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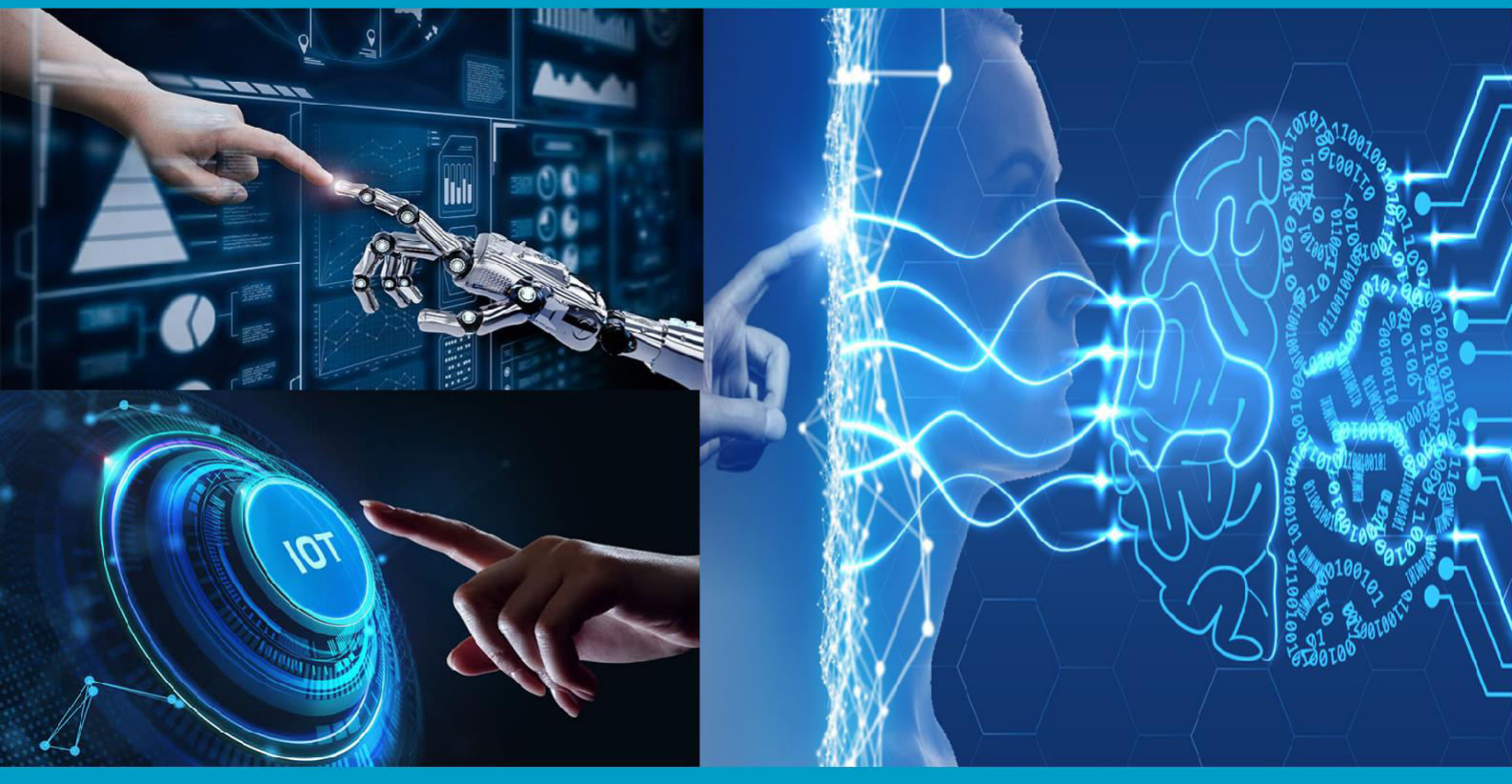


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# Role of Chromium in Blood Sugar Regulation

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**ABSTRACT:** Chromium is an essential mineral that plays a role in how insulin helps the body regulate blood sugar levels. Insulin is a hormone your body uses to change sugar, starches, and other food into the energy you need for daily activities. Some evidence suggests that chromium supplements may help people with diabetes lower blood sugar levels. People with diabetes either do not make enough insulin, or cannot properly use the insulin that their bodies make. As a result, glucose or sugar builds up in the bloodstream. Low chromium levels can increase blood sugar, triglycerides (a type of fat in the blood), cholesterol levels, and increase the risk for a number of conditions, such as diabetes and heart disease. Chromium is often advertised as a weight-loss aid and a way to improve lean muscle and reduce body fat. Chromium from food is generally considered safe. As a supplement, very high doses of this mineral can reduce how effective insulin is at controlling blood sugar and cause stomach irritation, itching, and flushing.

