

Full Length Research Paper

The effect of supplemental dietary chromium on blood glucose, body weight and liver enzymes of rabbits

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Dietary trivalent chromium as chromium picolinate supplementation is an essential nutrient for human life and been used at higher dosages to offset problems of malabsorption or to pharmacologically influence the chemistry of blood sugar control in diabetics and has been previously studied on the basis of non-randomized clinical trials. It is also recognized as one of 15 trace elements critical for proper physiological functioning of lipid and carbohydrate metabolism. The present study was unique, as it has been the first ever study in which the effect of different doses of chromium supplementation (200/400 µg chromium chloride) at different time intervals on body weight, bilirubin, serum glutamate pyruvate transaminase, serum glutamate oxaloacetate transaminase and alkaline phosphatase has been investigated in normal and diabetic rabbits. Twenty four healthy Newzeland white rabbits were randomly selected, half of them were made diabetic with the help of alloxan at the dose of 300 mg/kg body weight orally for two weeks on a daily basis. Both normal and diabetic groups were divided into two treatment groups; 200 and 400 µg/L supplemental chromium was provided by chromium chloride incorporated into drinking water daily for sixty days. Blood glucose levels were checked on 0, 15, 30 and 60 days. In supplemental chromium, chloride did not affect bilirubin ($P < 0.05$) in any rabbit type, while results revealed increased secretion of SGPT (93.00 to 134.50 i.µ) and decreased ALK-PHOS levels (133.17 to 45.1 i.µ) in normal group. In contrary, decreased secretion of SGPT (83.50 to 75.17 i.µ) and an increased ALK-PHOS level (115.83 to 167 i.µ) has been observed in diabetic group at doses of 200/400 µg chromium chloride supplementation in all rabbits, while SGOT level showed increased effect in both normal and diabetic groups. The bodyweight profile was affected in all rabbit's type by supplemental chromium. Bodyweight increased as dietary chromium. Chloride content increased from 0 to 200 µg statistically, experimental data evaluated as significant at ($P < 0.05$, $P < 0.01$).

Key words: Chromium chloride, blood glucose level, alloxan, body weight, liver enzymes, rabbits.

INTRODUCTION

The role of trace elements along with metals, are essential for proper functioning of biochemical reactions in particular as enzyme cofactors and in vast set of processes involved in regulation of glucose metabolism

or in hormonal control, especially insulin (Wiernsperger and Rapin, 2010). Chromium is a mineral which is required in trace amounts by the human body and is one of the most popular and widely used supplements. It is sold as a single-ingredient supplement as well as in combination formulas, particularly those marketed for weight loss and performance enhancement (Wiernsperger and Rapin, 2010). Chromium has

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Table 1. Effect of supplemental chromium chloride on blood glucose profile of rabbits.

Dose ($\mu\text{g/L}$)	Baseline (Mean \pm S.D)	After 15 days (Mean \pm S.D)	After 30 days (Mean \pm S.D)	After 60 days (Mean \pm S.D)
Normal (200)	79.50 \pm 0.207	82.54 \pm 0.307	82.54 \pm 0.307	88.67 \pm 0.49
Normal (400)	88.67 \pm 0.49	92.54 \pm 0.507	82.54 \pm 0.307	95.17 \pm 0.52
Diabetic (200)	125.1 \pm 0.68	109.83 \pm 0.781	100.33 \pm 0.461	92.8 \pm 0.528
Diabetic (400)	125.1 \pm 0.68	110.23 \pm 0.861	114.56 \pm 0.561	108.2 \pm 0.561

extensively been area of concern since long for its probable connection to various health conditions. Among the most active areas, chromium is used in supplement form to treat diabetes, lower blood lipid levels, promote weight loss, and improve body composition (Albarracin et al., 2008). Chromium is renowned to enhance the action of insulin by increasing insulin binding with receptor, phosphorylation, and protein kinase activity and finally results in decreased insulin resistance and has therefore been recommended that might help to control Type 2 diabetes or the glucose and insulin responses in persons at high risk of developing the disease (Cefalu and Hu, 2004).

