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Review on chromium:therapeutic uses and toxicological effects on human health

N. Adamu[1], N. Jithendra Kumar[1], N. Venkata Sreenatha Reddy[1], R.Prasanna Kumar[2], K. Swathi Krishna[3]

1. B Pharmacy final year student, Saastra College of Pharmaceutical Education and Research, Nellore.
2. Assistant Professor, Dept.of Pharmacy practice, Saastra College of Pharmaceutical Education and Research, Nellore
3. Principal, Saastra College of Pharmaceutical Education and Research, Nellore.

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Abstract

Chromium is an essential trace element whose deficiency can cause impairment of glucose tolerance, growth and various biological functions. There are two isotopes of chromium-trivalent chromium and hexavalent chromium. Both the isotopes of chromium have quite different effects on the human body. The objective of this narrative review is to compile the different effects of the two isotopes of chromium and give a comprehensive analysis of the effects of hexavalent and trivalent chromium. Data from various studies across different forums were compared to provide a concrete analysis of the therapeutic and harmful effects of two isotopes of chromium on human health. Chromium plays a vital role in the biological functions of the body. It might be helpful in balancing the glycaemic levels, triglyceride levels and cholesterol levels in the body. Excessive intake of chromium is harmful for health. Overexposure to chromium can lead to carcinogenic effects. Consumption of an insufficient amount of chromium might not be adequate as well. Trivalent chromium can be quite beneficial if taken in proper quantities. Hexavalent chromium can cause cancer. Trivalent chromium is beneficial, while hexavalent chromium is harmful to human health.

Keywords: Chromium, Chromium toxicity, Therapeutic use of chromium, Chromium interactions.

***Corresponding Author**

R.Prasanna Kumar

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Introduction

Chromium (Cr) is a crucial trace element. The total body content of chromium decreases with age [1]. Radioactive chromium is used to label red blood cells to calculate the rate of haemolysis [2]. Effects like decreased fertility, sperm count and impairment of growth can occur due to chromium deficiency [3]. Laboratory investigations in a clinical trial suggested certain conditions associated with a specific risk of chromium deficiency, including low birth weight in infants, insulin-dependent juvenile diabetes, gestational diabetes and protein-calorie malnutrition in some people [4].

Inhalation of chromium increases the chances of hypersensitivity reactions like asthma, nasal irritability, nasal ulcers, skin lesions or rashes, lung cancer and contact dermatitis [5]. A lot of workers in the tanning industry get affected by chromium toxicity [6]. Chromium is partly responsible for the carcinogenic effects of tobacco that can affect human health adversely [7]. Chromium deficiency would cause disorders in lipid, carbohydrate and protein metabolisms due to the generation of electrons from reactive oxygen species [8]. Herbal drugs may be a source of chromium [9]. Various mechanisms of the immune system are affected by chromium. It may result in immune stimulation or immune suppression. The estimated safe and adequate daily dietary intake for Cr is 50–200 μg [10]. Chromium can have some therapeutic uses, but there seem to be some toxic effects. Chromium has two isotopes [11]. The risk of trivalent chromium is insignificant due to its less severe toxicity [12]. Severe oral toxicity could happen if the amount ranges from 50 mg/kg to 150 mg/kg [12].

Chromium acts as mutagen, carcinogen and allergen.5 Exposure to chromium dust in occupational setups is hexavalent primarily chromium in the sources [13]. It is essential to know the difference between the effects of both isotopes of chromium. The objective of the succeeding review is to bring light to the different effects of the two isotopes of chromium, classifying them as chromium deficiency due to less intake of chromium or toxicity if exposed to chromium even in small quantities or huge quantities for another type of chromium.

Materials and Methods

Different studies and research papers gave us information on the actions of two isotopes of chromium on human health. Studies from various forums can be categorised and compared to give information on the therapeutic uses and toxicological effects of chromium. It can provide a stable idea of the aspects we need to be aware of before chromium can be beneficial for human health. This study is a narrative review that summarises the various effects of two isotopes of chromium. The study is ethically acceptable, and no harm has been done to any human or animal during the process of the comparative analysis. Around 81 research articles from PubMed and various other forums were considered for this narrative review, and only 50 papers were selected for the final review article. The words used for the search strategy are toxicological effects of chromium and its positive effects, the molecular basis of chromium interaction, chromium (VI) and chromium (III).

