chromium propionate obtained from the Kemin Industries Inc. USA, has been approved as an acceptable additive for swine feed by US Food and Drug Administration. Studies on genotoxicity (Anon, 2007) showed the non-toxic effect of chromium picolinate. Significant differences in the levels of responses are known depending on the source of chromium. Studies in pigs (Mathews, *et al*., 1997) have shown significant different metabolic responses with chromium propionate supplementation when compared to the same responses when chromium picolinate is used as a supplement; this demonstrates excellent and reliable bioavailability.

Role of Chromium in Metabolism

Glucose metabolism

Chromodulin is a low molecular weight chromium binding substance and is assumed to be involved in the metabolism of glucose. Chromodulin is an oligopeptide which occurs naturally and is made up of glycine, cysteine, aspartate and glutamate (Yamamoto, *et al*., 1987). Chromodulin binds chromic ions in response to an insulin-mediated chromic ion influx and the metal saturated oligopeptide is then able to become bound to an insulin stimulated insulin receptor which activates the receptor's tyrosine kinase activity. Chromodulin thus appears to play a role in the auto amplification mechanism of insulin signaling (Vincent, 2000). Chromodulin binds four equivalents of Cr^{3+}, despite its low molecular weight and small size. It is believed to carry chromium into the urine after the intake of large doses of chromium in both the trivalent and hexavalent forms (Wada, *et al*., 1983) and can therefore assist in detoxification. Chromodulin has been shown to activate the tyrosine kinase activity of an insulin-activated insulin receptor (Davis *et al*., 1997; Davis and Vincent, 1997) and also to activate membrane phosphotyrosine phosphatase found in adipocyte membranes (Davis *et al*., 1996). Research findings (Davis

and Vincent, 1997) have shown that the addition of bovine liver Chromodulin to rat adipocyte membranes in the presence of 100nM-insulin results I an eight-fold stimulation of insulin-dependent protein tyrosine kinase activity, while no activity was observed in the absence of insulin. Chromium deficiency is found to cause a reduction in insulin sensitivity in the peripheral tissues as well as a decrease in growth rate (Linderman, 1996). The mechanism by which Chromodulin takes part in insulin signaling has been proposed by Vincent (2000). According to his proposal, apochromodulin is stored in insulin sensitive cells. As a response to increases in blood insulin concentrations, insulin binds to its receptor, bringing about conformational changes that result in the autophosphorylation of tyrosine residues present on the internal side of the receptor. This process transforms the receptor into an active tyrosine kinase and transmits the signal from insulin into the cell. In response to insulin concentrations, chromium is moved from the blood to insulin sensitive cells. Here the chromium flux results in the binding of apochromodulin with chromium forming holochromodulin, which then binds to the receptor assisting in the maintenance of the receptor in its active form, this amplifies the receptor's kinase activity. When the signaling is to be turned off, a decrease in blood insulin facilitates relaxation of the conformation of the receptor and the holochromodulin is excreted from the cells into the blood stream, thus Chromodulin is efficiently excreted in the urine. The Fe^{+}-transport protein (transferrin) has been shown to be responsible for maintaining Cr^{3+} levels in the blood plasma and for transporting chromium to tissues in an insulin-responsive manner (Vincent, 2000; Clodfelder *et al*., 2001). The mode of chromium action in enhancing insulin sensitivity may also be explained by its effect on increasing membrane fluidity and the rate of insulin internalization (Evans and Bowman, 1992). Moderate increases in plasma membrane fluidity have also been shown to increase glucose transport, also it has been shown that basal glucose transport is not fully active in fat cells, this can be increased by raising membrane fluidity (Pitch *et al*, 1980). The antidiabetic drug metformin has been shown to enhance insulin action by increasing membrane fluidity (Muller *et al*., 1997; Wiernsperger, 1999). As has been observed after chromium treatment (Cefalu *et al*., 2002), metformin treatment has been shown to increase Glucose Transporter 4 (GLUT4) translocation (Hundal et al., 1992; Pryor et al., 2000). It has been hypothesized that chromium enhances GLUT4 translocation through a cholesterol dependent mechanism. Plasma membrane cholesterol content has been shown to diminish in cells exposed to chromium and exogenous cholesterol replenishment was found to render the enhancement of insulin action by chromium ineffective (Chen *et al*., 2006).

