Dietary Chromium-methionine Chelate Supplementation and Animal Performance

Sang Jip Ohh* and Joon Yeop Lee

Department of Feed Science and Technology, Kangwon National University, Chuncheon, Korea

ABSTRACT : Chromium has emerged as an essential trace mineral in nutrition. However, it readily causes toxicity because of slightly excessive dose and/or form of chromium supplement. Therefore, developing a noble form of chromium supplement which is capable of not only an increased availability but also a reduced toxicity has been a critical issue in chromium nutrition. Chromium-methionine chelate has been, so far, one of the latest developments in its kind. Although not much information is available for the chromium-methionine chelate, especially in view of animal performances upon dietary supplementation, several studies indicated chromium methionine chelate could be effective to improve meat quality by increasing muscle mass but decreasing body fat. Highly-graded beef was produced by dietary chromium methionine supplementation during fattening stage of Korean native steers. Body muscle was increased in replace of decreasing body fat in both pig and rat that were dietary supplemented with chromium methionine chelate. However, a pig farm study did not show any significant improvement of body gain upon supplementation of chromium methionine. Immune responses of pig and rat were not always dependent upon chromium form but were varied by species. These results suggest there could be a different mode of responses due to species as well as onset time of dietary supplementation of chromium methionine. It is still early to conclude the bio-efficacy of chromium methionine chelate presumably due to its recent appearance into the field. But the chelate is certainly worth more application to animal since it certainly reduced the application level of dietary chromium.
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Key Words : Chromium-methionine Chelate, Animal Performances, Meat Quality, Immune Response

INTRODUCTION

Chromium is an essential trace mineral that is pivotal in glucose, protein and fat metabolism in animal tissue. The chromium is also known to be partially responsible in blood cholesterol regulation. Therefore, a dietary supplementation of chromium has suggested as a new approach to produce low-fat, low-cholesterol meat from the meat producing animals.

Chromium is a key constituent of glucose tolerance factor (GTF), which is responsible for regulating blood glucose level. Blood glucose level and its homeostasis were known to be related to body protein or fat synthesis especially in ruminant animal. Therefore, this interrelated regulation mechanism via glucose can be applied to control the muscular fat deposition for high marbled-beef production.

Quality meat production is also affected by how much the animal had stressed during their growth and fattening. Since chromium has known to strengthen the stress relieving mechanism and immune response, appropriate regimen of diet chromium could be a metabolic tool to lessen the stress and therefore improve the meat quality. The chromium could replace feed supplemented antibiotics due to its beneficial effect on immune response. This can be additional advantage of chromium as a feed supplement.

In spite of all the beneficial effect of chromium, risk of toxicity, poor absorption into the body and possibly subsequent accumulation into the soil, has been a barrier against the proactive feed supplementation. Even though animals just need trace amounts of chromium to meet their optimal nutritional needs, it was not easy to meet their requirements due to poor absorption and poor availability of inorganic chromium. Therefore, several chromium products have developed to claim an improvement in biological availability. Among them, organic chromium has received strong attention since organic form can be readily absorbed into the gastrointestinal gut due to their low molecular weight compared to inorganic form.

Consequently, many types of organic mineral complex have been developed and introduced to the market. Chromium methionine chelate is a newly developed organic mineral which is able to directly cross the intestinal cell membrane and be metabolized without any prior digestion since it was chelated with amino acid. Therefore, bioavailability of chromium methionine chelate is proposed to be higher than those of other organic chromium. But only limited information is currently available compared to other organic chromium complexes such as chromium picolinate and chromium yeast complex that are already in the market.

In this article, the author focused on chromium

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** Corresponding Author: Sang Jip Ohh. Tel: +82-33-250-8631, Fax: +82-33-255-5482, E-mail: sjohh@kangwon.ac.kr

Table 1. Signs and symptoms of chromium deficiency in pig and cattle

Deficiency symptoms	Animals
Impaired glucose tolerance	Pig
Elevated circulated insulin	Pig
Elevated serum cholesterol and triacylglycerol	Cattle, Pig
Decreased body lean mass	Pig
Elevated percentage of body fat	Pig
Increased humoral immune response	Cattle
Morbidity	Cattle

Reference : Anderson, 1994

methionine chelate as a new supplemental form of chromium. Effect on animal performances and metabolic responses was extensively discussed from the limited numbers of recent studies by comparing studies with other organic chromium complexes including chelated chromium and chromium enriched yeast as well. This article is also focused on the potential of chromium methionine to produce low fat good quality meat from the meat producing animal.

