




**Micronutrients:
Chromium**

Dr. Ritamarie Loscalzo

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Chromium General Info

- ✓ Chromium (Cr_0) is a ubiquitous trace metal
- ✓ It was first discovered in 1797
- ✓ The predominant chromium form in the body is **trivalent chromium (Cr_3^+)**, which plays a role in normal insulin function
- ✓ Trivalent chromium (Cr_3^+) is the **most stable oxidation state of chromium**
- ✓ Forms relatively inert complexes with proteins and nucleic acids
- ✓ Hexavalent chromium (Cr_6^+) is another common and stable form
- ✓ Hexavalent chromium is **highly toxic** and is classified as a human carcinogen when inhaled
 - Derived from trivalent chromium by heating at alkaline pH and used for industrial purposes
 - readily reduced to trivalent chromium in the acidic environment of the stomach which limits the absorption of hexavalent chromium

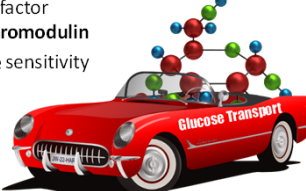


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INE: Micronutrients - Minerals: Chromium

Functions of Chromium

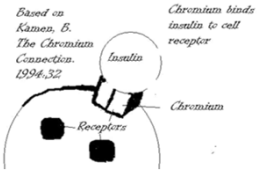
- ✓ Enhances the effects of insulin on target tissues
- ✓ Stimulates fatty acid and cholesterol synthesis
- ✓ Involved in carbohydrate, fat, and protein metabolism
- ✓ Inorganic chromium does not potentiate insulin action and must be **converted to an organic biologically active form**
- ✓ Trivalent chromium is the cofactor for an oligopeptide called **chromodulin**
- ✓ **Chromodulin** improve tissue sensitivity to insulin and facilitates glucose transport into cells



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Chromium and Insulin Sensitivity

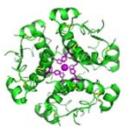
- ✓ Binding of insulin to insulin receptor stimulates movement of chromium into the cell
 - Chromium binds to **apochromodulin**, a form of chromodulin that lacks chromium
 - Chromodulin binds to the insulin receptor and upregulates insulin signaling molecules
 - This increases the translocation of **glucose transporters (GLUT-4)** into the cell membrane
- ✓ Chromium **inhibits the activity of protein tyrosine phosphatase-1B (PTP-1B)** and other negative regulators of insulin signaling
- ✓ Chromium improves insulin sensitivity under insulin-resistant conditions
- ✓ Chromium reduces insulin clearance and enhances insulin signaling by inhibiting the proteolysis of insulin
- ✓ Chromium **reduces oxidative stress and inflammation** known to contribute to insulin resistance



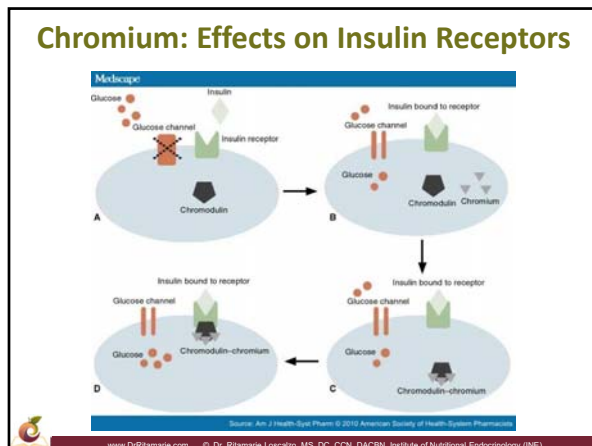
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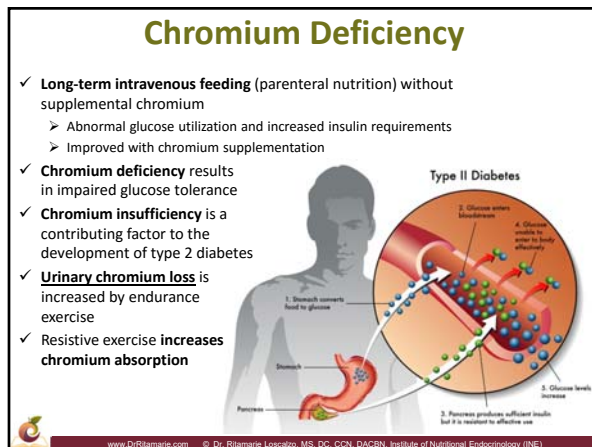
Chromium And Insulin Signaling

