

Studies on chromium picolinate pre-treated albino rats given high concentrations of glucose D

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Abstract: The status of chromium as an essential nutrient is an ongoing debate despite its widespread use as supplement. Chromium supplement has been reported to improve glucose tolerance, insulin action and promote weight loss. This study examined the effect of given high concentrations of glucose D to chromium picolinate pretreated rats. Male albino wistar rats (36) fed a standard diet for approximately 6 weeks, weighing (170-210g), were used for this study. After an overnight 12 hours fasting, the rats were divided into 2 groups (A and B). The Group A rats, further divided into 6 sub groups of three rats each, received oral glucose load of (0, 5, 10, 20 40 and 80 g/kg of body weight) respectively within 3 hours. While group B rats, were all pre-treated with 4µg/kg of chromium picolinate one hour prior to administration of concentrations of glucose D in similar manner as in group A, respectively. Plasma insulin, plasma and urine glucose measured after 24 hours, showed no statistical significant differences ($P>0.05$) in the mean plasma glucose, urine glucose, and plasma insulin levels between the groups. In conclusion, Chromium picolinate does not appear to improve insulin sensitivity and change plasma glucose level.

Keywords: High Glucose concentration, Glucose Tolerance, Chromium Picolinate, Blood Glucose, Plasma Insulin

1. Introduction

Chromium is a transitional element that is ubiquitous in nature, occurring in air, water, soil and biological materials, over a range of concentrations. Chromium picolinate, derived from chromium (III) and picolinic acid is a chemical compound available as a nutritional supplement to prevent or treat chromium deficiency. Several studies have reported beneficial effects of chromium on glucose tolerance and or lipid metabolism. Chromium dietary supplements use is especially popular among patients with Type 2 Diabetes Mellitus (T2DM) or those attempting to lose weight (Shapiro and Gong, 2002). It has been reported (Martin et al, 2006) that Chromium picolinate supplementation in subjects with (T2DM) who are taking sulfonylurea agents, show significant improvement in insulin sensitivity and glucose control as well as significant attenuated body weight gain and visceral fat accumulation.

However, despite those claims, a meta-analysis of chromium supplementation studies showed no association

between chromium and glucose or insulin concentrations for non-diabetics, and inconclusive results for diabetics (Althuis et al, 2002). Interestingly, this study has been challenged by Kalman D.S (2003) because it excluded significant results. Over the years, there has been considerable interest on whether or not that chromium as an essential element could potentiate insulin action and thus, influences carbohydrate, lipid and protein metabolism. The nature of this relationship however, has not been clearly defined and findings gave mixed results. A study by Gunton et al, (2005) found no beneficial effect of chromium supplementation in the treatment of people with impaired glucose tolerance despite increases in serum chromium levels. Also recently, (Masharani et al, 2012) have reported that pharmacological doses of chromium picolinate therapy do not improve insulin sensitivity in normal non-diabetic subjects. However, Balk et al. (2007) have shown that chromium supplementation significantly improved glycemia among patients with diabetes. Studies by Singer and Geohas (2006) have shown that chromium

picolinate/biotin supplementation may represent an effective adjunctive nutritional therapy to people with poorly controlled diabetes and with the potential for improving lipid metabolism.

Therefore, since existing information from several studies are often confusing and misleading, the present studies were performed to investigate the effects of chromium on glucose concentration and glucosuria (a condition which is known to occur when renal threshold for glucose is exceeded) in rat. This study was to determine whether consumption of chromium picolinate prior to administration of high concentrations of glucose D, alters glucose metabolism significantly in albino rats.

2. Materials and Methods

Chromium picolinate tablets were purchased from Solgar Vitamin and Herb, UK while insulin RIA kit was from MP Biomedicals, New York. The assay kit for glucose was from Randox Laboratories, Co-Antrium, UK. All other reagents were of analytical grade.

2.1. Experimental Animals

Male, albino wistar rats (36), weighing (170-210g), obtained from the Animal House, Department of Pharmacology and Toxicology, University of Port-Harcourt, Nigeria were used for this study. The animals were housed for two weeks under similar conditions in standard cages at controlled atmosphere to acclimatize with 12 hours light/dark cycle prior to commencement of the studies. They were approximately 5–6 weeks old at the beginning of the studies. The rats were fed a standard diet, ad libitum (animal feed), and each animal had free access to drinking water.