THE ROLE OF CHROMIUM IN ANIMAL NUTRITION

Although chromium has been suggested as an essential mineral for human and animal, the exact role of chromium and its mode of action are not elucidated yet. Chromium exists in nature mostly in trivalent (Cr^{3+}) form. Hexavalent (Cr^{6+}) form can be existent but it is unstable and toxic in human and animal due to its strong oxidizing properties. Chromium requirement for human is relatively well known but not for animal. Chromium requirement seems to increase in animal and human as a consequence of stressors such as fatigue, trauma, pregnancy and other nutritional, metabolic, physical, environmental and emotional stresses.

Chromium, once ingested, is primarily absorbed in the small intestine. Inorganic forms of chromium such as chromium chloride and chromium oxide are poorly absorbed by animal with average absorption rate of the chromium estimated about 0.5 percent. The reason for the low availability of inorganic form of Cr^{3+} is related to the formation of insoluble compound and binding of free chromium to natural complexing agent in animal feed. Also chromium absorption is hindered by interference between chromium and other mineral such as Zn and Fe. Once chromium entered into the blood circulation and transported to tissues, it could be bound possibly as a component of GTF. After that, transported chromium can be accumulated in all tissue at a relatively low concentration. Chromium is excreted mainly in the urine and partially is lost in hair, perspiration and bile. Under the stressed condition, amounts of excreted chromium could be increased 10-300 folds.

Physiological function of dietary chromium in animal and human is proposed (Mertz, 1993) in view of carbohydrate metabolism, lipid metabolism, protein synthesis, growth and longevity. Schwarz and Mertz (1959) had recognized chromium as a component of GTF, which enhance not only tissue sensitivity to insulin but also glucose utilization. Therefore, glucose uptake, glucose use for lipogenesis, glucose oxidation to carbon dioxide, and glycogenesis are increased by addition of chromium plus insulin to animal tissue (Anderson, 1987). A human study also reported metabolic disorders such as diabetes-like symptoms, fasting hyperglycemia, and glycosuria that could be back to normal status after dietary chromium supplementation (JeeJeebhoy et al., 1977). Moreover, supplemental chromium exerted a beneficial effect on cholesterol, glycosylated hemoglobin, glucose and insulin in the blood of human with type II diabetes (Anderson et al., 1996)

Supplemental chromium also plays an important role in serum cholesterol homeostasis. Chromium supplementation decreased the level of blood total cholesterol, LDL cholesterol, and triglyceride but increased the level of HDL cholesterol (Anderson, 1995). However, effect of chromium supplementation on blood lipid in human was not always consistent, therefore, this effect on lipid metabolism seems to be independent from the effect on glucose metabolism. Possible mechanism of chromium on amino acid synthesis has been predicted due to the role of insulin in amino acid uptake, but other activities of chromium in protein metabolism have not been reported (Roginski and Mertz, 1969).

When both animal and human are under stressed statuses by either physical, physiological, environmental, pathological, or nutritional stressors, supplementation of organic chromium resulted in an improved recovery to normal statuses in growth performance, metabolic response, and disease susceptibility (Chang and Mowat, 1992; Mowat et al., 1993; Anderson, 1994; Burton et al., 1996; Yang et al., 1996; Hayirli et al., 2001). This means that the chromium would act as a metabolic modulator to balance the metabolism to get back to normal status.

The signs of chromium deficiency in farm animal are listed in Table 1. Chromium deficiencies in farm animal do not occur in usual state, but chromium requirement can be elevated in animal undergone nutritional, physiological, immunological and environmental stresses.

Since chromium have protein-precipitating and oxidizing properties, chromium, regardless of Cr^{6+} and Cr^{3+}, are known to be toxic. Although Cr^{3+} is much less toxic than Cr^{6+}, that does not insure Cr^{3+} is safe upon feed application. Since Cr^{3+} toxicity also caused a conditional intracellular iron deficiency (Ramana and Sastry, 1994) and a possible soil contamination by the excreted Cr after poor intrinsic absorption, the development of highly available form of chromium draws not only nutritionist but also environmentalist's attention.

