Effects of High-Chromium Bakers' Yeast on Glucose Tolerance and Blood Lipids in Rats[1]

G. S. RANHOTRA and J. A. GELROTH[2]

ABSTRACT

In rats fed a chromium-deficient diet for 17 weeks, a marginal elevation in blood glucose and cholesterol levels was observed. The potential of chromium in high-chromium bakers' yeast and chromium chloride to reverse these elevations was then examined. After a glucose challenge (200 mg/100 g body weight), bakers' yeast, but not chromium chloride, caused less elevation of blood glucose at 30, 60, and 90 min as compared to the chromium-deficient diet. Bakers' yeast also caused a significant ($P < 0.05$) lowering of serum cholesterol and triglyceride levels. A significant ($P < 0.05$) lowering effect on serum triglyceride level was also observed in animals fed chromium chloride.

Cereal Chem. 63(5):411-413

Several workers have hypothesized that a marginal chromium deficiency exists in the United States populace (Hambidge 1974, Offenbacher and Pi-Sunyer 1980, Anderson and Kozlovsky 1985). Chromium deficiency appears to be related to impairment (elevation) of blood glucose levels. This impairment can be reversed by biologically active chromium that, although the mechanism is not well understood, appears to stimulate the oxidation of glucose in the presence of insulin (Mertz 1969, Evans et al 1973). Biologically active chromium may also be involved in lipid homeostasis. Elevated blood cholesterol levels in animals and humans displaying chromium deficiency are reported (Schroeder 1969, Staub et al 1969, Doisy et al 1976, Stoecker and Oladut 1985). Some investigators link poor chromium status with atherosclerosis (Abraham et al 1980) and diabetes.

Brewer's yeast is recognized as an important source of biologically active chromium, generally termed the glucose tolerance factor (Mertz 1969). As isolated from brewer's yeast, glucose tolerance factor (GTF) seems to become available immediately to correct glucose intolerance (Evans et al 1973, Pi-Sunyer and Offenbacher 1984, Vinson and Hsiao 1985); chromium is thought to be an integral part of GTF, although a study by Haylock et al (1983) seems contradictory.

Bakers' yeast may also be a significant source of the GTF. However, bakers' yeast contains chromium in levels too low to permit meaningful experimental studies that might demonstrate this. High-chromium bakers' yeast, produced for human supplementation, is now more readily available. These studies were undertaken to examine the effect of high-chromium bakers' yeast on glucose tolerance and lipid metabolism, using rats as the test model.

MATERIALS AND METHODS

Test Animals

Thirty-six weanling male Sprague-Dawley rats (Harlan Sprague-Dawley, Indianapolis, IN) were fed a diet deficient in chromium for 17 weeks (basal diet, Table I). The animals were then divided into three equal groups that were assigned to one of the three experimental diets, A, B, or C (Table I). Experimental diets were fed on a staggered basis for nine days. The oral glucose tolerance (OGT) test was performed by intubating the animals with glucose (200 mg per 100 g of body weight) as a 50% (w/v) solution. Only six rats (two per group) were tested in a day.

Throughout the study, the animals were housed individually in clear plastic cages to minimize chromium contamination. They were housed in an environmentally controlled room, however, no modification of the room air was made. During the initial 17-week chromium deprivation period, rats were offered the diet (in ceramic cups) and distilled deionized water ad libitum. During the nine-day chromium repletion period, however, each rat was fed a restricted diet of 10 g/day.

Test Diets

The chromium-deficient (basal) diet was formulated by analyzing potential ingredients individually and then using those lowest in chromium. By analysis, this diet contained 6 μg of chromium per 100 g. Chromium-supplemented diets were prepared by adding chromium (45 μg/100 g) to the basal diet. The level of chromium addition represented 150% of the chromium requirement of the rat (NAS/NRC 1978). Chromium was added either as high-chromium yeast (diet B) or as chromium chloride (diet C). All diets were equalized for calcium, phosphorus, and zinc contents.

Biological Tests

The OGT test in rats was performed after the rats were fed the experimental diets for four days, and fasted overnight, by drawing a blood sample (tail blood), administering the glucose load, and drawing blood samples again at 30, 60, 90, 120 and 180 min for glucose determination. The feeding of experimental diets was continued for another five days. On the final day, rats were again fasted overnight, anesthetized, and a blood sample was obtained by heart puncture for lipid analysis.

Analytical

Chromium in diets and diet ingredients was determined by the department of Chemistry, Kansas State University, using DC

[1]This paper was presented at the AACC 71st Annual Meeting, Toronto, Canada, October 1986.