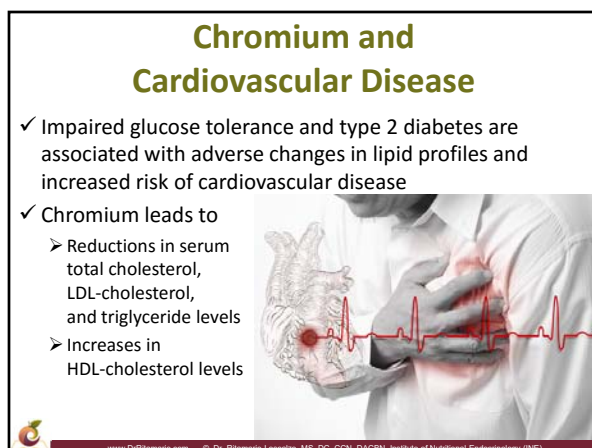
- ✓ Oligopeptide low-molecular-weight chromium-binding substance (LMWCr) tightly binds four chromic ions
- ✓ Binds to the tyrosine kinase active site of the insulin receptor
- ✓ Chromium is readily transferred from transferrin to apoLMWCr at near neutral pH
- ✓ Release of chromium is related to a mechanism by which Cr_3 may generate hydroxyl radicals in cells
- ✓ Trivalent chromium might be the cofactor of a low-molecular-weight chromium-binding substance, LMWCr or chromodulin
- ✓ Chromodulin believed to **enhance the cascade of signaling events** induced by the binding of insulin to extracellular α -subunit of the insulin receptor (IR)
- ✓ Upon insulin binding, the tyrosine kinase domain of the intracellular β -subunit of the IR becomes activated
 - Causes the **phosphorylation of tyrosine residues** in the β -subunit itself
 - Insulin receptor activation triggers a series of rapid phosphorylation reactions
 - Activates many downstream effectors
 - Results in an increase in glucose uptake and storage



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Chromium and Muscle Mass

- ✓ Chromium supplementation increases lean body mass and decreases body fat due to the relationship between chromium and insulin action
- ✓ Insulin affects fat and protein metabolism
- ✓ Also regulates glucose metabolism



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Chromium and Diabetes

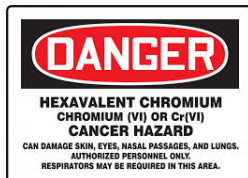
- ✓ Chromium regulates insulin sensitivity and blood glucose levels
- ✓ Those with overt type 2 diabetes for over two years have **higher rates of urinary chromium loss** than healthy individuals
- ✓ Chromium supplementation with type 2 diabetics **reduced insulin concentrations and improved blood lipid profiles**
- ✓ Chromium supplementation beneficial in the treatment of type 2 diabetes
- ✓ Chromium either 200 mcg/day or 1,000 mcg/day is associated with **reduced insulin concentrations**
- ✓ Hemoglobin A1c (HbA1c) is also significantly reduced
- ✓ Chromium intake of at least 250 mcg/day for no less than three months significantly **reduces fasting glucose concentrations** in diabetics but has no effect on the levels of HbA1c
- ✓ **Greater doses of chromium needed** to observe beneficial effects of chromium supplementation
- ✓ Women with gestational diabetes supplemented with 4 mcg of chromium picolinate/kg for eight weeks had **decreased fasting blood glucose** and insulin concentrations compared to those who took a placebo



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Chromium Toxicity

- ✓ **Hexavalent chromium** (Cr_6^+) is a recognized carcinogen
- ✓ **Exposure to hexavalent chromium in dust**
 - Associated with an increased incidence of lung cancer
 - Known to cause inflammation of the skin (dermatitis)
- ✓ Little evidence that trivalent chromium (Cr_3^+) is toxic to humans
- ✓ The toxicity from oral intakes is considered to be low
 - Ingested chromium is poorly absorbed
 - Most absorbed chromium is rapidly excreted in the urine
- ✓ Because no adverse effects have been convincingly associated with excess intake of trivalent chromium from food or supplements, **the Food and Nutrition Board (FNB) of the Institute of Medicine did not set a tolerable upper intake level (UL) for chromium**



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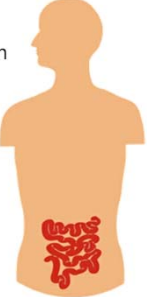
INE: Micronutrients - Minerals: Chromium


Chromium Absorption

- ✓ Small intestine, mainly in jejunum
- ✓ Absorbed via active transport and diffusion

Chromium Transport and Storage


- ✓ Transferrin (competes with iron)
- ✓ Albumin
- ✓ Stored in
 - Kidney
 - Liver
 - Pancreas
 - Muscle
 - Heart
 - Bone




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Influences on Chromium


<u>Decreases</u>	<u>Increases</u>
✓ Simple carbohydrates (sucrose, fructose, glucose)	✓ Vitamin C
✓ Phytates	✓ Methionine
✓ Zinc supplements	✓ Histidine
✓ Horsetail	
✓ Corticosteroids	
✓ Antacids, H2 blockers, proton pump inhibitors	
✓ Vitamin B3 (niacin)	
✓ Beta blockers (propranolol)	
✓ Insulin	
✓ NSAIDs	




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Chromium Iron Interactions

- ✓ Chromium competes for one of the binding sites on the iron transport protein, **transferrin**
- ✓ Iron overload in hereditary hemochromatosis may interfere with chromium transport by competing for transferrin binding
- ✓ Decreased chromium transport might contribute to the pathogenesis of diabetes mellitus in patients with hereditary hemochromatosis