The exclusion criteria for the studies excluded in the narrative review comprise studies of chromium interactions in animals that cannot be correlated to effects on human health, studies of chromium interactions in animals that cannot be correlated to effects on human health and studies of chromium complexes not indicating any therapeutic or harmful effects on the human body. The inclusion criteria or selection criteria for this narrative review are the studies showing differences in chromium interactions in the human body, studies on toxic effects of chromium, reports on therapeutic effects of chromium, clinical trials involving animals that can be correlated to human health, the interaction of chromium with other drugs and the molecular basis of chromium interaction. The aim of the review is to discuss the difference in positive effects, therapeutic uses, adverse effects and toxicological effects of the two isotopes of chromium to determine the role of chromium in health and well-being. The references are cited using Google Scholar and Zotero.

Role of Chromium in Enhancing the Human Health

Chromium plays a significant role in fat and carbohydrate metabolism. Ameliorate diabetes patients could potentially use high-chromium yeast as a nutritional supplement [14]. Results from research showed that fasting blood glucose levels decreased considerably in the individuals taking yeast enhanced with chromium; better glycaemic control was indicated with HbA1c values improved; and the total cholesterol level, triglyceride levels and low-density lipoprotein (LDL) levels were significantly lowered [15]. However, more studies must be done to implement the effectiveness of chromium to a greater extent and recommend it to patients with type 2 diabetes mellitus for glycaemic contro [16].

Hexavalent chromium, at a lysosomal acidic pH of 4.5, can induce oxidation of human LDL. Chromium (III) is not capable of causing the oxidation of LD [17]. Deficiency of chromium in patients with type 2 diabetes mellitus can play a part in insulin resistance and hyperlipidaemia; hence, they require supplementation of chromium to counter its loss in urine [18]. A randomised controlled trial for effects of chromium supplementation related to menstruation suggests that Cr could be advantageous for monotherapy or secondary therapy for fewer mood symptoms and satisfaction in overall health in women affected by symptoms related to the menstrual cycl [19]. A study suggested positive effects of administering chromium for 8 weeks in infertile women subjects suffering from the polycystic ovarian syndrome, opting for in-vitro fertilisation on the control of glucose levels and lower risk of cardiovascular, metabolic and oxidative stress [20]. However, a chromium supplementation meta-analysis for women suffering from polycystic ovarian syndrome did not show relevant positive effects [21]. There has been evidence that shows that the risk of cardiovascular disease and insulin resistance was decreased with the supplementation of chromium picolinate [22]. The chances of atherosclerosis in individuals, heart attack and cholesterol levels are found to be lowered with sufficient chromium intake [23]. Although research provides slight evidence on the therapeutic role of chromium on body composition, it might be beneficial for people suffering from obesity and those who want to improve their body composition [24]. A study showed that serum iron concentration was likely to be lower and affected postprandial metabolism

of glucose in healthy young men on acute chromium supplementation [25]. Attenuating insulin resistance and low plasma cholesterol levels could be attained with chromium supplements, particularly niacin-bound chromium or chromium nicotinate [26].

Therapeutic Uses of Chromium

A study states that chromium mono-supplementation of greater than 200 μg per day can control glycaemic levels [27]. Sportspersons and bodybuilders might take chromium as a dietary supplement, and healthy individuals might consume it in total parenteral nutrition or through vitamin pills. Sufficient chromium supplementation would help with the excellent insulin efficacy required for high-level athletic performance [28].

Chromium has been claimed to increase muscle mass and decrease body fat, and athletes might take foods rich in chromium or mineral supplements. Chromium levels fluctuate with regular exercise, hence supplementation is required [29]. Chromium deficiency in patients with type 2 diabetes mellitus can play a part in insulin resistance and hyperlipidaemia; hence, they require supplementation of chromium to counter its loss in urine [30]. A randomised controlled trial for effects of chromium supplementation related to menstruation suggests that Cr could be advantageous for monotherapy or secondary therapy for less mood symptoms and satisfaction in overall health in women affected by symptoms related to menstrual cycle [19].