Lipid metabolism

Chromium has been observed to increase the synthesis of fats in adipose tissues and decrease the net release. This is assumed to be through a linkage of Chromodulin with the insulin receptor and the increase glucose flux into the adipocyte. Chromium is also found to influence the metabolism of cholesterol and triglycerides; however the mechanism has not been fully established. It is assumed to occur by processes similar to the action of the antidiabetic drug metformin. Research findings (Zhou *et al*., 2001) have shown that metformin activates 5_-AMP-activated kinase (AMPK) and the metformin stimulated AMPK activity suppresses the expression of a sterol regulatory element binding protein SREBP-1 which belongs to a family of key lipogenic transcription factors directly involved in the expression of more than 30 genes involved in the synthesis and uptake of cholesterol, fatty acids, triglycerides and phospholipids, as well as the NADPH cofactor required for the synthesis of these compounds (Brown and Goldstein, 1997).

Protein metabolism

Increased amino acid and glucose uptake by skeletal muscles of rats incubated with chromium has been demonstrated (Evans and Bowman, 1992). This increase in uptake of these nutrients is associated with the alteration of insulin parameters which is dependent on chromium. It has been observed (Roginski and Mertz, 1969) that chromium supplementation increases amino acid uptake by tissues and also intensifies the incorporation of amino acids into the proteins of the heart in rats.

Nucleic acid metabolism

Chromium in the trivalent state is assumed to be involved in the structural integrity and expression of genetic information in animals. Chromium protects RNA against heat denaturation. Chromium participates in gene expression by binding chromatin, causing an increase in initiation loci and consequently, an increase in RNA synthesis. An interaction of chromium with DNA templates that resulted in a significant stimulation of RNA synthesis in vitro has been observed (Okada *et al*., 1982). During in vitro studies, chromium is believed to have a role in nucleic acid metabolism due to an increase in stimulation of amino acid incorporation into liver (Weser and Koolman, 1969).

Chromium and Stress

The effect of chromium in relieving stress has been well documented. Stress factors stimulate the hypothalamus leading to the production of corticotrophin releasing factor,

which stimulates the pituitary to produce adrenocorticotropic hormones, which in turn stimulates the adrenal cortex to increase the production and release of corticosterone (Siegel, 1995). Corticoids depress the immune system function and reduce serum protein concentrations. Blood glucose concentration is also increased and there is reduction in glucose utilization by peripheral tissues, thus functioning as insulin antagonists. Chromium is known to influence the secretion of corticosteroids. A number of reports have confirmed decreased sensitivity to stress in animals fed chromium supplements as a result of reduced concentrations of cortisol in the blood (Chang and Mowat, 1992; Moonsie-Shageer and Mowat, 1993; Pechova *et al*., 2002). It has also been observed that all-stress inducing factors enhance chromium excretion in the urine (Mowat, 1994).

Chromium and Immune Function

Chromium is an essential nutrient required to promote the action of insulin in body tissues so that the body can metabolize the major nutrient molecules in living cells. Chromium is of importance in altering the immune response by immunostimulatory or immunosuppressive processes as shown by its effects on T and B lymphocytes, macrophages, cytokine production and immune responses that may induce hypersensitivity reactions (Shrivastava *et al*., 2002; Borella *et al*., 1990; Glaser *et al*., 1985; Boscolo *et al*., 2000; Burton *et al*., 1993; van de Ligt *et al*., 2002).

