**Chromium (Cr)**

**Synonyms/Common Names/Related Substances:**
- Atomic number 24, chromate, chromic chloride, chromic oxide, chromium (III), chromium 3, chromium 3+, chromium acetate, chromium chloride, chromium III picolinate, chromium III, chromium nicotinate, chromium picolinate, chromium polynicotinate, chromium trichloride, chromium tripicolinate, chromium yeast, chromium, chromium-3+, chromium-enriched yeast, chromodulin, Cr III, Cr, Cr-3, Cr-3+, Cr-6+, Cr-III, glucose tolerance factor, glucose tolerance factor-Cr, GTF, GTF-Cr, hexavalent chromium, LMWCr, low molecular weight chromium, nicotinic acid, oligopeptide, picolinic acid, trivalent chromium, tryptophan amino acid metabolite.
- **Combination product examples:** Arsenal X (contains vitamin B12, *Paullinia cupana*, *Theobroma cacao* (theobromine), caffeine anhydrous USP, magnesium salicylate, yohimbe extract, Zi Shi (synephrine), guggelsterones Z&E, and *Hypericum perforatum*).
- Core4Life™ Advanced Memory Formula™ (proprietary blend of chromium picolinate, PS (phospholipid), and DHA).

**Brief Background:**
- Chromium is an essential trace element that exists naturally in trivalent and hexavalent states. Trivalent chromium (Chromium/Cr III), typically found in foods and supplements, appears to have very low toxicity and a wide margin of safety. Hexavalent chromium (Chromic oxide, Chromate) is a known toxin; long-term occupational exposure may lead to skin problems, perforated nasal septum, and lung cancer.
- Chromium plays an important role in insulin's regulation of blood glucose and it acts as a cofactor for a number of enzymes involved in energy production. It has been used to treat diseases in which glucose regulation is dysfunctional (diabetes), in lipid disorders, and as a supplement for weight loss. Similar to metformin and troglitazone, experts believe that trivalent chromium decreases insulin resistance and in addition, has an acceptable side-effect profile (1). Chromium picolinate has gained popularity among Americans, especially those seeking a weight-reduction program (2).
- Research on chromium has been hindered by several factors, including an inability to accurately measure chromium status, as well as uncertainty about the effects of chromium intake on chromium status. While chromium may decrease blood sugar in subjects with hyperglycemia and increase blood sugar in hypoglycemic states through insulin regulation, it is difficult to determine whether large controlled trials or pharmacologic studies have assessed effective chromium replacement. Benefits of chromium supplementation appear to be related to several factors, including chromium intake/status and degree of glucose intolerance (3; 4).
- Chromium picolinate is the most studied synthetic chromium product. It is not clear whether its potential benefit in other areas, such as lipoprotein balance, is a direct effect or is secondary to improved insulin and glucose homeostasis (5). Adequate controlled trials are currently unavailable to support chromium's common use in weight loss/body composition. Nutrition 21, Inc. (NXXI), a manufacturer of chromium-based and omega-3 fish oil-based nutritional supplements, announced the results of a clinical study that reportedly indicated that daily supplementation with 1,000mcg of chromium, as chromium picolinate, improved cognitive function in older adults experiencing early memory decline.

**Scientific Evidence for Common/Studied Uses:**
<table>
<thead>
<tr>
<th>Indication</th>
<th>Evidence Grade</th>
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<tbody>
<tr>
<td>Hypoglycemia</td>
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</tr>
<tr>
<td>Polycystic ovary syndrome (glucose intolerance)</td>
<td>B</td>
</tr>
<tr>
<td>Bipolar disorder</td>
<td>C</td>
</tr>
<tr>
<td>Bone loss (postmenopausal women)</td>
<td>C</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>C</td>
</tr>
<tr>
<td>Cognitive function</td>
<td>C</td>
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<tr>
<td>Depression</td>
<td>C</td>
</tr>
<tr>
<td>Diabetes mellitus (glucose intolerance)</td>
<td>C</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>C</td>
</tr>
<tr>
<td>Immunosuppression</td>
<td>C</td>
</tr>
<tr>
<td>Parkinson's disease</td>
<td>C</td>
</tr>
<tr>
<td>Schizophrenia (body composition and mental states)</td>
<td>C</td>
</tr>
<tr>
<td>Obesity/weight loss (body composition)</td>
<td>F</td>
</tr>
</tbody>
</table>

**Historical, Common, or Theoretical Uses which Lack Sufficient Evidence:**
- Acne, antioxidant (6), atherosclerosis (7), athletic performance enhancement (8), glaucoma, hypothyroidism, migraine headaches, premenstrual syndrome (PMS), psoriasis, reproductive organ problems (Turner's syndrome).

**Expert Opinion and Folkloric Precedent:**
- Until the 1980s, scientists were still having difficulty with quantifying the presence of chromium in human tissue or fluids (9). The assessment of chromium status may still be limited to deduction from clinical effects following supplementation (10). Mertz has reviewed the major impediments to progress in this area, including: chromium analysis, interaction of chromium with other dietary substances; and diagnosis of chromium deficiency (11). Concerns about a high level of polarization and politicization in chromium research have emerged (12). In 1997, the Diabetes Prevention Program conducted a $150 million dollar, NIH (National Institutes of Health)-sponsored study designed to determine whether non-insulin-dependent diabetes mellitus can be prevented or delayed in individuals with impaired glucose tolerance (1). Researchers used metformin (Glucophage) or troglitazone with standard diet and exercise, but did not use trivalent chromium, which is known to potentiate the action of insulin.

**Brief Safety Summary:**
- **Likely Safe:** When used orally by otherwise healthy adults in amounts of 50-200mcg per day or when adequate intake guidelines are followed (13). Chromium is safe in amounts naturally occurring in foods.
- **Possible Safe:** When used orally in recommended doses during pregnancy or lactation (14).
- **Possibly Unsafe:** In doses greater than recommended or for long-term use, due to unknown long-term biological effects of chromium accumulation (15). When used in patients with renal or hepatic insufficiency, iron deficiency, or in patients on TPN (total parental nutrition). When used in patients with neurological or behavioral disorders or in those taking neurological agents, as picolinic acid may alter CNS metabolism of serotonin, dopamine, and norepinephrine (16). When used in patients with diabetes
or in those taking antidiabetic agents.

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**DOSE & TOXICITY**

**General:**
- Recommended doses are based on those most commonly used in available trials, or on historical practice. However, with natural products it is often not clear what the optimal doses are to balance efficacy and safety. Preparation of products may vary from manufacturer to manufacturer, and from batch to batch within one manufacturer. Because it is often not clear what the active component(s) of a product is, standardization may not be possible, and the clinical effects of different brands may not be comparable.

**Standardization:**
- There is no well known standardization for chromium. Chromium picolinate is the most studied synthetic chromium product. Concentration of chromium within foods is widely variable and may reflect contamination from growing and processing (17).

**Dosing:**

**Adult (age ≥ 18):**

**Oral:**

- **General:** The Reference Daily Intake (RDI) for chromium has not been established; the Optimal Daily Allowance (ODA) is 200-600mcg daily. Clinical studies have typically used 150mcg daily (18) to 1,000mcg daily (3; 19) of chromium picolinate (3) or chromium chloride (19).
- **Adequate dietary intake:** Adequate dietary intake of chromium in the United States is 50-200mcg daily (17). Other reports have suggested that adequate intake for men and women should range from 24 to 45mcg daily (13). In a study of self-selected diets, the average dietary intake for adults in the United States was reported to be 22-48mcg daily for males and 13-36mcg daily for females (20). A study of 40,000 patients found mean serum chromium levels to be 0.39mcg/L (21).
- **Bone loss (postmenopausal women):** In clinical study, 400mcg chromium has been used daily for 60 days (22).
- **Cognitive function:** 1,000mcg of chromium as chromium picolinate has been taken daily for 12 weeks, according to chromium product manufacturer data.
- **Depression:** 600mcg per day of elemental chromium, as provided by chromium picolinate (CrPic), has been studied (23).
- **Diabetes type 2:** Kleefstra et al. conducted a randomized controlled trial using 500 or 1,000mcg chromium daily in the form of chromium picolinate for six months with no evidence of benefit in Western patients with type 2 diabetes (24). Other chromium dosage forms that have been used for a six month duration period include: 400mcg of chromium daily in the form of chromium yeast (25); 1,000mcg chromium daily in the form of chromium picolinate (24); and sulfonylurea plus 1,000mcg of chromium as chromium picolinate (CrPic) (26). Other chromium doses include: 400mcg Cr daily as Cr-enriched yeast (27); chromium-containing milk powder (chromium 200mcg/20g milk powder) taken twice daily for 16 weeks (28); and 600mcg of chromium as chromium picolinate plus biotin (2mg daily) (Diachrome, Nutrition 21, Inc., Purchase, NY) in addition to a pre-study oral antihyperglycemic agent (29).
- **Hyperlipidemia:** In clinical study, doses of 150mcg to 1,000mcg chromium have been used daily for 2-4 months (30; 30; 31; 32; 33; 34; 35; 36; 37; 38; 39). Chromium in the form of brewer's yeast (supplying 5mcg-48mcg chromium) has been used daily for 8-10 weeks (40; 41; 42).
- **Hypoglycemia:** In clinical study, 200mcg chromium has been used daily for 12 weeks with significant improvements in insulin binding, insulin receptor number, and hypoglycemic symptoms reported (38). In patients with symptomatic hypoglycemia, 125mcg Cr (Biochrome; Pharma-Nord, Denmark) has been used daily for three months (43).
- **Obesity/weight loss:** In a randomized controlled trial, subjects received either 400mcg chromium daily
as a CP supplement or a placebo (45). Chromium picolinate (CrPic), 200mcg Cr daily has also been used in clinical study (46).

**INTERACTIONS**

**MECHANISM OF ACTION**

**Pharmacology:**

- **Constituents/chemical constitution:** Chromium (Cr) is a white, hard, brittle metal that occurs in multiple valence states ranging from 2- to 6+. The most prevalent oxidation states are trivalent (3+) and hexavalent (6+). Trivalent chromium is the most stable state and is found in the food supply.

- Concentration of chromium within foods is widely variable and may reflect contamination from growing and processing (17). Chromium is considered an essential metal in human and animal nutrition, required for normal carbohydrate and lipid metabolism.

- A review by Vincent et al. discussed the inconclusive search for a naturally occurring, biologically active form of chromium (136). The authors cited three possible materials that may be the active agent: chromium picolinate, glucose tolerance factor (GTF), and low molecular weight chromium-binding substance. Chromium picolinate is a synthetic product found in many nutritional supplements. Picolinic acid (contained in chromium picolinate) is an isomer of nicotinic acid and a tryptophan amino acid metabolite (137).

- Analogues of picolinic acid alter serotonin, dopamine, and norepinephrine metabolism in the central nervous system (16). GTF, isolated from yeast products, has been thought to stimulate glucose metabolism in initial animal studies. More recent review reports that GTF is merely a source of chromium (136); however, its exact structure is unknown (138). Naturally occurring low molecular weight chromium (LMWCr) binding substance has been suggested to possess intrinsic biological function in animal studies and has been isolated from animal livers and kidneys (139;140). It is an oligopeptide that binds chromic ions and may function in autoamplification of insulin signaling. This substance has been named chromodulin and its proposed activity has been described in detail (9;136).

- **Glucose metabolism effects:** Chromium picolinate may increase insulin sensitivity and stimulate insulin receptor sites in patients with type 2 diabetes (142). Regardless of form, the exact mechanism of action of chromium is uncertain. Chromium may act by potentiation of insulin activity to normalize insulin function. It may directly bind insulin, increase insulin binding to red blood cells, increase insulin receptor number or affect receptor proteins, increase insulin internalization in cells, or increase pancreatic b-cell glucose sensitivity (3;76;143;144). Restoring normal insulin activity may positively affect nitric oxide synthesis (145). Effects on lipid components, such as HDL, may be a manifestation of insulin activity (37) compared to a direct effect. Chromium may alter lean body mass by the regulation of lipid deposition and potentiation of amino acid entry into muscle (146).

- Deficiency states may provide insight into chromium's mechanism of action. Chromium deficiency may yield: glucose intolerance, elevated circulating insulin, glycosuria, fasting hyperglycemia, impaired growth, decreased longevity, elevated serum cholesterol and triglycerides, increased incidence of aortic plaques/CAD, peripheral neuropathy, brain disorders, and decreased fertility and sperm count (147;148;149).

- An article regarding dietary chromium deficiency stated that chromium deficiency may be a cause or an aggravating factor in the glucose intolerance of infants suffering from protein calorie malnutrition and juvenile and type 2 diabetes (150). The authors also identified the risks of chromium deficiency, which include a poor placental supply of glucose tolerance factor in a low birth weight neonate, fetal demand on maternal chromium reserves, variations in dietary chromium, and abnormal chromium metabolism in insulin-dependent individuals with diabetes.
Volek et al. investigated the effect of chromium on glycogen synthesis and insulin signaling in 16 overweight men (151). After four weeks of supplementation with 600mcg chromium picolinate per day and exercise challenge, elevations in glucose and insulin during recovery were not different, but the lactate response was significantly higher in the Cr group. There was a significant depletion in glycogen immediately after exercise, an increase at two hours, and a further increase above rest at 24 hours (p<0.05). The rate of glycogen synthesis during the two hours after exercise was not different between groups (Cr: 25.8 ± 8.0 and PI: 17.1 ± 4.7mmol.kg.h). Glycogen synthase activity was significantly increased immediately after exercise in both groups. Muscle phosphatidylglycerol 3-kinase (PI 3-kinase) activity decreased immediately after exercise and increased at two hours (p<0.05), with a trend for a lower PI 3-kinase response in Cr (p=0.08). The authors concluded that chromium supplementation did not augment glycogen synthesis during recovery from high-intensity exercise and high-carbohydrate feeding, although there was a trend for lower PI 3-kinase activity.

Chromium is often studied for its benefits in type 2 diabetes. In one variation of type-2 diabetes, the disease is not the result of an alteration in the insulin receptor or the glucose transporter, but a genetically determined defect of the postreceptorial intracellular signaling mechanism (152). There have been investigations to determine the role of chromium (III) ions in glucose metabolism and in the prevention of type 2 diabetes. It has also been investigated if chromium substitution can prevent or treat those forms of diabetes where chromium deficiency is suspected to be a causative factor. Kesztthelyi et al. investigated the role of chromium (III) compounds in glucose metabolism and concluded that chromium (III) may be an effective supplemental therapy in the treatment of patients' with decreased glucose tolerance or type 2 diabetes mellitus. Balk et al. conducted a systematic review of the effect of chromium supplementation on glucose metabolism and lipid levels (153). Among participants with type 2 diabetes, chromium supplementation improved glycosylated hemoglobin levels by -0.6% (95% CI-0.9 to -0.2) and fasting glucose by - 1.0mcM/l (-1.4 to -0.5), but not lipids. There was no benefit in individuals without diabetes. There were some indications of dose effect and differences among chromium formulations.

The Cr group (400mcg Cr per day as Cr-enriched yeast) in a randomized, double-blind, controlled trial showed a significantly greater increase in serum Cr compared to the placebo group (p<0.05), as well as a significant decrease in fasting serum glucose compared to placebo (p<0.01) (27). Blood markers of oxidative stress, glutathione peroxidase activity, and levels of reduced glutathione were essentially unchanged in the Cr group after 12 weeks, but decreased significantly in the placebo group (p<0.05, p=0.01, respectively). Serum HbA1c and glycated protein (fructosamine) were essentially unchanged in the Cr group, whereas HbA1c tended to increase in the placebo group (from 6.94% to 7.11%). Fasting serum insulin decreased in both groups, with a greater tendency in the Cr group (-16.5% vs. -9.5%). The authors suggested that the supplementation of well-controlled type 2 diabetics with Cr-enriched yeast may be safe and may result in improvements in blood glucose variables and oxidative stress.

In clinical study, subjects randomized to sulfonylurea/placebo, as opposed to those randomized to sulfonylurea/CrPic, have shown a significant increase in body weight (2.2kg, p<0.001 vs. 0.9kg, p=0.11), percent body fat (1.17%, p<0.001 vs. 0.12%, p=0.7), and total abdominal fat (32.5cm²), p<0.05 vs. 12.2cm², <0.10) from baseline (26). Subjects randomized to sulfonylurea/CrPic had significant improvements in insulin sensitivity corrected for fat-free mass (28.8, p< 0.05 vs. 15.9, p=0.4), GHb (-1.16%, p< -0.05 vs. -0.4%, p= 0.3), and free fatty acids (-0.2mM/L, p<0.01 vs. -0.12mM, p<0.03), as opposed to sulfonylurea/placebo.

