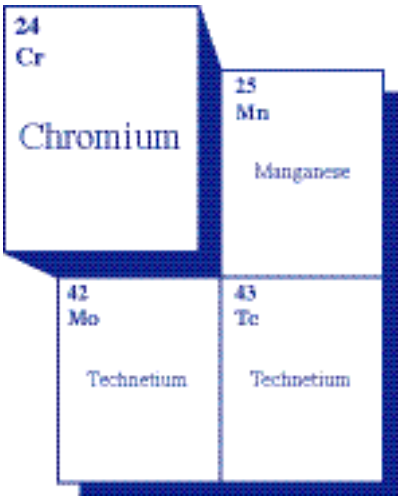

Chromium

Introduction

Chromium (Cr) is a transition element that can occur in several valence states (most commonly 0, +2, +3, and +6). Trivalent chromium (Cr^{+3}) is the most stable form in biological systems and the most abundant form found in the food supply.[1]

In early studies, an unknown factor was extracted from brewer's yeast that improved glucose tolerance in chromium-deficient rats.[1] Named Glucose Tolerance Factor (GTF), it was first identified in 1957. Chromium was later identified as the essential element of GTF that potentiates insulin action and restores normal glucose tolerance.[2] The GTF form of chromium was originally proposed as containing chromium bound to nicotinic acid, glycine, cysteine, and glutamic acid.[1] However, researchers have been unable to purify and isolate this compound to confirm its exact structure.

Chromium is widely distributed in foods, but in small quantities. Refining foods such as flour or sugar depletes them of chromium.[3] Stainless steel contains 11-30 percent chromium, which can be leached from containers when acidic foods (e.g., fruits and their juices) are stored or cooked in them.[4]

Pharmacokinetics

The bioavailability of chromium has been difficult to establish, owing to its rather low concentration in mammalian tissues. Intestinal absorption of chromium is low, with animal studies indicating rates in the range of less than 0.5-3 percent.[5]

Chromium is absorbed by an active transport mechanism and is transported to the liver bound to transferrin. It has been suggested iron interferes with the transport of chromium in patients with hemochromatosis.[6,7] This may partially explain the higher rate of diabetes seen in hemochromatosis patients. High-sugar diets increase chromium turnover and excretion in the urine.[8]

Mechanisms of Action

Chromium potentiates insulin by enhancing receptor binding, thereby stabilizing blood glucose levels. The chromium found in brewer's yeast was found in one study to be more effective than chromium chloride or torula yeast at stimulating glucose uptake.[9] In 12 of 15

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controlled clinical trials, chromium supplementation improved the action of insulin or exerted beneficial effects on blood lipid balance.[10]

Chromium has been found to decrease C-reactive protein (a marker for inflammation) and increase insulin receptor number and binding.[11]

Animal studies indicate chromium may affect immune status by activating specific immune responses and immunoglobulins.[12-14]

Deficiency States and Symptoms

Chromium deficiency is rare and difficult to produce experimentally because chromium is ubiquitous in the environment. No Cr-dependent metabolic enzymes have been identified. Animal studies suggest inadequate dietary intake may produce insulin insensitivity and reduced sperm count. However, the long-term consequences of intakes less than 50 mcg per day have yet to be determined.

Chromium may be important for growth, based on animal studies[15] and on the observation that patients on Cr-deficient total parenteral nutrition (TPN) lost weight that was later regained after chromium supplementation.[16,17]

Metabolic stress, such as experienced by trauma patients or persons who exercise strenuously, increases the excretion of and possibly the need for chromium.[18] Chromium needs may also increase during pregnancy due to maternal depletion.[19,20]

No effective clinical test exists to identify chromium deficiency. Serum chromium is not easily detected and is a poor indicator of Cr status. Low levels of chromium in tissues and the potential for easy contamination of samples make testing a challenge. Moreover, tissue concentrations do not accurately reflect metabolic pools.

Clinical Indications

Diabetes

Chromium-rich brewer's yeast has been recognized since the mid-nineteenth century as a useful therapy for diabetes. Chromium supplementation improves glucose levels and potentiates the action of insulin in people with glucose intolerance, diabetes (types 1 and 2), gestational diabetes, and diabetes caused by corticosteroids.[21] More than 10 trials of chromium supplementation in patients with glucose intolerance and diabetes have demonstrated clinical efficacy of supplemental chromium.[22]

In a four-month, double-blind trial, 180 people with type 2 diabetes were supplemented with either 100 mcg chromium (picolinate), 500 mcg chromium (picolinate), or placebo, twice daily. A significant lowering of fasting blood sugar was experienced by the 500-mcg group, but not in the other two groups. Glycosylated hemoglobin was significantly decreased in both chromium groups (more so in the high-dose group), and cholesterol decreased significantly in the high-dose chromium group.[23]

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In another study, 243 people with either type 1 or 2 diabetes took 200 mcg chromium daily. Subjects were asked to decrease oral hypoglycemic agents or insulin as needed to keep blood sugar within normal limits. Over one-half of the type 2 diabetics and one-third of the type 1 diabetics were able to decrease their medications significantly.[24]

Some studies have reported no therapeutic effect from chromium supplementation in diabetes;[25-27] however, these studies used daily doses of 200 mcg or less.