Chromium in Poultry

Egg production and egg quality

Supplementation of poultry diet with chromium has been shown to positively affect egg production and performance in laying birds (Sahin *et al*., 2001; Sahin *et al*., 2002).The beneficial effects of chromium could be more efficiently noticed in conditions of dietary, environmental and hormonal stresses. It has been shown that chromium supplementation alleviates the detrimental effects of cold stress especially in laying hens reared under low ambient temperatures (Sahin and Sahin, 2002). In a similar vein the egg production and egg quality of laying Japanese quails reared under heat stress, were found to be improved by chromium supplementation (Sahin *et al*., 2002). A threshold of 100-200ppb of chromium has been recommended as an optimum requirement for enhanced egg production in layers (Southern and Page, 1994). An increase of 5.3% in egg production at doses of 100ppb and a reduction in egg production at doses of 400ppb and above has been observed (Southern and Page, 1994). Few studies have recommended higher doses of chromium (Sahin and Sahin, 2002; Sahin *et al*., 2001). Other studies (Odgaard and Greaves, 2001) have also suggested optimum doses of between 100 and 200 ppb chromium propionate as a livestock feed supplement. Variation in the optimum dosage of chromium is as a result of the different sources of chromium and the experimental conditions. Chromium supplementation in laying Japanese quails reared under heat stress was found to improve feed efficiency (Sahin *et al*., 2002). Studies by Uyanik *et al*. (2002) have shown improved efficiency of feed utilization by laying hens with supplementation of chromium as chromium chloride. Research findings (Sahin *et al*., 2001) have shown improved egg quality traits such as specific gravity, eggshell thickness, eggshell weight and Haugh unit, with chromium supplementation in the diets of laying hens reared under low ambient temperatures. In a similar vein, Sahin *et al*. (2002) observed improved egg quality traits in laying Japanese quails exposed to heat stress. However Lien *et al*. (1996) reported that shell thickness was not affected by chromium picolinate supplementation under thermally neutral conditions. Other studies (Southern and Page, 1994) observed that chromium supplementation did not affect significantly egg quality traits such as Haugh units and specific gravity, this could suggest that marked beneficial effects of chromium on egg quality is observed only under conditions of stress. Chromium supplementation markedly decreased blood cholesterol concentrations in Japanese quail under thermo neutral zones (Sahin *et al*., 2001). A lowering trend in egg cholesterol levels was also observed in hens when the diets were supplemented with 100 or 200ppb organic chromium (Southern and Page, 1994). Sahin *et al* (2002) have shown a significant reduction in serum corticosterone levels in laying Japanese quails supplemented with chromium. Sahin *et al*. (2001) found that chromium supplementation increased serum insulin concentration while markedly decreasing corticosterone concentration in laying hens reared under low ambient temperatures.

Broiler performance

Studies have revealed that heat stress has detrimental effects on the performance of broilers reducing feed intake and the growth rate and also affecting feed efficiency, carcass quality and the general health of the birds (Carmen et al., 1991; Yahav *et al*., 1996; Temim *et al*., 2000; Har *et al*., 2000). Chronic heat stress affects the time to reach market weight, since growth rate is affected; heat stress also increases the rate of mortality. Chromium supplementation has been shown to alleviate the adverse effects associated with heat stress in broilers. Chromium supplementation has also been shown to improve body weight gain and feed efficiency in broilers under conditions of heat stress (Sands and Smith, 1999). An increase in body weight gain and feed intake of broilers under heat stress when supplemented with chromium has been reported (Toghyani *et al*., 2006). The authors also observed an increase in carcass yield and a decrease in abdominal fats. Increase in carcass yield and decrease in

abdominal fat content in broilers has been observed when the diet of broilers was supplemented with chromium picolinate (Sahin *et al*., 2003) or with high chromium yeast (Debski *et al*., 2004). A decrease in weight gain and feed efficiency in broilers reared under heat stress conditions was alleviated by dietary chromium supplementation (Sahin *et al*., 2003). Chromium supplementation has been observed to improve feed conversion ratio by 6.2% (Zhang et al., 2002). It has been observed (Rosebrough and Steele, 1981) that turkeys fed diets supplemented with chromium had greater liver glycogen levels as a result of the increased activity of the enzyme glycogen synthetase and also chromium increased glucose transport by increasing insulin activity. Kim *et al*. (1995) reported increased HDL cholesterol and decreased total serum cholesterol in the diets of broilers supplemented with chromium. Some authors (Sands and Smith, 2002) however did not observe significant differences in serum cholesterol levels in broilers fed chromium supplemented diets. Anandhi *et al*. (2006) observed a significant reduction in breast and thigh muscle cholesterol levels and an increase in breast and thigh muscle protein levels in broilers fed diets supplemented with chromium. Chromium supplementation has been shown to decrease serum corticosterone and cholesterol levels in broilers reared under heat stress (Sahin *et.al*, 2002).