In a clinical study, the chromium group (chromium 200mcg plus20g milk powder) demonstrated a lower FPG and fasting insulin (-38.1 ± 9.2 vs. 63 ± 8.5mg/dL and -1.7 ± 0.2 vs. 1.9 ± 0.3mcU/mL, respectively; p<0.05), especially in male patients (-41 ± 9.2 vs. 85 ± 11.7mg/dL and -2.7 ± 0.2 vs. 3.1 ± 0.3mcU/mL, respectively; p<0.01), at the end of the study (28). Lower glycosylated hemoglobin was observed in chromium-treated male patients (-1.1 ± 0.5 vs. 0.7 ± 0.2; p<0.05). However, there were no significant changes in other metabolic parameters (lipid profiles including total cholesterol, triglyceride, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol), except improvement of insulin resistance (homeostasis model assessment for insulin resistance and insulin sensitivity index from frequently sampled intravenous glucose tolerance test) observed in male patients (26.1 ± 1.1 vs. -0.41 ± 1.12 and 0.18 ± 0.11 vs. -0.15 ± 0.2, respectively; p<0.05).

Singer et al. conducted a randomized, controlled pilot study to determine if supplementation with
Chromium picolinate and biotin may improve glycemic control in patients with type 2 diabetes mellitus with suboptimal glycemic control despite the use of oral antihyperglycemic agents (29). After four weeks, there was a significantly greater reduction in the total area under the curve for glucose during the two-hour oral glucose tolerance test for the treatment group (mean change -9.7%) compared with the placebo group (mean change +5.1%, p<0.03). Significantly greater reductions were also seen in fructosamine (p<0.03), triglycerides (p<0.02), and triglycerides/high-density lipoprotein cholesterol ratio (p<0.05) in the treatment group.

The potential for using urinary Cr response to glucose load as an indicator of Cr status has been investigated (154). Seventy-eight non-insulin dependent diabetes mellitus patients were divided randomly into two groups and given Cr supplements as brewer's yeast and CrCl3 sequentially with placebo in between, in a double-blind, crossover design of four stages, each lasting eight weeks. Subjects were weighed, had their dietary data and drug dosage recorded, and blood and urine samples collected for analysis of glucose and urinary chromium (fasting and two hours post-75-g glucose load) and fructosamine at the beginning and end of each stage of the study. The mean urinary Cr after the glucose load was significantly higher than the fasting mean at zero time (p<0.01). The authors noted, however, that only 52 of the patients showed an obvious increase; while the others showed a slight decrease or no change. Both supplements caused a significant increase in the means of urinary Cr and a significant decrease in the means of glucose and fructosamine. Only those subjects responding to Cr supplementation by improved glucose control showed an increase in post-glucose-load urinary Cr over fasting level, after supplementation, but not at zero time. The authors concluded that urinary Cr response to glucose load could be used as an indicator of Cr status.

Another study was conducted by Bahijri et al. investigating serum chromium status measurements (155). The effect of chromium supplements on glucose tolerance and lipid profile was studied in 44 normal, free living adults. A dose of 200mg chromium per day as CrCl3 or a placebo was given in a double blind cross-over study, with eight week experimental periods. Fasting, one hour and two hours post glucose challenge (75g of glucose) glucose, serum fructosamine, total cholesterol, high-density lipoprotein-cholesterol, triglycerides, chromium, and dietary intakes were estimated at the beginning and the end of each stage. Mean serum chromium increased significantly after chromium supplementation (p<.001) indicating proper absorption. The authors noted that chromium did not affect the total cholesterol; however, the mean high-density lipoprotein-cholesterol level was significantly increased (p<.001), the mean triglycerides levels significantly decreased (p<.001), and the mean fructosamine level significantly decreased (p<.05). Chromium supplementation also affected one hour and two hours post glucose challenge glucose levels in subgroups of subjects with two hour glucose level > 10% above or below fasting level and significantly differing to it (p<.05 in both cases), by decreasing or increasing them significantly (p<.05 in all cases) so that the two hour mean became not significantly different to the fasting mean. The authors concluded that improved glucose control and lipid profile following chromium supplementation suggests the presence of low chromium status in the studied population. However, the authors noted that serum chromium could not be recommended for use as an indicator of chromium status because subjects with widely varying levels responded favorably to the chromium supplement.

Urberg and Zemel reported that supplementation with 200mcg daily chromium chloride plus 100mg daily nicotinic acid, in five or six of 16 healthy elderly subjects after 28 days, caused a 15% decrease in a glucose area integrated total (p<0.025) and a 6.8% decrease in fasting glucose (p<0.10) (118). Patients were over the age of 65, in good health, and were not diabetic. The subjects could not be taking a chromium supplement, nicotinic acid, or brewers yeast. Fasting glucose and glucose tolerance were unaffected by either chromium or nicotinic acid supplements alone. The authors asserted that the results demonstrate that nicotinic acid and chromium are required together in order to optimize glucose metabolism. This may account for variation in the results of chromium supplementation trials, since human diets contain a variable level of nicotinic acid. The study was limited by its small sample size.

Lipid effects: A review of chromium in human nutrition by Offenbacher evaluated the role of chromium in chromium deficiency, lipid metabolism, and other conditions (159). Balk et al. conducted a systematic review of the effect of chromium supplementation on glucose metabolism and lipid levels (153). Among participants with type 2 diabetes, chromium supplementation improved glycosylated hemoglobin levels
by -0.6% (95% CI-0.9 to -0.2) and fasting glucose by - 1.0mcM/l (-1.4 to -0.5), but not lipids. There was no benefit in individuals without diabetes. There were some indications of dose effect and differences among chromium formulations.

**Metabolic effects:** Vincent et al. examined the potential mechanism of action of chromium and how it may relate to type 2 diabetes and other metabolic disorders (160).

**Weight loss effects:** Literature review has noted that chromium picolinate is widely used, especially by athletes, to increase lean body mass (89; 169). Woolven has investigated different chromium supplements and how they may cause weight loss (170). Clinical research has examined the effect of chromium on obesity/weight loss and/or weight maintenance and a number of variables related to body composition (30; 45; 46; 119; 120; 121; 122; 123; 124; 125; 126; 127; 128). There is currently insufficient evidence to support the use of chromium in the treatment of obesity/weight/body composition at this time.

**Pharmacodynamics/Kinetics:**

- Chromium is biologically active only in the trivalent state. It may form complexes with organic compounds, including niacin, glycine, glutamic acid, and cysteine. This complex is collectively known as glucose tolerance factor (GTF). GTF enhances the blood sugar-lowering effects of insulin, which facilitates the uptake of glucose into cells. Chromium is a cofactor in carbohydrate and lipid-metabolizing enzymes and may play a role in regulating LDL and HDL serum levels.

- Technological advancements only recently enabled reliable chromium analysis and are conducted in a limited number of laboratories worldwide (11).

- Approximately 0.5-2% of chromium is absorbed (20; 171). Based on unsubstantiated reports, absorption occurs primarily in the jejunum. Absorption is related to exposure and to the nature of the chromium salt or ligand (172). Absorption of chromium may be affected by interactions with other metals, including zinc, iron, vanadium, oxalate, and phytate.

- After absorption, trivalent chromium is bound to transferrin (9). The distribution may occur across fast, medium, and slow compartments, with serum chromium not in equilibrium with tissue-organ stores (138).

- Chromium retention decreases with aging, as found in a very large collection of hair, sweat, and serum samples (21). Whether this may be due to inadequate nutrition or normal physiology is unknown (173).

- Garland et al. performed a prospective, cohort study to observe the possibility of an association between toenail levels of five trace elements (arsenic, copper, chromium, iron, and zinc) and breast cancer in 62,641 women with follow up for four years (174). They found that there was no evidence to support these elements in the risk of breast cancer.

- Chromium is excreted mainly in the urine (172). Based on unsubstantiated reports, small amounts of absorbed chromium are excreted in bile, hair, and perspiration, whereas unabsorbed chromium is excreted in the feces. Stressors, such as elevated blood sugar, strenuous physical activity or work, infection, and emotional and physical trauma, may increase the loss of chromium (133; 175; 176; 177).

- Bunker et al. conducted a study to assess the daily intake and requirements of chromium by healthy elderly individuals (178). They observed 23 volunteers, who lived unassisted in their own homes and chose their own meals, and looked at their diet, feces, and urine for chromium over five days. The average intake of chromium from the diet was 24.5mcg, which was not statistically significant (p>0.05). It was determined that chromium dietary intake and excretion were in equilibrium and that dietary intake was adequate for their requirements. However, they did find that a patient, who ate a diet high in fiber, was in negative balance of chromium. Since this study was only conducted in 23 elderly subjects and over five days, it should not be generalized. In regards to the patient that was in a negative equilibrium of chromium, further studies should be performed to note the effects of fiber on chromium excretion. The authors never specified in the study what the subjects disease states were or what medications they were taking, which would be important in noting potential drug interactions and potential problems with a drugs' excretion.

- A similar study by Bunker et al., which examined trace elements, was carried out by the same methodology and time frame (179). The researchers used 24 elderly volunteers, 19 of which were
housebound, and excluded subjects that had hepatic, renal, or gastrointestinal disease, malignancies, or an acute illness. The dietary intake for these subjects was below the recommended daily allowance, but was balanced for both groups; a correlation was found between the intake and retention of chromium in healthy and housebound subjects (p<0.001, 95%CI). This study should be done with a larger sample size to observe if any difference does exist. In addition, since this data was extrapolated from 24 relatively healthy volunteers, it should not be generalized to all elderly people who have multiple disease states. The authors did not specify the patients' disease states or the medications they were taking, which would be important in noting potential drug interactions and potential problems with a drug's excretion.

- Gargas et al. examined the urinary excretion of chromium in eight healthy adults who ingested 400mcg of a chromium supplement for three days (180). The authors estimated that a person would have to ingest 7,000 to 52,000mg of chromium to see an increase in urinary excretion above 1.8mcg Cr/liter, which is normal dietary excretion of urine.

- Jannetto et al. conducted an in vitro study to examine the role of cytochrome b5 in combination with P450 reductase in order to better understand the reduction of chromium VI to chromium III, which releases toxic intermediates (181). They concluded that chromium VI reduction can be seen with cytochrome b5 and P450 reductase in the NADPH dependent pathway.

- Low-molecular weight and high-molecular weight chromium binding capacity was studied in mice (182). Low-molecular weight chromium binding capacity was also studied in the milk of bovine colostrums (183).

- In a clinical trial, serum and urinary Cr and biochemical indicators of iron status were measured before and serially every four weeks for 12 weeks (46). CrPic supplementation increased (p<0.0001) serum Cr concentration and urinary Cr excretion, compared with picolinic acid and placebo. CrPic did not affect body weight or fat, although all groups lost (p<0.05) weight and fat; it did not affect fat-free, mineral-free mass, or measurements of iron status.

- In a clinical trial, after four weeks of chromium supplementation, there was a significantly greater reduction in the total area under the curve for glucose during the two-hour oral glucose tolerance test for the treatment group (mean change -9.7%) compared with the placebo group (mean change +5.1%, p<0.03) (29). Significantly greater reductions were also seen in fructosamine (p<0.03), triglycerides (p<0.02), and triglycerides/ high-density lipoprotein cholesterol ratio (p<0.05) in the treatment group.

### HISTORY

- Animal studies in the 1950s by Schwarz and Mertz demonstrated that chromium is important for the expression of glucose tolerance in animals, and that the use of glucose is impaired in chromium deficiency. Follow-up studies suggested chromium's activity was linked to insulin (136). Mertz presented the first 20 years of chromium research in an extensive review (184).

- Wolf et al. determined the chromium content of refined vs. unrefined sugars in various countries and how the graphite furnace or ashing may cause the loss of organic chromium (185).

- Cobalt-chromium is a common material for hip replacements and is frequently used in bearing systems (186; 187; 188; 189) and stents (190; 191; 192; 193). Denture framework may also use chromium cobalt (194). Chromium 51-ethylene diaminetetra-acetate (51Cr-EDTA) has also been used as a diagnostic testing aid (195).

### EVIDENCE TABLE

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<th>Condition</th>
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weeks; significant improvements seen in insulin binding, insulin receptor number, and hypoglycemic symptoms; small study.

