J Food Sci Nutr
Vol 9, p 342~345 (2004)

J Food Science and Nutrition

# Effects of Different Forms of Chromium Supplements on Serum Glucose, Insulin and Lipids in Rats

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## Abstract

**This study evaluated the effects of different forms of chromium supplements on serum glucose, insulin and lipid concentrations in rats. Sprague-Dawley male rats were randomly assigned to one of three dietary groups and fed AIN-76 semi-purified basal diets supplemented with 300 ppb Cr from Cr methionine (CrMet) and Cr chloride ($CrCl_3$) or without Cr (control). By the end of the 4th week, all rats were decapitated, blood collected, and serum glucose, insulin and lipid concentrations were determined. The CrMet and $CrCl_3$ supplementation did not affect weight gain and feed efficiency ratio. However, feed intake was significantly higher in CrMet groups than control ($p<0.05$). CrMet-supplemented rats had markedly increased insulin levels ($p<0.05$) compared with controls. Serum lipids were not significantly different between the control and the CrMet groups. $CrCl_3$ supplementation decreased total cholesterol and triglyceride, but the decreases were only significant for the control group. $CrCl_3$ supplementation was associated with significant decreases in total cholesterol compared with CrMet supplementation. These results indicate that CrMet supplementation is effective for increasing serum insulin, and $CrCl_3$ may improve lipid concentrations, because we observed decreased serum total cholesterol and an improved total cholesterol/HDL-cholesterol ratio (THR).**

**Key words:** Cr methionine, glucose, insulin, lipid, THR

## INTRODUCTION

Cr is an essential mineral involved in carbohydrate and lipid metabolism (1-4). It is generally accepted that the source of dietary Cr affects bioavailability, with most organic sources of Cr having a higher bioavailability than inorganic sources (5). To increase the bioavailability of Cr, several studies have suggested using organically complexed Cr sources.

Organic forms of Cr have been shown to improve the insulin response to glucose and have been used with some success to control blood glucose levels in humans and animals (6-9). Supplemental Cr picolinate increased glucose clearance rate and decreased glucose half-life and area under the curve in calves (10,11). In calves, Cr nicotinate complex slowed the return to basal glucose concentration after an insulin infusion (12). Studies in humans and animals have shown lower concentrations of lipids in blood when diets were supplemented with Cr picolinate (13,14). Cr supplementation causes significant decreases in serum cholesterol concentrations with larger decreases observed in subjects with the highest concentration prior to supplementation (15). Bunting et al. (11) reported a greater reduction in plasma cholesterol in calves fed 370 μg/kg Cr picolinate than in calves fed a control diet.

Certain organically complexed Cr sources are suggested to be utilized more efficiently than inorganic Cr sources (16). Organic forms that seem to have greater biological availability include high-Cr yeast, Cr nicotinate, Cr-AA-nicotinate complex, and Cr picolinate. However, studies designed to compare the effectiveness of organically complexed and inorganic sources of Cr are few. Cr methionine (CrMet) is a newly available organic Cr source whose bioavailability has not been previously determined in rats. Therefore, the objectives of this study were to investigate the effects of an inorganic Cr with CrMet supplementation on serum glucose, insulin and lipid concentrations in rats.

## MATERIALS AND METHODS

### Animals and diets

Male Sprague-Dawley rats were divided into three treatment groups of nine each. All rats fed AIN-76 semi purified basal diet for 4 weeks (17). The animals were

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provided the diet and deionized water *ad libitum*. The animals were maintained in a controlled environment at 20°C and 40~50% humidity, with 12 h of light per 24 h period.

As shown in Table 1, the dietary treatment consisted of the basal diet supplemented with 300 ppb CrMet from an organic source or with 300 ppb $CrCl_3$ from an inorganic source or without Cr (control). Body weight was measured at frequent intervals in order to estimate weight gain.

**Blood glucose, insulin and lipids**

At the end of week 4, after an overnight fast, blood samples were collected by decapitation. Serum was separated by centrifugation at 4°C and kept frozen at -70°C for analysis of glucose, insulin and lipid concentrations. Fasting blood glucose was analyzed by an enzymatic procedure (Boeringer Manheim, Germany). Insulin was determined by an RIA method (Diagnostic Products Corporation, USA) which has been validated for the detection of rat insulin. Serum total cholesterol, HDL-cholesterol, and triglyceride concentrations were enzymatically determined using diagnostic kits (Boeringer Manheim, Germany).

