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The role of chromium compounds in reproduction, immune response and general health status

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ABSTRACT

Chromium (Cr), a first-series transition metal with a standard atomic mass of approximately 52 g/mol, plays a sophisticated role as an essential trace element in human and animal physiology. Characterized by its diverse oxidation states most notably the highly stable Cr^{3+} this micronutrient functions primarily as a biochemical potentiator of insulin action. Through the activation of the low-molecular-weight chromium-binding substance, chromodulin, chromium amplifies insulin receptor tyrosine kinase activity, thereby facilitating efficient glucose uptake and the metabolism of carbohydrates, proteins, and lipids. Beyond glycemic control, chromium serves as a critical modulator of lipid profiles, stimulating lipase activity to reduce very low-density lipoproteins (VLDL) and low-density lipoproteins (LDL) while elevating high density lipoproteins (HDL). Deficiencies in chromium have been linked to impaired lipid metabolism, atherosclerosis, and, in neonatal contexts, significant growth retardation or developmental delays. Furthermore, chromium exhibits immunomodulatory properties, influencing both innate and adaptive immune responses. This synthesis highlights the necessity of meeting gender specific Adequate Intake (AI) levels 35 µg/day for men and 25 µg/day for women to maintain metabolic homeostasis and prevent chronic gestational and systemic pathologies.

Keywords: Chromium, Insulin sensitivity, Chromodulin, Lipid metabolism, Immunomodulation, Trace elements.

Introduction

Chromium (Cr) is a transition metal belonging to the first transition series of the periodic table. Chromium has an atomic mass of approximately 52 g/mol (IUPAC, 2024). This element exhibits a variety of oxidation states, most commonly 0, 3+, and 6+ (Catherine, 2021). Among these, the 3+ state is considered the most stable due to its half-filled 2 g subshell configuration (3+), which provides extra kinetic and thermodynamic stability (Shupack, 1991; Housecroft, and Sharpe, 2018). Humans require trace amounts of naturally occurring chromium as a dietary supplement in order to maintain good health. Chromium helps blood glucose levels remain normal by supporting the action of the hormone insulin. The element may also be involved in the metabolism of macromolecules such as carbohydrates, proteins, and fats.

Towards the end of the 20^{th} century, the nutritional and health importance of chromium became clear.

Chromium is an essential trace element that functions by potentiating the action of insulin (Havel, 2004). The widely accepted mechanism involves a low-molecular-weight chromium-binding substance known as chromodulin. When insulin binds to its receptor, it triggers the movement of chromium into cells, where it binds to chromodulin (Vincent, 2000). This complex then binds to the insulin receptor, amplifying its tyrosine kinase activity and significantly increasing glucose uptake (Vincent, 2000; Wang et al., 2014).

However, the nutritional and metabolic roles of chromium (Cr) in humans and animals are extensively documented, particularly regarding its synergy with insulin and its influence on lipid profiles. Healthy Adults (19–50 years) need 35 µg/day for men and 25 µg/day for women, while a recommended daily intake of 400 µg, it is important to distinguish between the Adequate Intake (AI) for healthy individuals and the therapeutic dosages used in clinical or veterinary settings (IUPAC, 2024).

Chromium acts as a "cofactor" or amplifier for insulin rather than a primary trigger, it acts as a catalyst for insulin activity, increasing insulin receptor synthesis and stimulating lipase, thereby increasing the metabolism of very low-density lipoproteins (VLDL). In this way, chromium added to feed rations is effective in reducing VLDL and LDL levels and increasing high-density lipoproteins (HDL) (Sahin et al., 2001; Uyanik et al., 2002; Lien et al., 2004). Research has also shown a link between low chromium intake and impaired lipid metabolism, potentially leading to atherosclerosis. In other words, low chromium intake can cause impaired lipid metabolism and contribute to the development of atherosclerosis (Mirfendereski and Jahanian, 2015; Al-Saadde et al., 2023).

In premature and low-birth-weight infants, chromium status is critical due to its role in glucose and lipid metabolism, studies have also indicated that low chromium concentrations can cause growth retardation or developmental delays in the fetus and in the tissues of premature infants (Adams et al., 2021; Stephen, 2022).

Chromium (Cr) serves as a complex immunomodulator, where its influence on the immune system is determined by a delicate balance of dosage and chemical form (Dworzański et al., 2021), Its role as a nutritional supplement has been linked to the enhancement of both innate (non-specific) and acquired (adaptive) immunity While trivalent chromium (Cr^{3+}) is often viewed as a beneficial micronutrient that can enhance immune parameters, hexavalent chromium (Cr^{6+}) is primarily associated with systemic toxicity and immune suppression (Lee et al., 2022; Zemelka-Wiacek, 2025). The aim of this study was to investigate the role of chromium compounds in reproduction, immune response and general health status.