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<td>Polycystic ovary syndrome (glucose tolerance)</td>
<td>Clinical trial</td>
<td>Lydic, 2006</td>
<td>5</td>
<td>NA</td>
<td>P</td>
<td>NA</td>
<td>Obese subjects with polycystic ovary syndrome; 1,000mcg trivalent chromium, as chromium picolinate.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bipolar disorder</td>
<td>Clinical trial</td>
<td>Amann, 2007</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>Open-label pilot study of adjunctive chromium in patients with treatment-resistant rapid-cycling bipolar disorder.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bone loss (postmenopausal women)</td>
<td>Crossover trial, double-blind</td>
<td>Evans, 1993</td>
<td>27</td>
<td>Yes</td>
<td>2</td>
<td>Small</td>
<td>400mcg chromium or placebo for 60 days with a three month washout.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cognitive function</td>
<td>Randomized placebo controlled study, double-blind</td>
<td>Krikorian, 2007</td>
<td>21</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>1,000mcg chromium picolinate used for 12-weeks to assess its effects on cognition in the elderly.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>Randomized controlled trial</td>
<td>Docherty, 2005</td>
<td>113</td>
<td>Yes</td>
<td>P</td>
<td>P</td>
<td>600mcg daily elemental chromium, as chromium picolinate (CrPic).</td>
<td></td>
<td></td>
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<tr>
<td>Diabetes mellitus (glucose tolerance)</td>
<td>Randomized placebo controlled study, double-blind</td>
<td>Krikorian, 2007</td>
<td>21</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>1,000mcg chromium picolinate used for 12-weeks to assess its effects on cognition in the elderly.</td>
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<tr>
<td>Diabetes mellitus</td>
<td>Systematic</td>
<td>Balk, 2007</td>
<td>41</td>
<td>NA</td>
<td>NA</td>
<td>P</td>
<td>Systematic review</td>
<td></td>
<td></td>
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<tr>
<td>Diabetes mellitus</td>
<td>Systematic</td>
<td>Balk, 2007</td>
<td>41</td>
<td>NA</td>
<td>NA</td>
<td>P</td>
<td>Systematic review</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Condition</td>
<td>Study Design</td>
<td>Study Details</td>
<td>Participants</td>
<td>Results</td>
<td></td>
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<tr>
<td>Diabetes mellitus (glucose tolerance)</td>
<td>Randomized controlled trial</td>
<td>Amato, 2000; 1,000mcg/d chromium; no significant changes on insulin sensitivity, lipids, or body composition was found; healthy elderly high dose chromium.</td>
<td>19 No 5 None</td>
<td>NA NA</td>
<td></td>
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<tr>
<td>Diabetes mellitus (glucose tolerance)</td>
<td>Randomized controlled trial</td>
<td>Lee, 1994; 200mcg/d chromium for six months; no detected difference in glucose and HbA1C (possibly due to small sample size); predominantly Hispanic NIDDM subjects.</td>
<td>30 No 4 None</td>
<td>NA NA</td>
<td></td>
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<tr>
<td>Diabetes mellitus (type 2 diabetes)</td>
<td>Randomized controlled trial, double-blind</td>
<td>Kleefstra, 2007; 400mcg of chromium daily in the form of chromium yeast for six months in addition to hypoglycemic agents showed no significant differences in A1C when compared to placebo.</td>
<td>P No P None</td>
<td>NA NA</td>
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<tr>
<td>Diabetes mellitus (insulin-dependent patients with type 2 diabetes)</td>
<td>Randomized controlled trial</td>
<td>Kleefstra, 2006; 500 or 1,000mcg chromium daily in the form of chromium picolinate for six months did not show reductions in A1C.</td>
<td>46 No P None</td>
<td>NA NA</td>
<td></td>
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<tr>
<td>Diabetes mellitus (glucose tolerance)</td>
<td>Randomized controlled trial, double-blind</td>
<td>Martin, 2006; Sulfonylurea plus 1,000mcg chromium as chromium picolinate for six months significantly improved insulin sensitivity and glucose control.</td>
<td>37 Yes P P</td>
<td>NA NA</td>
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<tr>
<td>Diabetes mellitus (glucose tolerance)</td>
<td>Randomized placebo controlled trial, double-blind</td>
<td>Pei, 2006; Chromium-containing milk powder (chromium 200mcg/20g milk powder) twice daily for 16 weeks resulted in lowering of FPG, fasting insulin, and improvement of metabolic control.</td>
<td>60 Yes P Variable</td>
<td>NA NA</td>
<td></td>
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<tr>
<td>Study</td>
<td>Design</td>
<td>Authors, Year</td>
<td>Sample Size</td>
<td>Randomized</td>
<td>Double-blind</td>
<td>Placebo, 220mcg/d chromium, or 1,000mcg/d chromium; significant decrease in HbA1C in chromium groups when compared with placebo; large controlled trial; Chinese subjects.</td>
<td>Placebo or 160mcg/d chromium for six months; no significant changes in glucose tolerance; elderly, low chromium intake.</td>
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<tr>
<td>Diabetes mellitus (glucose tolerance)</td>
<td>Randomized controlled trial</td>
<td>Uusitupa, 1992</td>
<td>26</td>
<td>No</td>
<td>3</td>
<td>None</td>
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<tr>
<td>Diabetes mellitus (glucose tolerance)</td>
<td>Randomized controlled trial</td>
<td>Martinez, 1985</td>
<td>86</td>
<td>Yes</td>
<td>3</td>
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<tr>
<td>Diabetes mellitus (glucose tolerance)</td>
<td>Randomized controlled trial, double-blind</td>
<td>Jovanovic, 1999</td>
<td>30</td>
<td>Yes</td>
<td>2</td>
<td>Small</td>
<td>Compared 4mcg/kg and 8mcg/kg of chromium against</td>
<td></td>
<td></td>
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<tr>
<td>Study</td>
<td>Design</td>
<td>Duration</td>
<td>Randomization</td>
<td>Sample Size</td>
<td>Treatment</td>
<td>Outcome</td>
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<tr>
<td>Sherman, 1968</td>
<td>Controlled, double-blind</td>
<td>16 weeks</td>
<td>No</td>
<td>2</td>
<td>None</td>
<td>NA NA 150mcg chromium or placebo daily for 16 weeks; No significant difference in glucose level or glucose tolerance; small study, unclear randomization.</td>
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<tr>
<td>Rabinowitz, 1983</td>
<td>Randomized controlled trial, double-blind</td>
<td>16 months</td>
<td>No</td>
<td>2</td>
<td>None</td>
<td>NA NA 150mcg/d of chromium, brewer's yeast with or without GTF, or placebo for 16 months; no significant changes noted; poor description of randomization and blinding methods.</td>
<td></td>
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</tr>
<tr>
<td>Anderson, 1983</td>
<td>Randomized controlled trial</td>
<td>76 weeks</td>
<td>No</td>
<td>2</td>
<td>Small</td>
<td>NA NA 200mcg chromium or placebo daily for two three-month periods; unclear randomization; significant effects after grouping.</td>
<td></td>
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<tr>
<td>Uusitupa, 1983</td>
<td>Randomized controlled trial</td>
<td>6 weeks</td>
<td>Yes</td>
<td>2</td>
<td>Small</td>
<td>NA NA 200mcg chromium for six weeks; no significant changes in glucose tolerance and fasting or 2h post-glucose serum insulin levels; 1h post-glucose serum insulin level lower (p&lt;0.01); unclear randomization.</td>
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<td>Offenbacher, 1980</td>
<td>Randomized controlled trial, single-blinded</td>
<td>24 weeks</td>
<td>Yes</td>
<td>2</td>
<td>Small</td>
<td>NA NA Single-blinded, lack of placebo control.</td>
<td></td>
<td></td>
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<tr>
<td>Abraham, 1992</td>
<td>Randomized controlled trial</td>
<td>76 weeks</td>
<td>No</td>
<td>1</td>
<td>None</td>
<td>NA NA 250mcg/d chromium for 7-16 months; no changes in fasting blood glucose were noted.</td>
<td></td>
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<tr>
<td>Mossop, 1983</td>
<td>Case-series</td>
<td>39 weeks</td>
<td>NA</td>
<td>1</td>
<td>Small</td>
<td>NA NA 2mg of chromium or placebo daily for three months; lack of a control group; African diabetic patients; high dropout rate.</td>
<td></td>
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</tr>
<tr>
<td>Urberg, 1987</td>
<td>Randomized controlled trial</td>
<td>16 weeks</td>
<td>Yes (with combination)</td>
<td>1</td>
<td>Small</td>
<td>NA NA 200mcg/d chromium plus 110mg/d nicotinic</td>
<td></td>
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</tr>
</tbody>
</table>
Acid for 28 days lead to significant decrease in glucose area integrated total; responded to combination of Cr and nicotinic acid.

<table>
<thead>
<tr>
<th>Diabetes mellitus (glucose tolerance)</th>
<th>Case-series</th>
<th>Levine, 1968</th>
<th>10</th>
<th>NA</th>
<th>0</th>
<th>Small</th>
<th>NA</th>
<th>NA</th>
<th>150mcg/d chromium; lack of control.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes mellitus (glucose tolerance)</td>
<td>Case-series</td>
<td>Glinsmann, 1966</td>
<td>14</td>
<td>NA</td>
<td>0</td>
<td>Small</td>
<td>NA</td>
<td>NA</td>
<td>150-1,000mcg/d of chromium for 7-120 days; no significant effect after seven days of 150-1,000mcg chromium; 15-120 days of 150-1,000mcg chromium improved glucose tolerance; lack of control group.</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>Randomized controlled trial</td>
<td>Amato, 2000</td>
<td>19</td>
<td>No</td>
<td>5</td>
<td>None</td>
<td>NA</td>
<td>NA</td>
<td>1,000mcg daily chromium; no significant changes were noted; healthy, elderly subjects; high dose.</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>Randomized controlled trial</td>
<td>Roeback, 1991</td>
<td>72</td>
<td>Yes</td>
<td>5</td>
<td>Moderate</td>
<td>NA</td>
<td>NA</td>
<td>600mcg GTF-chromium or placebo for eight weeks; chromium lead to significant increase in HDL; subjects on beta-blockers.</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>Randomized controlled trial</td>
<td>Lee, 1994</td>
<td>30</td>
<td>Yes</td>
<td>4</td>
<td>Small</td>
<td>NA</td>
<td>NA</td>
<td>200mcg chromium daily for six months; significant reduction in triglyceride levels; no changes in LDL, HDL.</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>Randomized controlled trial</td>
<td>Press, 1990</td>
<td>32</td>
<td>Yes</td>
<td>4</td>
<td>Moderate</td>
<td>NA</td>
<td>NA</td>
<td>200mcg of chromium or placebo daily for 42 days; total cholesterol, LDL decreased significantly; crossover design.</td>
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<tr>
<td>Condition</td>
<td>Study Type</td>
<td>Authors, Year</td>
<td>n</td>
<td>Randomized</td>
<td>Placebo</td>
<td>Dose Description</td>
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<tr>
<td>Hyperlipidemia</td>
<td>Randomized controlled trial</td>
<td>Lefavi, 1993</td>
<td>34</td>
<td>Yes</td>
<td>4</td>
<td>Moderate</td>
<td></td>
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<td></td>
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<td>200mcg/1.8mg chromium/nicotinic acid or 800mcg/7.2mg chromium/nicotinic acid for eight weeks.</td>
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<tr>
<td>Hyperlipidemia</td>
<td>Randomized controlled trial</td>
<td>Riales, 1981</td>
<td>23</td>
<td>Yes</td>
<td>4</td>
<td>Small</td>
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<td></td>
<td>200mcg/d chromium for five days/week for 12 weeks; significant increase in HDL and weight reduction.</td>
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<tr>
<td>Hyperlipidemia</td>
<td>Randomized controlled trial</td>
<td>Uusitupa, 1992</td>
<td>26</td>
<td>No</td>
<td>3</td>
<td>None</td>
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<td></td>
<td>Placebo or 160mcg/d chromium for six months; no significant changes in lipid levels were seen; elderly subjects; low chromium intake.</td>
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<tr>
<td>Hyperlipidemia</td>
<td>Randomized controlled trial</td>
<td>Wilson, 1995</td>
<td>26</td>
<td>No</td>
<td>3</td>
<td>None</td>
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<td></td>
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<td>220mcg chromium daily for 90 days; no change in lipid levels; healthy, young, non-obese patients.</td>
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<td>Hyperlipidemia</td>
<td>Randomized controlled trial</td>
<td>Hermann, 1994</td>
<td>42</td>
<td>Yes</td>
<td>2</td>
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<td>150mcg/d chromium or placebo for 12 weeks; significant reductions in LDL and total cholesterol with chromium; subgroup analysis on small sample.</td>
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<tr>
<td>Hyperlipidemia</td>
<td>Controlled trial, double-blind</td>
<td>Boyd, 1998</td>
<td>35</td>
<td>Yes</td>
<td>2</td>
<td>Small</td>
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<td></td>
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<td>1,000mcg chromium daily or placebo for 13 weeks; significant reductions seen in cholesterol and LDL; 10 subjects removed due to poor compliance.</td>
<td></td>
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<td>Hyperlipidemia</td>
<td>Randomized controlled trial</td>
<td>Offenbacher, 1985</td>
<td>23</td>
<td>No</td>
<td>2</td>
<td>None</td>
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<td>200mcg/d chromium or brewer's yeast for 10 weeks; no significant change in lipids; healthy elderly volunteers.</td>
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<tr>
<td>Hyperlipidemia</td>
<td>Randomized controlled trial</td>
<td>Anderson, 1983</td>
<td>76</td>
<td>No</td>
<td>2</td>
<td>None</td>
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<td></td>
<td>200mcg chromium or placebo for two three-month periods; no significant effects noted; unclear randomization; six-month trial.</td>
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<tr>
<td>Hyperlipidemia</td>
<td>Randomized controlled trial, double-blind</td>
<td>Rabinowitz, 1983</td>
<td>43</td>
<td>No</td>
<td>2</td>
<td>None</td>
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<tr>
<td></td>
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<td></td>
<td>150mcg/d of chromium, brewer's yeast</td>
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<td>Condition</td>
<td>Design</td>
<td>Reference</td>
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<td>Randomization</td>
<td>Placebo</td>
<td>Effect Size</td>
<td>Publication Year</td>
<td>Description and Notes</td>
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<tr>
<td>Hyperlipidemia</td>
<td>Randomized controlled trial</td>
<td>Uusitupa, 1983</td>
<td>10</td>
<td>No</td>
<td>2</td>
<td>None</td>
<td>NA</td>
<td>200mcg chromium for six weeks; no significant changes in lipid levels were noted; unclear randomization.</td>
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<tr>
<td>Hyperlipidemia</td>
<td>Double-blind</td>
<td>Bourn, 1986</td>
<td>86</td>
<td>No</td>
<td>P</td>
<td>None</td>
<td>NA</td>
<td>Postmenopausal women; chromium chloride at a dose of 200mcg daily for 10 weeks.</td>
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<tr>
<td>Hyperlipidemia</td>
<td>Randomized placebo controlled trial</td>
<td>Abraham, 1992</td>
<td>76</td>
<td>Yes</td>
<td>1</td>
<td>Moderate</td>
<td>NA</td>
<td>250mcg CrCl3 per day chromium for 7-16 months; significant increase in HDL and decrease in triglycerides.</td>
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<tr>
<td>Hyperlipidemia</td>
<td>Comparative pilot study</td>
<td>Preuss, 2000</td>
<td>P</td>
<td>No</td>
<td>P</td>
<td>None</td>
<td>NA</td>
<td>Niacin-bound chromium alone and in combination with grapeseed extract; only the combination showed lipid-lowering effects.</td>
<td></td>
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<tr>
<td>Hyperlipidemia</td>
<td>Case-series</td>
<td>Mossop, 1983</td>
<td>39</td>
<td>NA</td>
<td>1</td>
<td>NA</td>
<td>NA</td>
<td>2mg chromium or placebo daily for three months; lack of a control group; African diabetic patients; high dropout rate.</td>
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<tr>
<td>Hyperlipidemia</td>
<td>Randomized controlled trial, single-blind</td>
<td>Wang, 1989</td>
<td>30</td>
<td>Yes</td>
<td>0</td>
<td>Small</td>
<td>NA</td>
<td>50mcg chromium or brewer's yeast (15mcg chromium) or placebo for five days a week for 12 weeks; cholesterol and LDL decreased significantly in chromium groups; single blinding; unclear randomization.</td>
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</tr>
<tr>
<td>Hyperlipidemia</td>
<td>Case-series</td>
<td>Trow, 2000</td>
<td>12</td>
<td>NA</td>
<td>0</td>
<td>NA</td>
<td>NA</td>
<td>100mcg chromium daily; no changes in lipoprotein concentrations; uncontrolled pilot study.</td>
<td></td>
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<td>Hyperlipidemia</td>
<td>Uncontrolled</td>
<td>Vinson, 1984</td>
<td>P</td>
<td>Yes (HDL at six months)</td>
<td>P</td>
<td>P</td>
<td>NA</td>
<td>218mcg chromium in the form of oral yeast capsule for six months.</td>
<td></td>
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<tr>
<td>Hyperlipidemia</td>
<td>Randomized controlled trial</td>
<td>Wang, 1989</td>
<td>30</td>
<td>Yes</td>
<td>P</td>
<td>P</td>
<td>NA</td>
<td>Chromium in the form of 50mcg</td>
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<td>Condition</td>
<td>Study Design</td>
<td>Reference</td>
<td>Study Size</td>
<td>P Value</td>
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<tr>
<td>Double-blind</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>CrCl₃ (Fisher Scientific Co, Fair Lawn, N.J) or brewer's yeast (containing 15mcg chromium) five times a week for 12 weeks.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immunosuppression</td>
<td>Randomized controlled trial</td>
<td>Rhee, 2000</td>
<td>40</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>0.394g lactose, 200mcg Cr, 3.0mg Cu, or 200mcg Cr and 3.0mg Cu/d for 12 weeks.</td>
<td></td>
</tr>
<tr>
<td>Schizophrenia</td>
<td>Randomized controlled trial</td>
<td>Hockney, 2006</td>
<td>P</td>
<td>No</td>
<td>P</td>
<td>None</td>
<td>NA</td>
<td>NA</td>
<td>Lack of benefit on body composition or mental states.</td>
</tr>
<tr>
<td>Obesity/weight loss</td>
<td>Randomized placebo controlled trial, double-blind</td>
<td>Lukaski, 2007</td>
<td>83</td>
<td>No</td>
<td>P</td>
<td>None</td>
<td>NA</td>
<td>NA</td>
<td>Women subjects; 200mcg chromium picolinate daily.</td>
</tr>
<tr>
<td>Obesity/weight loss</td>
<td>Randomized controlled trial, double-blind</td>
<td>Volpe, 2001</td>
<td>44</td>
<td>No</td>
<td>P</td>
<td>None</td>
<td>NA</td>
<td>NA</td>
<td>Women subjects; 400mcg per day of chromium.</td>
</tr>
<tr>
<td>Obesity/weight loss</td>
<td>Randomized controlled trial</td>
<td>Amato, 2000</td>
<td>16</td>
<td>No</td>
<td>5</td>
<td>None</td>
<td>NA</td>
<td>NA</td>
<td>1,000mcg daily chromium; no significant changes were noted; glucose, lipids, composition studied.</td>
</tr>
<tr>
<td>Obesity/weight loss</td>
<td>Randomized controlled trial</td>
<td>Kaats, 1998</td>
<td>130</td>
<td>Yes</td>
<td>5</td>
<td>Moderate</td>
<td>NA</td>
<td>NA</td>
<td>400mcg chromium vs. placebo for 90 days; significantly reduced weight, fat mass, percent body fat with chromium; dual energy X-ray absorptiometry; high dropout rate (29.7%).</td>
</tr>
<tr>
<td>Obesity/weight loss</td>
<td>Randomized controlled trial</td>
<td>Campbell, 1999</td>
<td>18</td>
<td>No</td>
<td>4</td>
<td>None</td>
<td>NA</td>
<td>NA</td>
<td>High dose Cr (924mcg daily) or low chromium placebo for 12 weeks; no significant changes with chromium seen; hydrostatic weighing.</td>
</tr>
<tr>
<td>Obesity/weight loss</td>
<td>Randomized controlled trial</td>
<td>Kaats, 1996</td>
<td>219</td>
<td>Yes</td>
<td>4</td>
<td>Small</td>
<td>NA</td>
<td>NA</td>
<td>200mcg chromium, 400mcg chromium or placebo for 72 days; body composition improvement score was significantly improved in both chromium groups over placebo; large sample; densitometry assessment.</td>
</tr>
</tbody>
</table>
| Obesity/weight loss        | Randomized controlled trial | Trent, 1995 | 212 | No | 4 | None | NA | NA | 400mcg chromium compared to placebo for 16
<table>
<thead>
<tr>
<th>Study Title</th>
<th>Study Design</th>
<th>Subjects</th>
<th>Gender</th>
<th>Dose</th>
<th>Outcome</th>
<th>Methodology</th>
<th>Notes</th>
</tr>
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<tbody>
<tr>
<td>Obesity/Weight Loss</td>
<td>Randomized controlled trial</td>
<td>Clancy, 1994</td>
<td>36</td>
<td>No</td>
<td>4</td>
<td>None</td>
<td>NA</td>
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<tr>
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<td>Hallmark, 1996</td>
<td>16</td>
<td>No</td>
<td>3</td>
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<td>NA</td>
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<tr>
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<td>20</td>
<td>No</td>
<td>3</td>
<td>None</td>
<td>NA</td>
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<tr>
<td>Obesity/Weight Loss</td>
<td>Randomized controlled trial</td>
<td>Pasman, 1997</td>
<td>33</td>
<td>No</td>
<td>3</td>
<td>None</td>
<td>NA</td>
</tr>
<tr>
<td>Obesity/Weight Loss</td>
<td>Randomized controlled trial</td>
<td>Lukaski, 1996</td>
<td>36</td>
<td>No</td>
<td>3</td>
<td>None</td>
<td>NA</td>
</tr>
<tr>
<td>Obesity/Weight Loss</td>
<td>Two placebo controlled trials, double-blind</td>
<td>Evans, 1993</td>
<td>10,31</td>
<td>NA</td>
<td>2</td>
<td>P</td>
<td>P</td>
</tr>
<tr>
<td>Obesity/Weight Loss</td>
<td>Randomized controlled trial</td>
<td>Grant, 1997</td>
<td>43</td>
<td>No</td>
<td>1</td>
<td>Small</td>
<td>NA</td>
</tr>
</tbody>
</table>
Hypoglycemia

**Summary**: Theoretically, chromium acts to correct hypoglycemia in addition to hyperglycemic states through insulin regulation. There have been suggestions that chromium may have an effect on the secretion of glucagon in hypoglycemic states by the down regulation of β-cell activity (196). There is currently insufficient evidence to support the use of chromium in the treatment of hypoglycemia at this time.