Chromium in Ruminants

Milk production

During the early lactation stages, high producing dairy cows are subjected to tremendous pressure and stress. This results in a negative energy balance, increased production of non esterified fatty acids (NEFA) and β-hydroxybutyric acid (BHBA) in the blood stream resulting in ketosis and other metabolic disorders leading to stress. Supplementation of the diets with chromium has been shown to be beneficial during such periods. Several studies (Debras *et al*., 1989; Prior and Christenson, 1978; Sano *et al*., 1991) have shown that insulin resistance begins before parturition and continues during early lactation. Thus, during periparturition, insulin resistance may be an important factor in the establishment of catabolic activities (Holstenius, 1993). In a study (Subiyatno *et al*., 1996), it was observed that supplementation with organic chromium at 0.5ppm in primiparous cows improved glucose tolerance and milk yield and reduced blood cortisol, NEFA and BHBA levels in the blood. It has been shown (Burton *et al*., 1994; Mallard *et al*., 1994; Chang *et al*., 1996), that supplementation with chromium reduced blood cortisol concentrations and improved immunological activities in transition dairy cows. Supplementing diets with organic chromium increased milk yield by 11% during the first 14 weeks of lactation in first parity cows (Yang *et al*., 1996). Chromium supplementation tends to increase dry matter intake in first parity cows during the first 4-6 weeks postpartum. Dairy cattle provided chromium in the form of chromium propionate, eat more feed and produce more milk than untreated cows (McNamara and Valdez, 2003). Increased milk production might be an indirect effect of increased glucose production. Increased production as a result of chromium supplementation is observed in primiparous cows and not multiparous cows. It has been observed (Popovic *et al*., 2000) that first lactation cows supplemented with 4mg/day of an organic chromium supplement, had higher average daily milk yield and higher milk fat , protein and lactose values when compared to a control group.

Calf growth

Normal husbandry practices in calf rearing, such as weaning, crowding and feedlot acclimation could lead to physiological stress and in turn to a deficiency of chromium. The excretion of chromium in the urine during stress periods normally increases the requirements of chromium. Chromium supplement frequently decreases serum cortisol in chromium deficient diets of stressed calves (Moonsie-Shageer and Mowat, 1993). Research findings (Dhiman *et al*., 2007) have shown that supplementation with chromium propionate in the diet decreased plasma cholesterol concentration in the blood of 6 month old buffalo calves. Chromium supplementation has been shown to improve the antibody response to infectious bovine *rhinotracheitis* vaccination in newly weaned calves (Burton *et al*., 1994). Recent studies (Mondal *et al*., 2007) have shown that chromium supplementation increased total weight gain, average daily weight gain and decreased blood cholesterol in young goats.

Chromium in Pigs

Growth and carcass composition

Several authors (Page *et al*., 1992, 1993; Lindermann *et al*., 1995: Mooney and Cromwell, 1995) have reported improvements in the carcass composition of pigs fed diets supplemented with chromium picolinate for the entire growing-finishing period. Research findings (Ward *et al*., 1995) however did not show improvement in carcass measurements of growing-finishing pigs fed diets supplemented with different sources of chromium which include chromium acetate, chromium oxalate, and chromium picolinate. Several authors (Evok-Clover *et al*., 1993; Mooney and Cromwell, 1997) have observed that the duration of supplementation is a major factor that determines the pig's response to chromium supplementation that there is little effect of chromium

supplementation over relatively short periods during early development. These authors have shown that chromium supplementation increased the rate of protein deposition and reduced the rate of fat deposition. Furthermore, chromium supplementation increased the amount of dissected lean in the ham by 5.4%, while the corresponding reduction in dissected fat was 8.2%.

CONCLUSION

Chromium has been shown to play a vital role in the metabolism of carbohydrates, proteins and lipids and in improving the immune function in livestock. Organic sources of chromium have been found to be highly bioavailable and the beneficial effects of chromium supplementation have been proven by various studies carried out with livestock. Chromium supplementation has been shown to alleviate the negative effects of stress thereby improving the performance and health of livestock.

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