Chromium Compounds: Chromium forms a diverse array of chemical species, ranging from organometallic sandwich complexes, which consist of two aromatic rings (aromatic compounds) where the metal is in a zero-oxidation state to classic coordination compounds with various ligands (Fischer and Hafner, 1955; Rayón and Frenking, 2002).

These complexes are sparingly soluble in water. Since the aromatic rings are uncharged, the compound contains chromium in the oxidation state (-O), i.e., uncharged, such as $Cr(C_6H_6)^2$. It can also form coordination complexes with water, cyanide, and oxalate molecules, such as $[Cr(H_2O)_6]^3$, $[Cr(CN)_6]^{3-}$, and $[Cr(C_2O_4)_3]^{3-}$. As for divalent chromium compounds, such as chromium chloride ($CrCl_2$), it is used as a strong reducing agent in laboratories, but its industrial use is limited. There are many chromium compounds in the oxidation state, such as chromium oxide ($Cr_2O_3.nH_2O$), which is used as a pigment in paints. Chromium chloride has the chemical formula $Cr(H_2O)_6Cl_3$. $Cr(H_2O)_4Cl_2$ is used in alkaline solutions for leather tanning (Tables 1), and chromium deposits in soil are in the trivalent oxidation state (Krishnamurty and Harris, 1961; Herndon, 2004).

The hexavalent oxidation state of chromium results from the oxidation of trivalent chromium in alkaline solution. Therefore, hexavalent chromium oxide precipitates when concentrated sulfuric acid is added to a sodium or potassium dichromate solution (Apte et al., 2006).

The chemical behavior of chromium across its major oxidation states is defined by its ability to transition between the relatively stable trivalent (Cr^{3+}) and the highly reactive hexavalent (Cr^{6+}) states depending on the pH and the presence of oxidizing agents (Shupack, 1991; Hartford, 1979; Britannica, 2026).

Table (1): Some common chromium compounds, their molecular weights, melting points and specific weights.

Chromium compounds	Molecular weights (g/mol)	Melting Point (°C)	Specific Weights (g/cm³)
Cr	51.996	1857	7.19
Cr_2O_3	151.99	196	2.70
CrO_3	99.99	2266	5.21
K_2CrO_4	194.20	196 Decomposes	2.10
$K_2Cr_2O_7$	294.19	968	2.73
$CaCrO_4 . 2H_2O$	192.04	2090	4.80
$CaCr_2O_4$	208.07	398	2.68

(WHO,1988; Lunk, 2015)

Chromium Complexes with Organic Compounds: Several organochrome compounds exist. These compounds result from the combination of a trivalent chromium molecule (Cr^{+3}) with three organic molecules, such as vitamins or certain proteins as in Figure (1) (Zinpro, 2003). Research indicates that the increased absorption of this complex is due to its similarity to a factor called the glucose tolerance factor, as well as the role of associated organic compounds, such as vitamins and proteins, which facilitate its absorption in the intestines (Alkhaledy and Mohammad, 2024).

Forms of Chromium in Biological Systems: Organic and inorganic chromium (Cr) exists in several forms or structures depending on its oxidation state. However, the most common forms are Cr^{+2}, Cr^{+3}, and Cr^{+6}. Generally, chromium is an inert element under normal conditions (Bell et al., 2022). The following are the most important forms of chromium and their oxidation states:

First: Divalent Chromium (Cr^{+2}): This form is called Bivalent Chromium, and it is the least common because divalent chromium is unstable and highly reactive, quickly combining with oxygen to become trivalent (Cr^{+3}). Therefore, it is not found in biological systems in this form (Poljsak et al., 2009; Lewicki et al., 2014).