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Chromium - Vitamin C Interactions

- ✓ Chromium uptake is enhanced when given at the same time as vitamin C
- ✓ In a study of three women, administration of 100 mg of vitamin C together with 1 mg of chromium resulted in higher plasma levels of chromium than 1 mg of chromium without vitamin C



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Cause of Chromium Deficiency

- ✓ Deficient soil
- ✓ Processed foods
- ✓ Fluoride in water
- ✓ Food antagonists: sugar, phytates
- ✓ Excess nutrient antagonists: iron, zinc
- ✓ Drugs



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Impact of Chromium Deficiency

- ✓ Diabetes
- ✓ Metabolic syndrome
- ✓ Insulin resistance
- ✓ Blood sugar swings
- ✓ Anxiety
- ✓ Fatigue
- ✓ Muscle weakness
- ✓ Mood swings



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Chromium Excess

- ✓ Daily doses of **up to 1,000 mcg** of chromium for several months have been found to be safe
- ✓ Little evidence to support concerns that trivalent chromium, especially chromium picolinate, may increase DNA damage
 - A study in 10 women taking 400 mcg/day of chromium picolinate found no evidence of increased oxidative damage to DNA
 - **Isolated reports** of serious adverse reactions to chromium picolinate
 - Kidney failure was reported five months after a six-week course of 600 mcg/day of chromium in the form of chromium picolinate
 - Kidney failure and impaired liver function reported after 1,200-2,400 mcg/day of chromium picolinate for four to five months
 - A 24-year old healthy male reportedly developed reversible, acute renal failure after taking chromium picolinate containing supplements for two weeks
- ✓ Individuals with **pre-existing kidney or liver disease** may be at increased risk of adverse effects and should limit supplemental chromium intake



<http://www.drRitamarie.com/go/ChromiumSafety>

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Assessing Status of Chromium

- ✓ Blood testing not accurate
- ✓ Hair test
- ✓ White blood cell - Spectracell
- ✓ Functional tests and physical exam
- ✓ Glucose tolerance test



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Chromium Adequate Intake


Life stage	Chromium, µg/ day	
	Male	Female
Infants, months		
0 – 6	0.2	0.2
7 – 12	5.5	5.5
Children, years		
1 – 3	11	11
4 – 8	15	15
Adults, years		
9 – 13	25	21
14 – 18	35	24
19 – 30	35	25
31 – 50	35	25



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Food Sources of Chromium

- ✓ Brewer's yeast (GTF)
- ✓ Broccoli
- ✓ Oats
- ✓ Green beans
- ✓ Tomatoes
- ✓ Apples
- ✓ Romaine lettuce
- ✓ Black pepper
- ✓ Bananas
- ✓ Beef
- ✓ Turkey breast




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Food Sources of Chromium

Food	Serving Size	Cals	Amount (mcg)	DRI/DV (%)
Broccoli	1 cup	54.6	18.55	53
Barley	0.33 cup	217.1	8.16	23
Oats	0.25 cup	151.7	5.38	15
Green Beans	1 cup	43.8	2.04	6
Tomatoes	1 cup	32.4	1.26	4
Romaine Lettuce	2 cups	16.0	1.25	4
Black Pepper	2 tsp	14.6	0.93	3


<http://www.drRitamarie.com/go/WHFoodsChromium>



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Herbs High In Chromium

- ✓ Wild yam
- ✓ Nettle
- ✓ Catnip
- ✓ Oat straw
- ✓ Licorice
- ✓ Horsetail
- ✓ Yarrow
- ✓ Red clover
- ✓ Sarsaparilla



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Chromium Supplementation

- ✓ Trivalent chromium in several forms
 - Chromium chloride
 - Chromium polynicotinate
 - Chromium picolinate
 - High-chromium yeast
- ✓ Doses range from 50 to 200 mcg of elemental chromium
- ✓ 19% of the US population uses chromium-containing supplements
- ✓ Highest proportion of users (29%) found in adults aged over 50 years
- ✓ Impaired glucose tolerance and type 2 diabetes – **Chromium polynicotinate or picolinate**



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Chromium Drug Interactions

- ✓ Little is known about drug interactions with chromium in humans
- ✓ Large doses of calcium carbonate or magnesium hydroxide-containing antacids decreased chromium absorption in rats
- ✓ In contrast, non-steroidal anti-inflammatory drugs, aspirin, and indomethacin can increase chromium absorption in rats



<http://www.drritamarie.com/go/DrugInteractionsChromium>

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- ✓ *PDR for Nutritional Supplements*. 2nd ed. – Hendler and Rorvik
- ✓ *Present Knowledge of Nutrition* – Erdman, Macdonald, and Ziesl
- ✓ WH Foods Website:
<http://www.drritamarie.com/go/WHFoodsChromium>
- ✓ Linus Pauling Institute:
<http://www.drritamarie.com/go/LPICromium>



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Chromium Research

- ✓ <http://www.drRitamarie.com/qa/PubMed10766445>
- ✓ <http://www.drRitamarie.com/qa/DrugInteractionsChromium>
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