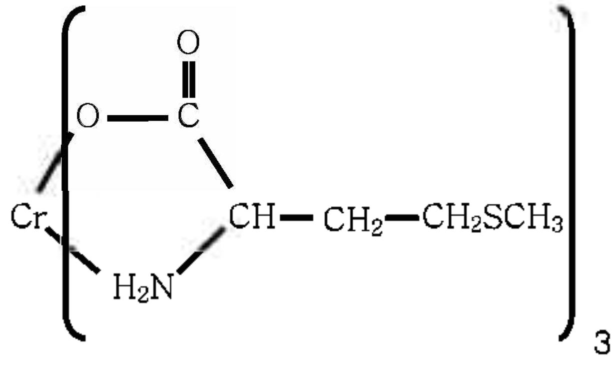

Figure 1. Proposed chemical structure of chromium methionine chelate.

DEVELOPMENT OF CHROMIUM METHIONINE CHELATE AND OTHER ORGANIC COMPLEX

By the definition of AAFCO (1998), commercial organic mineral complexes can be categorized into 4 groups; metal amino acid complex, metal amino acid chelate, metal polysaccharide complex, and metal proteinate. Among them, referred to the criterion of metal amino acid chelate, the amino acid chelate is considered to be mostly difficult in manufacturing due to a removal process of side chains of amino acid to attain less than 800 daltons of molecular weight.

When ligands, that contain two or more donor atoms capable of bonding to a metal ion, bind to metal ion via two or more donor atom, the resulting complex contains one or more heterocyclic rings with metal ions. These complexes are called 'chelate' and the amino acids are called ligands which bond to metal ions via oxygen in carboxyl group and nitrogen in amino group. Since there have been several mineral products, manufactured by chelation reaction, that means ligands used in the chelation reaction could also be various (Power and Horgan, 2000).

Currently available organic chromiums are yeast-bound chromium, chromium picolinate, chromium nicotinate, chromium chelate, chromium proteinate, and chromium methionine chelate. Classification of these compounds depends on their ligand substances and reaction method (Hynes and Kelly, 1995). Among the above organic chromiums, only yeast bound chromium, chromium picolinate, and chromium methionine chelate, have practically introduced to animal feed market.

Metal protein chelate that had marketed prior to the metal amino acid chelate is manufactured from the reactions between metal ion and hydrolyzed protein molecules. A disadvantage of this process is presumably the production of metal protein chelate greater than 800 daltons of molecular weight, since average molecular weight of hydrolyzed protein and amino acid from hydrolyzed protein used in this reaction could range from 1,000 to 100,000 daltons. These complexes are difficult to be absorbed directly into the intestinal gut because of heavier molecular weight.

Metal amino acid chelate is made from metal ion and individually purified amino acid which has known molecular weight. This process has an advantage of making an uniform quality product but its production cost could be increased due to relatively expensive cost of ingredient. However, once ingested by animal and human, this complex is considered to be rapidly and directly absorbed and metabolized easily in small intestine avoiding digestion by gastric juice. Consequently, efficacy of the metal amino acid chelate was claimed to be superior to other organic metal complexes especially in term of bioavailability upon feeding to animal and human.

A chromium methionine chelate is made recently by the author's laboratory via the reaction between one mole of chromium molecule and three moles of methionine molecules. This chromium methionine has evaluated through a series of animal feeding studies and a part of those results was employed in this article. The proposed chemical structure of the chromium methionine chelate is illustrated in Figure 1.

Trivalent chromium was selected since it is naturally better in uptake capability and less toxic than Cr^{6+}. The trivalent chromium was also known to form octahedral coordination complexes and polynuclear chelated complexes by hydrolysis in aqueous solution (Mertz et al., 1969). However, the hexavalent chromium has acidic properties and could be easily reduced to Cr^{3+}, therefore, it is speculated to be difficult to form complexes. Among amino acids, methionine was selected since methionine was found to be effective to reverse Cr^{6+} toxicity (Ramada and Sastry, 1994).

