

Review

Chromium, an essential nutrient and pollutant: A review

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The increased use of chromium (Cr) in several anthropogenic activities has led to the subsequent soil, surface water and ground water contamination. It has wide applications in the dyes, stainless steel, leather tanning, electroplating of chrome, and wood preservatives industries. Chromium exists in the environment in several diverse forms such as Cr(0), Cr(III) and Cr(VI) species. Cr toxicity depends on its valence state. Cr(VI) which is regarded as being highly mobile is toxic, while Cr(III) is less mobile and less toxic. Cr(VI) being more mobile in soil, more toxic and a stronger oxidant penetrates more readily into the cell membranes than the trivalent form. Chromium does not bioaccumulate in plants and animals therefore high levels of chromium in the environment are highly toxic to plants and animals. Chromium toxicity in human beings is expressed in liver and kidney damage as well as skin lesions or rashes. Symptoms of chromium toxicity in plants include alterations in the seed germination process, reduced growth of roots, stems and leaves, which results in low total dry matter production and yield. This paper reviews properties of trivalent and hexavalent chromium with respect to their essentiality as micronutrients and their toxic harmful effects. Trivalent chromium is essential to normal carbohydrate, lipid and protein metabolism, by making the action of the hormone, insulin, more effective while the hexavalent chromium is toxic and involved in mutagenicity, carcinogenicity, and teratogenicity.

Key words: Chromium, micronutrient, toxicity, pollutant, metabolism.

INTRODUCTION

Contamination of the environment by toxic heavy metals is a worldwide problem (Mahvi, 2008). The development of industries such as mining, electroplating, fertilizer, pesticides, metals finishing, leather, painting and dyeing has led to the discharge of metallic species into the environment causing serious environmental pollution to both flora and fauna (Cossich et al., 2002). Heavy metallic species are an environmental concern because of their toxicity, bio-accumulation tendency, persistency in nature and non biodegradability (Garg et al., 2007).

The toxicity of heavy metals is well documented, with past disasters in Minamata tragedy (Japan) due to methyl mercury contamination and "Itai-Itai" due to contamination

of cadmium in Jintsu river of Japan (Friberg and Elinder, 1985; Kjellstrom et al., 1977). In order to assess the risk caused by heavy metal pollution, knowledge of the bioavailability of the different chemical species of the metals is essential (Eary and Rai, 1989). Among the toxic metal ions, chromium (VI) is a threat due to its toxicity even at low concentrations (Mahvi, 2008).

CHROMIUM OCCURRENCE AND SOURCES

Chromium (Cr) is the 17th most abundant element in the Earth's mantle and naturally occurs as chromite (FeCr_2O_4)

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Table 1. Uses of Chromium.

Form	Uses
Cr(0)	Stainless steel production
	Alloy production
	Metal and alloy manufacturing
Cr(III)	Metal and alloy manufacturing
	Brick lining
	Chrome plating
	Leather tanning
	Textiles
Cr(VI)	Copying machine toner
	Chrome plating
	Leather tanning
	Textiles
	Copying machine toner

in ultramafic and serpentine rocks or complexed with other metals like crocoite (PbCrO_4), bentorite $\text{Ca}_6(\text{Cr,Al})_2(\text{SO}_4)_3$ and tarapacaite (K_2CrO_4), vauquelinite ($\text{CuPb}_2\text{CrO}_4\text{PO}_4\text{OH}$), among others (Avudainayagam et al., 2003; Babula et al., 2008). The anthropogenic sources of Cr in the environment stem from the use of Cr in the metallurgy, refractory and chemical industries (Zayed and Terry, 2003). Chromium from anthropogenic sources can be released to soils and sediments indirectly by atmospheric deposition, but releases are more commonly from dumping of Cr-bearing liquid or solid wastes such as chromate by-products (“muds”), ferrochromium slag, or chromium plating wastes. Such wastes can contain any combination of Cr (III) or Cr(VI) with various solubilities (Stanin and Pirnie, 2004).

