BMC JOURNAL OF SCIENTIFIC RESEARCH
A Multidisciplinary Peer Reviewed Research Journal
ISSN: 2594-3421 (Print), 2773-8191 (Online)

The Effect of Chromium on Human-Health: A Review

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Received: Aug. 04, 2022, Accepted: Nov. 30, 2022

Abstract

This review presents the health effects of chromium on the living organism based on previous studies. Chromium (Cr) belongs to the d-block element in the modern periodic table. Chromium has a wide range of oxidation states ranging from -2 to +6. Chromium mostly exists in the environment as trivalent (Cr^{3+}) and hexavalent (Cr^{6+}) states. Both trivalent and hexavalent states of chromiums are derived from the industrial effluents. Ingestion, dermal contact, and inhalation are the most common routes through which chromium enters the human body. Ion chromatography inductively coupled plasma-mass spectrometry (IC-ICP-MS) is mostly used for the speciation analysis of metals. Hexavalent chromium is highly soluble and mobile in alkaline and slightly acidic soils, whereas trivalent chromium is less soluble, adheres to the coarse material on the soil, and precipitates as Cr(III) hydroxide. Hexavalent chromium is more detrimental as compared to trivalent chromium. The detrimental effects of chromium are bronchial asthma, lung cancer, nasal ulcers, skin allergies, carcinogenicity, and genotoxicity. To protect from these adverse effects, WHO has suggested a provisional guideline value of chromium as 0.05 mg/L until further information is available and revalued.

Keywords Chromium, health hazards, carcinogenic, ingestion, toxicity.

1. Introduction

The disposal of industrial waste into water bodies has degraded the quality of water. The industries such as catalyst manufacturers, paint and pigment, glass, ceramic, chrome plating, chrome alloy, and chromium metal production use chromium and its salt in large amounts[1, 2, 3]. The industrial waste produced from the textile industries, tanneries, electroplating, and metallurgical mainly consists of chromium which causes serious health hazards to humans, animals, and marine life[4]. The living organisms present in water slowly degrade these wastes into harmless small molecules, whereas some of them cannot be easily degraded by the organisms and accumulate to a certain extent that causes considerable health hazards to living organisms. A very low concentration of certain heavy metals is essential for living beings, but a higher level than its permissible limit inhibits the enzyme activities which cause toxicity such as carcinogenicity and allergenicity[5].

Chromium (Cr) belongs to the d-block element in the modern periodic table and has an atomic number of 24. The relative atomic mass of chromium is 51.996. Chromium possesses -2 to +6 oxidation states. Chromium mostly exists in trivalent and hexavalent states. Both trivalent and hexavalent states of chromium are derived from the industries.

The compounds of chromium, such as chromium halides, oxides, and sulfides having oxidation states of +2, are the available forms and oxidize to +3 forms in the presence of air[6, 7].

The amount of chromium present in the soil varies from area to area, and the extent of contamination depends on anthropogenic sources of chromium. The oxidation states of chromium determine its toxicity, mobility, and bioavailability. Chromium mostly exists as the oxidation states of Cr^{+3}[Cr(III)] and Cr^{+6}[Cr(VI)]. The predominant species in the environment are Cr(III) and Cr(VI). Chromium as Chromate(CrO_4^{2-}), bichromate ($HCrO_4^-$), and dichromate ($Cr_2O_7^{2-}$) ion are hexavalent which are toxic and mutagenic. Chromium(VI) is highly soluble and mobile in alkaline and slightly acidic soils[8, 9]. In contrast, the trivalent chromium is less soluble, adheres to the coarse material on the soil, and precipitated as Cr(III) hydroxide[10,11]. Chromium has unique properties among toxic metals. Both trivalent [Cr(III)] and hexavalent[Cr(VI)] chromium species possess distinct chemical, toxicological, and epidemiological characteristics[12]. Cr(VI) is carcinogenic to humans. It oxidizes biological molecules and has the ability to diffuse through cell membranes[13]. It is also a potential epithelial irritant[14]. Cr(VI) is toxic to micro-organisms[15],aquatic animals[16]and many plants too[17]. Cr(III) is essential for sugar and lipid metabolism in humans. It is regarded asa micronutrient and basically not harmful[18]. At a very low concentration (i.e. 0.05 to 1.0 mg/L), it was realized to enhance the growth and yield in plants but not indispensable to plants[7, 19]. Its accumulation in cereals, vegetables, fruits, and edible parts of the plant is hazardous to animals and humans.