**Evidence**: Following preliminary results of benefit in hypoglycemic patients (38), Anderson et al. studied the effect of 200mcg daily of chromium supplementation (CrCl3) or placebo on eight patients with symptoms of reactive hypoglycemia, tested after six and 12 weeks (197). Inclusion and exclusion criteria were not discussed. The study was a double blind, crossover-designed trial. Subjects responded with an increase in glucose at six and 12 weeks following supplementation. Significant improvements in insulin binding, insulin receptor number, and hypoglycemic symptoms were reported (p<0.05).

Clausen studied chromium induced clinical improvement in symptomatic hypoglycemia in 20 Danish patients receiving 125mcg Cr (Biochrome; Pharma-Nord, Denmark) daily for three months (43). Inclusion and exclusion criteria were not discussed. One month after treatment, 10 patients demonstrated a decrease in the hypoglycemic area of the glucose tolerance curve; the significance was not discussed. Clinical symptoms improved in several patients as well. The study can be strengthened by mentioning the inclusion and exclusion criteria and statistical analysis. An important factor that was not mentioned was whether the patients with hypoglycemia had type 1 or type 2 diabetes and if they had decreased the medication strength to help with the hypoglycemia.

Diabetes mellitus

**Summary**: Chromium treatment has been reported to improve glycemic control in patients with type 2 diabetes. However, concern exists about the possible toxic effects of chromium picolinate. Preclinical studies have shown that the combination of chromium picolinate and biotin significantly enhances glucose uptake in skeletal muscle cells and enhances glucose disposal. Research has centered on patients with non-insulin dependent diabetics, glucose intolerance, and healthy subjects. Chromium has been studied as chromium chloride (trivalent chromium), chromium picolinate, chromium-enriched yeast, brewer's yeast, and chromium-containing milk. Despite the large number of randomized controlled trials, there is inconsistency in the literature, thus making strong conclusions difficult. For instance, studies investigating chromium as chromium picolinate or chromium yeast at doses of 500-1,000mcg with similar primary endpoints found a lack of benefit in patients with type 2 diabetes who were currently taking antihyperglycemics (24;25). However, there are numerous studies that have suggested benefit in improving insulin sensitivity and glucose control (3;40;134;202); these studies, however, typically have varied primary endpoints, outcome measures, and dosage forms. Controlled trials have not consistently demonstrated benefit (19), although negative findings may be due to poor methodology or lack of appropriate administration due to nutritional deficiency (i.e. binding agents, such as niacin). Furthermore, one proposed mechanism of action is that chromium (III) compounds may only be effective in select populations of decreased glucose tolerance or type 2 diabetes mellitus where the disease is not the result of an alteration in the insulin receptor or the glucose transporter, but a genetically determined defect of the postreceptorial intracellular signaling mechanism (152). Additional study with better endpoints and methodology is necessary to make any firm conclusions.

**Reviews (non-systematic)**: Kelly conducted a review of studies that focused on nutritional
interventions and how chromium affects glucose metabolism (37; 40; 203; 204; 205). Sharpiro et al. reviewed the efficacy and safety of natural products and concluded that based on the data available, several natural products can be used to decrease blood glucose levels in patients with diabetes (206). Mertz et al. conducted an early review of the literature on chromium in human nutrition, including only studies with controls and chemically-defined compounds (115). Fifteen trials were examined and are discussed individually.

- **Meta-analysis:** Althuis et al. conducted a meta-analysis on the glucose and insulin responses to dietary chromium supplements (207).

- **Systematic reviews:** Balk et al. conducted a systematic review of the effect of chromium supplementation on glucose metabolism and lipid levels (153). Literature search was conducted in MEDLINE and the Commonwealth Agricultural Bureau and meta-analyses were reportedly performed as appropriate. The 41 qualifying studies included: English language randomized controlled trials of chromium supplement intake ≥3 weeks, with ≥10 participants receiving chromium; all trials with glucose metabolism outcomes; and trials of individuals with diabetes or glucose intolerance for lipid outcomes. For subjects with type 2 diabetes, chromium supplementation improved glycosylated hemoglobin levels by -0.6% (95% CI-0.9 to -0.2) and fasting glucose by -1.0mcM/l (-1.4 to -0.5), but did not improve lipids. In individuals without diabetes, there was no benefit. There were reportedly some indications of dose effect and differences among chromium formulations and larger effects were seen in poor-quality studies. The authors reported that limitations of these results include: poor quality of the qualifying studies (reportedly almost half of included studies), heterogeneity in methodology and results, and a lack of consensus on the assessment of chromium status.

- **Evidence:** Kleefstra et al. conducted a randomized, double-blind controlled trial to determine the effect of chromium treatment in the form of chromium yeast on glycemic control in a Western population of patients with type 2 diabetes who were being treated with oral hypoglycemic agents (25). The primary efficacy parameter was a change in A1C and secondary endpoints were changes in lipid profile, BMI, blood pressure, body fat, and insulin resistance. Patients were randomly assigned to receive either a placebo or treatment with 400mcg of chromium daily in the form of chromium yeast for six months. No differences were found for the change in A1C between the intervention and placebo groups, nor were any differences found between the groups for the secondary endpoints. The authors concluded that there is no evidence that chromium in the form of chromium yeast is effective in improving glycemic control in Western patients with type 2 diabetes who are taking oral hypoglycemic agents.

- **Kleefstra et al.** conducted a randomized controlled trial to determine the effect of chromium treatment on glycemic control in a Western population of insulin-dependent patients with type 2 diabetes (24). Patients with an HbA(1c) (A1C) >8% and insulin requirements of >50 units per day were included in this trial. The primary endpoint was a change in A1C and secondary endpoints were changes in lipid profile, BMI, blood pressure, and insulin requirements. Patients were randomly assigned to receive treatment with placebo or 500 or 1,000mcg chromium daily in the form of chromium picolinate for six months. The authors found that in their per-protocol analysis (N=46), the decrease in A1C was approximately equal across the three groups (0.4%). All patients had a BMI >25kg/m(2). No differences were found in the secondary endpoints, but there was a weak relationship between an increasing serum chromium concentration and improvement of the lipid profile. The authors concluded that this study does not show evidence that high-dose chromium treatment is effective in obese Western patients with type 2 diabetes.

- **Racek et al.** conducted a randomized, double-blind, controlled trial to determine the effect of chromium (Cr)- enriched yeast on blood glucose and insulin variables, blood lipids, and blood markers of oxidative stress in individuals with type 2 diabetes mellitus (27). Thirty-six subjects (nine men, 27 women; mean age: 61.3 years; mean body mass index: 34.33kg/m2) were supplemented with 400mcg Cr per day as Cr-enriched yeast (N=19) or placebo (N=17) for 12 weeks. The Cr group showed a significantly greater increase in serum Cr compared to the placebo group (p<0.05), as well as a significant decrease in fasting serum glucose compared to placebo (p<0.01). Blood markers of oxidative stress, glutathione peroxidase activity and levels of reduced glutathione, were essentially unchanged in the Cr group after 12 weeks, but decreased significantly in the placebo group (p<0.05, p<0.01, respectively). Serum HbA1c and glycated protein (fructosamine) were essentially unchanged in the Cr group, whereas HbA1c tended to increase in the placebo group (from 6.94% to 7.11%). Fasting serum insulin decreased in both groups, with a greater tendency in the Cr group (-16.5% vs. -9.5%). The authors
suggest that supplementation of well-controlled type 2 diabetics with Cr-enriched yeast is safe and may result in improvements in blood glucose variables and oxidative stress.

- Martin et al. conducted a randomized double-blind, placebo controlled trial to determine the effect of chromium picolinate on insulin sensitivity, glycemic control, and body composition in subjects with type 2 diabetes (26). Thirty-seven subjects with type 2 diabetes were evaluated. After baseline, subjects were placed on a sulfonylurea (glipizide gastrointestinal therapeutic system 5mg per day) with placebo for three months. Subjects were then randomized in a double-blind fashion to receive either the sulfonylurea plus placebo (N=12) or the sulfonylurea plus 1,000mcg chromium as chromium picolinate (CrPic) (N=17) for six months. Body composition, insulin sensitivity, and glycemic control were determined at baseline, end of the three-month single-blind placebo phase, and end of study. Subjects randomized to sulfonylurea/placebo, as opposed to those randomized to sulfonylurea/CrPic, had a significant increase in body weight (2.2kg, p<0.001 vs. 0.9kg, p=0.11), percent body fat (1.17%, p<0.001 vs.0.12%, p=0.7), and total abdominal fat (32.5cm², p<0.05 vs. 12.2cm², p<0.10) from baseline. Subjects randomized to sulfonylurea/CrPic had significant improvements in insulin sensitivity corrected for fat-free mass (28.8, p< 0.05 vs. 15.9, p=0.4), GHb (-1.16%, p< 0.005 vs. -0.4%, p= 0.3), and free fatty acids (-0.2mM/L, p<0.001 vs. -0.12mM, p<0.03) as opposed to sulfonylurea/placebo. The authors concluded that CrPic supplementation in subjects with type 2 diabetes who take sulfonylurea agents may significantly improve insulin sensitivity and glucose control. Further, CrPic supplementation significantly attenuated body weight gain and visceral fat accumulation compared with the placebo group.

- Pei et al. conducted a randomized, double-blind, placebo-controlled trial to assess the efficacy and safety of chromium-containing milk powder in patients with type 2 diabetes mellitus (28). A total of 60 patients with type 2 diabetes mellitus, ages 30 to 75 years, and on a dose of gliclazide sulfonylurea agent (≤160mg/d) for at least three months, were enrolled. Their glycosylated hemoglobin ranged from 7.5% to 12%, fasting plasma glucose (FPG) from 140 to 250mg/dL, and body mass index from 20 to 35kg/m². The subjects were divided into two groups, one group to receive chromium-containing milk powder (chromium 200mcg/20g milk powder) and the other to receive placebo twice a day for 16 weeks. Frequently sampled intravenous glucose tolerance test (IVGTT) was performed before and after treatment. The chromium group demonstrated a lower FPG and fasting insulin (-38.1 ± 9.2 vs. 63 ± 8.5mg/dL and -1.7 ± 0.2 vs. 1.9 ± 0.3mcU/mL, respectively; p<0.05), especially in male patients (-41 ± 9.2 vs. 85 ± 11.7mg/dL and -2.7 ± 0.2 vs 3.1 ± 0.3mcU/mL, respectively; p<0.01), at the end of the study. Lower glycosylated hemoglobin was observed in chromium-treated male patients (-1.1 ± 0. 5 vs. 0.7 ± 0. 2; p<0.05). However, there were no significant changes in other metabolic parameters (lipid profiles including total cholesterol, triglyceride, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol), except improvement of insulin resistance (homeostasis model assessment for insulin resistance and insulin sensitivity index from frequently sampled intravenous glucose tolerance test) observed in male patients (-2.1 ± 1.1 vs. -0.41 ± 1.12 and 0.18 ± 0.11 vs. -0.15 ± 0.2, respectively; p<0.05). There were no adverse events in both groups, except for mild complaints in the chromium group of constipation (5%) and flatulence (5%). The authors concluded that intake of chromium milk powder for 16 weeks in subjects with type 2 diabetes mellitus resulted in lowering of FPG, fasting insulin, and improvement of metabolic control in male patients.

- Singer et al. conducted a randomized, controlled pilot study to determine if supplementation with chromium picolinate and biotin can improve glycemic control in patients with type 2 diabetes mellitus with suboptimal glycemic control despite the use of oral antihyperglycemic agents (29). Forty-three subjects with impaired glycemic control (2-h glucose >200mg/dL; glycated hemoglobin ≥7%), despite treatments with oral antihyperglycemic agents, were randomized to receive 600mcg of chromium as chromium picolinate and biotin (2mg per day) (Diachrome, Nutrition 21, Inc., Purchase, NY) in addition to their pre-study oral antihyperglycemic agent therapy. Measurements of glycemic control and blood lipids were taken at baseline and after four weeks. Results indicated that after four weeks, there was a significantly greater reduction in the total area under the curve for glucose during the two hour oral glucose tolerance test for the treatment group (mean change -9.7%) compared with the placebo group (mean change +5.1%, p<0.03). Significantly greater reductions were also seen in fructosamine (p<0.03), triglycerides (p<0.02), and triglycerides/high-density lipoprotein cholesterol ratio (p<0.05) in the treatment group. No significant adverse events were attributed to chromium picolinate and biotin supplementation. The author concluded that a combination of chromium picolinate and biotin in poorly
controlled patients with diabetes receiving antidiabetic therapy improved glucose management and several lipid measurements. Chromium picolinate/biotin supplementation may represent an effective adjunctive nutritional therapy for people with poorly controlled diabetes with the potential for improving lipid metabolism.

• Sherman et al. studied the effect of trivalent chromium on the blood sugar concentrations of four normal and 10 diabetic (seven NIDDM, three IDDM) adult subjects over two 16-week periods in a double blind trial (18). Subjects were inmates at a state penitentiary ages 28 to 47 years. They excluded two subjects because one required insulin and the other chlorpropamide. Subjects received 150mcg chromium chloride or placebo daily for 16 weeks and were crossed over for an additional 16 weeks, without a washout period. There were no significant differences in blood glucose concentrations or glucose tolerance between chromium and placebo. Due to a small sample size, the power to detect a significant difference may not have been adequate.

• Rabinowitz et al. studied the effects of chromium and yeast supplements in a double blind, randomized, crossover trial in 43 men diagnosed with non-insulin dependent diabetes mellitus or insulin dependent diabetes mellitus (208). Patients were excluded if they had a history of pancreatitis, hemochromatosis, diabetes secondary to other endocrine problems, any life-threatening illness, chronic infections, proteinuria, evidence of gastrointestinal malabsorption, required diuretics, or chronically ingested yeast. The 16-month trial was broken into three four-month study periods, with two-month periods in between treatments. Patients received three of the four possible treatments. The treatments included 150mcg daily of CrCl₃, brewer's yeast with or without GTF, or placebo. The researchers observed cholesterol, triglycerides, fasting glucose, integrated plasma glucose response to Sustacal, and plasma glucose decrement after tolbutamide. Results failed to reveal any significant changes in fasting plasma glucose, glucose response, or body weight. Mean change in chromium stores was not correlated with change in carbohydrate status. Limitations include a poor description of randomization and blinding methods.