Chromium exists in the environment in three stable oxidation states, Cr(0), Cr(III) and Cr(VI) which have different toxicities and transport characteristics (Papassipoi et al., 2009). Cr(0) is the metallic form, produced in industry and is a solid with high fusion point usually used for the manufacturing of steel and other alloys. Cr (VI) typically exists as the oxyanion chromate (CrO_4^{2-}), dichromate ($\text{Cr}_2\text{O}_7^{2-}$) and the trioxide (CrO_3) have a high solubility in soils and water and very mobile in the environment. Additionally, Cr(VI) is considered the most toxic form of chromium, as it presents high oxidizing potential, high solubility, and mobility across the membranes in living organisms and in the environment (Becquer et al., 2003). The trivalent chromium, Cr(III), in contrast forms oxides, hydroxides and sulphates and is less toxic due to its insolubility in water. It presents lower mobility and is mainly bound to organic matter in soil and aquatic environments (Oliveira, 2012). Cr(III) has a tendency of forming hydroxide precipitates with Fe at typical ground water pH values. At high concentrations

of oxygen or Mn oxides, Cr(III) can be oxidized to Cr (VI) (Peralta-Videa et al., 2009).

USES OF CHROMIUM

Chromium and its compounds are very useful in everyday life, as presented in Table 1. It is used on a large scale in many different industries, including metallurgical, electroplating, production of paints and pigments, tanning, wood preservation, chromium chemicals production, and pulp and paper production (Zayed and Terry, 2003). Chromium is resistant to ordinary corrosive agents at room temperature, which explains its uses as an electroplated, protective coating. It is also used in ferrous and non-ferrous alloys, in refractories, and in chemicals. Ferrous alloys, mainly stainless steels, account for most of the consumption. These steels have a wide range of mechanical properties as well as being corrosion and oxidation resistant (Bielicka et al., 2005).

CHROMIUM CHEMISTRY

Chromium is a polyvalent element, found naturally in the air, soil, water and lithosphere (Vasilatos et al., 2008). Chromium can exist in several chemical forms displaying different oxidation states from zero to six, but in the natural environment, only trivalent and hexavalent chromium are stable (Skovbjerg et al., 2006; Zayed and Terry, 2003). Cr(III) is the most stable state in water with a standard potential of -1.74V as shown in Figure 1, therefore a considerable amount of energy would be needed to convert it to lower or higher oxidation states. The chromium oxidation states of I - III have negative potentials thus oxidation is favored while oxidation states

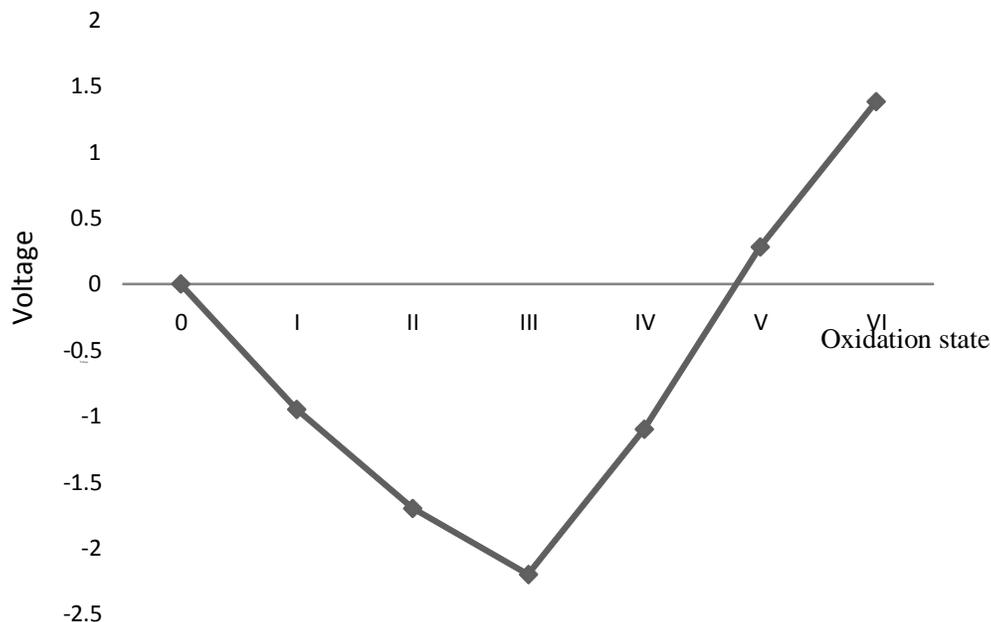


Figure 1. Oxidation state free energy diagram for chromium.

of IV - VI have positive potentials thus reduction is favored.