[2]Nutrition Research, American Institute of Baking, Manhattan, KS 66502.

plasma emission after wet ashing (HNO_3/$HClO_4$) of the samples. Calcium and zinc contents of the basal diet were determined by an IL model 251 atomic absorption spectrophotometer (Allied Analytical Systems, Andover, MA). Phosphorus was determined by the method of Fiske and Subbarow (1925). Samples for blood glucose determination were collected in heparinized capillary tubes, centrifuged, the plasma separated, and glucose in plasma determined by the glucose oxidase method using a YSI model 27 glucose analyzer (Yellow Springs Instrument Co., Yellow Springs, OH). Glucose determination was made immediately after the blood sample was obtained and the plasma separated. For determining blood lipids, blood was allowed to clot and the serum was separated. Total cholesterol in serum was determined by the modified Lieberman-Burchard method (Kim and Goldberg 1969). Serum triglycerides were determined enzymatically using diagnostic kit no. 336 from Sigma Chemical Co., St. Louis, MO. The data were analyzed statistically by analysis of variance (Snedecor and Cochran 1980) and by Duncan's (1955) multiple-range test.

RESULTS AND DISCUSSION

During feeding of the chromium-deficient diet (diet A, Table I), the fasting plasma glucose level in the rats was periodically monitored to indirectly assess their chromium status. By week 17, fasting glucose levels averaged about 115 mg/dl. In rats fed chromium-deficient diets, Jain et al (1981) reported a value of 114 mg/dl of plasma after 11 weeks, whereas Schroeder (1966) reported a value of 137 mg/dl after 43 weeks. Normal blood glucose levels in rats rarely exceed 100 mg/dl of plasma, although values ranging from 50 to 115 mg/dl are often quoted. A diet extremely low in chromium is difficult to formulate and, although airborne chromium contamination can be minimized, it is difficult to control completely. Because of this, chromium deficiency tends to develop slowly. In the present studies, after 17 weeks rats were probably in a borderline chromium deficiency state, with plasma glucose levels simulating that of a mild type II (adult-onset) diabetes.

TABLE I
Experimental Tests

	Diet		
		Chromium Supplemented	
Diet Components (g/100 g)	Basal[a] (A)	As Yeast (B)	As Chloride (C)
Casein	15	15	15
Soybean oil	5	5	5
Vitamin mix[b]	1	1	1
Mineral mix[c]	2	2	2
$CaSO_4 \cdot H_2O$[d]	2.14	2.14	2.14
$NaH_2PO_4 \cdot H_2O$[d]	1.36	1.36	1.36
$ZnCl_2$	0.002	0.002	0.002
Choline chloride	0.13	0.13	0.13
Sucrose	73.4	73.4	73.4
Added chromium (μg/100 g)			
As bakers' yeast[e]	...	45	...
As chromium chloride[f]	...	...	45

[a] Contained (by analysis) 6 μg Cr/100 g of diet.
[b] AIN mixture 76 from U.S. Biochemicals, Cleveland, OH.
[c] Chromium-free mixture. Contained (mg, in sucrose base): Mg, 40; Mn, 5; Fe, 3.5; Cu, 0.5; I, 0.015; Se, 0.01; Na, 50; and K, 360.
[d] Total amount (mg/100 g of diet) with sources added: Ca, 500; P, 400.
[e] High-chromium (3,002 μg/g) yeast from Universal Foods, Milwaukee, WI.
[f] Obtained from Sigma Chemical Co., St. Louis, MO, and added dissolved in distilled/deionized water.

Glucose Tolerance

The reported indirect method to assess the body's chromium status is chromium supplementation followed by improvement in glucose tolerance. Measurements of serum insulin activity and lipid levels also provide valuable clues to chromium nutriture (Schroeder 1969, Doisy et al 1976, Stoecker and Oladut 1985).

In chromium-deficient animals, biologically active chromium acts rapidly to improve glucose tolerance (Pi-Sunyer and Offenbacher 1984). Because of this, in the present studies the OGT test was performed just four days after feeding rats the chromium-supplemented diets. The glucose responses obtained after the glucose load are outlined in Table II.

For rats on all diets, plasma glucose levels returned to the preload (0 min) levels in 180 min. The degree of elevation of plasma glucose levels during this period, however, differed among the three diets. On the yeast-based diet, this elevation was appreciably, although not significantly ($P > 0.05$), less at 30, 60 and 90 min as compared to the control (basal) diet. This is graphically illustrated in Figure 1. Animals fed the diet supplemented with inorganic chromium (as chromium chloride), on the other hand, failed to have a similar response.