After an overnight 12 hour fasting, the rats were divided randomly into 2 groups (A and B) of approximately equal initial mean body weights and identified by tail tattoo (marks). Then blood samples were collected from tail bleeds from each rat for measurement of plasma glucose and insulin levels. The rats in each group were further divided into 6 subgroups consisting of three rats each (in group A, subgroups are A1-A6 while in group B, subgroups are B1-B6). Thereafter, the rats in group A, received oral glucose load (0, 5, 10, 20 40 and 80 g/kg of body weight) respectively within 3 hours. While group B rats, were all pre-treated with 4µg/kg of chromium picolinate one hour prior to oral administration of doses of glucose D in similar manner as in group A respectively. The rats were

subsequently incubated in metabolic cages and observed for 24 hours, thereafter, blood and urine samples were collected for determination of glucose using spectrophotometer based on glucose oxidase method as described by Trinder, (1969). Plasma insulin was measured using MPBiomedicals Immuchem™ Radioimmunoassay kit as described by the manufacturer. It involves the use of Lyophilized insulin labeled with iodine-125 (¹²⁵I), anti-insulin coated tubes, insulin standard prepared in insulin buffer(phosphate buffered saline solution at pH 7.0 containing horse serum, with 10% sodium azide as preservative), insulin controls supplied in phosphate buffered saline containing bovine serum albumin). To assay, the lyophilized insulin-¹²⁵I was reconstituted with 5.0ml of distilled water and allowed to sit at room temperature for 60 minutes. The reconstituted insulin tracer solution was poured directly into a clean glass flask. The tracer solution vial was washed out three times with buffer and the washes added to the glass flask. The remaining buffer solution was added to the flask and mixed thoroughly. All standards, coated tubes and insulin-¹²⁵I were brought to room temperature prior to use. The required number of anti-insulin tubes was placed in a test tube rack. Then 100µL each of insulin standards, control and samples were added to their respective tubes. Thereafter, 900µL of Tracer/ buffer solution was added to all tubes. After then, all tubes were vortex thoroughly and incubated at room temperature for 18 hours. Thereafter, all tubes were decanted and blotted except the total count tubes. The radioactivity count was done in a gamma counter for one minute. The concentration of insulin was obtained from a standard curve where % bound was plotted against concentration.

Statistical Analysis: The results were expressed as the mean and standard deviation and were analyzed using the students' tests. The difference in mean at P>0.05 was considered statistically not significant.

3. Results

3.1. Effects of Chromium Picolinate and Increase Oral Glucose Loads on the Rats Behavioral Pattern

No noticeable changes were observed in the behavioral pattern of the rats 24 hours after oral administration of chromium picolinate and glucose D even with increase doses of glucose D. No visible changes with regard to onset of pallor, sedation, respiratory distress, coma or death were noticed 24 hours after the onset of the studies.

Table 1. Fasting glucose and insulin levels of rats assigned and arranged as (Group A) and those for (Group B).

Parameters	Group A Rats (For glucose load only) Mean ±SD (n=18)	Group B Rats (For administration of chromium picolinate & glucose load) Mean ±SD(n=18)	P-value
Fasting blood glucose level (mmol/L)	4.32±0.24	4.29±0.35	P> 0.05
Fasting plasma insulin level (mIU/L)	15 ± 3.2	16 ± 1.8	P>0.05

Note: the values are Mean ± SD while P>0.05 indicates that difference in their mean values is statistically not significant

3.2. Effects of high concentrations of glucose D given to Chromium Picolinate pretreated rats on Insulin, Plasma and Urine Glucose Levels

The plasma glucose levels (Mean \pm SD) of rats fed with varying concentrations of glucose D only (Group A) compared with those fed with 4 μ g/dl chromium picolinate prior to administration of oral glucose loads (Group B) is shown in Table 2 while the 24 hours urine glucose levels (Mean \pm SD) of rats fed with varying concentrations of glucose D only (Group A) compared with those fed with 4 μ g/dl chromium picolinate prior to administration of oral

glucose loads (Group B) is shown in Table 3. The results show that there was no statistical significant differences ($P>0.05$) in the mean plasma glucose level and urine glucose levels between the groups (See tables 2 and 3). Figure I show a plot comparing the plasma insulin levels (Mean \pm SD) between the rats fed with oral glucose loads only (Group A) and those fed with 4 μ g/dl chromium picolinate prior to administration of oral glucose loads (Group B). According to the figure shown, there was also no significant difference observed in plasma insulin levels (mean) between the two groups.

Table 2. Plasma Glucose levels of rats fed with oral glucose loads only (Group A) compare with those fed with 4 μ g/dl chromium picolinate and oral glucose loads (Group B).

Dose of Oral Glucose administered (g/kg)	Plasma Glucose levels (mol/L)		P-value
	Group A (Glucose load only) (n=3 each)	Group B (4 μ g/kg chromium picolinate & Glucose load) (n=3 each)	
0	3.03 \pm 0.38	1.92 \pm 0.29	$P>0.05$
5	4.59 \pm 0.57	4.05 \pm 0.69	$P>0.05$
10	5.47 \pm 2.09	4.71 \pm 0.68	$P>0.05$
20	5.90 \pm 1.28	5.53 \pm 0.78	$P>0.05$
40	6.47 \pm 1.57	5.78 \pm 0.18	$P>0.05$
80	7.13 \pm 1.25	6.78 \pm 0.54	$P>0.05$

Note: the values are Mean \pm SD while $P>0.05$ indicates that difference in their mean values is statistically not significant

Table 3. The 24 hours collected urine glucose levels of rats fed oral glucose loads only (Group A) compare with those fed 4 μ g/dl chromium picolinate and oral glucose loads (Group B).