Hazardous Nature of Chromium

Acute oral toxicity for chromium (VI) is possible if the dose is between 1.5 mg/kg and 3.3 mg/kg [31]. The severe toxicity could be due to the strong oxidising properties of hexavalent chromium. It harms the blood cells, the kidneys and the liver through oxidative reactions when it enters the bloodstream. It could lead to haemolysis, damage to neural tissues and renal and liver failure. According to a review, a chromium compound, chromate, was found to be deposited in the proximal convoluted tubule selectively where necrosis happened. On the contrary, information on proteinuria of low molecular weight (LMW) and other kidney diseases in chromium workers suggests that they are caused by chromium exposure in low doses for a long time [32].

Prolonged exposure to hexavalent chromium compounds can result in chrome ulcers, skin diseases like irritant dermatitis and allergic contact dermatitis [33]. It is mostly seen in people working in tanning, electroplating and chrome-producing companies. Individuals exposed to low doses of Cr dust might suffer brain injuries [34]. According to a review, hexavalent Cr may be genotoxic and should not used as insulin enhancers, supplements in regular diet or anti-diabetic drugs [14]. Trivalent chromium, however, is not genetically toxic if taken in a moderate amount [35]. Automobile exhaust may lead to human lung cancers and skin irritation due to excess chromium. Allergy to chromium is commonly seen in people who work in the cement or leather industries. Inhaling hexavalent chromium at high concentrations is considered carcinogenic [12,36]. Tobacco is rich in chromium, which partly leads to the carcinogenic effects of smoking [7]. Thus, Cr concentrations in drugs should be within limits. Hexavalent chromium has pro-oxidative effects, which inhibit enzymes with antioxidant properties and use up glutathione present in the intracellular matrix of living organisms to serve as hemotoxic, immune-toxic, hepatotoxic, pulmonary-toxic and nephrotoxic agents. According to a study, garlic might act as a protective antioxidant to increase lipid peroxidation and reactive oxygen species produced, where hexavalent chromium acts as an inducer [37].

Findings of a review article suggest that the atypical glucose tolerance tests in Turner patients are due to chromium deficiency. Although more research needs to be done, chromium can be a factor in promoting the prevalence of Turner's syndrome in women.38 People with lipoprotein abnormalities, diabetes and an augmented risk of cardiovascular disease might have positive effects on their health with chromium supplementation [22]. If minimal amounts of chromium can aid in the prevention of such deadly diseases, it might be beneficial to have chromium-rich foods in a regular diet. The LDL and high-density lipoprotein (HDL) levels are positively altered in the blood due to chromium intake in the diet [17]. Thus, it helps in the prevention of atherosclerosis and various heart-related diseases. Insulin- resistance-related disorders could be corrected using the technology of nutrigenomics to recognise genes regulated by chromium supplementation. Lack of insulin leads to type 2 diabetes mellitus in the body. Chromium in the blood can influence insulin production and affect insulin levels in the body [30]. An increase in the levels of insulin in the body would help decrease the glucose levels in the blood. It can be a factor in preventing diabetes mellitus. If further research is done, we might also find evidence on how to find a cure for diabetes mellitus. Hexavalent chromium is mutagenic [7]. Allergic contact dermatitis

(ACD) and stomach tumours could be caused by the consumption of chromium (VI) through the water.39 Water should be filtered before consumption, and hexavalent chromium should be removed to prevent severe diseases or disorders. There has been evidence of hexavalent chromium negatively affecting human health due to its highly unstable nature.