2. Analytical methods for chromium

Atomic absorption spectroscopy (AAS) is the most widely used technology to measure the total concentration of chromium, but it cannot measure the different species of chromium[20, 21]. For a long time, Neutron absorption analysis[20]and particle-induced X-ray emission analysis had been better options for detecting very low chromium levels(μg/g) in tissues[22]. The different species of chromium can be efficiently measured using various modern chromatographic methods[23, 24]. Now a days, ion chromatography inductively coupled plasma-mass spectrometry(IC-ICP-MS) is better for metal speciation. To efficiently separate Cr(III) and Cr(VI) species[25], liquid chromatography coupled with inductively coupled plasma mass spectrometry (IC-ICP-MS) can be used. Simultaneous determination of the Cr(III) and Cr(VI) through a single chromatographic column is difficult due to the cationic nature of Cr(III) and the anionic nature of the Cr(VI) species. This problem has been solved using two alternative methods; a) using an anion–exchange column and cation-exchange guard column in series or mixed-mode column to retain both species[26] and b) using an appropriate ligand to form anionic Cr(III)-ligand complex that can be separated from Cr(VI) simultaneously using an anion exchange column on ion chromatography[27]. 1, 2– cyclohexanediamine tetraacetic acid(CDTA), diethylene triamine pentaacetic acid(DTPA), and Ethylene diamine tetracetic acid (EDTA) can be used to convert Cr(III) into the anionic complexes[28, 29].

3. Absorption and metabolism

Chromium and its compound are entered into the human body through inhalation, oral and dermal routes. Chromium(VI) is more easily absorbed than chromium(III), leading to a difference in the mode of transport in cells. Chromium(III) enters the cell through passive diffusion whereas Cr(VI) enters the cell through a non-specific anion channel by diffusion. The concentration of chromium in human kidneys, liver, and spleen measures higher as compared with other organs[30]. The Cr(VI) enters the RBC and then converts to Cr(III), which binds with the cellular components and cannot leave the RBC. In some extent of the similarity in structure between cells and RBC, Cr(VI)can be taken by other cells. The administration of Cr(VI) through oral, intratracheal, and intravenous routes increases its concentration in tissue[31, 32, 33]. The size of the particle, oxidation states, and solubility of chromium determines its fate of absorption and interaction with biomolecules in cells. Cr(VI) is mainly reduced to Cr(III) in the lung tissues[34].

The trivalent chromium is poorly absorbed into the human body. In oral administration, about 99% of its dose is retrieved in faeces, approx. 94% recovered after duodenal processing, and only about 0.5% discharge through the urine proves its poor absorption[2]. Cr(VI)has strong oxidative power. As a result, it binds with oxygen and forms chromate and dichromate. The oxidative nature of Cr(VI) made it possible to cross the biological membrane and make changes in the molecules of protein and nucleic acid. Its small amount can be absorbed in the digestive tract is proved through10% of its dose retained in the faecal test. Pulmonary alveolar macrophages in the lower respiratory tract help to reduce Cr(VI) into Cr(III). Thus, as the Cr(VI) enters the bloodstream, it is carried up by RBC, gets reduced, and confines with hemoglobin. Cr(VI) can be excreted from the human body in three different intervals, i.e., at about seven hours, 15 to 30 days, and 3 to 5 years[35].