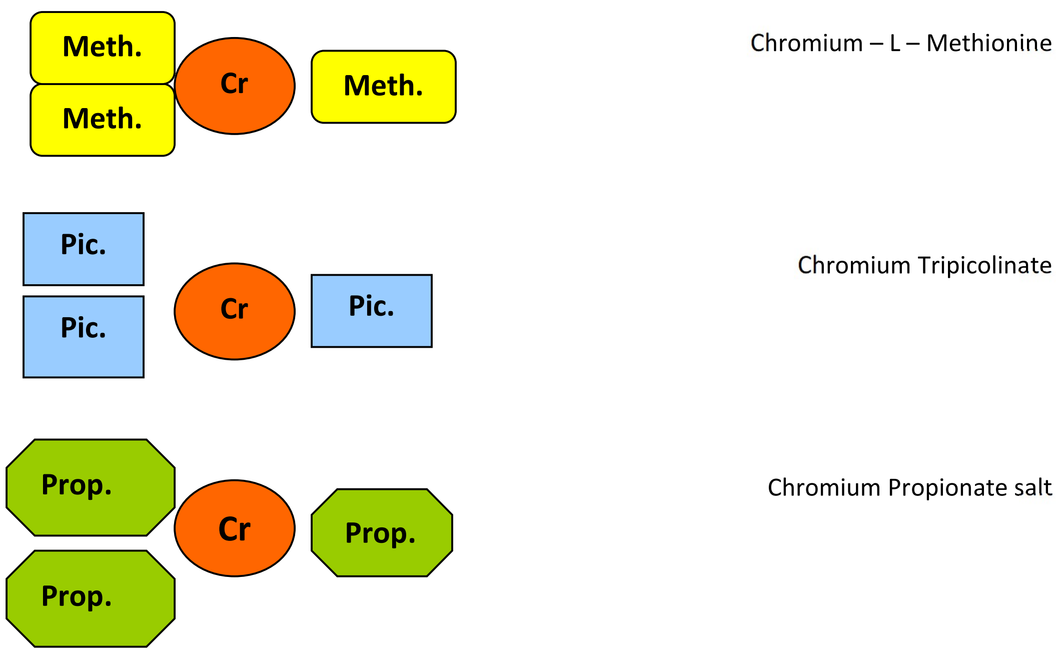

Figure (1): Trivalent chromium molecule (Zinpro, 2003)

Second: Trivalent Chromium (Cr^{+3}): This is called Trivalent Chromium and is the most stable form of chromium in living tissues and biological systems. Its reactions are similar to other forms of chromium, but its oxidizing power is weak (Vincent, 2018).

Third: Hexavalent Chromium (Cr^{+6}): This is called Hexavalent Chromium. It is a form of chromium that exists combined with oxygen as monovalent chromates (CrO_4^{-2}) or divalent chromates ($Cr_2O_7^{-2}$). It has the properties of a strong oxidizing agent. Hexavalent chromium readily crosses cell membranes and binds to proteins and nucleic acids, converting to the trivalent chromium ion. Reaction with proteins and nucleoproteins is carcinogenic and dangerous; therefore, trivalent chromium is preferred over this form (Britannica, 2026).

Chromium in foods: Good dietary sources of chromium include Vegetables such as lettuce and green beans, fruit such as apples and bananas, juices such as grape, orange, and tomato juices Brewer's yeast and nuts (Thor et al., 2011; Shaikh, 2022; Henriksen and Arnesen, 2023). Also, broccoli, grapes, whole wheat, potatoes, and garlic. Because chromium is only needed in trace amounts, chromium deficiency is rare (National Institute Health, 2022), Figure (2) Cr content in in various foods.