• Offenbacher et al. conducted a follow-up trial to an earlier study conducted in 1980 by the same research team (42). In this randomized-placebo controlled study, 23 healthy elderly patients consuming well-balanced diets received chromium chloride (200mcg per day) or brewer's yeast supplementation for 10 weeks. Subjects were excluded if they had ketosis-prone insulin-dependent diabetes, marked obesity, hyperuricemia, major intestinal disease, and mental incompetence. Outcomes observed were glucose, insulin, lipids, triglycerides, and total lipids. Glucose tolerance was not affected. Due to a small sample size, the power to detect a significant difference may not have been adequate.

• Glinsmann and Mertz conducted an early, uncontrolled study of the effect of chromium chloride on glucose tolerance in 14 patients with diabetes mellitus and 10 patients with normal glucose control (19). The 14 patients were U.S. army personnel, in good health except for their diabetes, and were hospitalized or followed for evaluation and control of diabetes as part of an Army requirement to determine fitness for military service. The authors used a glucose tolerance test before, during, and after supplementation with chromium. The first group of seven diabetics (three with IDDM) did not demonstrate significant changes in glucose following one to seven days of 150-1,000mcg chromium daily. In contrast, three of six diabetic subjects treated with 15-120 days of supplementation (150-1,000mcg daily) responded with an improved glucose tolerance. Limitations included a small sample size or exclusion criteria.

• Mossop et al. enrolled 39 African diabetic patients in a trial in which patients either received 2mg of chromium chloride or placebo daily for three months (36). No inclusion or exclusion criteria were given. Only 26 patients completed the trial due to multiple reasons, including non-attendance. The researchers looked at the patients' fasting blood glucose, fasting cholesterol levels, and fasting HDL levels. There was a decrease in fasting glucose levels (mean 7.7mM/L) in five of the 13 chromium treated subjects; significance was not discussed. The fasting cholesterol average dropped by 0.21mcM/l in the subjects taking chromium; the difference was not significant, and no p value was given. The fasting HDL levels rose by 0.08mcM/l in the chromium subjects, which was insignificant, and p value was not given. This study was limited in its methodology.

• Anderson et al. conducted a double blind, crossover study of 76 healthy subjects given 200mcg chromic chloride or a placebo daily for two three-month periods (38). Patients were excluded if they were taking more than three times the RDA of vitamins or minerals, those consuming brewer's yeast, those on medication, and those with overt illnesses. All patients were between 21 to 69 years of age. No
significant effects occurred in glucose or insulin levels (p>0.05). However, subjects with an elevated 90-minute glucose level following glucose challenge responded to chromium supplementation with a decrease in glucose level, whereas glucose levels in subjects with normal glucose challenge response were unchanged. The authors did not state if there was a washout period. This study was limited in its methodology.

- Uusitupa et al. investigated the effect of chromium supplementation (200mcg daily) on glucose tolerance, insulin response, long-term diabetic control, and serum lipids (209). Inclusion and exclusion criteria were not discussed. This six week, double blind, controlled crossover trial included 10 men with non-insulin dependent diabetes mellitus. No significant differences were seen in outcomes, specifically glucose tolerance and fasting or two-hour post-glucose serum insulin levels. The one hour post-glucose serum insulin level was slightly lower in the chromium supplementation (p<0.01) group. Limitations of the study include its small sample size and methodology.

- Martinez et al. examined the effects of chromium on 85 elderly Canadian women in a 10-week double blind controlled trial (210). Subjects (N=85) received either 200mcg chromium or placebo daily. Inclusion and exclusion criteria were not defined. Five women had diabetes that was not treated with insulin. Women at risk for impaired glucose tolerance (glucose >100 mg/dL two hours after challenge) who were not on medications demonstrated a small significant decrease (p=0.03) in glucose response to challenge following chromium treatment. This group had a lower mean chromium intake than one other subgroup. The authors concluded that women who were not on medication, but at risk for glucose intolerance, were chromium depleted and showed benefit from a chromium supplement. The study was limited by its methodology and sample size.

- Urberg and Zemel reported that supplementation with 200mcg daily chromium chloride plus 100mg daily nicotinic acid, in five or six of the 16 healthy elderly subjects after 28 days, caused a 15% decrease in a glucose area integrated total (p 0.025) and a 6.8% decrease in fasting glucose (p<0.10) (118). Patients were over the age of 65 years, in good health, and were not diabetic. The subjects could not be taking a chromium supplement, nicotinic acid, or brewers yeast. Fasting glucose and glucose tolerance were unaffected by either chromium or nicotinic acid supplements alone. The authors asserted that the results demonstrated that nicotinic acid and chromium are required together in order to optimize glucose metabolism. This may account for the variation in the results of chromium supplementation trials, since human diets contain a variable level of nicotinic acid. This study was limited by its small sample size.

- In a randomized, placebo controlled trial, Abraham et al. studied the effects of chromium supplementation (250mcg daily of CrCl₃) on serum glucose and lipids in 76 patients with established atherosclerotic disease, with and without non-insulin dependent diabetes mellitus, for seven to 16 months (110). The subjects were 42 to 83 years old. All patients had established atherosclerotic disease. No initial or long-term changes in fasting blood glucose concentrations were demonstrated. Serum triglycerides were lower in the chromium group (1.68 ± 0.11 versus 2.10 ± 0.14mcM/l respectively, p<0.02). A limitation of this study was a small sample size.

- A systematic review by Anderson examined the literature on glucose intolerance and diabetes (3). The author referenced 23 trials of chromium supplementation of subjects without diabetes mellitus. Several trials were not mentioned by the aforementioned Mertz review (34;40;113;118;211;212;213;214).

- Levine et al. completed an uncontrolled study of chromium deficiency in the impairment of glucose tolerance in 15 elderly subjects, who were at least 74 years of age (211). Patients had to: have been in the home for six months or longer, have no family history of diabetes, be alert with no known disease, and not be taking any medication that might have interfered with glucose tolerance tests. All the subjects had fasting plasma glucose levels below 120mg/100mL. Sixteen healthy young adults were used as a control group. Chromium supplements (150mcg/day) were given to 10 apparently healthy elderly subjects whose oral glucose tolerance tests (GTGs) were abnormal on at least one occasion. Mean GTT became normal in four of the 10 elderly subjects. Serum chromium concentration was found to rise significantly (p<0.05) after the glucose load, but to a lower level in the six elderly chromium non-responders.

- Offenbacher et al. conducted a single blind controlled trial of 24 elderly (mean age of 78) volunteers, of which eight subjects had mild non-insulin dependent diabetes mellitus (40). Subjects were excluded if they had ketosis-prone insulin-dependent diabetes, marked obesity, hyperuricemia, major intestinal
disease, and mental incompetence. Subjects were randomly assigned to 9g daily of brewers yeast or (chromium poor) torula yeast for eight weeks. Outcomes that were observed were glucose, insulin, lipids, triglycerides, and total lipids. Glucose tolerance improved significantly (p<0.05) and insulin output was reduced following chromium supplementation; mean glucose area index totals decreased from 632mg-h/dL to 549mg-h/dL (p<0.01). Cholesterol decreased significantly (p<0.001) in the experimental group, with the biggest decrease seen in patients with hypercholesterolemia. The authors concluded that chromium-rich brewer's yeast improved glucose and cholesterol. A limitation of the study was the sample size and age of subjects, which cannot be generalized to younger subjects.

Uusitupa et al. performed a double-blind, parallel-placebo group study evaluating daily chromium rich yeast (containing 160mcg chromium) supplementation, compared to placebo, in order to observe 26 elderly patients with impaired glucose tolerance for six months (113). Inclusion and exclusion criteria were not reported. The outcome measures were glucose tolerance, insulin secretion, and serum and lipoprotein lipids. No significant changes were observed in the oral glucose tolerance test, HbA1C, plasma insulin C-peptide, serum and lipoprotein-cholesterol, serum total triacylglycerols, and apolipoproteins; p value was not given. The authors concluded that chromium does not improve glucose tolerance in elderly patients with stable, impaired glucose tolerance. A limitation to the study is the sample size and methodology.

Wilson et al. conducted a double-blind, randomized trial to study the effects of chromium supplementation (220mcg daily) on fasting insulin levels and lipid parameters in 26 healthy, non-obese young subjects after 90 days (34). The study excluded patients with: chronic kidney, liver, pulmonary, or cardiac disease; obesity; a known history of diabetes mellitus; a history of hypertension or a resting diastolic blood pressure of greater than 90mmHg; those receiving treatment for hypertension; those being treated for hyperlipidemia; patients who had recently experienced a significant weight loss or gain; or patients who were competitive athletes, dancers, or gymnasts. The outcome measures were fasting glucose, immuno-reactive insulin level, and serum lipids. There were no statistically significant differences in fasting glucose, insulin level, or lipids compared to placebo. However, the 15 individuals in the chromium group with initial fasting insulin levels >35pmol/L had a significant decrease in post-supplemental insulin (p<0.03). The authors concluded that these subjects may benefit from chromium by improvement of insulin sensitivity and cardiovascular risk over time. A larger sample size would prove to be more conclusive.

A review by Anderson referenced an additional 16 trials (five trials overlapped with the first set and three reported lipid levels) of patients with non-insulin dependent diabetes mellitus (215). Those studies not already reviewed included an uncontrolled trial (216), studies with small sample size (146) or short duration (217), as well as the widely cited Anderson et al. (3) trial.

In a widely cited, large, double blind, placebo controlled study, Anderson et al. examined supplemental chromium in the control of type 2 diabetes in China (3). 180 subjects were enrolled, with 155 subjects completing the study. Subjects were 35-55 years old and had diabetic histories for five to eight years. Most were taking oral hypoglycemic agents. Subjects were randomized into the following groups: placebo, low dose chromium picolinate (200mcg), and high dose chromium picolinate (1,000mcg). Compared with placebo, HbA1C significantly decreased in both chromium groups by four months of treatment, while fasting blood glucose and glucose concentrations post-GTT only decreased significantly in the high dose group. Fasting insulin levels decreased significantly in both chromium groups. It has been noted (218) that differences in the Chinese and American diet may partly account for these findings. Further limitations may include the absence of documented chromium status, no information on compliance with treatment, and uncertain applicability to other populations (12).

Another review by Anderson was conducted on the subject of prevention and control of diabetes (76). The author stated that there have been more than 17 prior trials involving chromium supplementation in patients with diabetes. The review covered trials or case reports of patients with glucose intolerance and insulin sensitivity (219), insulin dependent diabetes mellitus (218), non-insulin dependent diabetes mellitus (220), gestational diabetes (134;202), and steroid induced diabetes (114).

Jovanovic et al. conducted a randomized, placebo controlled trial to examine the efficacy of chromium supplementation in 30 gestational (20-24 gestational weeks) diabetic women (134;202). Subjects were randomized to receive 4mcg/kg bodyweight of chromium picolinate, 8mcg/kg of chromium picolinate, or placebo for eight weeks. Although exclusion/inclusion criteria were not specified, the author did state
that all groups were matched for body weight, age, and gestational week. Three women in the 4mcg/kg Cr group, one in the 8mcg/kg Cr group, and four in the placebo group failed diet therapy and required insulin. Outcome measures assessed included concentrations of insulin, glucose, and C-peptide. Results at eight weeks showed that the 4mcg/kg Cr group had significantly lower HbA1C when compared to baseline (5.6±0.4% dropped to 5.2±0.6%, p<0.05). The 8mcg/kg and placebo groups had no change. Both 4mcg/kg and 8mcg/kg Cr were shown to significantly decrease glucose and insulin when compared to placebo. Limitations include lack of blinding.

Cefalu et al. conducted a long term, double blind placebo controlled trial with 29 obese patients with a family history of non-insulin dependent diabetes mellitus (219). Chromium picolinate at a dose of 1,000mcg daily over eight months had a demonstrated significant effect on insulin sensitivity.

Cheng et al. conducted a follow-up trial to the study by Anderson et al. (3) involving over 800 individuals with non-insulin dependent diabetes mellitus, in which symptoms of hyperglycemia improved in over 80% of subjects (220).

Ravina et al. conducted a trial of 50 patients on steroids, with steroid induced signs and symptoms of diabetes (221). All patients had fasting blood glucose values >13.9mcM/L that did not respond to hypoglycemic drugs or insulin therapy. Chromium picolinate at a dose of 600mcg daily was given for two weeks and then reduced to 200mcg daily or discontinued by some individuals. A majority (47/50) of patients responded to supplementation, with fasting blood glucose levels <150mg/dL and two hour postprandial glucose <180mg/dL. The authors did not mention any significance in the study or p values. The study was also limited by its methodology.

There have been several additional trials further examining dosages and efficacy. Lee et al. investigated the effect of chromium picolinate supplementation (200mcg daily) on the lipid profile of 28 predominantly Hispanic non-insulin dependent diabetes mellitus subjects in a six-month double blind crossover controlled trial (31). The study excluded patients with untreated thyroid dysfunction, pregnancy, acute medical or psychiatric illness, renal insufficiency, liver disease, ethanol or illicit drug use, steroid use, and poorly controlled diabetes. Each patient was randomized to receive either chromium or placebo for two months, followed by a two-month washout period, after which patients were crossed-over to receive the alternate capsule for an additional two months. Results failed to reveal any significant differences between the chromium and placebo groups in the endpoints of fasting blood glucose and HbA1C. The sample size may have been too small for adequate power to detect a statistical difference.

A randomized placebo controlled trial of high dose chromium (1,000mcg daily) was conducted with 19 healthy, non-obese older men and women (30). The outcome measures for the study were insulin sensitivity, serum lipids, and body composition. No significant effect on insulin sensitivity, lipids, or body composition was found. The P value was not given. The study was limited by its small sample size, which would make it difficult to detect a significant difference.

Trow et al. conducted an uncontrolled pilot study to examine the effects of daily supplementation with high chromium yeast on the parameters of glucose tolerance, plasma insulin, and lipoprotein concentrations (222). Patients had to have been diagnosed with type 2 diabetes for at least three months. The patients were between the ages of 45 to 67 years and had a body mass index of 22-30. Healthy volunteers (N=12) with type 2 diabetes were selected and tested for chromium content at baseline and after the initiation of treatment. Chromium was given at a dose of 100mcg daily. Fasting glucose concentrations and glucose area under the curve profiles were not altered significantly after chromium supplementation. No significant changes (no p values given) in insulin and lipoprotein concentrations were found during the trial. This study was limited by the omission of p values.

Aharoni et al. conducted an uncontrolled, non-randomized study to observe if a possible etiology for gestational diabetes could be the impaired utilization of chromium (105). The study compared the hair chromium concentrations in 42 pregnant women with gestational diabetes to 68 pregnant women without gestational diabetes. None of the women were taking chromium supplements at the time of the study. The women were subdivided in regards to their maternal age, number of children, and gestational age. The authors found that there was a statistically significant difference (t = 3.06, p<0.005, 95% CI) in the hair chromium concentration and the concentrations were higher in all patients with gestational diabetes than those without. This may support the hypothesis that glucose intolerance in gestational diabetes may be from impaired glucose utilization and not chromium deficiency. This study used a small study population to base its conclusion. Further studies should be performed on a larger population to
establish a concise correlation between hair chromium concentrations and impaired chromium utilization.

A randomized, placebo-controlled trial was performed by Anderson et al. to examine if people with type 2 diabetes would receive benefit from taking chromium as a supplement (205). The researchers randomized 180 adults with type 2 diabetes to receive oral doses of either a placebo, 100mcg of chromium picolinate twice a day, or 500mcg of chromium picolinate twice a day. Participants were instructed not to change their diet or living habits during the four-month trial. Glycated hemoglobin improved significantly after two months in the 1,000mcg daily group (placebo, 8.5 ± 0.2%; 200mcg Cr, 7.5 ± 0.2% and 1,000mcg Cr, 6.6 ± 0.1%) and in both chromium groups after four months. The authors stated that there was significance in the decrease of fasting (Cr 1,000mcg daily, placebo, 8.8 ± 0.3mcM/l; 1,000mcg Cr, 7.1 ± 0.2mcM/l) and two-hour post-prandial blood glucose (placebo, 12.3 ± 0.4mcM/l; 1,000mcg Cr, 10.5 ± 0.2mcM/l) for both chromium groups, although values were not given for the 200mcg daily group. They also found that plasma total cholesterol also decreased after four months in the group receiving 1,000mcg daily of chromium. The authors concluded that a chromium supplement had a significant beneficial effect on cholesterol, glycated hemoglobin, glucose and insulin variables, and that 500mcg chromium taken twice daily was more beneficial than 100mcg chromium taken twice daily. This study was only conducted over four months, which is not considered a significant amount of time to observe the effects on a patient's glycated hemoglobin. Glycated hemoglobin is a three-month marker of how a patient's glucose has been controlled over the previous three months. The authors evaluated the patients' hemoglobin at two months into the trial and at four months. These values would have more significance if they were taken at baseline and then again at four months, to more clearly show the patients' benefit from receiving chromium.