Chromium has been utilized to reduce body fat mass and increase lean body mass (Lai, 2008). In addition, dietary chromium supplementation significantly improves body mass index and lipid profile as well as improve insulin resistance and in the prevention and treatment of obesity and Type 2 diabetes as insulin resistance has been revealed to be the chief contributing factor to the metabolic syndrome, comprising obesity, dyslipidemia, hypertension, and hyperglycemia (Lau et al., 2008). Dietary supplementation of chromium compound may be efficacious in athletes due to excessive chromium loss and insignificant chromium intake. This has been supported by recent studies that have shown that chromium supplementation increase the muscle mass thus can attract athletes for its use to improve their muscle strength (Martin et al., 2006). Chromium potentiates insulin activity and is responsible for normal insulin function. As chromium potentates the activity of insulin, therefore, it affects different liver enzymes as well (Riales et al., 1981). The results from one of the studies has suggested that trivalent chromium (CRC454) showed significant reduction of hyperglycemia under insulin-deficient conditions as compared to improvement of body weight gains and blood levels of creatine kinase, aspartate transaminase, and alanine transaminase (Machalinski et al., 2006). The present study was undertaken so as to find out the effect of different doses of chromium supplementation (200/400 μg chromium chloride) at different time intervals on body weight, bilirubin, serum glutamate pyruvate transaminase, serum glutamate oxaloacetate transaminase and alkaline phosphatase has been investigated in normal and diabetic rabbits.

MATERIALS AND METHODS

Animals

Twenty four healthy Newzeland white rabbits of two years of age were assigned to two treatments in a completely randomized design at start of study. In each treatment, twelve normal and twelve diabetic rabbits were used. This study was conducted at the animal house of National Institute of Health, Islamabad, Pakistan from January, 2010 to June, 2010. They were fed until two months with chromium chloride to determine the effect of different doses of chromium on body weight, Bilirubin, SGPT, SGOT and ALK-PHOS of normal and diabetic rabbits at different time intervals.

Induction of diabetes

The next step was to induce diabetes in the second group that is, the diabetic group. The diabetic group was made diabetic with the help of alloxan tetrahydrate (Sigma 6316) at the dose of 300 mg/kg body weight orally for two weeks on a daily basis (John et al., 1983). Blood glucose level was estimated initially and at every three days interval. Induction of diabetes was confirmed by measuring the blood glucose level.

At the end of two weeks, a rise in blood sugar was noticed in the group, which was compared with the standard normal blood glucose value in rabbits, that is, 75 to 100 mg/dL. Rabbits with blood glucose level 125 mg/dL and above were selected as diabetic (Table 1).

Dietary treatments

In the experiment, various levels of chromium provided by chromium chloride ($\text{CrCl}_3 \cdot 6 \text{H}_2\text{O}$) were given. The chromium chloride was purchased from Sigma Aldrich (Chromium (III) chloride, anhydrous flakes, 99 to 99%, and product number 450790). The treatments consisted of 200 $\mu\text{g/l}$ (Treatment 1) and 400 $\mu\text{g/l}$ (Treatment 2) of supplemental chromium. The dose of chromium chloride was calculated per body weight of rabbit equivalent to normal body weight of man and was administered orally in drinking water on a daily basis (Kazi et al., 2008).

Sample collection and laboratory analysis

Twenty four Newzealand rabbits were fed until two months with chromium chloride to determine the effect of different doses of chromium on Body weight, Bilirubin, SGPT, SGOT and ALK-PHOS of normal and diabetic rabbits. Bodyweight was recorded by using triple beam balance whereas Kits of following Bilirubin (Merk 60050198), SGPT (Merk 60055778), SGOT (Merk 60056153) and ALK-PHOS (Randox) were used. All the parameters were recorded

on 0, 15, 30 and 60 days in both the groups of normal and diabetic rabbits.

Statistical analysis

For each group (normal and diabetic) difference among treatments for body weight, bilirubin, SGPT, SGOT and ALK-PHOS at baseline and after 60 days was analyzed by using SPSS V.16 and Paired t-Test.

RESULTS

Effect of supplemental chromium chloride on blood glucose profile (mg/dL) of rabbits