Chromium enhances the action of insulin, i.e., glucose metabolism[36], even though chromium-containing enzyme has not been identified. Brewers'yeast and kidney powder have been found to contain the biologically active type of chromium which is named "Glucose tolerance Factor"(GFT). GFT is a complex containing trivalent chromium and nicotinic acid, amino acids such as glutamic acid, glycine, and cysteine[37]. GFT acts as a carrier of chromium to chromium deficient cells of proteins[38]; however, its action sequence is yet unknown. Low mol. wt. chromium binding substance(LMWCr) is assumed to act as an insulin signal amplification mechanism[39]. Cysteine, glutamate, aspartate, and glycine are the moiety of LMWCr oligopeptide[39]. The stabilization of active conformation of insulin receptor tyrosine takes place due to the sticking of chromium to the inactive form of LMWCr and hence facilitates the action of insulin[40].

4. Routes of exposure to humans

Chromium is omnipresent in nature in different concentrations. The toxic form, Cr(VI), is released into the environment due to human activities, whereas the least toxic form, Cr(III), occurs in the environment. The use of Cr(VI) in industries as an anticorrosive agent in the cooling and combustion system leads to its exposure in the environment[3].

Almost all food materials contain some chromium but it scales from 20-500µg/kg. The foods derived from the meats, mollusks, and crustaceans were found in the highest amount[14]. Respiratory and dermal contacts are the potential way to enter the Cr(VI) into the human body for the workers who worked in Chromium industries[30]. Food is the major source of chromium exposure. Rowbotham et al.(2000) reported that the oral intake of chromium is restricted to 33-45 µg/day for infants of 1 yr, to123-171µg/day for 11 yr and to 246-343 µg/day for adults[41].

Chromium is mainly exposed to the human body through ingestion, inhalation, and dermal contact. Exposure to Chromium (VI) through either of the routes has carcinogenic effects. Chromium-containing aerosols are of primary concern pertaining to chromium compounds inhalation. Chromium exposure adversely affects human health and is categorized into carcinogenic and noncarcinogenic effects. The duration of exposure is categorized into three different types[42]: Acute exposure (up to fourteen days, Intermediate exposure (75 to 364 days), and chronic exposure (365 days or more). Well-water is the main source of oral exposure to chromium in humans[34]. Chromium concentration in drinking water depends on the nearby industrial sources and the soil types. However, exposure to industrial waste in the water source is of major concern. Acute tubular necrosis, kidney failure, abdominal pain, mouth ulcer, indigestion,vomiting, and even death have been reported in chromium poisoning[43].

Oral exposure: Trivalent chromiumCr(III) plays a vital role in protein and lipid metabolism[44]. Oral ingestion of Cr(III) containing food caused toxicity in the mouth and increased mortality rate in the workers (gold miners) in Ontario, Canada, due to stomach cancer[44].

Inhalation: The major source of chromium is the waste from the chromium industries, which consists of a mixture of Cr(III) and Cr(VI). Both of these oxidation states of chromium are then inhaled. The lung tissue absorbs the Cr(III) as the Cr(VI) undergoes metabolic reduction into Cr(III)[45].

5. Studies on animal

Cr(VI) easily crossed the placenta and reached foetal tissue when it was given to rats and mice through drinking water[46, 47]. The cellular infiltration of Cr(VI) in the liver, pancreas, and small intestines of rats and mice was also observed in the experiment performed by the Office of Environmental Health Hazard Assessment[30]. When Cr(VI) was supplied through drinking water, both the sex of rats and mice also showed the symptoms of carcinogenicity. When Cr(VI) was supplied through the drinking water, skin tumors and small intestine carcinogenicity resulted in mice, whereas carcinogenicity at the oral cavity was reported in rats[48]. The growth of skin tumors in hairless mice was accelerated when exposed to UV light and Cr(VI) simultaneously. The presence of potassium dichromate($K_2Cr_2O_7$) in drinking water proliferates UV-induced skin tumors. It alarms human health for the exposure to Cr in drinking water[49].

The oral lethal dose to kill 50% of the rats' test populations were 20-250 mg of hexavalent chromium and 185-615 mg of trivalent chromium based on the dichromates

and chromates compound used as administrating chemicals per kg body weight, respectively[50].