Hypoglycemia

In a double-blind, crossover study,[28] eight female patients with hypoglycemia were given supplemental chromium chloride (200 mcg per day elemental chromium) or placebo for three months. Chromium supplementation alleviated symptoms of hypoglycemia and raised the glucose nadir at 2-4 hours after a glucose load. In an uncontrolled trial,[29] chromium supplementation (125 mcg per day as a yeast supplement) produced improvement of chilliness in 47 percent of participants, with 15 percent indicating the chilliness disappeared entirely. Trembling, emotional instability, and disorientation improved as well. One case was reported of chromium supplementation inducing hypoglycemia.[30]

Hypercholesterolemia

Although one group of researchers found no beneficial effect of chromium supplementation on blood lipid levels,[27,31] several well-controlled clinical trials of chromium supplementation have demonstrated it can lower total[32,33] and LDL cholesterol,[34,35] and increase HDL cholesterol.[33,36] In one double-blind trial, 500 mcg chromium per day in combination with regular exercise reduced total cholesterol levels by 20 percent in 13 weeks.[37] It is impossible in this study to know which was more important, the chromium or the exercise. Supplementation with chromium-rich brewer's yeast has also lowered serum cholesterol.[38]

Dysthymia

After one patient reported a dramatic response to the addition of a chromium supplement to sertraline (Zoloft®) therapy for dysthymic disorder, a series of single-blind and open-label trials were undertaken to evaluate the effects of chromium picolinate or chromium polynicotinate on the treatment of antidepressant-refractory dysthymic disorder. In five patients, chromium supplementation led to remission of dysthymic symptoms. Single-blind substitution of other dietary supplements in each of the patients demonstrated specificity of response to chromium supplementation.[39]

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Athletic Performance

Research in animals[40] and humans[41,42] have found chromium picolinate supplementation might increase fat loss and lean muscle gain when used in conjunction with a resistance-training program. These findings were validated by the results of two double-blind trials.[43,44]

However, more evidence exists that chromium supplementation has little or no effect on strength or body composition.[45-48] In one study, changes in body weight, a sum of three body circumferences, a sum of three skin folds, and the one-repetition maximum for the squat and bench press were examined in 59 college-age students over a 12-week weightlifting program. Half the students were given 200 mcg per day elemental chromium as picolinate, while the other half received a placebo. No treatment effects were seen for the strength measurements. The only significant treatment effect found was an increase in body weight observed in females supplementing with chromium.[48]

Several other studies using 200 mcg[49,50] or 400 mcg[51,52] chromium as picolinate found similar lack of effect on body composition or strength.

Weight Loss

Because chromium supplementation has been reported to increase lean body mass and decrease the percentage of body fat, chromium has been touted as a weight-loss product. The effect of chromium supplementation on body composition is controversial, although theoretically supported by animal studies.[47] According to one human study, chromium picolinate supplementation increased lean body mass in obese patients in the maintenance period after a very low-calorie diet without counteracting the weight loss achieved.[53] In another double-blind trial, 400 mcg per day of chromium as picolinate was ineffective in enhancing body fat reduction in healthy U.S. Navy personnel who exercised aerobically three times per week for at least 30 minutes.[51]

Drug-Nutrient Interactions

Chromium absorption is enhanced by vitamin C,[54] oxalates,[55] aspirin,[56] and indomethacin.[57] On the other hand, absorption of chromium is decreased by a high fiber meal, due to the presence of phytic acid.[58] It is therefore likely that dietary supplements containing phytic acid (i.e., inositol hexaphosphate; IP-6) would also chelate the mineral and decrease its absorption. Several antacids have been found to significantly reduce 51Cr in the blood and tissues compared to controls.[59]

Side Effects and Toxicity

Trivalent chromium is safe, not well absorbed, excreted rapidly with large exposures, and has low potential for toxicity. Trivalent chromium should not be confused with the toxic

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hexavalent chromium (Cr^{6+}), which is generated from the welding of stainless steel. Toxicity symptoms of Cr^{6+} include allergic dermatitis, skin and nasal septum lesions, and increased incidence of lung cancer and possibly other diseases.

Chromium picolinate supplementation has been linked with individual cases of systemic contact dermatitis[60] and acute, generalized, exanthematous pustulosis.[61] Another case was reported of a woman who took 1,200-2,400 mcg chromium per day for 4-5 months and suffered toxicity symptoms including weight loss, anemia, thrombocytopenia, hemolysis, and elevated liver enzymes.[62] Previous animal studies have shown, variously, that chromium picolinate produced chromosomal damage[63] or that is has no toxicity.[64] Toxicity of other supplemental forms of chromium (e.g., chromium polynicotinate) has not been reported.

Dosage

Mean chromium intake is 33 mcg per day in adult men, 25 mcg per day in women. The estimated safe and adequate daily dietary intake (ESADDI) is currently set at 50-200 mcg per day for adults; the ESADDI for infants (10-40 mcg per day) may not be attainable because human breast milk provides less than 1 mcg per day.[9]

In the studies cited above, effective doses range from 150-1,000 mcg per day. Typical dosage amounts used to treat diabetes and dysglycemia — conditions for which the strongest evidence exists in favor of chromium supplementation — are 200-1,000 mcg per day.

Warnings and Contraindications

Caution should be used in combining chromium supplements with any blood-sugar lowering medication, as the combination may induce hypoglycemia.

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