Blood glucose (mg/dL) profile has also been observed in normal and diabetic groups which were subjected to supplemental chromium chloride at two different doses 200/400 µg chromium chloride for 60 days treatment. Effects of supplemental chromium chloride on normal and diabetic groups were recorded in Tables 1 and 2. It has been observed that there is significant decrease ($P < 0.05$ and $P < 0.01$) in blood glucose level (125.1 to 92.8 mg/dL) of diabetic group when subjected to dose 200 µg chromium chloride. While significant ($P < 0.01$) decrease in blood glucose level has also been observed at dose 400 µg chromium chloride (125.1 to 108 mg/dL) in diabetic group. Whereas, increase in blood glucose level (79.50 to 88.67 mg/dL) of normal group has been observed at dose 200 µg chromium chloride and further increase in blood glucose has been observed at dose 400 µg chromium chloride. Results are quiet similar at both observation time periods (30 and 60 days). So results revealed that dose of 200/400 µg chromium chloride prove to be more effective in diabetic groups as it decrease significantly blood glucose levels (mg/dL) which is crucial for diabetic condition. Simultaneously, it can also be evaluated from experimental data of normal group, that dose range 200/400 µg chromium chloride supplementation up to 60 days of observation time, showed continuous increase in blood glucose levels, so this dose range is not effective for normal group.

Effect of supplemental chromium on body weight profile of rabbits

The effect of chromium supplementation on the body weight profile of rabbits, has been observed at doses of 200/400 µg chromium chloride in diabetic and normal groups (observation time of 60 days), comparatively evaluated and mentioned in Table 3. It has been found that chromium supplementation does not show pronounced change in body weight of normal groups, while in diabetic group, significant decrease in body weight has been observed. Statistically, these results are highly significant ($P < 0.05$, $P < 0.01$) which clearly indicates

effects of chromium supplementation particularly in diabetic group.

Effects of supplemental chromium chloride on LFT's profile of rabbits

The effect of supplemental chromium as chromium chloride on LFT's profile of rabbits has been observed both in normal and diabetic groups at two different doses of 200/400 µg chromium chloride. Bilirubin, SGPT, SGOT and ALK-PHOS levels of both groups were recorded by using Kit method and results has been mentioned in Table 4. Results revealed significant variation specifically related to SGPT and ALK-PHOS levels in normal and diabetic groups. In normal group doses of 200/400 µg Chromium Chloride supplementation cause increased secretion of SGPT (93.00 to 134.50 i.µ) and while ALK-PHOS levels has decreased (133.17 to 45.1 i.µ) has been observed. In contrary, decreased secretion of SGPT (83.50 to 75.17 i.µ) and an increased ALK-PHOS level (115.83 to 167 i.µ) has been observed in diabetic group at doses of 200/400 µg Chromium Chloride supplementation. While Bilirubin levels showed minor increase in both groups. Whereas results revealed that SGOT level has been increased significantly ($P < 0.05$, $P < 0.01$) under the effect of chromium chloride supplementation.

DISCUSSION

Chromium plays a critical role in carbohydrate and lipid metabolism in mammals, being a part of a glucose/insulin system, which maintains homeostatic control of blood glucose in the animals. Chromium deficiency is associated with hyperglycemia in animals as well as in humans. The condition can be reversed by supplementation (Schwartz and Mertz, 1959; Anderson et al., 1997; Lamson and Plaza, 2002; Ibrahim et al., 2010). Blood glucose (mg/dL) profile has also been observed in normal and diabetic groups of animals (rabbit) which were subjected to supplemental chromium chloride at two different doses 200/400 µg chromium chloride. Experimental analysis showed that there is significant decrease in blood glucose level, when subjected to dose 200 µg chromium chloride and same results were observed at dose 400 µg chromium chloride in diabetic group. Previous studies support these findings, that supplemental chromium had lower blood glucose concentration in broilers but these observation were obtained on lower level of chromium rather than higher levels (Debski et al., 2001; Juturu and Komorowski, 2007). In present study, it has been observed that effects on blood glucose level of normal group are in contrast to, those of diabetic group, as increase in blood glucose level has been observed at dose 200 and 400 µg chromium chloride. In contrast to it, previous studies

Table 2. Comparison of blood glucose (mg/dL) profile after 200 and 400 µg of oral chromium chloride. Chloride administration in normal and diabetic rabbits (n = 12).

Group	Baseline (mean)	After 60 days (mean)	Baseline (mean)	After 60 days (mean)
	200 µg CrCl	200 µg CrCl	400 µg CrCl	400 µg CrCl
Normal	79.50 ± 0.207	88.67 ± 0.49	88.33 ± 0.163	95.17 ± 0.522
Diabetic	125.1 ± 0.68**	92.8 ± 0.528**	125.1 ± 0.68*	108.2 ± 0.561*

Values were expressed as (Mean ± S.D) significant, ** show for both (P<0.05) and (P<0.01), * show for (P<0.05).