The chromium methionine chelate was tested and found to be effective for dietary supplementation to ruminant animal since the chelate remained intact by rumen microorganism (Kim et al., 2003a). The study, however, indicate higher uptake of trivalent chromium by rumen microbes, therefore could reduce the portion of chromium that can be transported to small intestine.

EFFECT OF CHROMIUM METHIONINE CHELATE ON THE ANIMAL PERFORMANCES

A series of animal feeding studies with chromium methionine or chelated chromium in ruminant could not find any adverse effect on animal performances. Effects of chelated chromium on growth and lactation performances in ruminants are respectively summarized in Table 2 and 3. Beef steer fed chromium methionine chelate supplemented diet at concentrations of 400 μg and 800 μg of chromium per kg of diet did not show any additional benefit on growth performances and feed efficiency compared to steers that were not supplemented with dietary chromium. But the

Table 2. Effect of chelated chromium on growth performance in cattle

Animals	Cr source	% increase vs w/o Cr	References
Stressed calves	Chelated Cr 1 ppm	ADG 12.9% ↑	Mowat et al., 1993
		DMI 9.4% ↑	
		Gain/feed 6.8% ↑	
Beef steer	Cr-met, 400 ppb/kg of DM	ADG 0%	Kegley et al., 2000
		DMI 1.4% ↑	
		Gain/feed 1.2% ↓	
	800 ppb/kg of DM	ADG 2.8% ↓	
		DMI 1.3% ↓	
		Gain/feed 4.8% ↓	
Beef steer	Chelated Cr		Mathison and Engstrom, 1995
- Growing		ADG 3.3% ↑	
		DMI 1.7% ↓	
- Finishing		ADG 3.5% ↓	
		DMI 0.2% ↓	
- Overall		ADG 1.3% ↓	
		DMI 0.6% ↓	
Korean native steer	Cr-met 400 ppb, Low forage diet	ADG 11.4% ↑	Hong et al., 2002
		DMI 1.0% ↑	
		Gain/feed 9.3% ↑	
	High forage diet	ADG 5.5% ↑	
		DMI 0.3% ↓	
		Gain/feed 5.5% ↑	

Table 3. Effect of chelated chromium on lactation performance in dairy cows

Animals	Cr source	% increase vs. w/o Cr	References
Periparturient dairy cows	Cr-met (Kg of $BW^{0.75}$), 30 ppb	Dry matter intake 7.9% ↑	Hayirli et al., 2001
		Body weight 1.9% ↓	
		Milk yield 1.5% ↑	
	60 ppb	Dry matter intake 24.5% ↑	
		Body weight 0.5% ↑	
		Milk yield 14.9% ↑	
	120 ppb	Dry matter intake 18.1% ↑	
		Body weight 1.4% ↑	
		Milk yield 5.1% ↓	
Cows at early lactation	Chelated Cr, 500 ppb/kg of DM		Yang et al., 1996
- Primiparous		DMI 2.4% ↑, 2.64% ↑	
		Milk yield 13.1% ↑, 6.63% ↑	
- Multiparous		DMI 0.5% ↑, 0.5% ↓	
		Milk yield 1.4% ↑, 1.4% ↓	

chromium supplementation enhanced a glucose clearance rate and increased a serum insulin concentration of growing steer after intravenous insulin and glucose injection (Kegley et al., 2000).

However, a little bit different result was reported with Korean native steer. 400 ppb of chromium methionine inclusion in high forage diet improved feed efficiency in Korean native steers during growing period but with no difference in daily gain and dry matter intake. Serum insulin concentration was the highest in chromium supplemented steer (Hong et al., 2002). This result means that chromium methionine chelate has a potential to induce positive effect in nutrient utilization in relatively well nourished animal without any adverse effect on growth performances.

Questionable effect on cattle performances was observed with other organic chromium supplement (Mowat et al., 1993; Methison and Engstorm, 1995). Mowat et al. (1993) reported that daily gain in stressed feeder calves, fed chelated chromium supplemented diet was increased by 46% in the first 21 d in the feedlot due to a remarkably reduced morbidity compared to calves with no chromium supplementation. But another chelated chromium supplementation for stressed steers could not change growth performances and feed efficiency during growing, finishing and overall period (Mathison and Engstorm, 1995). Therefore, it is still unclear how a chelated chromium supplementation for growing cattle and calves does respond under the stress condition like transportation and weaning.