**Table 1.** Composition of diets (g/kg diet)

| Components | Groups[1] | | |
|---|---|---|---|
| | Control | CrMet | $CrCl_3$ |
| Casein | 200 | 200 | 200 |
| DL-methionine | 3 | 3 | 3 |
| Sucrose | 500 | 500 | 500 |
| Corn starch | 150 | 150 | 150 |
| Cellulose | 50 | 50 | 50 |
| Corn oil | 50 | 50 | 50 |
| Mineral mix[2] | 35 | 35 | 35 |
| Vitamin mix[3] | 10 | 10 | 10 |
| Choline bitartate | 2 | 2 | 2 |
| Chromium methionine | - | 300[4] | - |
| $CrCl_3$ | - | - | 300[4] |

[1]Control: AIN-76 diet.
CrMet: AIN-76 diet with Cr methionine.
$CrCl_3$: AIN-76 diet with Cr chloride, $CrCl_3$.
[2]AIN-76 mineral mixture.
[3]AIN-76 vitamin mixture.
[4]Cr doses are expressed as micrograms of Cr per kilogram of diet, or parts per bilion.

**Statistical analysis**

Statistical analysis was performed by the GLM procedure of SAS (SAS Institute, Cary, NC USA) (18). Duncan's multiple range test was conducted to evaluate significant main effects. The differences between control and treatments were statistically significant considered at $p<0.05$.

## RESULTS

**Body weight gain, feed intake and feed efficiency ratio**

The average weight gain, feed intake and feed efficiency ratio are shown in Table 2. Body weight gain and feed efficiency ratio were not significantly different among groups. Compared with control and $CrCl_3$ groups, rats supplemented with CrMet had slightly, but significantly, increased feed intake ($p<0.05$).

**Serum glucose and insulin**

The concentrations of glucose and insulin in serum of rats fed CrMet were determined (Table 3). Rats supplemented with CrMet had slightly lower fasting serum glucose concentrations compared with control and $CrCl_3$ rats. Serum insulin levels were significantly higher in the CrMet-treated rats than controls ($p<0.05$).

**Serum lipids**

Serum lipid concentrations of rats supplemented with different forms of Cr are shown in Table 4. There was no effect of CrMet supplementation on serum lipids; however, triglyceride was lower in CrMet-treated rats than controls. In the $CrCl_3$ group, the total cholesterol

**Table 3.** Effect of different forms of dietary chromium on serum glucose and insulin concentrations of rats

| Groups[1] | Glucose (mg/dL) | Insulin (μU/mL) |
|---|---|---|
| Control | 124.88±3.04[2)NS3)] | 17.28±6.07[b4)] |
| CrMet | 115.22±5.65 | 43.03±6.27[a] |
| $CrCl_3$ | 123.00±3.60 | 37.24±3.42[a] |

[1]See the legend of Table 1.
[2]Values are mean±SE.
[3]Not significant.
[4]Means with different letters are significantly different at $\alpha$ = 0.05 as determined by Duncan's multiple range test.

**Table 2.** Effect of different forms of dietary chromium on body weight gain, feed intake and feed efficiency ratio in rats

| Groups[1] | Weight gain (g) | Feed intake (g/day) | Feed efficiency ratio |
|---|---|---|---|
| Control | 130.36±5.33[2)NS3)] | 21.20±0.24[b4)] | 0.16±0.01[NS] |
| CrMet | 142.76±6.10 | 22.07±0.18[a] | 0.16±0.08 |
| $CrCl_3$ | 137.41±3.82 | 21.18±0.21[b] | 0.16±0.01 |

[1]See the legend of Table 1.
[2]Values are mean±SE.
[3]Not significant.
[4]Means with different letters are significantly different at $\alpha$=0.05 as determined by Duncan's multiple range test.

**Table 4.** Effect of different forms of dietary chromium on serum lipid concentrations in rats

| Groups[1)] | Total cholesterol (mg/dL) | HDL-cholesterol (mg/dL) | Triglyceride (mg/dL) | Total cholesterol/ HDL-cholesterol ratio |
|---|---|---|---|---|
| Control | 93.63±7.06[2)a3)] | 67.50±4.29[NS4)] | 212.50±35.00[a] | 1.39±0.06[NS] |
| CrMet | 92.56±3.43[a] | 68.56±2.31 | 149.78±22.54[ab] | 1.35±0.03 |
| $CrCl_3$ | 74.67±3.38[b] | 59.33±3.03 | 103.89±11.16[b] | 1.26±0.02 |

[1)]See the legend of Table 1.
[2)]Values are mean±SE.
[3)]Means with different letters are significantly different at $\alpha$=0.05 as determined by Duncan's multiple range test.
[4)]Not significant.

and triglyceride concentrations were significantly lower compared to control ($p<0.05$). In addition, $CrCl_3$-treated rats had lower total cholesterol levels compared to CrMet rats ($p<0.05$). $CrCl_3$ decreased lipid levels, as demonstrated by a decrease in total cholesterol and a reduced THR.