A three-month, double blind, crossover study was performed to determine the effects of a chromium supplement on serum chromium and related variables (223). The study included 76 adult patients who were given placebo or 200mcg chromium, as chromic chloride. There was no inclusion or exclusion criteria for enrollment in the study. The basal serum chromium was 0.13 ± 0.02ng/mL and after three months of chromium supplement, it significantly increased (p<0.05) to 0.38 ± 0.02ng/mL, which demonstrates that this increase is due to the intake of chromium. These levels were also checked following a 90-minute glucose load and no significance was found between the two groups. This suggests that following a glucose load, serum chromium concentration does not indicate chromium status. A larger study population should be evaluated in order to observe any significant changes in serum chromium concentrations. In addition, this study utilized patients who did not have diabetes; therefore, the 90-minute blood glucose sample would show no benefit with taking a chromium supplement. The authors did not state what patients were excluded from the trial, if any, which is why this study cannot be generalized.

Cefalu et al. conducted an in vivo double-blind, placebo controlled trial to determine the effects of chromium supplements on insulin sensitivity and on specific body fat depots (224). The study evaluated 26 moderately obese, non-diabetic patients, who received either placebo or chromium picolinate 1,000mcg/d and were followed for eight months. The authors found that there was a significant effect (p<0.001) as insulin sensitivity increased from 2.6 to 4.0 x 10^{-4} μU^{-1} in patients receiving chromium. Intra-abdominal fat was not statistically significant between the two groups (p value not given). The authors concluded that chromium picolinate, over the eight month trial, increased insulin sensitivity in moderately obese non-diabetic patients and no effect was seen with abdominal fat distribution. Future studies should be done in a larger study population to note a stronger correlation between chromium and insulin sensitivity.

Insulin sensitivity was determined by using the artificial beta cell in six patients with type 2 diabetes who were given chromium-rich brewer's yeast supplementation (225). They received three heaped tablespoonfuls (52g of brewer's yeast and 0.4mcg/g of trivalent chromium) per day for the two weeks of the study. Baseline data was compared to the two-week data and it was found that all patients had an increase in insulin sensitivity, which was seen as a decrease in fasting glucose concentration (baseline, 121.8 ± 24.1; after chromium 105.2 ± 13.9) and insulin requirement during a glucose challenge (p<0.02). The authors concluded that peripheral effects of insulin could be due to chromium or other elements in the brewer's yeast. In a study that only looks at six people, it is hard to make a conclusive decision about chromium or brewer's yeast. Since inclusion and exclusion criteria were not given, this data should not be generalized. Additional studies should be performed on more subjects and over a
Hair samples were collected from 33 children who were seemingly normal (without diabetes), and 19 children with juvenile diabetes, who had been receiving insulin for several years, to determine the concentration of chromium between the two groups (226). The children lived in the same area and with no relation to each other. There was no standardization with regards to hair length or the site of the sample. They found that in the 33 normal children, the chromium mean was 0.85mcg/g (range, 0.36-1.87mcg/g), and in the children with juvenile diabetes, the mean was 0.56mcg/g (range, 0.26-1.19mcg/g). The authors concluded that there was a statistical difference, using the student's test, between the two groups (p<0.001), and that further studies should be performed in juvenile diabetes to determine the precise role of chromium. Due to the small sample size of the study, further studies are needed to determine the significance of chromium in type 1 diabetes. The authors also failed to mention how long the children had diabetes, length of treatment, and control. The authors further described, in another study, the methods for hair washing and external environmental factors that may affect hair chromium concentrations (227). They also examined the concentration of chromium with regards to the distance the sample was taken from the hair roots (228).

Case study has reported that chromium supplementation in a nine-year-old boy with insulin-dependent diabetes mellitus (IDDM) lead to significant reductions (p=0.005) in his blood glucose within 24 hours after taking 200mcg of chromium (229). In October, prior to his chromium supplementation, the HbA1C was 6.5. After taking the chromium supplement, the HbA1C in January was 6.0; in April it was 5.6, and in July it was 5.3, which shows a control of his diabetes for three month periods. Further studies are needed to support or reject the use of chromium in type 1 diabetes.

A randomized, double-blind 12-week study of 35 patients, with no metabolic or cardiac abnormalities, was done to observe if there was any effect from resistance training, with or without 500mcg of a chromium picolinate supplement twice daily, on glucose metabolism (230). The subjects' mean age was 62 years, with a BMI of 29.1kg/m². Subjects were required to participate in resistance training twice a week. Before performing glucose metabolism assessment, patients in weeks one and 13 had to eat meals that were provided, which ensured that all patients consumed a standardized diet. The authors used repeated-measure ANOVA and found no changes in insulin or c-peptide concentrations in all 32 patients, which suggests that in patients with no metabolic disorders, high doses of chromium picolinate has no effect on glucose metabolism. The study had 100% compliance with regards to resistance training, but the authors failed to mention the compliance rate with the chromium supplement. The authors did state that they determined compliance by counting the pills that were returned to them on a weekly basis, by an interview, and by noting a 50-fold increase in the 24 hour urine chromium excretion during weeks seven and 13. The study could have been stronger if the authors stated the compliance rate with chromium.

A case-control panel study of 400 consecutively chosen ophthalmologic patients was conducted that included an 809-item quantitative-food-frequency inventory to estimate the prior two month intake of minerals and erythrocyte enzymes (231). It was found that patients with primary open-angle glaucoma seemed to have a deficiency of erythrocyte chromium and ascorbic-acid intake and an increase in vanadium, which is the antagonist to chromium. The authors reported that a deficiency of either substance is associated with an increase in intraocular pressure (t =-3.18, p=0.0003).

In a controlled trial by Liu et al., researchers studied 20 college students with normal insulin secretion and divided them into two groups: subjects with high insulin secretors and subjects with low insulin secretors (232). Each group fasted for 14 hours overnight and then were administered 100g of glucose dissolved in 275mL of water. At several time intervals, ranging from a half-hour to an hour to three hours, random blood samples were taken. Outcome measures included serum glucose, serum insulin, serum chromium, percentage of ideal body weight, and triceps skinfold thickness. The subjects' insulin peaked between a half-hour to one hour, and no significant difference was found between the groups in their serum chromium levels at either the baseline or peak insulin level. Results may have been influenced by the strong family history of diabetes in 14 of the subjects. The study was not randomized, controlled, had no placebo group, and it also had a small study sample.

A comparison of 93 type 2 diabetic patients and 33 healthy volunteers was done to measure the chromium homeostasis using fasting blood samples and second morning voiding of urine samples (233). The type 2 diabetic patients had a 33% lower plasma level and a 100% higher urine level.
compared to healthy volunteers, suggesting that patients with type 2 diabetes were at an increased risk of chromium deficiency, which may lead to the development of insulin resistance. A larger sample size would be needed for future studies.

A double-blind, randomized, cross-over trial was conducted in which chromium trichloride (a brewer's yeast that contains chromium as glucose-tolerance-factor (GTF)), a brewer's yeast without GTF supplement, and placebo, were given to 43 men with diabetes to observe the effects on fasting plasma glucose, plasma cholesterol, and plasma triglycerides (234). The study excluded subjects that had a history of pancreatitis, hemochromatosis, diabetes secondary to other endocrine problems, any life-threatening illness, chronic infections, proteinuria, evidence of gastrointestinal malabsorption, required diuretics, or chronically ingested yeast. In group I, 21 subjects required daily insulin due to ketosis; in group II, seven subjects were not ketosis-prone and were not obese; and in group III, 15 subjects were not ketosis prone but were obese. The men were instructed to take the experimental drugs for four months each with a two-month wash out period. The total study duration was 16 months. Since there were four tablets to be dispensed and only three treatment periods, no one group received all four treatments. At the end of the trial, body weight was constant in all patients. Some men on insulin needed an increase of 3.6 ± 1.5 units a day, which is not statistically significant (p value not given). Increases in creatinine levels were noticed but with no correlation between the formulation. None of the groups showed significant change regarding their fasting plasma glucose, cholesterol, or triglyceride levels. The study did not indicate why they used all male subjects and did not indicate a further study that would require all female subjects to compare the results. However, the authors did have baseline measurements and results shown in tables to clarify the data presented.

Romero et al. used 112 adult subjects and divided them according to type 2 diabetes with chronic renal failure, non-diabetics with chronic renal failure, type 2 diabetics, and healthy subjects, to evaluate blood levels of chromium (235). Inclusion and exclusion criteria were not mentioned. It was found that patients who had diabetes and chronic renal failure had a significantly higher blood chromium level (p<0.01) than non-diabetic patients with chronic renal failure; chromium levels in the blood were also statistically significant when compared to the control group, and when compared to patients with diabetes (p<0.05). The groups were equivalent with regards to age, sex, and size. The study did not mention the duration of the disease state (patient receiving hemodialysis for many years vs. just starting), which might alter the results of the study. The inclusion and exclusion criteria are not necessary in this study since the subjects did not receive any study drugs.

138 tannery workers who were occupationally exposed to chromium were compared to 150 subjects who were not exposed, in order to determine if there was an association between chromium levels and glucose and fat metabolism (236). Subjects in the control group were randomly selected to have the same male to female ratio and mean age as the tannery group with no exclusion criteria. The study used hair samples, pre-shift urine, and thermally-induced sweat. It was found that the tannery workers absorbed 13 times the level of chromium than the control group and were significantly higher (p<0.01) in all three lab samples (tannery, hair: mcg Cr/g; urine: Chromium/creatinine 1.7mcg Cr/g; sweat: 25mcg Cr dm-3; control group: hair: 0.16mcg Cr/g; urine: Chromium/creatinine 0.13mcg Cr dm-3). There was no statistical significance found with lipid levels between the groups. However, when the groups were individually subdivided by age, the percentage of obese, glucose-intolerant subjects was significantly lower (p<0.01) in the tannery subjects. This was not the case with comparison of all tannery subjects. The authors mentioned that the control group was selected without regard to medical health status, which may have made a difference in the study results. A better comparison would have been established if the researchers selected patients in the control group with the same mean lipid panel and glucose intolerance. Employment in the tannery ranged from two to 40 years; this range should have been narrowed. Also, the authors did not state the length of the study, which was assumed to be one day.

Another study in 1999 by Wróbel et al. looked at tannery workers and the effects of chromium on their glucose, serum cholesterol, and triglyceride levels (237). The study used three study groups of nine tannery workers, eight patients with type 2 diabetes, and 10 healthy volunteers. Randomization and inclusion and exclusion criteria were not discussed. The researchers administered oral glucose and glucose levels were checked at a half-hour, hour, and two hours. The tannery workers had higher levels of serum chromium, lower serum insulin, cholesterol, and better glucose tolerance when compared to
the control group; no significance was reported. The authors concluded that patients with diabetes had an altered mechanism of action for the chromium. The sample size was too small to be generalized.

Hyperlipidemia

**Summary:** There have been inconsistent results on chromium's effect on serum lipids, with most support for an increase in HDL levels. It is unclear whether improvement of serum lipids in these studies was a direct effect of chromium intake on lipid metabolism and/or an indirect consequence related to improved glucose and insulin homeostasis. There is insufficient evidence to support the use of chromium in the treatment of hyperlipidemia at this time.

**Evidence:** Balk et al. conducted a systematic review of the effect of chromium supplementation on glucose metabolism and lipid levels (153). Literature search was conducted in MEDLINE and the Commonwealth Agricultural Bureau and meta-analyses were reportedly performed as appropriate. The 41 qualifying studies included: English language randomized controlled trials of chromium supplement intake ≥3 weeks, with ≥10 participants receiving chromium; all trials with glucose metabolism outcomes; and trials of individuals with diabetes or glucose intolerance for lipid outcomes. For subjects with type 2 diabetes, chromium supplementation improved glycosylated hemoglobin levels by -0.6% (95% CI-0.9 to -0.2) and fasting glucose by -1.0mcM/l (-1.4 to -0.5), but did not improve lipids. In individuals without diabetes there was no benefit. There were reportedly some indications of dose effect and differences among chromium formulations and larger effects were seen in poor-quality studies. The authors reported that limitations of these results included: poor quality of the qualifying studies (reportedly almost half of included studies), heterogeneity in the methodology and results, and a lack of consensus on the assessment of chromium status.

A randomized placebo controlled trial of high dose chromium (1,000mcg daily) was conducted with 19 healthy, non-obese older men and women (30). The outcome measures for the study were insulin sensitivity, serum lipids, and body composition. No significant effect on insulin sensitivity, lipids, or body composition was found. P value was not given. The study was limited by its small sample size, which would make it difficult to detect a significant difference.

Lee et al. investigated the effect of chromium picolinate supplementation (200mcg daily) on the lipid profile of 28 predominantly Hispanic non-insulin dependent diabetes mellitus subjects in a six-month double blind crossover controlled trial (31). The study excluded patients with untreated thyroid dysfunction, pregnancy, acute medical or psychiatric illness, renal insufficiency, liver disease, ethanol or illicit drug use, steroid use, and poorly controlled diabetes. There were no differences between the groups in glucose control, HDL-cholesterol levels, or LDL-cholesterol. However, triglyceride levels significantly decreased (17.4%, p<0.05) at endpoint. By report, this was the first demonstration of a reduction in TG in non-insulin dependent diabetes mellitus patients treated with chromium. The sample size may have been too small to detect a difference.

A randomized, double blind controlled trial was conducted in which chromium-nicotinic acid (supplied by ChromeMate®, Interhealth Inc, Concord, CA) was given to 34 college bodybuilders (32). Subjects were randomized to placebo, 200mcg/1.8mg chromium/nicotinic acid, or 800mcg/7.2mg chromium/nicotinic acid for eight weeks. Outcome measures included total cholesterol, triglyceride, HDL, TC:HSL, LDL, and one hour post-challenge insulin and glucose values. Mean triglyceride concentrations decreased in the Cr and as well as the combination group (147.9 to 126.8mg/dL and 159.2 to 131.3mg/dL respectively; p<0.03). Mean TC:HDL ratio decreased from 3.62 to 3.37 and 3.43 to 3.27 in the Cr and combination groups, respectively (p<0.04). In contrast, the mean triglyceride and TC:HDL ratio increased in the placebo group. No significant differences were seen in insulin and glucose concentrations. Limitations include a poor description of randomization procedure.

Hermann et al. examined 42 healthy older (>60 years old) subjects in a 12-week, randomized, placebo controlled trial using 150mcg chromium (CrCl3) (33). The average age of the subjects was 73 years. Patients self reported no known debilitation or chronic diseases. No significant differences were found in the total sample. However, sub-group analysis of patients with higher baseline total cholesterol (>6.21mcM) found significant reduction in total, LDL cholesterol (p<0.03), and apolipoprotein B (p=0.05) in the chromium treated subjects compared to placebo. Subgroup analysis was based on a smaller sample. A limitation to the study was self-reporting of the presence of chronic diseases, rather than physician approval regarding the patients' disease status. Many subjects in this age group have chronic
disease (such as hyperlipidemia and hypertension), which may have interfered with the study results.

- Wilson et al. enrolled 26 young, healthy volunteers in a 90-day randomized double blind trial of 220mcg/day chromium nicotinate (supplied by Nutrition 21 Inc. San Diego, CA) compared to placebo (34). The study design was a double-blind, randomized trial. The study excluded patients with chronic kidney, liver, pulmonary, or cardiac disease; obesity; a known history of diabetes mellitus; a history of hypertension or a resting diastolic blood pressure of greater than 90mmHg; patients receiving treatment for hypertension; those being treated for hyperlipidemia; patients who had recently experienced a significant weight loss or gain; and patients who were competitive athletes, dancers, or gymnasts. The outcome measures were fasting glucose, immuno-reactive insulin level, and serum lipids. There was no significant difference between chromium and placebo groups across several lipid parameters. The study was limited by its small sample size.