Table 4. Effect of chelated chromium on animal performances in non-ruminants

Animals	Cr source		% increase vs w/o Cr	References
Laying hen	Cr aminoniacinate	47 ppm	Egg production 1.6% ↑	Piva et al., 2003
			Feed intake 4.3%↑	
			Egg weight 1.1% ↓	
Rat	Cr-met	300 ppb/ kg of diet	Weight gain 1.0% ↑	Ohh et al., 2003
			Feed intake 6.0% ↑*	
			Gain/Feed 5.6% ↓	
		600 ppb/ kg of diet	Weight gain 3.9% ↑	
			Feed intake 9.0% ↑*	
			Gain/Feed 5.6% ↓	
		1,200 ppb/ kg of diet	Weight gain 1.1% ↑	
			Feed intake 9.4% ↑*	
			Gain/Feed 8.3% ↓	
Rat fed high fat diet	Cr-met	300 ppb/ kg of diet	Weight gain 6.5% ↓	Kim et al., 2003
			Feed intake 4.4% ↓	
			Gain/Feed 6.7% ↑	
Broiler	Cr-met	200 ppb/ kg of diet	Weight gain 11.5% ↑*	Ohh et al., 2004d
			Feed intake 3.5% ↑	
			Gain/Feed 7.9% ↑	
		400 ppb/ kg of diet	Weight gain 2.5% ↑	
			Feed intake 0.3% ↓	
			Gain/Feed 1.7% ↑	

* Significant difference ($p<0.05$).

Assessment of performance and metabolic responses upon dietary chromium supplementation in lactating dairy cattle has focused on the transition, periparturient and early-lactation cow (Subiyatno et al., 1996; Yang et al., 1996; Hayirli et al., 2001). Supplemental chromium methionine as a chromium source at concentrations of 30, 60 and 120 ppb per kg of $BW^{0.75}$ to periparturient dairy cow linearly increased dry matter intake during prepartum and postpartum and quadratically increased milk, fat and lactose yield while serum glucose and insulin:glucose ratio decreased significantly (Hayirli et al., 2001). Dietary addition of 5 mg of chelated chromium increased milk yield during the first 16 wk lactation of primiparous cows by about 13% in the first experiment and 7% in another experiment, but not in multiparous cows (Yang et al., 1996).

From the above result, it is postulated that the first parity cows may be more sensitive than multiparous cow against the exposure to stressed circumstances. Hence, primiparous cows that are deficient in chromium during late pregnancy may need more chromium to maximize dry matter intake to return to normal metabolic status (Subiyatno et al., 1996). Increased milk yields due to chromium supplementation may be explained by the altered insulin sensitivity. During glucose-tolerance test, chromium supplementation increased glucose/insulin ratio in primiparous cows after parturition. This means that chromium supplementation seems to improve insulin sensitivity for these primiparous cows before calving.

In stressed animals, information about blood serum traits, as summarized in Table 5, can be an important criterion to assess metabolic status of the animal. Chromium supplementation for repartee primiparous cows fed chelated chromium resulted in a decreased plasma triglyceride and a peak insulin level, but not in postpartum primiparous cows (Subiyatno et al., 1996). Yang et al.(1996) reported that there was no effect of chelated chromium supplementation on serum nonesterified fatty acid(NEFA) and β-hydroxybutyric acid level in cows during lactation. However, with unstressed calves, a supplementation of chromium picolinate lowered blood cholesterol (Bunting et al., 1994). This result is contradictory to the result of Hong et al. (2002), who reported that serum total cholesterol was increased by supplementation of chromium methionine in Korean native steer. However, in the same study, HDL cholesterol has remarkably increased whereas LDL cholesterol has decreased as to result the net increase of total cholesterol.