In acidic solutions, Cr(VI) has a very high positive redox potential (1.38 V) denoting that it is strongly oxidizing and unstable in the presence of electron donors (Figure 1). Under common environmental conditions of pH and Eh, Cr(III) compounds are sparingly soluble in water but Cr(VI) compounds are quite soluble (Swietlik, 1998). The resulting Cr(VI) solutions are powerful oxidizing agents under acidic conditions, but less so under basic conditions. For example, H_2CrO_4 is used for cleaning glassware in chemical laboratories by oxidizing organic residues. Thus, Cr(VI) is much more toxic and mobile in groundwater than the relatively immobile Cr(III). Depending on the concentration and acidity, Cr(VI) can exist either as chromate ion (CrO_4^{2-}) or as dichromate ion ($\text{Cr}_2\text{O}_7^{2-}$). The common dissolved Cr entities of Cr(VI) are the hydrogen chromate ion (HCrO_4^-), CrO_4^{2-} and $\text{Cr}_2\text{O}_7^{2-}$ (Testa, 2005). The entity that will dominate in a particular environment depends upon the specific conditions like pH, Eh, total concentration of Cr and the aqueous chemistry (Figure 2) (Rai et al., 1987).

At $\text{pH} > 6.5$, CrO_4^{2-} species dominate while at $\text{pH} < 6.5$, HCrO_4^- counterparts dominates at low concentrations ($< 0.03 \text{ mol/L}$), but at concentrations greater than 0.001 mol/L , HCrO_4^- ions begin to change to $\text{Cr}_2\text{O}_7^{2-}$ which becomes the dominant entity at concentrations greater than 0.03 mol/L (Palmer and Puls, 1994). HCrO_4^- imparts a yellow colour to the water while $\text{Cr}_2\text{O}_7^{2-}$ imparts an orange colour (Testa, 2005). In aqueous solution, Cr(III) dominates as soluble Cr^{3+} at $\text{pH} < 3$. As pH increases, Cr(III) hydrolyzes to $\text{Cr}(\text{OH})^{2+}$, $\text{Cr}(\text{OH})_3$ and $\text{Cr}(\text{OH})_4^-$ species. In slightly acidic to alkaline conditions, Cr(III)

precipitates as amorphous $\text{Cr}(\text{OH})_3$ which subsequently crystallize to $\text{Cr}(\text{OH})_3 \cdot \text{H}_2\text{O}$ (Rai et al., 1987).

The Chromium Eh-pH diagram (Figure 2) provides a generalized depiction of the aqueous species stabilities in different redox conditions. Chromium introduced into or existing naturally in the environment may undergo changes in oxidation state if the redox chemistry of the environment is altered or if chromium that is migrating as aqueous species encounters different redox conditions (Vasilatos et al., 2008).

Chromium(VI) is strongly oxidizing only under high redox potentials (Figure 3), and it reacts rapidly with numerous reducing agents found commonly in the environment. Eary and Rai (1988, 1989) reported that Cr(VI) is reduced in seconds by ferrous ions and in a matter of hours to days by ferrous-iron containing oxide and silicate minerals. Similar reactions were reported to occur in low-pH soils that contain small amounts of ferrous iron in clay minerals (Rai et al., 1988). Reduction might occurred rapidly even in the presence of dissolved oxygen. Chromium(VI) is also reduced by organic matter (Schroeder and Lee, 1975; Bartlett and Kimble, 1976; James and Bartlett, 1983) and by $\text{H}_2\text{S}(\text{g})$ (Smillie et al., 1981). Ferrous iron and organic matter are ubiquitous in soils and ground waters. Consequently, Cr(VI) is reduced to Cr(III) in many natural environments.