Dose of Oral Glucose administered (g/kg)	Urine glucose levels (Mean \pm SD) (mol/L)		P-value
	Group A (Glucose load only) (n=3 each)	Group B (4 μ g/kg chromium picolinate & Glucose load) (n=3 each)	
0	0.18 \pm 0.02	0.15 \pm 0.02	$P>0.05$
5	0.77 \pm 0.29	0.50 \pm 0.04	$P>0.05$
10	1.37 \pm 0.2	1.19 \pm 0.06	$P>0.05$
20	5.7 \pm 2.15	5.32 \pm 0.05	$P>0.05$
40	7.93 \pm 7.16	6.39 \pm 0.08	$P>0.05$
80	24.3 \pm 1.56	22.50 \pm 0.15	$P>0.05$

Note: the values are Mean \pm SD while $P>0.05$ indicates that difference in their mean values is statistically not significant

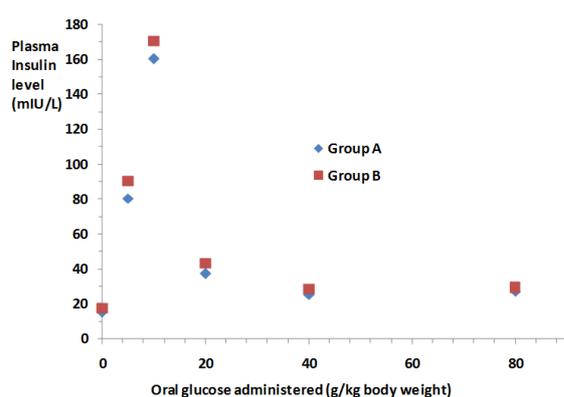


Figure 1. Plasma insulin levels (mean) of rats fed varying concentrations of oral glucose loads only (Group A) and those fed 4 μ g/kg chromium picolinate and varying concentrations of oral glucose load (group B).

4. Discussion

In investigating the effects of given high concentrations of glucose D to chromium picolinate pretreated albino rats, we

found no evidence that chromium picolinate had significant impact on the concentration of plasma glucose in the rats. Several previous studies have examined the effects of chromium supplementation on glucose metabolism with inconsistent results, with some studies reporting a positive effect on glucose and/or insulin levels whereas others failing to show benefit. This is most likely due to significant variability among these studies with respect to the preparation and dose of chromium given, the duration of use and the study population. In this study, we use rats because it was easier to control their feeding pattern and life style effectively. Whereas most of the studies have been in patients with diabetic mellitus (Balk et al. 2007; Phung et al, 2010), while some studies have been performed in patients at high risk of developing diseases, such as Impaired Glucose Tolerant (IGT), obesity, or a family history of Type 2 Diabetic Mellitus (T2DM) (Anderson et al, 1991; Cefalu et al. 1999). However, our finding is intriguing because some other studies were also unable to demonstrate any beneficial effect of chromium picolinate supplementation on glucose metabolism (Amato et al. 2000; Masharani et al.

2012) despite claims of it beneficial effects.

This study also examined the effect on the concentration of plasma insulin in chromium picolinate pretreated rats given high concentrations of glucose D. This study found no significant sensitization or amplification or changes in the plasma insulin levels compared with those not given chromium picolinate. However, the result of this study shows that the plasma insulin levels were lower at higher oral doses of glucose. This is consistent with the report by Craighead (1994) that insulin receptor activity increase as plasma insulin levels fell. This suggests that with increase in the plasma glucose levels, there was also increase in the uptake of insulin by insulin receptor resulting in a fall in plasma insulin levels. Although, there are studies suggesting that chromium can improve blood sugar control and insulin sensitivity among diabetics. Most studies found no such effects among non-diabetics subjects (Amato *et al.* 2000; Balk *et al.* 2007). Hence, we suggest that chromium picolinate does not increase insulin binding to cells even though there was increased insulin receptor numbers.

The rise in plasma glucose levels of the rats as shown in this study resulted in glucosuria which increased with increase in oral glucose load. Glucose is usually filtered by the renal glomeruli and almost totally reabsorbed by the kidneys tubules. Hence in the rats, the renal threshold for glucose was exceeded for both groups.

5. Conclusion

In conclusion, administration of chromium picolinate on rats prior to given high concentrations of glucose D does not improve insulin sensitivity or influence changes in the glucose level in the rats. Hence, extensive studies of chromium status in normal subjects and pre-diabetics should be undertaken.

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