Dietary inorganic chromium must be converted into a biologically active form to function physiologically (Mertz et al 1974, Anderson et al 1978, Vinson and Hsiao 1985). In the present studies, such conversion of chromium chloride may have been slow or even entirely lacking as studies with mice by Tuman and Doisy (1977) seem to indicate. Large doses of chromium as chromium chloride may, in fact, even induce hyperglycemia as indicated by Ghafghazi et al (1977) in studies with animals. In humans, Vinson

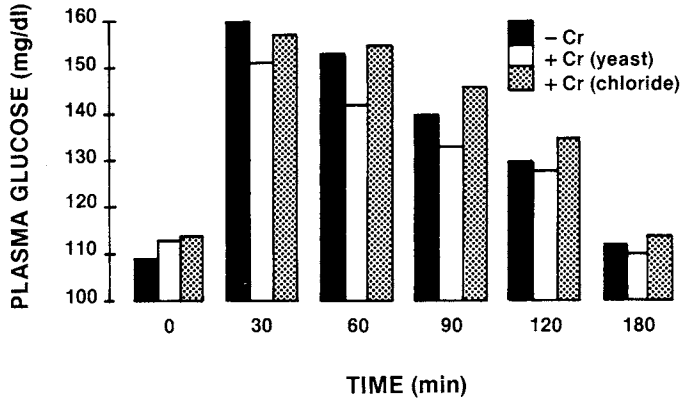

Fig. 1. Oral glucose tolerance test in rats fed chromium-deficient (−Cr) or chromium-supplemented (+CR) diets. Diets were supplemented either with bakers' yeast or chromium chloride.

TABLE II
Oral Glucose Tolerance Test in Rats[a]

	Body Weight	Plasma Glucose (mg/dl)					
Diet	(g)	0 min	30 min	60 min	90 min	120 min	180 min
A (Chromium deficient)[b]	341 ± 36	109 ± 9	160 ±17	153 ± 17	140 ± 18	130 ± 14	112 ± 9
B (Yeast-based)[c]	337 ± 29	113 ± 10	151 ± 14	142 ± 13	133 ± 8	128 ± 8	110 ± 7
C (Chloride-based)[d]	341 ± 29	114 ± 9	157 ± 16	155 ± 15	146 ± 15	135 ± 11	114 ± 10

[a] Values represent the average (10–11 rats/diet) ± SD. Averages in each column were not significantly different ($P > 0.05$). Glucose dose administered: 200 mg/100 g of body weight.
[b] 6 μg Cr/100 g of diet.
[c] 45 μg added Cr/100 g of diet; supplied by high-chromium bakers' yeast.
[d] 45 μg added Cr/100 g of diet; supplied by $CrCl_3$.

TABLE III
Blood Lipids in Rats[a]

Diet	Blood Lipid (mg/dl serum)	
	Cholesterol	Triglycerides
A (Chromium deficient)[b]	102 ± 10 a	60 ± 12 a
B (Yeast-based)[c]	93 ± 11 b	38 ± 8 b
C (Chloride-based)[d]	101 ± 7 a	45 ± 14 b

[a] Values represent the average (11–12 rats/diet) ± SD. Averages in each column followed by different letters were significantly different ($P<0.05$).
[b] 6 μg Cr/100 g of diet.
[c] 45 μg added Cr/100 g of diet; supplied by high-chromium bakers' yeast.
[d] 45 μg added Cr/100 g of diet; supplied by $CrCl_3$.

and Hsiao (1985) reported some biological activity of chromium chloride, but it was significantly less than that of chromium in regular bakers' yeast. Thus, the content of total chromium in a diet may bear little relationship to its effectiveness as biologically active chromium.

Serum Lipids

An elevated blood cholesterol level is recognized as a significant risk factor in atherosclerosis. Marginal chromium deficiency in the present studies caused only a mild elevation in blood cholesterol level. However, the yeast-based diet still caused a significant ($P<0.05$) lowering of serum cholesterol level (Table III). No such lowering was observed on diet C (chloride-based).

An elevated blood triglyceride level is also recognized as a contributory risk factor in atherosclerosis. Although serum triglyceride levels in these studies did not appear elevated, both chromium-supplemented diets caused a significant ($P < 0.05$) lowering of these levels (Table III). It is likely that such would also be the case when triglyceride levels are excessively elevated. The triglyceride-lowering effect was more pronounced on the yeast-based diet than on the chloride-based diet, however. Thus, while these studies relate to high-chromium yeast, regular bakers' yeast or yeast with somewhat higher chromium levels may be equally beneficial in correcting impairments of glucose and lipid metabolism. This may be particularly true if the GTF is not necessarily complexed with chromium as studies by Haylock et al (1983) seem to suggest.