Table 3. Effect of supplemental chromium on body weight profile of rabbits. Comparison of Bodyweight profile after 200 and 400 µg of oral CrCl administration in normal and diabetic rabbits (n = 12).

Group	Baseline (Mean ± S.D)	After 60 days (Mean ± S.D)	Baseline (Mean ± S.D)	After 60 days (Mean ± S.D)
	200 µg CrCl	200 µg CrCl	400 µg CrCl	400 µg CrCl
Normal	1.7335 ± 0.75*	1.93 ± 0.90*	1.93 ± 0.950*	1.70 ± 0.95*
Diabetic	1.79 ± 0.900*	2.2 ± 0.154*	1.94 ± 0.1164*	2.02 ± 0.165*

Values were expressed as (Mean ± S.D.) significant ** show for both (P<0.05) and (P<0.01) * show for (P<0.05).

Table 4. Effect of supplemental chromium chloride on LFT's profile of rabbits. Comparison of LFT profile after 200 and 400 µg of oral CrCl administration in normal and diabetic rabbits (n = 12).

Group	Baseline (Mean ± S.D)	After 60 days (Mean ± S.D)	Baseline (Mean ± S.D)	After 60 days (Mean ± S.D)
	200 µg CrCl	200 µg CrCl	400 µg CrCl	400 µg CrCl
Normal				
Bilirubin	0.300 ± 0.03	0.367 ± 0.035	0.33 ± 0.03	0.433 ± 0.04
SGPT	93.00 ± 0.97	167.83 ± 0.172	101.67 ± 0.102	134.50 ± 0.132
SGOT	57.17 ± 0.57**	112.67 ± 0.11**	60.00 ± 0.59	96.50 ± 0.97**
ALK-PHOS	133.17 ± 0.133	123.33 ± 0.118	159.00 ± 0.160	45.1 ± 0.162
Diabetic				
Bilirubin	0.283 ± 0.030	0.35 ± 0.030	0.417 ± 0.040	0.367 ± 0.0350
SGPT	83.50 ± 0.83	76.50 ± 0.75	98.50 ± 0.102	75.17 ± 0.77
SGOT	36.82 ± 0.35**	85.67 ± 0.94**	56.50 ± 0.59**	68.83 ± 0.67**
ALK-PHOS	115.83 ± 0.112	173.50 ± 0.171	170.00 ± 0.172	167 ± 0.166

Values were expressed as (Mean ± S.D.) significant, ** show for both (P<0.05) and (P<0.01), *show for (P<0.05).

showed that there is no association between chromium and glucose or insulin concentrations among non diabetic subjects (Althuis et al., 2002). Findings of present study coincide with another study, conducted in healthy volunteers and diabetic patients, treated with chromium supplementation (200 mcg/day of trivalent chromium as chromium picolinate), which revealed that Chromium showed, a positive influence on individuals with no diabetic symptoms. While in diabetic patients, it significantly lowers glucose and insulin level so, leading to improved glucose tolerance (Lamson and Plaza, 2002; Al-Bandr et al., 2010).

The positive effect of chromium in human and animal

health is due to its role as an integral component of the glucose tolerance factor (Schwartz and Mertz, 1959). Research studies showed that glucose tolerance factor GTF, which contain chromium, was deficient in animals with impaired glucose tolerance and supplemental chromium improved has glucose tolerance. Chromium is a co-factor of insulin, promoting insulin activity, enhancing amino acid uptake, promoting lipogenesis from glucose and lipid storage in the liver and adipose tissues (Ibrahim et al., 2010). According to reported proposed mode of action of Chromium in the regulation of insulin, Chromium increases insulin binding to the target cells by increasing sensitiveness and number of insulin

receptor, which are present mostly in all cells, but their concentration varies in different cell types. Structurally, insulin receptor is composed of two extracellular alpha subunits, which contain the insulin-binding site, and two trans membrane beta subunits. Structural features suggest that, chromium like insulin, affects protein phosphorylation-dephosphorylation reactions. Once insulin binds to the alpha subunit of the insulin receptor, a specific phosphorylation of the beta subunit occurs through a cascade of intermolecular phosphorylation reactions. Insulin receptor tyrosine kinase enzyme partly responsible for the phosphorylation, which is activated by chromium. Chromium binding the absence of insulin does not affect the protein kinase activity of rat adipocytes in but stimulates kinase activity 8-fold in the presence of insulin. Chromium also inhibits phosphotyrosine phosphatase (PTP-1), that inactivates the insulin receptor. Both effect of chromium would lead to increased phosphorylation of the insulin receptor, which is associated with increased insulin sensitivity, leading to significantly lowers glucose level which in turn cause improvement in diabetic condition (Anderson, 1998; Debski et al., 2001).