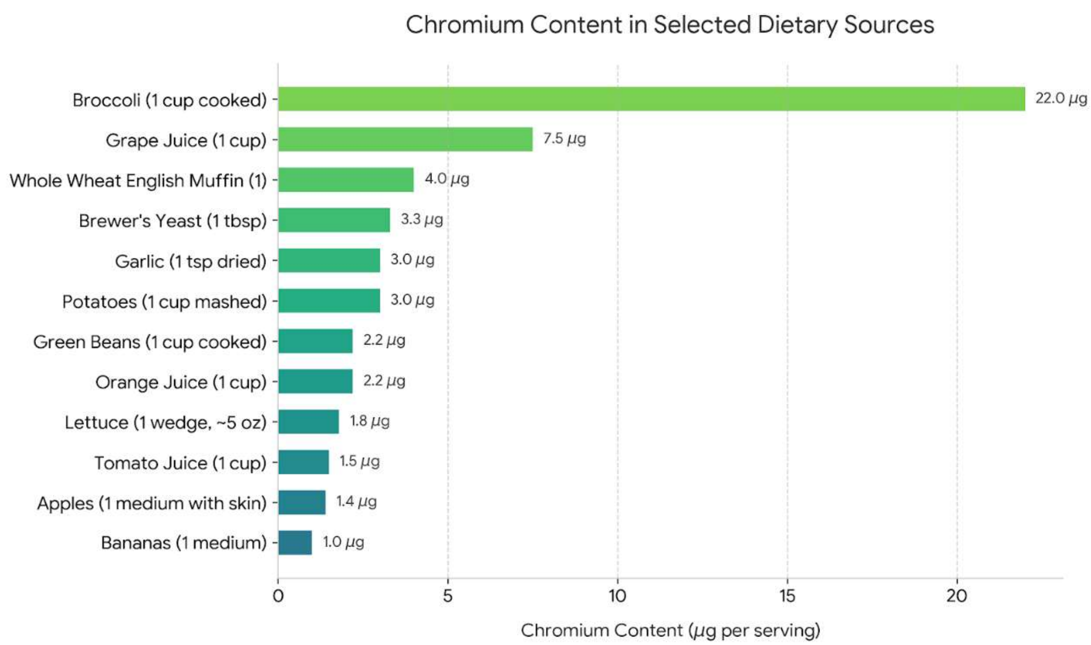

Figure (2): Chromium content in various foods

Chromium Absorption and Metabolism in the Digestive Tract: Chromium is primarily absorbed by the small intestine, with the jejunum being the most efficient site for its absorption. It can also be absorbed by the duodenum and ileum, as with other minerals (Kiela and Ghishan, 2016; Vincent and Edwards, 2025).

Inorganic chromium exists in several forms, all of which have a very low absorption coefficient compared to organic chromium (Anderson, 1987; EFSA, 2014). The absorption coefficient of trivalent chromium (Cr^{+3}) is estimated at about 0.5%, but its absorption increases to about double, and sometimes even quadruple, in diabetic individuals. Most inorganic chromium forms in nature are trivalent (Cr^{+3}), but it can also be found synthetically as hexavalent chromium (Cr^{+6}). Hexavalent chromium (Cr^{6+}) is a highly toxic, non-essential form of chromium primarily associated with industrial contamination (DesMarias and Costa, 2019). This form (Cr^{6+}) is not present in biological systems and does not reach the human or animal body except through industrial contamination, specifically when workers in chemical plants are exposed to this element. This form is more soluble than trivalent chromium and has an absorption coefficient about 3-5 times greater. Therefore, it penetrates through membranes and accumulates in external tissues such as skin and hair, in addition to very limited deposition in muscle tissue (Anderson et al., 1991; Zhitkovich, 2011; DesMarias and Costa, 2019; Islam et al., 2023)

Tissue Chromium Concentration: The first comprehensive surveys of tissue chromium concentration were conducted by Henry A. Schroeder in conducted in the 1960s and early 1970s, chromium was analyzed using spectrography and the samples of various tissues, carefully collected to avoid contamination, were analyzed. The results were as follows: lung 15.6 mg/kg, aorta 9.1 mg/kg, pancreas 6.5 mg/kg, heart 3.8 mg/kg, testis 3.1 mg/kg, kidney 2.1 mg/kg, liver 1.8 mg/kg, and spleen 1.7 mg/kg as in Figure (3) (Schroeder et al., 1962). Chromium concentrations in other tissues ranged from 0.5 mg/kg in bone marrow to 1.5 mg/kg in the adrenal glands, the values you provided correspond to the mean chromium concentrations in ash for subjects aged 30–40 years (WHO, 1988). Tissue chromium concentration gradually decreases from birth to age 10, continuing until age 80. It is not established whether this decrease is due to the physical mechanisms of chromium metabolism or dietary deficiency. Research has found that chromium concentration in lung tissue is higher in workers at chromate processing plants than in other locations. A study conducted on 16 chromate processing workers revealed that 11 of them had lung cancer (Mancuso, 1998; Ishikawa et al., 1994).