LITERATURE CITED

ABRAHAM, A. S., SONNENBLICK, M., EINI, M., SHEMESH, O., and BATT, A. P. 1980. The effect of chromium on established atherosclerotic plaques in rabbits. Am. J. Clin. Nutr. 33:2294.

ANDERSON, R. A., and KOZLOVSKY, A. S. 1985. Chromium intake, absorption and excretion of subjects consuming self-selected diets. Am. J. Clin. Nutr. 41:1177.

ANDERSON, R. A., BRANTNER, J. H., and POLANSKY, M. M. 1978. An improved assay for biologically active chromium. J. Agric. Food Chem. 26:1219.

DOISY, R. J., STREETEN, D. H. P., FREIBERG, J. M., and SCHNEIDER, A. M. 1976. In: Trace elements in human health and disease. A. Prasad, ed. Academic Press: New York.

DUNCAN, D. B. 1955. Multiple range and multiple F test. Biometrics 11:1.

EVANS, G. W., ROGINSKI, E. E., and MERTZ, W. 1973. Interaction of the glucose tolerance factor (GTF) with insulin. Biochem. Biophys. Res. Comm. 50:718.

FISKE, C. H., and SUBBAROW, Y. 1925. The colorimetric determination of phosphorus. J. Biol. Chem. 66:375.

GHAFGHAZI, T., MAGHBAREH, A., and BARNETT, R. 1979. Chromium-induced hyperglycemia in the rat. Toxicol. 12:47.

HAMBIDGE, K. M. 1974. Chromium nutrition in man. Am. J. Clin. Nutr. 27:505.

HAYLOCK, S. J., BUCKLEY, P. D., and BLACKWELL, L. F. 1983. The relationship of chromium to the glucose tolerance factor.. J. Inorg. Biochem. 19:105.

JAIN, R., VERCH, R. L., WALLACH, S., and PEABODY, R. A. 1981. Tissue chromium exchange in the rat. Am. J. Clin. Nutr. 34:2199.

KIM, E., and GOLDBERG, M. 1969. Serum cholesterol assay using a stable Liebermann-Burchard reagent. Clin. Chem. 15:1171.

MERTZ, W. 1969. Chromium occurrence and function in biological systems. Physiol. Rev. 49:103.

MERTZ, W., TOEPFER, E. W., ROGINSKI, E. E., and POLANSKY, M. M. 1974. Present knowledge of the role of chromium. Fed. Proc. 33:2275.

NAS/NRC. 1978. Nutrient requirements of domestic animals: Nutrient requirements of laboratory animals. Bull. no. 10. National Academy of Sciences, National Research Council: Washington, DC.

OFFENBACHER, E. G., and PI-SUNYER, F. X. 1980. Beneficial effects of chromium-rich yeast on glucose tolerance and blood lipids in elderly subjects. Diabetes 29:919.

PI-SUNYER, F. X., and OFFENBACHER, E. G. 1984. Chromium. In: Present knowledge in nutrition. 5th ed. Nutrition Foundation: Washington, DC.

SCHROEDER, H. A. 1966. Chromium deficiency in rats: A syndrome simulating diabetes mellitus with retarded growth. J. Nutr. 88:439.

SCHROEDER, H. A. 1969. Serum cholesterol and glucose levels in rats fed refined and less refined sugars and chromium. J. Nutr. 97:237.

SCHWARZ, K., and MERTZ, W. 1959. Chromium (III) and the glucose tolerance factor. Arch. Biochem. Biophys. 85:292.

SNEDECOR, G. W., and COCHRAN, W. G. 1980. Statistical Methods. 7th ed. Iowa State University: Ames, IA.

STAUB, H. W., REUSSNER, G., and THIESSEN, R. 1969. Serum cholesterol reduction by chromium in hypercholesterolemic rats. Science 166:746.

STOECKER, B. J., and OLADUT, W. K. 1985. Effects of chromium and ascorbate deficiencies on glucose tolerance and serum cholesterol of guinea pigs. Nutr. Rep. Int. 32:399.

TUMAN, R., and DOISY, R. 1977. Metabolic effects of glucose tolerance factor in normal and genetically diabetic mice. Diabetes 26:820.

VINSON, J. A., and HSIAO, K. H. 1985. Comparative effect of various forms of chromium in serum glucose: An assay for biologically active chromium. Nutr. Rep. Int. 32:1.

[Received February 28, 1986. Revision received May 27, 1986. Accepted May 27, 1986.]