**KEYWORDS:** chromium, blood sugar, regulation, diabetes, insulin, weight-loss, triglycerides

## I. INTRODUCTION

Chromium -- specifically, trivalent chromium -- is an essential trace element that's used by some people as a supplement. Perhaps most importantly, chromium forms a compound in the body that seems to enhance the effects of insulin and lower glucose levels. However, it also had risks and its use is somewhat controversial. Some studies have shown that chromium supplements may be helpful for people with type 2 diabetes and insulin resistance (prediabetes). [1,2] There's good evidence that chromium can lower glucose levels and improve insulin sensitivity, although not all studies have shown a benefit. It may be that chromium works better if someone is chromium deficient, which is usually only seen if a person has poor overall nutrition. Other studies have also found that chromium may help with polycystic ovary syndrome (PCOS), which is linked to insulin resistance.Chromium supplements have also been studied for their effects on cholesterol, heart disease risk, psychological disorders, Parkinson's disease, and other conditions. However, the study results have been contradictory or unclear. Some people use chromium supplements to build muscle or trigger weight loss. Some chromium studies have shown these benefits, but others have not.[3,4]

| Adequate Intakes (AI) of Chromium | |
|---|---|
| Women, aged 19-50 | 25 mcg/day |
| Women, aged 51 and older | 20 mcg/day |
| Men, aged 19-50 | 35 mcg/day |
| Men, aged 51 and over | 30 mcg/day |

Many people get more chromium than that. However, no one knows exactly how much more is safe. Some researchers suggest that 1,000 micrograms a day should be considered the upper limit. Excessive doses of chromium may actually worsen insulin sensitivity.The doses used in clinical studies vary. For example, for diabetes, people have taken 200-1,000 micrograms daily, split two to three times a day.

Most people get enough chromium from food. Foods that are good sources of chromium include:

- Vegetables such as broccoli, potatoes, and green beans
- Whole-grain products
- Beef and poultry
- Fruits, including apples and bananas; grape juice

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- Milk and dairy products[5,6]

Chromium seems to have few side effects. There have been some reports of chromium causing occasional irregular heartbeats, sleep disturbances, headaches, mood changes, and allergic reactions. Chromium may increase the risk of kidney or liver damage. If you have kidney or liver disease, do not take chromium without talking to your doctor first. Since chromium may affect blood sugar levels, it is crucial that anyone taking diabetes medications, like insulin, only use chromium under the care of a medical doctor. Chromium may also interact with drugs like antacids, acid reflux drugs, corticosteroids, beta-blockers, insulin, thyroid medicine and NSAID painkillers. These interactions may cause the chromium to be poorly absorbed or amplify the effect of the other medicine. Pregnant and breastfeeding women should not take chromium supplements. For children, consult a doctor. Some experts recommend that no one should take more than 200 mcg/day without medical advice. The Institute of Medicine has not set a tolerable upper intake level (UL) because few serious side effects have been seen with high chromium intake.[7,8]

## II. DISCUSSION

The notion of chromium as a potential regulator of glucose metabolism began in the 1950s when Walter Mertz and his co-workers performed a series of experiments controlling the diet of rats. The experimenters subjected the rats to a chromium deficient diet, and witnessed an inability of the organisms to respond effectively to increased levels of glucose within the blood. They then included "acid-hydrolyzed porcine kidney and Brewer's yeast" in the diet of these rats, and found that the rats were now able to effectively metabolize glucose. Both the porcine kidney and Brewer's yeast were rich in chromium, and so it was from these findings that began the study of chromium as a regulator of blood glucose.

The idea of chromium being used for the treatment of type II diabetes was first sparked in the 1970s. A patient receiving total parenteral nutrition (TPN) had developed "severe signs of diabetes", and was administered chromium supplements based on previous studies that proved the effectiveness of this metal in modulating blood glucose levels. The patient was administered chromium for a total of two weeks, and by the end of this time-period, their ability to metabolize glucose had increased significantly; they also now required less insulin ("exogenous insulin requirements decreased from 45 units/day to none"). It was these experiments that were performed in the 1950s and 1970s that paved the foundation for future studies on chromium and diabetes.In 2005, the U.S. Food and Drug Administration approved a Qualified Health Claim for chromium picolinate with a requirement for very specific label wording: "One small study suggests that chromium picolinate may reduce the risk of insulin resistance, and therefore possibly may reduce the risk of type 2 diabetes. FDA concludes, however, that the existence of such a relationship between chromium picolinate and either insulin resistance or type 2 diabetes is highly uncertain." In 2010, chromium(III) picolinate was approved by Health Canada to be used in dietary supplements. [9,10]

Approved labeling statements included: "...provides support for healthy glucose metabolism." The European Food Safety Authority (EFSA) approved claims in 2010 that chromium contributed to normal macronutrient metabolism and maintenance of normal blood glucose concentration.A 2016 review of meta-analyses concluded that whereas there may be modest decreases in fasting plasma glucose or gylcated hemoglobin that achieve statistical significance, the changes were rarely large enough to be expected to be relevant to clinical outcome.