The oxidation potential for transforming the trivalent chromium into the hexavalent one is high, and the probability of transformation into a higher oxidation form in environmental conditions is reduced. Due to the high redox potential of the Cr(VI)/Cr(III), there are few oxidants present in natural systems that are capable of oxidizing Cr(III) to Cr(VI). Common oxidants include

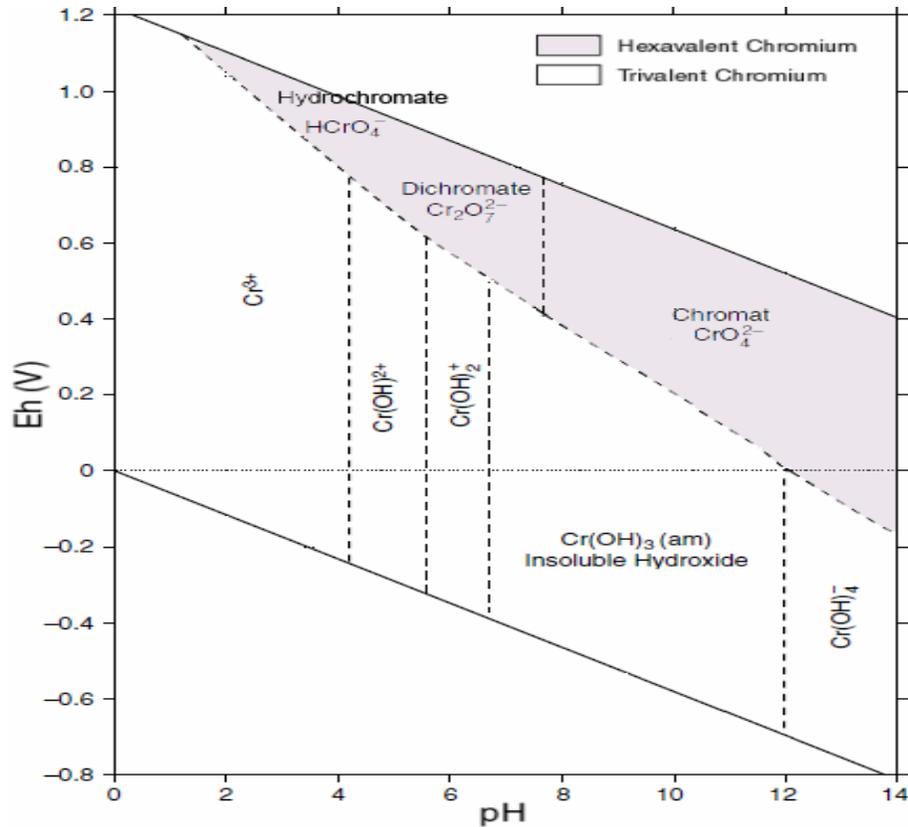


Figure 2. Eh-pH diagram for Chromium (Palmer and Wittbrodt, 1991).



Figure 3. Human carcinogen. Ingesting large amounts of it can cause kidney and liver damage and skin contact is known to lead to skin ulcers (Das and Mishra, 2008).

dissolved oxygen and manganese oxides. However, the oxidation of Cr(III) by dissolved oxygen is reported to be very slow (Schroeder and Lee, 1975; Eary and Rai, 1988), while the oxidation of Cr(III) by manganese oxides is reported to be more rapid. Therefore, manganese oxides are more important oxidants for Cr(III) in

groundwater systems (Rai et al., 1989). Despite the wide range of chromium in the soil and plants, the hexavalent chromium is rarely found in natural water above the concentration of the natural background, (1 $\mu\text{g/L}$). Higher concentrations indicate anthropogenic pollution (Brilly et al., 2003).

Table 2. Effects of Cr (III) and Cr (VI) on humans.

Cr(VI) Toxicant	Cr(III) Bio-element
Dermatitis	glucose metabolism (glucose tolerance factor)
Allergies	cholesterol and triglyceride levels decrease
Cancers	enzymes reactions
Mutations	body fat decrease
Teratogenic impact	muscle mass increase

CHROMIUM TOXICOLOGY

Chromium exists in the environment in several diverse forms such as trivalent (Cr(III)) and hexavalent, of which hexavalent chromium (Cr(VI)) is a carcinogen and a potential soil, surface water and ground water contaminant, while its reduced trivalent form (Cr³⁺) is much less toxic, insoluble and a vital nutrient for humans. Cr(III) occurs naturally in the environment and is an essential nutrient required by the human body (De Flora, 2000; Flegal et al., 2001; Gibb et al., 2006).