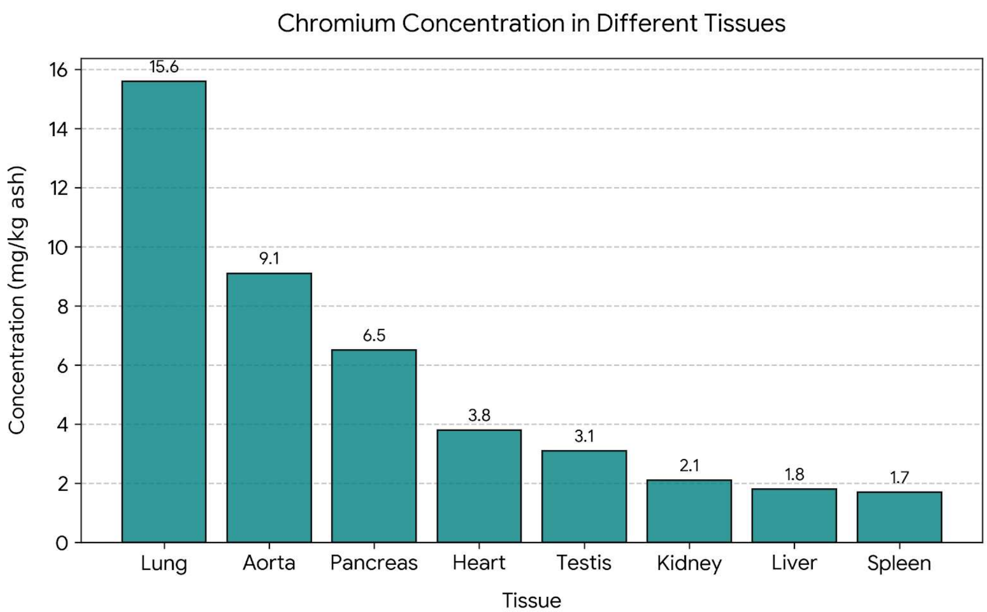

Figure (3): Chromium content in different human tissues.

Chromium concentration in the blood: Researchers have indicated that the concentration of chromium in the blood of humans not exposed to chromium pollution ranges from 0.2 to 70 micrograms per liter (parts per billion) in serum or plasma, and the concentration in red blood cells ranges from 5 to 45 micrograms per liter (Schroeder et al., 1962; WHO, 1988). There is insufficient evidence to suggest that the concentration of this element in the air affects its concentration in the blood. When a person is exposed to chromium, its concentration in blood serum increases to between 5 and 170 micrograms per liter. After cessation of exposure to chromium pollution, there was no decrease in the concentration of this element in the blood, even after 7 days. Red blood cells have a high affinity for hexavalent chromium; therefore, any increase in the concentration of hexavalent chromium in the air will be reflected in an increase in its concentration in red blood cells (Ottenwaelder et al., 1988; Ray, 2016; Jiang et al., 2025).

Urine Chromium Concentration: Normal urinary chromium concentration ranges from 1.8 to 11 micrograms/liter. It increases with exposure to high concentrations of chromium so it can used as Urinary Chromium as a Biomarker (Georgaki et al., 2026), modern analytical methods and population studies often find lower baseline levels in non-exposed populations, typically averaging around 0.17 to 2.7 µg/L (Georgaki et al., 2026; Thompson et al., 2026). Males have higher concentrations than females, and urinary chromium excretion decreases with age. Studies have indicated significant variations in urinary chromium concentration, attributed to individual differences and various factors, including environmental conditions (Ottenwaelder et al., 1988; WHO, 1988; Georgaki et al., 2026).

Milk Chromium Concentration: Milk chromium concentration was determined by manually collecting 261 breast milk samples from 45 American women. The total chromium level in all samples was measured using a Graphic-Furnace AAS instrument and standard methods. The average milk chromium content was found to be 0.30 mg/L, with a range of 0.06 to 1.56 mg/L. No significant changes were observed during lactation. In a study conducted on frozen samples taken from mothers at different stages of breastfeeding and obtained from the milk bank at the Children's Hospital in Helsinki, the average concentration of chromium was found to be 0.667 mg/L of milk (WHO, 1988; Case et al., 1984; Casey and Hambidge, 2007; Björklund et al., 2012).

The Role of Chromium in Lipid Metabolism and Heart Disease: Increasing research has shown a link between low chromium intake and impaired lipid metabolism, leading to the development of atherosclerosis. In other words, low chromium intake disrupts lipid metabolism and contributes to the development of atherosclerosis. For example, feeding rats a low-chromium diet impairs glucose tolerance, resulting in elevated cholesterol levels. Extensive studies have shown that a larger proportion of these rats suffered from aortic occlusion compared to the control group. Similar results were observed in an experimental study conducted on rabbits (Schroeder, 1962; Lewicki et al., 2014; Ganguly et al., 2017). Furthermore, studies involving human populations through large-scale epidemiological surveys have found that individuals with significantly low chromium levels experienced higher rates of cardiovascular morbidity and mortality compared to the control group of healthy individuals, these human studies complement the animal research by demonstrating that individuals with existing cardiovascular diseases (CVDs) often possess significantly lower plasma or serum chromium concentrations than healthy controls (Chen et al., 2022; Nayyar et al., 2026). Researchers have indicated that low chromium levels have proven to be a better predictor of coronary heart disease in the presence of risk factors such as age, sex, cholesterol and triacylglycerol levels, and systolic and diastolic blood pressure (Newman et al., 1978; Simonoff et al., 1984; Guallar et al., 2005). Some researchers have suggested that one reason for the high incidence of coronary artery disease observed in individuals with chromium deficiency is their inability to maintain normal insulin levels (Abraham et al., 1980, 1982; Cefalu and Hu, 2004; Cabrera-Abreu et al., 2023).