Chromium picolinate is a complex of chromium. Chromium picolinate might lower the risk of insulin resistance and type 2 diabetes mellitus, but it is not yet fully certain [40]. More research needs to be done in this aspect to help us understand the various effects of chromium in complex forms. It might lead to multiple positive developments in medical science. There is a need for more studies related to supplementation of chromium reducing fatigue or tiredness and maintaining body weight. There might be a chance that chromium could help to get rid of tiredness. Chromium might enhance the metabolism of the body. Chromium supplementation in the diet might help with getting rid of fatigue. Proper metabolism would also support maintaining the proper weight.

Chromium complexes can be proven to be beneficial to human health. Chromium complexes might favour the rate of metabolic reactions in the body. It could lead to various processes involving the catabolism of substances to produce energy. As a result, fatigue can be prevented with the help of chromium supplementation in the diet.

Compounds with trivalent Cr are insoluble; chromium metal does not pose a threat to health, while hexavalent chromium is toxic and can cause cancer.41 The insolubility of trivalent chromium is a big factor in making trivalent chromium beneficial to human health. Trivalent chromium may be consumed in desirable quantities in limited amounts in a regular diet through chromium-rich foods, unlike hexavalent chromium. The unstable and mutagenic properties of hexavalent chromium might lead to cancer. Due to definite transport mechanisms, only restricted amounts of trivalent Cr go into the cells. Chromium supplementation should not be done in large quantities as excess chromium is not good for health. If chromium is supplemented in inadequate amounts, it would not be beneficial or harmful. Chromium deficiency leads to diseases or malfunctions, but it might not be life-threatening in most cases. However, intake of chromium in excess amounts is injurious to health. Excessive intake of chromium can lead to severe complications.

On the basis of the assessment of various research works, it is evident that chromium can affect human health in many ways. A person needs to take chromium in proper quantities as prescribed by a consultant to ensure the appropriate functioning of the body. Thus, chromium might be taken in a proper quantity to promote health and prevent diseases.

The collated data of different studies gave results that came out to be quite reasonable, with a solid division in terms of the use of the two isotopes of chromium to our advantage. Trivalent chromium has been proved to have health benefits when consumed or supplemented with diet. In contrast, hexavalent chromium has dismissive effects on human health and can lead to less severe health issues and more serious health complications.

Cellular Effects of Chromium in the Body Metabolism

The glycaemic index of the body undergoes some alterations due to interaction with chromium. Chromium toxicity can induce inflammation [42]. Trivalent chromium can also react with DNA and cause damage, but it can be controlled under restricted access [35]. Trivalent chromium, on binding with DNA, enhances the activity of DNA polymerases and changes a few parts of DNA, promoting mutations in the biological system [43,44]. In insulin signalling, with the help of the anomalous difference Fourier method and crystallographic analysis of trivalent chromium and insulin crystals, the binding site for trivalent chromium is found to be B21 Glu.45 Chromium is responsible for promoting phosphorylation of Akt, tyrosine phosphorylation of the insulin receptor substrate-1 protein and PI-3-kinase activity that are stimulated by insulin. Chromium also increased the insulin receptor tyrosine kinase activity in the chromium-treated cell membrane [45,46]. Chromium has also increased the rate of biological and physiological processes involving a membrane- bound transcription factor that is responsible for regulation of sterol and cellular cholesterol balance in the body [47].

Risk Factors of the Chromium Available in the Environment

Hexavalent chromium can lead to a runny nose, nosebleed, coughing, sneezing, skin cancers, lung cancers [7,10]. and also lead to tumours in the body when it is inhaled or consumed. Its toxicity is a widely known hazardous health effect. Contaminated water bodies should be purified properly to remove hexavalent chromium that is toxic in nature. Wastes from industries should be filtered properly before discharging into water bodies through bioremediation strategies.48 Polluted water with hexavalent chromium is injurious to marine animals and human beings.

Hexavalent chromium might affect vision and smell. It affects eyesight and the sensation of smell. Hexavalent chromium is toxic due to the fact that it is soluble in nature. It pollutes the water, which affects human health negatively. This negative effect of chromium is chiefly seen in the tanning industry [6]. Usually, it is hexavalent chromium that is responsible for the harmful effects of chromium on human health.