The sources of trivalent chromium include many fresh vegetables and fruits, meat, grains, and yeast (Das and Mishra, 2008). Relatively insoluble, it is the most prevalent form in surface soils where reduction processes (which convert chromium from the hexavalent to trivalent form) are most common. The hexavalent chromium also occurs naturally and most notably in water-saturated (reducing) conditions and is an indicator of human pollution. Inside cells, Cr(III) can complex with organic compounds and this interferes with metallo-enzyme systems at high concentrations (Kotas and Stasicka, 2000).

Oliviera (2012) noted that, of the several chromium oxidation states, only the trivalent and hexavalent forms are of interest. Chromium in its trivalent oxidation state is considered to be essential for human and animal nutrition, while the hexavalent species have been identified as being toxic, carcinogenic and destroy the DNA structure (Oliviera, 2012). Bielicka et al. (2005) also gave the positive effects of Cr(III) as well as the harmful effects of Cr(VI) (Bielicka et al., 2005) (Table 2).

CHROMIUM(VI) TOXICITY

Exposure to Cr(VI) exerts toxic effects on biological systems (Das and Mishra, 2008). Inhalation of Cr(VI) has been shown to cause perforation of the nasal septum, asthma, bronchitis, pneumonitis, inflammation of the larynx and liver and increased incidence of bronchogenic carcinoma while exposure due to dermal contact of Cr(VI) compounds can induce skin allergies, dermatitis, dermal necrosis and dermal corrosion (Bielicka et al., 2005). Cr(VI) is a powerful epithelial irritant and also considered a human carcinogen (IARC, 1990).

Studies of workers in various industries with exposure

to chromium compounds (including production of chromate and chromate pigments and chromium plating) showed that they are at risk of developing various cancers such as of the nasal or sinonasal cavity, the lung and the stomach (Beaumont et al., 2008). Several chromium(VI) compounds like calcium chromate, lead chromate (and its derived pigments), chromium trioxide and sodium dichromate have been tested for carcinogenicity by several routes in several animal species and strains and were shown to cause various cancerous tumors (IARC, 1990). Other Cr(VI) containing compounds such as sodium dichromate dehydrate (NTP, 2008), potassium chromate (Davidson et al., 2004) have also been shown to be carcinogenic.

Chromium(VI) compounds are known to exert genotoxicity both *in vivo* and *in vitro*. Several studies have shown lymphocytes of workers exposed to dusts of chromium(VI) compounds to have elevated frequencies of DNA strand breaks (Gambelunghe et al., 2003), sister chromatid exchange (Wu et al., 2001), and micronuclei (Benova et al., 2002). DNA single-strand as well as double strand breaks may arise due to the reaction of chromium(VI) with hydrogen peroxide, forming hydroxyl radicals (Quievryn et al., 2003). This induces mismatches during replication, leading to aberrant mismatch repair. Thus chronic exposure to toxic doses of chromium(VI) provokes the selective outgrowth of mismatch-repair-deficient clones with high rates of spontaneous mutagenesis, and thus, genomic instability (Reynolds et al., 2007). The binding of Cr(VI) to double stranded deoxyribonucleic acid (DNA), alters gene replication, repair, and duplication, a proposed mechanism for cancer formation (Kendrick et al., 1992).

Cr(VI) is capable of penetrating cell membranes and get reduced to Cr(III), with the released electrons damaging the membrane (Namieśnik and Rabajczyk, 2012). This reduction ($\text{Cr}^{6+} + 3e \rightarrow \text{Cr}^{3+}$) contributes to mutagenic changes in the organism. It is also one of the ways in which Cr⁶⁺ is removed from organisms. Reduction of Cr(VI) to Cr(III) in the immune system forms reactive intermediates, which, in combination with oxidative stress, tissue damage (the result of oxidation), and a cascade of cell collisions, give rise to cytotoxicity, genotoxicity, and carcinogenicity (Shrivastava et al., 2002). It is known that the reduction of Cr(VI) produces the following free radicals: Cr(V), Cr(IV) and Cr(III), which are responsible for the observed toxic and carcinogenic

effects (Li et al., 2011; Das and Mishra, 2008).