Another study found that the highest incidence of atherosclerosis was in individuals with very low hair chromium concentrations compared to healthy individuals of the same age. Later, another report indicated that those who died from coronary artery disease had significantly lower chromium levels in their aortic tissue compared to those who died from accidents (Cote et al., 1979; WHO, 1988). Chromium acts as a catalyst for insulin sensitivity, increasing insulin receptor synthesis and stimulating lipase activity, thereby increasing the metabolism of very low-density lipoproteins (VLDL). In this way, chromium added to diets is effective in reducing VLDL and LDL levels and increasing beneficial high-density lipoproteins (HDL) (Pei et al., 2018; Vincent, 2000). A study conducted involving 14 healthy individuals and 5 individuals with diabetes, showed that 200 mcg of chromium and nicotinic acid led to a decrease in cholesterol, LDL, and glucose levels in the blood of diabetic patients. Another human trial using chromium picolinate at a daily dose of 200 mcg for 6 months observed a decrease in both LDL and total cholesterol levels, thus maintaining normal blood lipid levels and the body, and reducing the risk of heart disease such as hardening and blockage of the coronary arteries, trials confirmed that chromium supplementation consistently lowers LDL cholesterol, triglycerides, and systolic blood pressure all primary contributors to coronary artery blockages (Shao et al., 2024; Liu et al., 2025).

The Role of Chromium in Protein Synthesis: Animal experiments have shown that high concentrations of chromium are found in the cell nucleus, with the remainder distributed between the mitochondria and chromosomes. Other experiments have demonstrated that dietary chromium deficiency leads to impaired amino acid synthesis, particularly of glycine, serine, and methionine in proteins. Chromium plays a crucial role in nucleic acid metabolism and synthesis, and high concentrations of this trace mineral are found in nucleoproteins (Macfie et al., 2009; Ray and Jankar, 2022).

The Role of Chromium in Reproduction: Experiments conducted on rats fed a diet with a low chromium level showed a significant decrease in sperm count and reduced fertility compared to the control group fed a diet with a good chromium content (Anderson, 1981; European Commission, 2003). This is because low chromium concentration in the body inhibits nucleic acid synthesis. Modern reviews suggest that chromium may play a role in regulating oxidative stress within the testis; a lack of essential trace elements can lead to lipid peroxidation of sperm membranes and DNA fragmentation, ultimately impairing fertility potential. Chromium also plays a fundamental role in maintaining the stability of protein and amino acid structures (Pereira et al., 2021). Furthermore, animal studies have shown that this element is important for embryonic growth and development. Studies conducted on humans to date have shown that premature infants and those with intrauterine growth restriction have a lower level of hair chromium compared to full-term infants, and that women who have given birth multiple times have a very low level of chromium in their bodies compared to those who have not given birth. Research confirms that chromium (Cr) is a crucial trace element for fetal development, primarily through its role in regulating maternal glucose metabolism and supporting the formation of fetal tissues (Zhang et al., 2016; Stephen, 2022). While moderate deficiency affects metabolism, excessive exposure to certain forms of chromium (such as hexavalent chromium) is toxic and can cause reduced birth weight and intrauterine growth restriction in fetal rats (Fang et al., 2026).

The effect of chromium on the immune response: The immune system is divided into two parts: specific immunity and non-specific immunity, which relates to aspects of the host's own defense. Non-specific immunity is called innate immunity and is related to the body's basic defensive elements, including physiological and physiological barriers, phagocytic cell function, and immune mediators, which in turn stimulate the immune response in specific immunity, also known as acquired immunity, is mediated by T and B lymphocytes. It differs from innate immunity in that it exhibits memory properties and the ability to differentiate between self and non-self (foreign substances or even the body's own cells in autoimmune diseases). This characteristic is not observed in innate immunity inflammation (Janeway et al., 2001; Romo et al., 2016; Abbas et al., 2021). Despite these differences, the mechanisms of innate and acquired immunity do not operate independently. For example, phagocytic cells, such as macrophages, are crucial for antigen presentation and the stimulation of specific (acquired) immunity; after engulfing a microbe, macrophages process its proteins and present the resulting fragments on their surface using Major Histocompatibility Complex (MHC) class II molecules (Abbas et al., 2021; Santa, 2023). Furthermore, soluble factors, such as cytokines, produced during lymphocyte activation, accelerate phagocytosis. Phagocytosis, compounds such as the metal chromium have the ability to modify the host body's defense (Alter Host Defense), and are referred to as immunomodulators, which work to raise the level of the body's defensive immunity, whether acquired or non-acquired (Abbas et al., 2021; Kafi et al., 2021). Cytokines produced during lymphocyte activation (e.g., IL-2, TNF-α) act as potent stimulators that enhance the microbicidal and tumoricidal capabilities of macrophages (Kafi et al., 2021; Santa, 2023).