Result of organic chromium studies with non-ruminant animal are summarized in Table 4. Pig studies, so far, have largely done with chromium picolinate by comparison with inorganic chromium chloride. Although the chromium requirement of pig is not known yet, NRC has recognized chromium as an essential mineral for swine. Effect of chromium supplementation in pig was mostly evaluated by growth performances and carcass quality. However, reported growth performances of growing-finishing pigs fed chromium supplemented diet have been inconsistent, presumably because basal diets used in the experiment may already meet the requirement of chromium. Some studies suggested that organic chromium could have a potential to decrease accretion rate of carcass fat and to increase that of protein (Mooney and Cromwell, 1997; Ohh et al., 2004b).

Table 5. Effect of chromium methionine and chelated chromium on blood metabolites

Animals	Cr source and dosing level	Metabolic parameters	Reference
Beef steers	Cr-met 400, 800 ppb	Increased insulin:glucose ratio	Kegley et al., 2000
Cows	Chelated Cr 500 ppb	Increased plasma cortisol production	Yang et al., 1996
Feeder calves	Chelated Cr 1 ppm	Unstressed Decreased serum glucose and cortisol* Stressed No difference in serum cortisol	Mowat et al., 1993
Dairy cows	Cr-met 30, 60, 120 ppb/ Kg of BW $^{0.75}$	Prepartum Attenuated insulin sensitivity Postpartum Decreased serum glucose* Decreased insulin:glucose ratio*	Hayirli et al.,2001
Korean native steer	Cr-met 400 ppb	Low forage diet and High forage diet Increased HDL cholesterol* Decreased LDL cholesterol* Increased serum insulin Increased serum glucose	Hong et al., 2002
Rat fed high fat diet	Cr-met 300 ppb	Decreased obesity index* Decreased total cholesterol Increased HDL cholesterol*	Kim et al., 2003
Rat	Cr-met 300, 600, 1,200 ppb	Decreased obesity index (1,200 ppb) Decreased body fat* (1,200 ppb)	Ohh et al., 2003
Rat	Cr-met 300 ppb	Increased serum insulin* Decreased serum triglyceride	Ohh et al., 2004a
Growing-finishing pig	Cr-met 100,200 ppb	No difference in serum cholesterol No difference in serum glucose No difference in serum insulin	Ohh et al., 2004b
Broiler	Cr-met 400 ppb	No difference in serum cholesterol No difference in serum glucose	Ohh et al., 2004d

* Significant difference ($p<0.05$).

Effect of chromium on sow reproductivity was once confirmed that 200 μg of chromium supplementation per kg of diet to gilt over two parities had increased litter size (Lindemann, 1995).

As shown in table 4, there was no difference in egg production, feed intake, egg weight, yolk weight and yolk color of laying hens fed diet supplemented with either $CrCl_3$, chromium yeast, or chromium amino niacinates as a dietary chromium form (Piva et al., 2003). On the other hand, Kim et al. (1997) reported that chromium picolinate inclusion to laying hen diet at concentrations of 0, 200, 400 or 800ppb of chromium per kg of diet decreased cholesterol contents in egg yolk and increased egg weight and egg mass. And similar result was reported by Lien et al. (2003). With broiler chickens, dietary chromium methionine supplementation was effective for improving body gain and feed efficiency (Ohh et al., 2004d). Decreases in serum cholesterol by chromium picolinate supplementation (Lee et al., 2003) and by chromium methionine (Ohh et al., 2004d) were also observed in broiler. These results indicate that supplementation effect of chromium on production is still inconsistent but is fairly consistent to control cholesterol in blood and egg.

In studies with rat, Kim et al. (2003) showed that serum total cholesterol was decreased whereas HDL cholesterol was increased by 300 ppb of chromium methionine addition when rats were fed high fat diet. In relation to this result, Ohh et al. (2003) reported that rats fed chromium methionine chelate at 0, 300, 600, 1,200 ppb of chromium levels exerted a decrease in obesity index. These results showed dosage dependent decrease in body fat with increasing dosage of chromium methionine and suggested intervention by chromium methionine in lipid metabolism.