- Rabinowitz et al. studied the effects of chromium and yeast supplements in a double blind, randomized crossover trial of 43 diabetic men, including insulin dependent diabetes mellitus and non-insulin dependent diabetes mellitus patients (208). Subjects were excluded if they had a history of pancreatitis, hemochromatosis, diabetes secondary to other endocrine problems, any life-threatening illness, chronic infections, proteinuria, evidence of gastrointestinal malabsorption, or chronically-ingested yeast. They assessed chromium in insulin requirements, fasting plasma glucose, plasma cholesterol, triglycerides, plasma glucose, glucagons, and insulin or C-peptide. The 16-month trial was broken into three four-month study periods, with two-month periods in between. Patients received three of four treatments; 150mcg/day of CrCl3, a brewer's yeast containing GTF, a brewer's yeast extract without GTF, or a placebo. No significant change was noted in fasting plasma glucose, cholesterol, or triglycerides. Mean change in chromium stores was not correlated with change in lipids. Limitations include a poor description of randomization and blinding methods.

- Boyd et al. studied 35 college-aged, healthy, exercising men and women in a double blind (randomization not mentioned) trial comparing 1,000mcg daily chromium picolinate (supplied by Nutrition 21 Inc. San Diego, CA) to placebo over 13 weeks (35). Inclusion and exclusion criteria were not given. Both groups continued exercise (resistance + aerobics) classes twice a week for 50 minutes. Ten subjects were removed from final analysis due to poor compliance; it is unclear from which group. Significant reductions in cholesterol (p<0.001), LDL cholesterol (p<0.002), and insulin concentration (p<0.02) were found in the chromium group, comparing pre- and post-exercise values. The study is limited by its sample size.

- Following two to four months of supplemental chromium (600mcg chromium chloride) in a sample of 39 diabetic patients (26 subjects completed the study), there was no significant change in total cholesterol. HDL levels rose in 12/13 chromium subjects (mean increase 0.44mcM/L) compared to a decrease in 11/13 controls (36). The study did not discuss inclusion or exclusion criteria. The authors assessed patients' fasting blood glucose, fasting cholesterol levels, and fasting HDL levels. The study was limited in its methodology (non-randomized, no placebo control).

- A randomized placebo controlled trial of high dose chromium (1,000mcg daily) was conducted with 19 healthy, non-obese older men and women (30). All subjects were nonsmokers and not obese. Patients with a medical illness were excluded. The authors observed the effects of chromium picolinate on insulin sensitivity, serum lipids, and body composition. No significant effect on insulin sensitivity, lipids, or body composition was found. The study was limited by its small sample size.

- Offenbacher studied the effect of low dose chromium on glucose tolerance and blood lipids in 24 elderly volunteers (eight mildly non-insulin dependent diabetes mellitus) for eight weeks (40). The subjects had to live at a retirement home for the elderly. The study excluded patients who were ketosis-prone insulin dependent diabetics, markedly obese, hyperuricemic, had major intestinal disease, and mental incompetence. Outcomes observed were glucose, insulin, lipids, triglycerides, and total lipids. Subjects were randomized to either chromium-rich brewer's yeast (10.8mcg chromium) or torula yeast (<0.45mcg chromium). In the chromium-rich yeast group, glucose tolerance improved significantly and cholesterol (by 30mg/dL; p<0.001) fell significantly after supplementation. Triglyceride reduction was significant in a small subgroup of subjects with cholesterol >300mg/dL. Due to a small sample size, the power to detect a significant difference may not have been adequate.

- Citing possible benefit on lipid profiles from chromium's effect on insulin sensitivity, Riales and Albrink conducted a randomized, double blind, placebo-controlled trial of chromium (CrCl3) (37). Inclusion and
exclusion criteria were not discussed. The outcome measures were weight, body mass index, serum lipids, and insulin. Twenty-three healthy men received 200mcg daily of chromium five days a week for 12 weeks. The increase in HDL (35-39mg/dL) was statistically significant by week 12 (p<0.05). A significant decrease in body weight in the chromium group is important to note in interpreting these findings (113). The study was limited in its sample size and methodology.

- In an open trial, Elwood et al. administered 20g/day high chromium brewer's yeast (48mcg chromium daily) to 11 normal and 16 hyperlipidemic patients over eight weeks, and then 10g a day high chromium brewer's yeast (24mcg chromium daily) to 19 patients over eight weeks (41). Subjects were excluded if they required insulin or took hypoglycemic medication, had major intestinal disease, or were overtly ill. The outcome measured was serum lipids. A significant decrease in total cholesterol was found in each trial (p<0.01), while HDL significantly increased in the higher dose chromium trial only. The average HDL increase in combined normal subjects and controls was 6mg/dL. The study was limited by its small sample size.

- Anderson et al. conducted a double blind, crossover study of 76 healthy subjects given 200mcg chromic chloride or a placebo daily for two, three-month periods (38). Patients were excluded if they were taking more than three times the RDA of vitamins or minerals, were consuming brewer's yeast, were on medication, or if they had overt illnesses. All patients were between 21 to 69 years of age. No significant change in lipid levels was found across the six-month study period. There was no significant effect on weight, unlike the positive study by Riales and Albrink (37).

- Trow et al. conducted an uncontrolled pilot study to examine the effects of daily supplementation with high chromium yeast on the parameters of glucose tolerance, plasma insulin, and lipoprotein concentrations (222). Healthy volunteers (N=12) with type 2 diabetes were selected and tested for chromium content at baseline and after the initiation of treatment. Patients had to have been diagnosed with type 2 diabetes for at least three months. The patients were between the ages of 45 to 67 and had a body mass index of 22-30. Chromium was given at a dose of 100mcg daily. Fasting glucose concentrations and glucose area under the curve profiles did not significantly alter post-chromium supplementation. No significant changes in insulin and lipoprotein concentrations were found during the trial. P values were not discussed.

- Uusitupa et al. investigated the effect of chromium supplementation (200mcg daily) on glucose tolerance, insulin response, long-term diabetic control, and serum lipids in a six-week, double blind, controlled crossover trial of 10 men with non-insulin dependent diabetes mellitus (209). Inclusion and exclusion criteria were not discussed There was no significant effect upon serum lipids. Limitations to the study included a small sample size.

- High potency yeast was used in a study of a mixed sample of normal subjects, diabetics, and hyperglycemic patients (238). Inclusion and exclusion criteria were not discussed. The authors measured HbA1C and serum lipids. In this uncontrolled trial, each subject served as control as well. Subjects received 218mcg chromium in the form of oral yeast capsules for six months. The small sample of hyperglycemic patients (5 subjects) had a significant reduction in mean blood glucose and a significant increase in HDL at six months. There was no significant effect on cholesterol or HDL in the remainder of the sample. Limitations to this study are a lack of definition of statistical significance, small sample size, and lack of inclusion and exclusion criteria.

- Offenbacher et al. examined the effects of inorganic chromium (200mcg daily as CrCl3), brewer's yeast (containing 5mcg of chromium), or placebo on glucose tolerance, plasma lipids, and plasma chromium in 23 well-nourished, healthy elderly volunteers for 10 weeks (42). Subjects were excluded if they had ketosis-prone insulin-dependent diabetes, marked obesity, hyperuricemia, major intestinal disease, or mental incompetence. Outcomes observed were glucose, insulin, lipids, triglycerides, and total lipids. There were no significant changes in glucose tolerance, insulin, cholesterol, or triglycerides after supplementation in any of the groups. This study suggests that age by itself is not a factor leading to chromium deficiency. Due to a small sample size, the power to detect a significant difference may not have been adequate.

- Press et al. studied the effect of chromium picolinate on serum cholesterol and apolipoprotein fractions in 32 healthy subjects (baseline cholesterol levels of 220-320mg/dL) receiving either 200mcg chromium picolinate or a placebo daily over a 42 day trial (39). Subjects had no history of hypothyroid disease, renal failure, liver disease, diabetes mellitus, known familial lipid disorder, alcohol or drug abuse,
bleeding disorders, multiple allergies, or any other serious medical illness and were not pregnant at the outset of the study. None of the subjects were using β-blockers, thiazide diuretics, steroids, chromium supplements, or any investigational drugs. The study was a double blind, randomized, crossover design. Levels of total cholesterol (p<0.007), LDL-cholesterol (p<0.015), and apolipoprotein B (p<0.003) decreased significantly in the group that began with a six-week trial of chromium. Consolidated results of the trial demonstrated a 7% decrease in total cholesterol and a 10.5% decrease in LDL (200-178mg/dL) with chromium treatment. The study was limited by its small sample size.

- Wang et al. examined serum glucose, insulin, total blood lipids, urinary chromium, and creatinine concentrations in 30 healthy adults with elevated serum cholesterol (>200mg/dL) (112). Patients were excluded if they were taking medication that would interfere with the study results. Each of the three groups received supplemental chromium of 50mcg CrCl3 (Fisher Scientific Co, Fair Lawn, NJ), brewer's yeast (containing 15mcg chromium), or placebo five times a week for 12 weeks. Serum total cholesterol decreased significantly with a mean decline of 14 mg/dL in the chromium group and 12mg/dL in the yeast group (p<0.005). Also compared to the controls, LDL decreased significantly from 164-150mg/dL. There was no significant change in body weight. The study was limited by its methodology.

- Following the improvements in HDL cholesterol demonstrated in smaller studies, Roeback et al. conducted an eight week, randomized, double blind controlled trial of 72 patients on beta-blockers, previously reported to reduce HDL (111). Patients were excluded if they had cancer, insulin-dependent diabetes, active liver or kidney disease, or a history of poor medication compliance. The outcome measures were serum levels of total cholesterol and HDL cholesterol. Subjects received 600mcg daily GTF-Chromium (supplied by Nutrition 21 Inc; San Diego, CA) or placebo. Chromium supplementation resulted in a statistically significant 16% increase in HDL-cholesterol (by 0.15mcM/L). Based upon population based studies of HDL and heart disease, and assuming long term benefit, the authors suggested that this improvement may lead to a 12% to 17 % decreased risk for coronary heart disease. Further studies should be performed with a larger sample size.

- In a trial of more extended duration, Abraham et al. studied the effects of chromium supplementation (250mcg/day CrCl3) on serum glucose and lipids in 76 patients with established atherosclerotic disease, with and without non-insulin dependent diabetes mellitus, for seven to 16 months (110). The average age of the subjects was 42 to 83. All patients had established atherosclerotic disease. Significant decreases in serum triglycerides (p<0.02) and VLDL cholesterol (p<0.05) and a significant increase in serum HDL cholesterol (by 0.20mcM/L; p<0.005) with chromium were demonstrated in this placebo controlled randomized trial. In addition, serum chromium levels were monitored and were increased when the supplement was administered. A limitation of the study was a small sample size.

- Elderly patients (N=26) with stable impaired glucose tolerance were studied by Uusitupa et al. in a double blind, placebo controlled trial over six months duration (113). Inclusion and exclusion criteria were not reported. The outcome measures were glucose tolerance, insulin secretion, and serum and lipoprotein lipids. Subjects received 160mcg daily chromium yeast in addition to ongoing diuretic or beta-blocker medication in several cases. No significant change in cholesterol levels, including apolipoprotein A & B, was noted in the sample (p value was not given). The study was limited by its sample size and methodology.

- Bourn et al. conducted a double-blind trial assessing the benefits of chromium supplementation on serum lipid concentrations in postmenopausal women (109). Subjects (N=86) received either placebo or chromium chloride at a dose of 200mcg daily for 10 weeks. Patients were classified according to the potential effects of their current medications on their serum lipid levels. Total cholesterol, HDL cholesterol, and triglyceride concentrations were monitored at baseline and after supplementation. The outcome measurement was serum lipid levels. Results showed no significant differences in the mean serum total cholesterol or triglyceride concentrations between treatment and placebo groups. Both treatment and placebo groups showed an increase in mean serum HDL concentrations. A small decrease in the mean total cholesterol:HDL ratio was seen in one of the subgroups (women on medication and receiving chromium supplementation) (p<0.01). The study was limited by a weak study methodology.

- A pilot study evaluated the effects of niacin-bound chromium alone and in combination with grapeseed extract on hyperlipidemic patients (129). Significant reductions in total cholesterol and LDL cholesterol were seen only with the combination of niacin-bound chromium and grapeseed extract.
• **Case reports:** In order to observe the effects of chromium and nicotinic acid supplementation on patients with hypercholesterolemia, Urberg et al. chose two patients with untreated hypercholesterolemia to be followed for one year while taking supplements of 200mcg chromium chloride and 100mg of nicotinic acid tablets daily (239). The first patient was a moderately obese 55 year-old woman with hypertension and hypercholesterolemia. Her serum cholesterol was 399mg/dL initially; after four weeks of supplementation, her cholesterol was 342mg/dL. The supplement was stopped for an unknown period of time and her cholesterol increased slightly. The supplements were started again and at one year her cholesterol was 280mg/dL. The second patient was a 62 year-old, moderately obese woman who had hypertension and was being treated for a previous nervous breakdown. Her initial cholesterol level was 308mg/dL and after four weeks, it was 260mg/dL. When the supplement was discontinued, the levels rose slightly; the supplement was started again and her level declined. The authors concluded that hypercholesterolemia might be due in part to chromium and nicotinic acid deficiency. The authors based this conclusion on two patients. Larger studies with more patients should be utilized to draw a conclusion. Other factors that may have influenced the results could have been a change in the patient's diet and exercise during the study.

• **Studies using combination products (not included in table):** A randomized, double-blind, placebo-controlled trial was conducted to determine the lipid-lowering activity of a dietary supplement containing chitosan 240mg, *Garcinia cambogia* extract 55mg, and chromium 19mg, added to a weight-reduction program (240). One hundred fifty obese patients, all receiving a hypocaloric diet, received two capsules a day of placebo, one dietary supplement and one placebo capsule, or two dietary supplement capsules, for a total of four weeks. The study included patients between the ages of 20 and 70, who were mildly obese (10%-25%) and had hyperlipoproteinemia. The study excluded patients with known hypersensitivity to the supplement, patients who did not guarantee a total adherence to the trial protocol, patients with severe hepatic or gastrointestinal diseases, renal insufficiency, severe chronic disease, pregnancy, or patients taking drugs that could interfere with the study results. All groups were equal with regards to sex, age, weight, height, percent overweight, serum total cholesterol, HDL, LDL, and triglycerides. The study concluded that there was a statistical significance in all groups, and that the groups on a supplement were statistically significant compared to placebo with regards to a reduction in weight, total, HDL, LDL cholesterol, and triglycerides (p<0.01). This study could be performed better if the patients were not started on the hypocaloric diet at the same time as the dietary supplement. Patients who are on a hypocaloric diet would notice a difference in their lipid panel from the weight loss alone, so by adding a dietary supplement to the diet it is difficult to distinguish whether the difference is from the supplement or the diet. The study also did not state whether their patients were to exercising, which may also have created a difference in lab values.

**Obesity/Weight loss (body composition)**

• **Summary:** Literature review has noted that chromium picolinate is one of the most widely used dietary supplements, especially by athletes, because it is believed to increase lean body mass (89;169). Research has examined the effect of chromium on obesity/weight loss and/or maintenance and a number of variables related to body composition. Complicating the interpretation of the results, a number of these trials did not find beneficial effects of exercise itself on body composition (102). There is insufficient evidence to support the use of chromium in the treatment of obesity/weight/body composition at this time.

• **Reviews (non-systematic):** Williams (242) briefly cited the literature on chromium, including Evans (146), Hasten et al. (128), Evans et al. (22), Hallmark et al. (126), and Clancy et al. (125). An article written by McArdle (243) gives a review of studies (123;125;126;128;146;244). In a review article of nutritional supplements for bodybuilders and strength athletes, Kelly (245) mentioned several articles (123;125;126;128;130). Clarkson expanded the examination of chromium in a more detailed review (124). The author evaluated the above trials, as well as those by Hallmark et al. (126), Lukaski et al. (130), and Trent et al. (123). Anderson has extensively studied carbohydrate metabolism and chromium. In a review by Anderson (215), the author discussed the controversial literature on body composition and weight loss; citing positive and negative findings (120;121;246;247;248;249;250). Following an earlier review, O'Mathuna (122) discussed additional trials from 1997-1998 onward (30;119;219). Additional reviews can be found elsewhere (122;251). Lukaski (251) cited evidence of
increased chromium needs or altered excretion during exercise (252; 253). In the latter study, basal urinary chromium excretion and excretion in response to exercise are related to the degree of physical fitness (253).