## DISCUSSION

We examined in the rat the effects of two different forms of Cr supplement on serum glucose, insulin and lipids. The present study indicates that Cr supplementation does not influence weight gain and feed efficiency ratios in rats. This is in agreement with results obtained by Cefalu et al. (19) with supplemented Cr picolinate. Ward et al. (20) reported that Cr tripicolinate supplementation did not affect weight gain, feed intake, and feed conversion. The same results were not found when Cr was supplemented from an inorganic source $CrCl_3$ (21).

Cr is involved in the control of the glucose-insulin system and the amount, and likely form of Cr, is critical when evaluating the role of Cr in this system. The finding of this study is that dietary CrMet supplementation affects fasting glucose and insulin concentrations. Similar to results of this study, Sahin et al. (22) found that Cr picolinate supplementation markedly decreased blood glucose and increased insulin concentration in laying hens. Offenbacher and Pi-Sunyer (23) showed no significant decreases in fasting glucose concentrations with Cr supplementation. Anderson et al. (24) showed a significant decrease in fasting glucose in the group receiving 1000 μg Cr compared with placebo, but not in the group receiving 200 μg Cr. Abraham et al. (25) on the other hand, reported no significant increase in fasting glucose concentrations. Wilson and Gondy (26) reported that Cr nicotinate had no effect in reducing insulin in healthy young subjects, but had a positive effect in those subjects with elevated fasting insulin levels.

CrMet supplementation did not improve lipid parameters, whereas supplemental $CrCl_3$ had a positive effect on serum lipids, as demonstrated by a decrease in total cholesterol, triglyceride and a reduced THR. Abraham et al. (25) with 250 ppb $CrCl_3$, increased HDL-cholesterol and decreased triglyceride, and Anderson (27) observed significant effects of $CrCl_3$ on blood lipids. Two human studies showed no significant effects on lipids with Cr nicotinate or Cr picolinate supplementation (28,29). Press et al. (14) reported a slight, but not significant elevation in HDL-cholesterol concentration among human subjects receiving Cr picolinate supplementation. Similarly, reports are conflicting regarding the effect of Cr on triglycerides. Some human $CrCl_3$ supplementation studies have reported decreased serum triglyceride concentration (30,31), whereas other human Cr supplementation studies have reported no effect on plasma triglyceride concentration (32,33). These inconsistent responses of lipids to Cr supplementation may reflect differences in the Cr status or in a failure to control the dietary factors that influence circulating lipid levels.

In conclusions, CrMet supplementation is effective for increasing serum insulin, and $CrCl_3$ may improve lipid levels because we observed decreased serum total cholesterol and an improved THR ratio. Further work is needed to elucidate the impact of this supplemental bioavailable Cr source.

## ACKNOWLEDGEMENTS

This study was proceeded in part by Korea Research Foundation Grant (KRF-99-005-G00011).

## REFERENCES

1. Anderson RA. 1986. Chromium metabolism and its role in disease processes in man. *Clin Phy Bioch* 4: 31-41.
2. Anderson RA. 1993. *Recent advances in the clinical and biochemical effects of chromium deficiency.* Wiley Liss, New York. p 221-234.
3. Anderson RA. 1995. Chromium, glucose tolerance, diabetes and lipid metabolism. *J Adv Med* 8: 37-49.
4. Mertz W. 1993. Chromium in human nutrition: a review. *J Nutr* 123: 626-633.
5. NRC. 1997. *The Role of Chromium in Animal Nutrition.* National Academy Press, Washington, DC.
6. Hasten DL, Hegsted M, Keenan MJ, Morris GS. 1997. Effects of various forms of dietary chromium on growth and body composition in the rat. *Nutr Res* 17: 283-294.