EFFECT OF CHROMIUM METHIONINE CHELATE ON MEAT QUALITY

Chromium supplementation has been employed to manipulate the quality of meat due to its biological function on body fat and muscle metabolism (Page et al., 1993). Chromium picolinate have widely been tested to increase lean muscle but to decrease back fat in pig. However, the result was varied presumably due to other extrinsic factors such as onset and level of supplementation, nutrients and Cr

Table 6. Effect of chromium methionine chelate and other organic chromium on meat quality

Animals	Cr source	Quality parameters	References
Korean native steer	Cr-Met 400 ppb	Marbling score Cr:control = 4.7:4.2 Carcass grade (>prime grade; %) Cr:control = 72:66	Hong et al., 2002
Beef steer	Chelated Cr 3 mg(6 days)+1.5 mg(21days)/kg of concentrates	Lean muscle percentage (%) Cr:control = 58.5:58.4	Mathison and Engstrom, 1995
Beef cattle	Cr yeast 400 ppb	Loin eye area(cm^2) Cr:control = 82:78	Pollard and Richardson, 1999
Growing-finishing pig	Cr-Met 200 ppb	Avg. back fat thickness (mm) Cr:control = 16:27 Lean muscle percentage (%) Cr:control = 63:58	Ohh et al., 2004b
Broiler	Cr yeast 150 ppb 300 ppb 400 ppb	Breast meat (% of carcass) Cr:control = 21.5:20.3 Cr:control = 21.6:20.3 Cr:control = 20.9:19.3	Hossain, 1998

Table 7. Effect of chelated chromium and chromium methionine supplementation on immune response

Animals	Cr source	Immune response	References
Lactating dairy cow	Chelated Cr 0.5 ppm	Elevated anti-OVA antibody response Increased mitogen stimulated blastogenic response	Burton et al., 1993
Pregnant dairy cow	Chelated Cr 0.5 ppm	No effect on neutrophil phagocytosis Increased *in vitro* PBL blastogenic effect	Chang et al., 1995
Feeder calves	Chelated Cr 0.14 ppm	Enhanced peripheral blood lymphocyte blastogenic response	Chang et al., 1994
Periparturient cow	Chelated Cr 0.5 ppm	Decreased cytokine, IL-2, TNF-α and INF-γ *in vitro*	Burton et al., 1996
Weaned pig	Cr-Met 100 ppb	Increased cell-mediated immune response Enhansed peripheral blood lymphocyte blastogenic response Enhansed neutrophil phagocytosis	Ohh et al., 2004c
Broiler	Cr-Met 200, 400 ppb	Significantly elevated anti-LPS antibody response	Ohh et al., 2004d

level of basal diet, breed and species (Page et al., 1993; Ward et al., 1995; Crow et al., 1997).

The recent supplemental form of chromium, methionine chelate was also introduced by authors as shown in Table 6, to modulate meat quality of the animal. In addition, function of chromium to regulate glucose level in the tissue has recently hypothesized to produce marbled beef via phase-regulated supplementation of dietary chromium (Hong et al., 2002). For this purpose, chromium methionine chelate was suggested since the chelate is generally safer than other organic chromium and could be required relatively less than others due to its higher bioavailability.

However, presumably due to the limited amount of time since the animal application of chromium methionine chelate, concrete result is not available especially in view of meat quality. In Table 6, numbers of data on meat quality by organic chromium including chromium yeast were summarized. The result of organic chromium supplementation on meat quality in farm animal is varied with animal species, form of dietary chromium and the level of chromium supplementation. There was no difference on lean muscle percentage in steers fed chelated chromium supplemented diet (Meathison and Engstrom, 1995). A similar result was also reported with beef cattle by Pollard and Richardson (1999), who showed no effect of chromium yeast on loin eye area. However, in recent study, the supplementation of chromium methionine chelate to Korean native steer showed the tendency to improve marbling score of beef and significantly increased carcass grade (Hong et al., 2002). With this result, it should be noted that the meat quality parameter was different from the above two results.

Studies with organic chromium supplementation in non-ruminant animals, however, showed a promising result on meat quality. Average backfat thickness in pig fed 200 ppb of chromium methionine supplemented diet during growing-finishing period was remarkably reduced along with increased lean muscle percentage (Ohh et al., 2004b). Breast meat percentage of broiler fed chromium yeast was significantly increased regardless the level of chromium supplementation (Hossain, 1998). This means that the effect of dietary chromium supplementation could be relatively remarkable with non-ruminants compared to ruminant. The above difference could be partly explained by difference in species dependent lipid metabolism between rumen and single stomach and interference by rumen microorganism.