Based on epidemiologic investigations of workers and of experimental studies with animals, hexavalent chromium compounds were confirmed to be carcinogenic (Das and Mishra, 2008). Epidemiological studies conducted 40 years ago in the USA indicated a 10 to 30 fold- increased risk of lung cancer among workers in the chromate industry compared to the general population (Das and Mishra, 2008). In most studies, a positive correlation between the duration of exposure and lung cancer death was found. Gastrointestinal bleeding, tuberculosis and asthma infertility, birth defects, skin cancers, skin ulcers (Figure 3) and stillbirths have also been recorded among workers exposed to high levels of chromium(VI), (Das and Mishra, 2008). The International Agency for Research on Cancer (IARC) in 1990 concluded that there was sufficient evidence in humans for the carcinogenicity of chromium(VI) compounds as encountered in the chromate production, chromate pigment production, and chromium plating industries for the carcinogenicity of chromium(VI) compounds in humans based on the combined results of epidemiological studies, carcinogenicity studies in experimental animals, and evidence that chromium(VI) ions generated at critical sites in the target cells are responsible for the carcinogenic action observed.

Accidental or intentional ingestion of high doses of chromium (VI) compounds results in acute, potentially fatal, effects in the respiratory, cardiovascular, gastrointestinal, hepatic, renal, and neurological systems (IPCS, 2006; ECB, 2005; ATSDR, 2000). Some of these effects can be attributed to the corrosive nature of the compound (HSE, 2005). Typically, in one case a 17-year-old male died 14 h from respiratory distress with severe hemorrhages after ingesting potassium dichromate ($29 \text{ mg chromium(VI) kg}^{-1}$) in an attempted suicide (ATSDR, 2000). Caustic burns in the stomach and duodenum and gastrointestinal hemorrhages were noted (ATSDR, 2000). Several other cases have reported fatalities following ingestion of lower doses of chromium(VI). In one case, a 14-year-old boy suffered gastrointestinal ulceration and severe liver and kidney damage and died 8 days after hospitalization after ingesting potassium dichromate ($7.5 \text{ mg chromium(VI) kg}^{-1}$), while in another case, a 44-year-old man died of severe gastrointestinal hemorrhage one month after ingesting chromic acid ($4.1 \text{ mg chromium(VI) kg}^{-1}$) (ATSDR, 2000).

Developmental toxicity of Cr(VI) has been observed in animals, but to date there is not enough evidence to determine the potential for developmental effects on humans (Banu et al., 2008). Chromium has also been shown to be transferred from mother to young through the placenta and mother's milk and increased birth and developmental defects in children have been informally noted in areas of poorly regulated chromite mining, leather tanning (using Cr) and chrome production (Blacksmith Institute, 2007). However, no scientific

studies investigating the potential relationship between these effects and specific chromium exposures in these locations have been conducted. A study on chrome plating workers occupationally exposed to chromic acid (mean 2 to $200 \mu\text{g m}^{-3}$ chromium(VI) for 8 h a day for 0.2 to 23.6 years) found that at low concentrations (mean $<2 \mu\text{g m}^{-3}$), chromium(VI) workers developed smeary, crusty and atrophied septum mucosa and at higher concentrations ($2 \text{ to } 200 \mu\text{g m}^{-3}$ chromium(VI)) nasal irritation, mucosa ulceration and atrophy and septum perforation were observed (IPCS, 2006). These effects may not have resulted from exposure levels actually measured, but also from earlier exposures. Another study on electroplating workers exposed to chromic acid ($>0.1 \text{ mg m}^{-3}$ chromium(VI)) for less than 1 year reported frequent incidences of coughing, expectoration, nasal irritation, sneezing, rhinorrhea, nose-bleed, nasal septum ulceration and perforation (ATSDR, 2000).