## III. RESULTS

Looking at the results from four meta-analyses, one reported a statistically significant decrease in fasting plasma glucose levels (FPG) and a non-significant trend in lower hemoglobin A1C (HbA1C). A second reported the same, a third reported significant decreases for both measures, while a fourth reported no benefit for either. A review published in 2016 listed 53 randomized clinical trials that were included in one or more of six meta-analyses. It concluded that whereas there may be modest decreases in FPG and/or HbA1C that achieve statistical significance in some of these meta-analyses, few of the trials achieved decreases large enough to be expected to be relevant to clinical outcome. The mode of action through which chromium aided in the regulation of blood glucose levels is poorly understood. Recently, it has been suggested that chromium interacts with the low-molecular weight chromium (LMWCr) binding substance to potentiate the action of insulin. LMWCr has a molecular weight of 1500, and is composed solely of the four amino acid residues of glycine, cysteine, aspartic acid and glutamate. It is a naturally occurring oligopeptide that has been purified from many sources: rabbit liver, porcine kidney and

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kidney powder, bovine liver, colostrum, dog, rat and mouse liver.Widely distributed in mammals, LMWCr is capable of tightly binding four chromic ions. The binding constant of this oligopeptide for chromium ions is very large, ($K \approx 1021$ $M-4$), suggesting it is strong and tightly binding. LMWCr exists in its inactive or apo form within the cytosol and nucleus of insulin-sensitive cells.[11]

When insulin concentrations within the blood rise, insulin binds to the external subunit of the insulin-receptor proteins, and induces a conformational change. This change results in the autophosphorylation of the tyrosine residue located on the internal ß-subunit of the receptor, thereby activating the receptor's kinase activity. An increase in insulin levels also signals for the movement of transferrin receptors from the vesicles of insulin-sensitive cells to the plasma membrane. Transferrin, the protein responsible for the movement of chromium through the body, binds to these receptors, and becomes internalized via the process of endocytosis. The pH of these vesicles containing the transferrin molecules is then decreased (resulting in increased acidity) by the action of ATP-driven proton pumps, and as a consequence, chromium is released from the transferrin. The free chromium within the cell is then sequestered by LMWCr. The binding of LMWCr to chromium converts it into its holo or active form, and once activated, LMWCr binds to the insulin receptors and aids in maintaining and amplifying the tyrosine kinase activity of the insulin receptors. In one experiment that was performed on bovine liver LMWCr, it was determined that LMWCr could amplify the activity of protein kinase receptors by up to seven-fold in the presence of insulin. Furthermore, evidence suggests that the action of LMWCr is most effective when it is bound to four chromic ions.

When the insulin signaling pathway is turned off, the insulin receptors on the plasma membrane relax and become inactivated. The holo-LMWCr is expelled from the cell and ultimately excreted from the body via urine. LMWCr cannot be converted back into its inactive from due to the high binding affinity of this oligopeptide for its chromium ions. As of currently, the mechanism through which apo-LMWCr is replaced within the body is unknown.[12]

## IV. CONCLUSIONS

The key role that chromium plays in the human body is by supporting blood sugar balance. It does this by influencing efficient transport of glucose into the cells. Once glucose is delivered to the cells, it can be used for energy and blood sugar levels become more balanced and stable. Chromium also helps support carbohydrate, fat, and protein metabolism.As a trace mineral, not a lot of chromium is needed to have it influence health. According to the National Institutes of Health, the adult recommended adequate intake is between 50–200 mcg daily. The best food source of chromium is broccoli, which contains about 11 mcg per ½ cup serving. One cup of grape juice contains 8 mcg. A three-ounce pork chop contains 8.5 mcg and a whole wheat English muffin has about 4 mcg.Although chromium deficiency is thought to be rare, it can be difficult for some patients to get enough chromium from diet alone. In addition, chromium levels tend to decline with age. Some medications such as antacids, proton-pump inhibitors, steroids, and H2 blockers may also reduce chromium absorption. For these and other reasons, integrative healthcare practitioners often look to dietary supplements to fill the gap.[13]

The most common forms of chromium sold as a dietary supplement are chromium picolinate, chromium polynicotinate, glucose-tolerance factor chromium (chromium GTF), and chromium cruciferate. Because chromium absorption can be an issue, many of these forms of chromium have been shown to be more easily absorbed and safer than other forms of chromium. When chromium is combined with picolinic acid, it is known as chromium picolinate, a substance that has been featured in the scientific research. Chromium GTF is found in Brewer's yeast and that form is also very popular among integrative practitioners. A chelated chromium nicotinate glycinate is also available.

Other vitamins and minerals can be added to supplement formulations to enhance the health-supporting effects and absorption of chromium. For example, vitamin C has been shown to enhance chromium absorption. Other nutrients that have been shown to support blood sugar balance are vitamin E, magnesium, and vanadium.[14]

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