**Evidence:** Lukaski et al. conducted a randomized double-blind, placebo controlled trial to assess the effects of chromium picolinate (CrPic) for decreasing body weight, altering body composition, and reducing iron status of women fed diets with constant energy and nutrients (46). Eighty three women were included in this study and administered either 200mcg chromium picolinate (CrPic) daily, an equivalent amount of picolinic acid (1,720mcg) in CrPic daily, or a placebo. The women were also fed nutritionally balanced diets. The authors used anthropometry and dual x-ray absorptiometry to assess body composition and measured serum and urinary Cr and biochemical indicators of iron status before and serially every four weeks for 12 weeks. CrPic supplementation increased (p<0.0001) serum Cr concentration and urinary Cr excretion compared with picolinic acid and placebo. CrPic did not affect body weight or fat, although all groups lost (p<0.05) weight and fat; it did not affect fat-free, mineral-free mass, or measurements of iron status. The authors concluded that CrPic supplementation did not independently influence body weight or composition or iron status in these women.

Volpe et al. conducted a randomized controlled trial to investigate the effect of chromium picolinate (CP) supplementation on body composition, resting metabolic rate (RMR), selected biochemical parameters, and iron and zinc status in moderately obese women participating in a 12-week exercise program (45). Forty-four women, 27 to 51 years of age, were randomly assigned to two groups based on their body mass index. Subjects received either 400mcg per day of chromium as a CP supplement or a placebo in double-blind fashion and participated in a supervised weight-training and walking program two days per week for 12 weeks. Body composition and RMR were measured at baseline and at six and 12 weeks. Selected biochemical parameters and iron and zinc status were measured at baseline and 12 weeks. The authors reported no significant changes in body composition, RMR, fasting plasma glucose, serum insulin, plasma glucagon, serum C-peptide and serum lipid concentrations, or in iron and zinc indices. Serum total cholesterol concentration significantly decreased (p=0.0016) over time for all subjects combined, which the authors ascribed to the exercise training. Exercise training significantly reduced total iron binding capacity (TIBC) by three percent for all subjects combined (p=0.001).

A randomized placebo controlled trial of high dose chromium 1,000mcg daily for eight weeks was conducted with 19 healthy, non-obese older men and women (30). All subjects were non-smokers, not obese, and with a body mass index between 22 and 28kg/m². Patients with a medical illness were excluded. The authors observed the effects of chromium picolinate on insulin sensitivity, serum lipids, and body composition. No significant effect on insulin sensitivity, lipids, or body composition was found.

Kaats et al. conducted a 90-day, randomized controlled trial of 130 subjects comparing 400mcg chromium picolinate to placebo (119). The study followed previous positive findings and sought to address several methodological questions, including the high dropout rate (29.7%). Both groups had significant reductions in weight. However, after controlling for differences in caloric intake and energy expenditure, the chromium group demonstrated significantly reduced weight (7.8 compared to 1.8kg) and fat mass (7.7 compared to 1.5kg), as well as a reduction in percent body fat (6% compared to 1%) compared to placebo. Dual energy X-ray absorptiometry was utilized in this trial.

Campbell et al. studied the effects of high dose chromium picolinate supplementation (924mcg daily) or a low-Cr placebo on 18 men (56-69 year old) for 12 weeks while participating in a high resistance training (RT) program twice per week (120). Recruitment criteria included men, ranging in age from 50-75 years, with a body mass index range of 27-34kg/m², and who were non-diabetic, physically able to engage in all aspects of the study protocol, and who had clinically normal cardiac, blood pressure, liver, and kidney functions. High dose Cr picolinate supplementation did not enhance muscle size, strength, power development, or lean body mass in study subjects.

Kaats et al. conducted a 72-day trial of 219 patients (154 subjects completed the study) given two doses of chromium (200 or 400mcg daily) compared to placebo (121). Inclusion and exclusion criteria were not discussed. Body composition improvement score (sum net gains nonfat + sum net loss fat) by underwater testing was significantly improved in the 200mcg (p=0.015) and 400mcg (p=0.0002) chromium groups compared to placebo, increasing by a mean 2.16-2.75kg (121). The study was limited by its methodology. Overall diet and exercise, as well as the chromium amount ingested, was not well controlled (122).
Trent et al. added to the literature with a study on overweight individuals (123). Chromium picolinate (400mcg) was compared to placebo in a 16-week trial of Navy personnel with >22-30% (men-women) body fat. Subjects were involved in three times a week aerobic exercise. Inclusion and exclusion criterion were not discussed. Primary outcome measures were percent body fat, body weight, and lean body mass. There was no significant difference in body weight change or percent body fat and p values were not given. Diet was not controlled and it is arguable whether the body composition assessment method was adequate (124). The limitations of the study are that inclusion or exclusion criteria and statistical values were not indicated.

Improvements in the accurate assessment of body composition were found in the Clancy et al. trial (125). Thirty-six college football players in resistance training were given either chromium picolinate (200mcg daily) or placebo over this nine-week trial. Inclusion and exclusion criteria were not discussed. The measures assessed were chromium loss by urinalysis, determination of mass and stature, skinfold measurements at seven sites, girth measurements at 20 sites, strength, percent body fat, and lean body mass. Underwater weighing assessed body composition. No significant difference between groups was found in skinfold, body fat, lean body mass, or strength (p<0.05). Urinary excretion increased following supplementation compared to placebo.

Hallmark et al. attempted to improve upon methodology of prior trials, by conducting a double blind, randomized controlled trial of 16 healthy young males (126). Subjects were between the ages of 18 to 35, had stopped resistance training at least six months before the study, and were free of medical conditions that would interfere with their participation in the study. The study assessed diet records, strength, body composition, and urinary chromium. The level of detecting a significance was p<0.05 for all analyses. Subjects engaged in a 12-week trial of progressive resistance training. Chromium picolinate 200mcg was taken daily (provided by Nutrition 21, San Diego, CA). Estimated dietary records were completed. Body composition was assessed by hydrodensitometry. The authors did not find significant differences in LBM, percent fat, or strength compared to placebo. The study was limited by its small sample size.

Walker et al. investigated the effect of chromium picolinate 200mcg daily or placebo on body composition and muscular performance in 20 college wrestlers during the final 14 weeks of a 16-week preseason resistance and conditioning program (127). Patients were between the ages of 18 to 23 years and could not have taken any ergogenic aids. The authors measured body composition, neuromuscular performance, metabolic performance, and serum insulin and glucose. Wrestlers were grouped according to weight and then randomized. There were no significant changes in body weight, lean body mass, percent body fat, fat mass, muscular parameters, or metabolic performance between groups. Assessment was by hydro-densitometry. Repeated measures by ANOVA showed that there was no significant difference in body composition, but aerobic power increased significantly (p<0.002) in all groups, which was not conclusive of the chromium supplement alone. The chromium group showed significant difference in upper body endurance (p=0.006). The authors concluded that chromium picolinate combined with a training program does not enhance body composition or performance compared with training alone.

College students in a weight training program (N=59) completed 12 weeks of chromium (200mcg chromium picolinate) or placebo supplementation (128). The subjects were between 18 to 36 years old, and had not participated in any type of weight lifting for at least two years prior, or were not in any type of physical conditioning program. Since there was a large number of variables, the significance level for this study was set at p<0.01. Differences in body weight, circumference, and skinfold measures were observed. Gain in bodyweight was highest in the female group (2.5kg), although there was no significant difference in strength analyses. The subjects were instructed to attend a weight training class, designed to increase muscle, which weighs more than fat. The increase seen in the female group might have been from a muscle gain due to the weight training and not the chromium.

Pasman et al. investigated the effects of supplementation of combined carbohydrate (50g), chromium picolinate (200mcg), soluble fiber (20g), and caffeine (100mg) supplement or carbohydrate alone or placebo on weight maintenance in 33 obese women for 16 months (248). Inclusion and exclusion criterion were not discussed. The study measured body weight, body composition, energy intake, and blood parameters. The amount and course of relapse of body weight was equal for the supplemented and control groups. Chromium intake did not result in significant changes in body composition or blood
parameters ($p>0.05$). It is possible that the carbohydrate supplement portion affected the absorption of chromium (102).

- Lukaski et al. studied chromium supplementation (3.3-3.5mcM CrCl3 or Cr picolinate) or placebo (0.01umol Cr) and resistance training in a sample of 36 young, untrained men for eight weeks (130). Subjects were between 19 to 29 years of age and not involved in physical training at the time of the study. Anthropometry, physique, body composition, strength gain, dietary intake, hematocrit, and biochemical determinations were observed. Subjects were matched according to physical and nutritional characteristics. Despite state of the art techniques (102), there was no beneficial effect on body composition or strength. The authors cited earlier trials using skinfold assessment as limited in accuracy and sensitivity. A larger sample size may be needed to detect a difference.

- Evans presented two double blind studies of benefit in lean body mass (146). Ten young men in resistance training had increased lean body mass (LBM) following 200mcg daily chromium picolinate for 40 days; 73% of the 2.2kg gain was LBM compared to 1.25kg gain in the placebo group. In the second cited six-week study, 31 athletes involved in resistance training and administered chromium (200mcg daily) gained 2.6kg LBM compared to 1.8kg in the placebo group. The chromium group lost 3.4kg of fat compared to 1kg in the placebo group. Caution in interpretation of this data has been recommended, due to inappropriate statistical analysis; separate paired t-tests were done for each group. In addition, body fat percentage was estimated by skinfold only (124).

- Grant et al. examined the effects of chromium supplementation (400mcg daily) or placebo, with or without exercise training, in 43 young obese women for nine weeks (249). Obesity was defined as being higher than the recommended body fat percentage for young women (20-25%) and the age range was 18 to 35 years old. Outcome measures were body weight, body fat, fat mass, and fat free mass. Chromium picolinate supplementation (Shaklee, Inc., San Fran, CA) resulted in significant mean weight gain in this population (66 to 68kg). Exercise training combined with chromium nicotinate supplementation resulted in significant weight loss (70.6 to 69.5kg). Multivariate ANOVA was used to establish a significant difference of $p<0.05$. There was no significant difference in fat mass, body fat percentage, or fat-free mass. The study was limited in its methodology and small sample size.

- In a long-term placebo controlled weight reduction trial of 36 obese non-diabetic patients, Bahadori et al. supplemented a low calorie (800kcal/day) diet with 200mcg chromium picolinate or chromium yeast over six months (250). Lean body mass was significantly increased ($p<0.029$) in the chromium picolinate group at 26 weeks.

- Bulbulian et al. conducted a study that demonstrated significant benefit over placebo at 24 weeks (not at 12 weeks) in a sample of 40 swimmers taking 400mcg daily chromium picolinate (247). Lean body mass was increased by 3.3% and fat mass was conversely decreased by 4.6%. In this study, females had a greater change in percentage of body fat. Assessment was by hydrodensitometry.

- Cefalu et al. conducted an eight month, double blind placebo controlled trial of 29 obese patients with a family history of non-insulin dependent diabetes mellitus (219). Chromium picolinate (1,000mcg daily) had a demonstrated significant effect on insulin sensitivity, with a non-significant greater increase of intra-abdominal fat in the placebo group (6.5% compared to 1%).

- Almada et al. conducted a 28-day, blinded, placebo controlled trial of 20 matched-paired males to observe if supplementation of chromium as picolinate and boron would alter body composition during resistance training (244). Patients supplemented their diet with either 190g daily of maltodextrin, which was the placebo, or Gainers Fuel 1000™ containing 290g daily of carbohydrate, 60g daily of protein, 1g daily of fat, 800mcg daily of chromium as picolinate, and 6mg daily of boron as citrate, aspartate, and glycinate. The authors did not state how frequently these supplements were to be taken. ANCOVA was used to analyze data and it was found that both groups had a significant increase ($p<0.05$) in total weight and lean tissue weight and that fat weight and percent body fat was significantly increased in the Gainers Fuel 1000™ group. The authors concluded that lean tissue accretion or the promotion of fat weight loss was not enhanced by the ingestion of a supplement containing 800mcg daily of chromium as picolinate and 6mg daily of boron. The sample size was comprised of 20 subjects, who resistance-trained 7.7 ± 3 hours/week, but inclusion and exclusion data was not given so this data should not be generalized.

- **Studies using combination products (not included in table):** Opala et al. conducted a randomized, double blind, placebo controlled clinical trial to evaluate the efficacy and safety of a combination product
containing chromium yeast for weight loss (254). The primary outcome measure was weight loss and secondary measures included body composition change. Of 105 subjects enrolled, five of them withdrew consent and there were two dropouts not related to the study preparation. Patients were administered one tablet containing extracts of asparagus, green tea, black tea, guarana, mate, and kidney beans one hour before meals and two tablets containing extracts of kidney bean pods, *Garcinia cambogia*, and chromium yeast a half-hour after meals; this dosing was given twice daily with two main meals. A significant change of the Body Composition Improvement Index and the decrease in body fat was statistically significant in subjects given active extract compared to placebo. A change in some outcome measures such as weight and BMI failed to produce significant differences between groups. One limitation of this study is the use of a combination product, which makes the effect of chromium alone difficult to determine.

Preuss et al. re-examined the weight-loss efficacy of a water-soluble, calcium-potassium salt of (−)-hydroxycitric acid (HCA-SX), a combination of HCA-SX 4,667mg, niacin-bound chromium (NBC) 4mg (providing 400mcg elemental chromium), and *Gymnema sylvestre* extract (GSE) 400mg (providing 100mg gymnemic acid), or placebo in three equally divided doses 30-60 minutes before each meal in 90 obese subjects (BMI: 30-50.8kg/m2) for eight weeks (78). All subjects were provided a 2,000kcal diet per day and participated in a supervised walking program for 30 minutes per day, for five days per week. Eighty-two subjects completed the study. HCA-SX and, to a greater degree, the combination of HCA-SX plus NBC and GSE, reduced body weight and BMI, suppressed appetite, improved blood lipid profiles, increased serum leptin and serotonin levels, and increased fat oxidation more than placebo.

Hoeger et al. conducted a double-blind, randomized, controlled, comparative study to determine whether a natural chromium containing dietary supplement produced favorable changes in body composition during a four-week diet and exercise program (255). Participants were randomly assigned to either a diet/exercise/supplement group (N=56) or a diet/exercise/placebo group (N=67). The active compound contained a patented combination of chromium picolinate, inulin, capsicum, L-phenylalanine, and other lipotropic nutrients. Caloric intake was reduced to 1,500kcal per day and participants walked for 45 minutes, five days a week, to attain between 60% and 80% of predicted maximal heart rate. Analysis of covariance (ANCOVA) showed significant differences (p<0.05) between groups in percent body fat, fat mass, and fat-free mass; no significant differences were found (p>0.05) in body weight, body mass index, or energy intake. Independent t tests showed no significant differences (p>0.05) in diet composition between groups. The authors concluded that the addition of a natural dietary supplement during a four-week diet and exercise weight-loss program accelerates the rate of body fat loss and helps maintain fat-free mass (lean tissue), thereby producing favorable changes in body composition. One limitation of this study is the use of a combination product, which makes the effect of chromium alone difficult to determine.

**Brands used in statistically significant clinical trials:**

- The majority of the statistically significant research studies did not specify brands of chromium supplements used, except Chromax®, which is a registered trademark of Nutrition 21, Purchase, NY.
- Chromax® chromium picolinate is a patented complex of the essential mineral chromium and picolinic acid. The types and formulations of the chromium supplements used included: CrCl₃ tablets, Cr-nicotinate gelatin capsules, Cr III hexa-aquo Cl₃ in capped vials, CrCl₃-H₂O, Baker Analyzed Reagent in 5mL of syrup, Cr III-rich yeast, brewer's yeast (with or without GTF) and NBS brewer's yeast, CrCl₃ dissolved in deionized H₂O and pipetted into sugar cubes, and Bio-Chrome tablets (Cr incorporated into yeast protein by fermentation).
- Core4Life™ Advanced Memory Formula™ (proprietary blend of chromium picolinate, PS (phospholipid) and DHA).

**Brands shown to contain claimed ingredients through third-party testing:**

- **Consumer Lab**: Nutrilite® Chrompic Extra. Last accessed 7/1/08.
- **Consumer Reports**: NA. Last accessed 7/1/08.
• **Natural Products Association**: NA. Last accessed 7/1/08.
• **NSF International**: Medicine Shoppe® Chromium Picolinate 200mcg, Perrigo® Chromium Polynicotinate. Last accessed 7/1/08.

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