Current evidence suggests the benefits of chromium supplementation on both innate and adaptive defense mechanisms, as well as its impact on infection rates and improved animal production (Al-Shadeedi et al., 2009; Kafilzadeh et al., 2012).

Chromium role in the immune response to the vaccinated animals: Chromium (Cr), specifically in its trivalent form (**Cr III**), serves as a potent immunomodulator that enhances both the magnitude and duration of the immune response in vaccinated animals. It acts primarily by improving the proliferation of lymphocytes and increasing the production of specific antibodies, often while mitigating the immunosuppressive effects of stress hormones like cortisol (Kafilzadeh et al., 2012; Dworzański et al., 2021).

1. **Enhancement of Antibody Response (Humoral Immunity):** Dietary chromium supplementation has been shown to significantly elevate antibody titers following vaccination against several viral and bacterial pathogens in livestock and poultry.

- **Viral Vaccines:** In broiler chicks, chromium picolinate supplementation (up to 1500 ppb) resulted in significantly higher antibody titers against Newcastle Disease and Avian Influenza (H_5N_1 and H_5N_8) compared to non-supplemented groups (Hajializadeh et al., 2017; Talib and Ulaiwi, 2023).
- **Bovine Respiratory Disease:** In dairy cows, supplemental chromium increased antibody production against **Bovine Viral Diarrhea Virus (BVDV)** and **tetanus**, although its effect can vary depending on the specific antigen and the animal's stress levels (Burton et al., 1993; Faldyna et al., 2003).
- **Immunoglobulin Levels:** Research indicates that chromium can specifically increase serum concentrations of **IgG** and **IgM**, providing a more robust primary and secondary immune response (Hajializadeh et al., 2017; Lu et al., 2019).

2. **Stimulation of Cell-Mediated Immunity (CMI):** Beyond antibody production, chromium

strengthens the cellular branch of the immune system, which is critical for fighting intracellular pathogens.

- **Lymphocyte Proliferation:** Chromium acts as a mitogen that stimulates the proliferation of **T and B lymphocytes** (Kafi et al., 2021). Supplementation has been shown to increase the population of **CD4+ (helper T cells)**, which are essential for coordinating the overall immune response to vaccines (Lu et al., 2019).
- **Cytokine Production:** It modulates the production of pro-inflammatory and immunoregulatory cytokines such as **IL-2, IL-6, and TNF-α**, which are necessary for the activation and maturation of immune cells post-vaccination (Kafi et al., 2021).

3. Mitigation of Stress-Induced Immunosuppression: Vaccination often coincides with stressful periods (e.g., weaning, transport, or heat stress). Chromium helps maintain vaccine efficacy during these times:

- **Cortisol Reduction:** Stress triggers the release of cortisol, which suppresses lymphocyte function and antibody synthesis. Chromium reduces serum cortisol levels, effectively "shielding" the immune system and allowing for a normal response to the vaccine (Soltan, 2010; Kafilzadeh et al., 2012).
- **Heat Stress Protection:** In poultry exposed to high temperatures, chromium supplementation prevents the typical decline in antibody titers, maintaining protective immunity where non-supplemented birds might fail (Hajializadeh et al., 2017).

The role of cytokines is to dually regulate the body's acquired and innate defense mechanisms, including antibody production and cell-mediated immune responses. Specifically, high concentrations of IFN-γ and IL-2 associated with T-helper 1 cells tend to support cell-mediated immune responses and the production of IgG 2a antibodies in mice and humans. Conversely, high concentrations of interleukin-4 (IL-4), interleukin-5 (IL-5), and interleukin-10 associated with T-helper 2 cells, known for their strong support of antibodies such as immunoglobulin A (IgA), immunoglobulin E (IgE), and immunoglobulin G1, are also associated with T-helper 2 cells (Ig G1) (Abbas et al., 2010; Romo et al., 2016; Stephen, 2022).