7. Hasten DL, Hegsted M, Keenan MJ, Morris GS. 1997. Dosage effects of chromium picolinate on growth and body composition in the rat. *Nutr Res* 17: 1175-1186.
8. Anderson RA, Bryden NA, Polansky MM. 1997. Lack of toxicity of chromium chloride and chromium picolinate in rats. *J Am Coll Nutr* 16: 273-279.
9. Evans GW. 1989. The effect of chromium picolinate on insulin controlled parameters in humans. *Int J Biosocial Med Res* 11: 163-180.
10. Striffler JS, Law JS, Polansky MM, Bhathena SJ, Anderson RA. 1995. Chromium improves insulin response to glucose in rats. *Metabolism* 44: 1314-1320.
11. Bunting LD, Fernandez JM, Thompson DL Jr, Southern LL. 1994. Influence of chromium picolinate on glucose usage and metabolic criteria in growing Holstein calves. *J Anim Sci* 72: 1591-1599.
12. Kegley EB, Spears JW, Eisemann JH. 1997. Performance and glucose metabolism in calves fed a chromium and nicotinic acid complex or chromium chloride. *J Dairy Sci* 80: 1744-1750.
13. Anderson RA. 1987. *Trace elements in human health and diseases.* Academic, New York. p 225.
14. Press RI, Geller J, Evans GW. 1990. The effect of chromium picolinate on serum cholesterol and apolipoprotein fractions in human subjects. *West J Med* 152: 41-45.
15. Doisy RJ, Streeten DHP, Freiberg JM, Schneider AJ. 1976. *Trace elements in human health and diseases.* Academic, New York. p 79-104.
16. Anderson RA, Kozlovsky AS. 1985. Chromium intake, absorption and excretion of subjects consuming self-selected diets. *Am J Clin Nutr* 41: 177-1183.
17. American Institute of Nutrition. 1977. Report of the American Institute of Nutrition ad hoc committee on standards for nutritional studies. *J Nutr* 107: 1340-1348.
18. SAS Institute Inc. 1996. *SAS User's Guide: Statistics.* SAS Institute, Cary, NC.
19. Cefalu WT, Wang ZQ, Zhang XH, Baldor LC, Russel JC. 2002. Oral chromium picolinate improves carbohydrate and lipid metabolism and enhances skeletal muscle Glut-4 translocation in obese, hyperinsulinemic (JCR-LA corpulent) rats. *J Nutr* 132: 1107-1114.
20. Ward TL, Southern LL, Boleman SL. 1993. Effect of dietary chromium picolinate on growth, nitrogen balance and body composition of growing broiler chicks. *Poultry Sci* 72: 37-45 (suppl. 1).
21. Rosebrough RW, Steele NC. 1981. Effect of supplemental dietary chromium or nicotinic acid on carbohydrate metabolism during basal, starvation and refeeding periods in poults. *Poult Sci* 60: 407-417.
22. Sahin K, Kucuk O, Sahin N, Ozbey O. 2001. Effects of dietary chromium picolinate supplementation on performance, insulin and corticosterone in laying hens under low ambient temperature. *J Anim Physiol Anim Nutr* 85: 142-147.
23. Offenbacher E, Pi-Sunyer F. 1980. Beneficial effect of chromium-rich yeast on glucose tolerance and blood lipids in elderly subjects. *Diabetes* 29: 919-925.
24. Anderson RA, Cheng N, Bryden NA, Polansky MM, Cheng N, Chi J, Feng J. 1997. Elevated intakes of supplemental chromium improve glucose and insulin variables in individuals with type 2 diabetes. *Diabetes* 46: 1786-1791.
25. Abraham AS, Brooks BA, Eylah U. 1992. The effects of chromium supplementation on serum glucose and lipids in patients with and without non-insulin-dependent diabetes. *Metabolism* 41: 768-771.
26. Wilson BE, Gondy A. 1995. Effects of chromium supplementation on fasting insulin levels and lipid parameters in healthy, non-obese young subjects. *Diabetes Res Clin Pract* 28: 179-184.
27. Anderson RA. 1998. Chromium, glucose intolerance and diabetes. *J Am Coll Nutr* 17: 548-555.
28. Sun Y, Mallya K, Ramirez J, Vincent JB. 1999. The biomimetic $[Cr_3O(O_2CCH_2CH_3)6\ (H_2O)_3]^+$ decreases plasma cholesterol and triglyceride in rats: towards chromium-containing therapeutics. *J Biol Inorg Chem* 4: 838-845.
29. Thomas VL, Gropper SS. 1996. Effect of chromium nicotinic acid supplementation on selected cardiovascular disease risk factors. *Biol Trace Elem Res* 55: 297-305.
30. Riales R, Albrink MJ. 1981. Effect of chromium chloride supplementation on glucose tolerance and serum lipids including high-density lipoprotein of adult men. *Am J Clin Nutr* 34: 2670-2678.
31. Anderson RA, Polansky MM, Bryden NA, Roginski EE, Mertz W, Glinsman W. 1983. Chromium supplementation of human subjects; Effects on glucose, insulin and lipid variables. *Metabolism* 32: 894-899.
32. Hermann J, Arquitt A, Stoecker B. 1994. Effects of chromium supplementation on plasma lipids, apolipoproteins, and glucose in elderly subjects. *Nutr Res* 14: 671-674.
33. Uusitupa MI, Mykkanen J, Siitonen O, Laasko M, Sarlund H, Kolehmainen P, Rasanen T, Kumpulainen J, Pyorala K. 1992. Chromium supplementation in impaired glucose tolerance of elderly: effects on blood glucose, plasma insulin, C-peptide and lipid levels. *Br J Nutr* 68: 209-216.

(Received August 23, 2004; Accepted October 19, 2004)