Further studies could be promising once the onset of chromium methionine chelate supplementation is carefully controlled to regulate fat deposition mechanism at different phases of growth.

EFFECT OF CHROMIUM METHIONINE CHELATE ON IMMUNE RESPONSE

Various metals are known to be responsible for many biochemical, immunological and physiological activities of body (Shrivastava et al., 2002). Recently, dietary chromium has been evidenced due to its important role in not only glucose metabolism but also immunomodulation, affecting health and resulting performances (Mallard and Borgs, 1997). Reduction of hexavalent chromium to trivalent form results in the formation of reactive intermediates that may aggravate cytotoxicity, genotoxicity and carcinogenecity by hexavalent chromium-containing compounds. This could indirectly reveal that chromium can be a mediator of immune response

Effect of chromium on bovine immune response was extensively reviewed by Burton (1995) and Shrivastava et al. (2002). Burton et al. (1993) investigated the effect of chelated chromium on immune response in physically and metabolically stressed cows during periparturient and early lactation. Several studies with chromium supplementation on immune response were summarized in Table 7. In humoral immune response, higher serum antibody response to ovalbumin antigen were observed in cows fed supplemental chelated chromium (Burton et al., 1993) and in broiler fed chromium methionine (Ohh et al., 2004d). In the same study, supplementation of chelated chromium increased *in vitro* lymphocyte proliferative responses to the mitogen Con A.

Similar to this result, proliferative activities in peripheral blood cell from chelated chromium supplemented calves was higher than those from calves fed $CrCl_3$ as inorganic chromium (Chang et al., 1994). On the other hand, in other *in vitro* study, an inorganic chromium addition in the medium containing insulin or cortisol, increased proliferative response better than organic chelated chromium (Chang et al., 1996). Differences between chelated chromium and inorganic chromium to lymphocyte proliferative activity can be explained by the fact that inorganic chromium has more free binding sites therefore, it is easier than chelated chromium to be transported through the membrane of lymphocyte (Chang et al., 1994).

A different effect of chelated chromium on non-specific immune response, in term of neutrophil phagocytosis, was observed in dairy cows (Chang et al., 1996) and in weaned pig (Ohh et al., 2004c). This result suggests that chromium in immune system may act differently between non ruminant and ruminant animal

To know how chromium improve a humoral immune response and a cell mediated immune response, several studies have been conducted by measuring the concentration of acute phase cytokines released from mitogen-stimulated peripheral blood mononuclear cell. IL-2, TNF-α and INF-γ concentrations in blood of periparturient cows fed chelated chromium supplemented diet were significantly decreased (Burton et al., 1996). Since TNF-α and INF-γ have antiproliferative activities in mitogen-stimulated hepatopoietic and lymphoid cells, increased proliferative responses in peripheral blood mononuclear cell could be explained by the concentration of acute phase cytokines such as TNF-α and INF-γ.

CONCLUSIONS

It is expected that the organic chromium instead of inorganic form would be more beneficial due to its higher bioavailability and lesser risks of toxicity and environmental accumulation. Among the several products that have introduced in the market, chromium methionine chelate was focused since it is the very new one and theoretically highly available. However, it is still very difficult to assess the bioavailability of chromium methionine in farm animals due to lack of appropriate tool and applied studies. Although mode of action of chromium methionine chelate in physiological, nutritional, and immunological metabolism is fairly understood, practical benefit of chromium methionine chelate supplementation is still varied and uncertain. Among the several proposed potentials of chromium methionine chelate, firstly, the recovery function in stressed animals draws an attention in view of animal health and immune response modulation. Biological functions of chromium methionine chelate for both lowering cholesterol and altering muscle fat during lipid metabolism was evidenced as an alternative regimen to produce novel animal products such as low cholesterol, high lean and low fat meat. However, it is still early to conclude the effect of chromium methionine chelate as a meat quality modulator and a stress reducer. In conclusion, this article indicates that chromium methionine chelate has nothing detrimental but worth animal application especially in view of meat quality modulation as well as stress relieving modulation in animals.

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