However, trivalent chromium is safe for use when taken in small quantities. According to research, trivalent chromium helps individuals with high blood glucose levels to lower their blood sugar. Trivalent chromium helps in the proper functioning of the body as it increases the basal metabolic rate of the body. This process helps in the breakdown of many substances that help in increasing the body mass index. Studies have shown that athletes and weightlifters experience positive effects on the regulation of mass in the body. Thus, trivalent chromium is helpful to athletes as a supplement. Trivalent chromium intake in adequate amounts in the diet helps with the prevention of various heart diseases and complications in the future. Trivalent chromium helps in the prevention of atherosclerosis. Trivalent chromium helps increase levels of HDL in the blood, which is known to be good cholesterol. Trivalent chromium favours the decrease of serum LDL in the blood, which is known to be bad cholesterol in layman's language. This alteration in the levels of LDL and HDL in the blood helps in the prevention of heart diseases in the body. There is evidence that chromium supplementation in postprandial meals has a positive effect on young men's health. Usually, whenever chromium is mentioned in a positive manner, trivalent chromium is what is meant. Trivalent chromium is insoluble in water. This insolubility of chromium plays a big factor in leading to trivalent chromium being beneficial to human health. Further research needs to be done to support these benefits of trivalent chromium with more substantial evidence. Even though trivalent chromium is known to affect human health in a positive manner, it is prevalent in patients with Turner's syndrome due to chromium deficiency. Biotechnology can help change the structures of genes to create genes regulated by chromium supplementation to regulate insulin levels in the body [26]. This method can lead to the prevention of insulin-related disorders that include type II diabetes mellitus. The technology of nutrigenomics can be used to identify the genes regulated by chromium supplementation, highlight the underlying mechanisms of chromium-gene interactions [49] and thus provide strategies to alleviate and avoid insulin-resistance-related disorders.

Precautions to Prevent Adverse Effects of Chromium

Trivalent chromium should be used in limited and prescribed amounts in drugs. Overexposure to hexavalent chromium dust should be avoided. Protective gear and helmets should be worn by workers in the tanning, leather or cement industries. Trivalent chromium consumption should be in moderate amounts through supplementation. Water infected with chromium waste should not be consumed or used for domestic work.

Limitations of the Review

The limitation of the review is the lack of studies on the effects of trivalent and hexavalent chromium together. Most of the studies are observational type, giving reports on the observed conditions in the study population. Most of the experimental studies have not passed the level of animal trials to be implemented on humans. The role of chromium in human health and disease is still ambiguous, with little concluding information. The analysis made from the studies included in the review has not given any solid proof of the positive effects of trivalent chromium without any adverse effects on human health and disease. Hexavalent chromium is well known to be hazardous for human health.

Conclusion

Trivalent chromium is beneficial to the human body, while hexavalent chromium causes tumours and severe health diseases. Hexavalent chromium can lead to skin diseases. Chromium promotes insulin function, and its deficiency leads to impaired glucose tolerance. This finding might help patients with type 2 diabetes mellitus. Chromium promotes the utilisation of glucose by the cells of the body. The various processes involved help in the production of ATP in the body. Chromium reduces serum cholesterol. Chromium, thus, helps in preventing cardiovascular diseases. Chromium performs several biological functions. It helps by increasing the basal metabolism of the body. As a result, chromium helps by maintaining body weight. ATP produced during the breakdown of various molecules and the formation of new compounds is taken up by the cells of the body. Since the metabolism of the body is enhanced, it helps get rid of fatigue. Sometimes, chromium is taken as a supplement by athletes. Chromium lowers the total serum cholesterol level. It is involved in lipoprotein metabolism. It is believed that

chromium participates in the transport of amino acids into the cells of the heart and liver. Chromium decreases serum LDL and increases HDL levels. These changes in levels of lipoproteins help in promote health and prevent diseases. It prevents atherosclerosis and various other cardiovascular diseases. Older people are mostly affected by chromium deficiency. The body's requirement for chromium increases with age for various metabolisms in the body, like lipid metabolism, carbohydrate metabolism and lipid metabolism. As a result, elderly people may include adequate amounts of chromium in their daily diet.

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