Further evidence also suggests that exposure to chromium(VI) may induce occupational asthma and chromate sensitive workers acutely exposed to chromium(VI) compounds may develop asthma and other signs of respiratory distress (IPCS, 2006; ATSDR, 2000). For example, a study of 5 individuals with a history of contact dermatitis to chromium, found that exposure via nebulizer to a potassium dichromate aerosol containing 0.035 mg ml^{-1} chromium(VI) resulted in decreased forced expiratory volume, facial erythema, nasopharyngeal pruritis, blocked nose, coughing and wheezing (IPCS, 2006; ATSDR, 2000).

Some studies of workers exposed to airborne chromium(VI) have found increased levels of low-molecular-weight urinary proteins, such as retinol binding protein, β 2-microglobulin and tubular antigens, indicative of early kidney changes, for example one such study identified a lowest - observed - adverse - effect - level (LOAEL) of $4 \mu\text{g m}^{-3}$ chromium(VI) (IPCS, 2006). Work-related cough or dyspnoea, production of phlegm, and shortness of breath was also noted in workers exposed to dust containing chromium oxide at an approximate concentration of 240 to $480 \mu\text{g m}^{-3}$ chromium(III) (IPCS, 2006).

CHROMIUM(III) AS AN ESSENTIAL NUTRIENT

Trivalent chromium is found in a wide range of foods, including egg yolks, whole-grain products, high-bran breakfast cereals, coffee, nuts, green beans, broccoli, meat, brewer's yeast, and some brands of wine and beer (Cefalu and Hu, 2004). Chromium is also present in many multivitamin/mineral supplements, and there are also specific chromium picolinate (CrP) supplements that contain 200 to 600 μg chromium per tablet (FSA, 2002). The U.S. National Academy of Sciences has established the Recommended Daily Allowances for chromium as 50 to 200 $\mu\text{g/day}$ for adult men and women, which is also

the Estimated Safe and Adequate Daily Dietary Intake (ESADDI) for chromium for children aged 7 years to adulthood (Anderson, 1997; 1998). Trivalent chromium is essential for animal and human health at trace levels (Ali and Aboul-Enein, 2006) and plays an essential role in many metabolic processes (García et al., 1999). Chromium(III) is present in the active centers of many enzymes, which is why it is classified as one of the essential elements. It facilitates the transport of glucose from the blood to the cells (Chen et al., 2009). The presence of Cr reduces the demand for insulin (the hormone regulating the level of glucose in the blood), thus Cr(III) helps to regulate blood sugar levels by collaborating with insulin in facilitating the uptake of glucose into cells (Horvath et al., 2008; Sahin et al., 2007; Lai et al. 2006). It also cooperates with insulin in protein synthesis. Cr(III) is an important bioelement, a deficiency of which disturbs glucose tolerance. It has been found, inter alia, that the glucose tolerance factor (GTF) contains Cr(III), which positively affects the action of insulin (Brown et al., 1986).

In the +3 oxidation state, chromium has been shown to reduce the risk of myocardial infarction (heart attack) and the development of atherosclerosis by lowering the concentration of total cholesterol and its low-density lipoprotein (bad cholesterol) fraction and raising the high-density lipoprotein (good cholesterol) level (USA- EPA, 1991b). Its deficiency has been associated with impaired glucose tolerance, fasting hyperglycemia, glucosuria, elevated percent body fat, decreased lean body mass, maturity-onset diabetes, cardiovascular disease, decreased sperm count, and impaired fertility (Valko et al., 2005). On the other hand, Cr(III) has been shown to have a detrimental effect on various components of the immune system, giving rise to immune stimulation or immune inhibition (Shrivastava et al., 2002). Chromium(III) also plays an important function in lipid metabolism thus reducing the risk of atherogenesis (Pechova and Pavlata, 2007), increase in lean body mass (Anderson, 2000), and promotion of weight loss (Morris et al., 1995).

CONCLUSION

This review has highlighted the two sides of Chromium (Cr) as an essential nutrient and a health hazard. Specifically Cr(VI), is considered harmful even in small doses while Cr(III) is considered essential for good health in moderate intake. As a micronutrient, Cr(III) is required for carbohydrate, lipid and protein metabolism while on the other hand the hexavalent form is predominantly involved in mutagenicity, carcinogenicity, and teratogenicity.

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