Compounds such as chromium, which may induce cytokine production and the management of the immune response, have significant practical value in vaccine formulation and drug modification in human medicine (Shrivastava et al., 2002; Dworzański et al., 2021). Current studies are seeking to further characterize the immunomodulating properties of chromium, and in particular its remarkable ability to modulate cytokine production in bovine cattle (Wang et al., 2025).

Mechanisms of Chromium Action: Numerous scientific studies have attempted to explain the mechanism of action of organic chromium in improving the productive, reproductive, and physiological performance. Several theories have been proposed, but the precise details remain unclear (Wang et al., 2020; Panchal et al., 2023; Domínguez et al., 2024; Haloi et al., 2025; Magnus and Lali, 2025). Among these proposed theories are:

1. Increased glucose metabolism through its role as an accelerator of glucose consumption within tissues and cells. Organic chromium plays a crucial role as part of a factor called the Glucose Tolerance Factor (GTF) in live bodies. In humans, the processing unit is insulin, which responds directly to the effects of chromium. Since insulin is the hormone that stimulates catabolic processes and inhibits anabolic processes within muscle tissue and the liver, as well as breaking down fat tissue, any stimulation by chromium will increase the response to insulin. This, in turn, will prevent fat deposition, increase muscle tissue, and enhance metabolic rates and nutrient utilization.
2. Increased amino acid and glucose consumption within living tissues increases nutrient uptake, particularly of amino acids and glucose. Chromium also alters insulin concentration, leading to increased consumption and absorption of amino acids within muscle tissue, increased insulin deposition, and consequently, increased muscle tissue growth.
3. Activation of phosphatyrosine phosphatase, this is a relatively recent theory explaining the role of organic chromium in improving productive and reproductive performance. It explains chromium's role through its binding to an unknown, low-molecular-weight protein. This protein originates from protein concentrates and meal in feedstuffs, forming a complex called the Cr^{+3}-protein complex. This complex activates the phosphotyrosine phosphatase enzyme, which increases the responsiveness of insulin receptors in tissues, thus increasing insulin sensitivity and enhancing insulin action on glucose metabolism and preventing fat deposition. 4. Increase Reproduction is attributed to its effect on increasing the level of luteinizing hormone (LH)

and the number of pulses of this hormone, thus increasing the ovulation rate.
5. Increasing the absorption rates of amino acids and nutrients and preventing their binding to chelating agents.
6. Enhancing the immune response.
7. Preventing all types of stress by lowering cortisol levels and reducing cholesterol concentration in blood serum.
8. Reducing the severity of bacterial infections by decreasing pathogenic stress factors, in addition to increasing the concentration of nutrients absorbed by the intestines and providing the body with these nutrients.

Conclusions

Based on previous information of chromium's biological and physiological pathways, we can conclude a comprehensive conclusion regarding its role in metabolism, growth, and overall health:

1. Chromium supplementation shifts the metabolic balance from fat storage to nutrient utilization. It effectively increases metabolic rates by accelerating glucose consumption and preventing the deposition of adipose tissue, while simultaneously promoting the development of lean muscle mass.
2. Increasing the sensitivity of muscle tissue to insulin, chromium facilitates a higher uptake of amino acids. This creates a highly anabolic environment that supports tissue repair and muscle growth, making it a critical micronutrient for optimizing physical development and nutrient absorption.
3. Chromium does not just "assist" insulin; it structurally enhances the receptor's responsiveness. By activating specific enzymes that sensitize tissues, chromium prevents the metabolic "numbness" (insulin resistance) that leads to obesity and inefficient energy use.
4. Chromium significantly improves fertility by modulating Luteinizing Hormone (LH). By increasing the frequency and magnitude of LH pulses, it directly enhances ovulation rates and reproductive success, addressing issues of reduced fertility often seen in trace-mineral-deficient subjects.
5. Chromium acts as a physiological buffer against stress. It prevents the spike of cortisol (the "stress hormone"), which is known to break down muscle and suppress the immune system. By lowering cortisol and cholesterol, chromium maintains internal stability (homeostasis) during environmental or physical challenges.
6. Supplementation strengthens both the innate and adaptive immune systems. Furthermore, by increasing nutrient absorption in the intestines and reducing "pathogenic stress factors," chromium minimizes the severity of bacterial infections and ensures the body has the necessary nutritional reserves to fight disease.

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