The 3-month-old inbred BD rats(5-14/sex/dose) showed a dose-related decrease (15% to 35%) in the weight of the liver and spleen when exposed to 0%, 2%, or 5% of insoluble anhydrous Cr_2O_3 pigment[51], which correspond to 0, 480 and 1210 mg/kg body weight per day[49], for 90 days (5 days per week)[51].

When Cr(III) was supplied for one year through the drinking water having 25 mg per liter of Cr(III) (as a chromium trichloride) to Sprague Dawley albino rats from five weeks old age (9 males and 12 females), only the accumulation of chromium in various tissue were observed but no any effect has been observed on the feeding, increase in body weight and the macroscopic and microscopic manifestation of organ tissue[52].

When Cr(VI) was supplied for one year through the drinking water up to the highest dose of 25 mg per liter of Cr(VI) (as potassium chromate) to the 5-week old Sprague Dawley albino rats (8 to 12/sex/dose), the decreased water consumption by 20% and chromium accumulation were observed in various tissues, but no effects were observed on the feeding, body weight, and the macroscopic/microscopic manifestation of organ tissue[52].

There was no effect on survival parameters and body weight of Swiss mice of the Charles River CD strain, conducted by supplying 5.0 mg/L Cr(VI) in drinking water during the entire lifetime[53]. The exposure of NMRI mice to 135 mg/L of Cr(VI) (as potassium chromate) through drinking water for up to 29 months, three-generation did not affect survival or growth[54].

The carcinogenic effect of calcium, lead, strontium, and zinc chromate(Chromium (VI)) has been proven in experimental animals. Chromium trioxide and sodium dichromate have revealed limited evidence for the carcinogenic influence, whereas others (such as Cr(VI), Cr(III) compounds, and metallic chromium) have inadequate evidence for carcinogenicity[55, 14].

6. Effects on human

The safe and adequate requirement of absorbable Cr(III) for adults is calculated to be 0.5-2 μg per day. If 25% of the available Cr(III) in food is considered to be absorbed, that will be supplemented from the everyday diet of 2 to 8 μg of Cr(III), corresponding to 0.03 to 0.13 μg Cr(III) per kg of body weight per day for a 60 kg adult[50].

The severe acute effects such as digestive tract disorder, hemorrhagic diathesis, and convulsion take place with the ingestion of about 1-5 g of chromate and ultimately cause death due to cardiovascular shock[50]. The workers exposed to Cr(VI) compounds showed genotoxic effects such as chromosomal abbreviations and the exchange of sister chromatids[50].

Occupational exposure of hexavalent chromium, Cr(VI), compounds shows a relation to death rate due to lung cancer. Humans exposed to Cr(VI) and a mixture of Cr(VI) compounds of diverse solubilities result in the greatest risk of respiratory carcinogenicity[55, 14]. Cr(VI) has been placed in Group 1 (carcinogenic to humans) and

Cr(III) in Group 3 (not carcinogenic to humans) by International Agency for Research on Cancer[55, 14].

7. Conclusion

Chromium being a primary toxic agent causes carcinogenicity in animals and humans. The extent of the health effect of chromium depends on its oxidation states. Cr(VI) is carcinogenic on inhalation and causes genotoxicity. As compared with Cr(III), Cr(VI) is more responsible for carcinogenicity. Without any ambiguity, chromium causes asthmatic responses on inhalations. It causes dermatitis allergy, ruptures nasal septum, and causes lung cancer. Exposure to Cr(VI) causes genetic alteration and is detrimental to human health.

On the other hand, excess exposure to chromium in mice develops patches on skin and lung cancer. Therefore, WHO (1984) recommended a maximum allowable concentration of 0.05mg/L of chromium as an international standard for drinking water. Even though hexavalent chromium is detrimental to health, the value of 0.05 mg/L is a provisional guideline for chromium until further information is available. There are many techniques for removing excess Cr(VI) from water, such as chemical precipitation, ion exchange, coagulation and flocculation, adsorption, and membrane filtration. Hence, any one of the above methods should be followed for the safe use of drinking water to reduce the intake of Cr(VI). The simple but effective technology should be disseminated in the local level to reduce the further risk of chromium intake in the future.

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