Although, both genetic and dietary factors influence the manifestation of Type 2 diabetes, several researchers concluded from nonrandomized studies, that dietary chromium supplementation can be an attractive option for the management of Type 1 diabetes and Type 2 diabetes for glycemic control in persons at high risk of Type 2 diabetes, as well as for women with diabetes that occurs during pregnancy (gestational diabetes). Further convincing findings in animal support this conclusion. Randomized clinical trials show conflicting evidence related to the fact that chromium deficiency can be a cause for emergence of Type 2 diabetes (Althuis et al., 2002; Anderson et al., 1997). So results from present analysis revealed that dose of 200/400 μg chromium chloride prove to be more effective in diabetic groups as it decrease significantly blood glucose levels (mg/dL) which is crucial for diabetic condition. Research studies also supports and have reported positive effects of supplemental chromium usually involved 400 mg or more of chromium. In another study, a decrease in fasting glucose has been observed in diabetic patients with daily supplementation of 600 mg of chromium as chromium chloride. Furthermore, positive effects with 500 mg/day, and 1000 mg/day of chromium as chromium chloride have also been reported (Anderson, 1998). Dietary chromium supplements are low-cost, and the safety evaluation data suggest that chromium is safe even at high doses. Therefore, in the form of dietary chromium supplementation, it would be an attractive preference for management of diabetes particularly for persons, at high risk of Type 2 diabetes (Althuis et al., 2002). It can also be evaluated from present experimental data of normal group, that dose range 200/400 μg chromium chloride supplementation showed continuous increase in blood

glucose levels, so this dose range is not effective for normal group. The fact is that, as chromium is a nutrient rather than a drug, therefore it will be beneficial for only those who are deficient or slightly deficient in chromium and among all other causes, it is also one of the causes of Type 2 diabetes (Anderson, 1998).

The effect of chromium supplementation on the body weight profile of rabbits has been observed at doses of 200/400 μg chromium chloride in diabetic and normal groups which indicates that chromium supplementation does not show pronounced change in body weight of normal groups, while in diabetic group, significant decrease in body weight has been observed. Previously, a study was conducted particularly on healthy overweight human adults, showed decrease in body fat from baseline in adults, due to sustained ingestion of chromium picolinate and suggested chromium a weight loss aid (Yazaki et al., 2009). These present studies also suggest that chromium cause an increase in live mass when given at lower dose level 200 μg chromium chloride, while when fed at much higher dose level 400 μg chromium chloride and in combination they had a non-significant effect and similar to the finding resulted, from previous experimental analysis conducted on broilers (Hossain et al., 1998; Lein et al., 1999).

The effect of supplemental chromium as chromium chloride on LFT's profile of rabbit has been observed both in normal and diabetic groups at two different doses of 200/400 μg chromium chloride. Results revealed that in normal group doses of 200/400 μg . Chromium chloride supplementation causes increased secretion of SGPT and while ALK-PHOS levels has decreased. In contrary, decreased secretion of SGPT and an increased ALK-PHOS level has been observed in diabetic group at doses of 200/400 μg chromium chloride supplementation. While bilirubin levels showed minor increase in both groups. These results were similar to those of Yazaki et al. (2009) as they also reported increase in SGOT, Alkaline phosphate and SGPT level because of chromium supplementation. Whereas, present study revealed that SGOT level has been increased significantly and similar type of results has been recorded from the study conducted by Al-Bandr et al. (2010) which also support elevated level of SGOT in animal (broilers) treated with supplemental chromium.

Conclusion

The result of the investigation indicates that both doses of chromium chloride supplementation had no significant effect on bilirubin, SGPT and ALK-PHOS but has significant effect on body weight and SGOT in both normal and diabetic rabbits. Thus, on the basis of results obtained after conducting our study, it can be concluded that both doses of 200 and 400 μg chromium chloride supplementation are safe to administer in both normal

and diabetic rabbits and are beneficial but still higher doses of chromium supplementation should be recommended with caution and not for long-term use in both healthy and diabetic subjects as fluctuations have been observed.

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Competing interests

The author(s) declare that they have no competing interests.

Ethical approval

This study was approved by the Institutional Review Board of the Sargodha University, Sargodha, Pakistan.

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