ISSN NO. 2320-5407

Journal homepage: http://www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH

RESEARCH ARTICLE

Chromium Toxicity and its Health Hazards

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Manuscript Info

Manuscript History:

Received: 22 May 2015
Final Accepted: 21 June 2015
Published Online: July 2015

Key words:
Carcinogenic, chromium, health hazards, ingestion, toxicity

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Abstract

This research article presents a review on the toxicity of chromium and its health hazards on living organism based on the previous researches done. Chromium is a toxic heavy metal which is found in environment in different oxidation states ranging from -2 to +6. But the most stable forms are trivalent and hexavalent chromium. Trivalent chromium has poor absorption inside the cell as compared to hexavalent chromium. The most common exposure routes of chromium to humans are ingestion, dermal contact and inhalation. The primary health hazards caused by chromium are bronchial asthma, lung and nasal ulcers and cancers, skin allergies, reproductive and developmental problems and this chromium is carcinogenic in nature. When taken in excess it may cause death also.

INTRODUCTION

Many industrial wastes are discharged into water regularly. Most of these wastes are degraded slowly by living organisms into smaller harmless molecules; however some are not easily broken down by them instead they accumulate to levels which could pose serious health hazards to organisms. Some heavy metals in low concentrations are essential for life but at high concentration they cause toxicity, carcinogenicity, allergenicity and sometimes they also inhibit the activity of sensitive enzymes (Koropatrick and Leibbrandt, 1995). Chromium (Cr) is one of the major industrial wastes produced from many industries like textiles, tanneries, electroplating, metallurgical which causes health issues in humans and animals and also affects marine life (Ajmal et al., 1996, Moncur et al., 2005).

Chromium is the most abundant mineral in Earth's crust. Cr has an atomic number 24 in periodic table and has a relative atomic mass of 51.996 and it occurs in almost all oxidation states ranging from -2 to +6. But in environment Cr is mostly stable in trivalent and hexavalent form. Cr which is present in 0 oxidation state is biologically inert and is not naturally present in Earth's crust while Cr (III) and Cr (VI) are originated from industries. The available form of chromium is as halides, oxides and sulphides. It is the +2 oxidation state of chromium which is unstable and can be easily be oxidized to +3 forms in the presence of air.

The concentration of chromium in drinking water i.e. the federal maximum concentration level (MCL) is 100µg/l (USEPA, 1998). In California MCL value is 50µg/l (Calder, 1988).According to Indian Standard the maximum tolerance for total chromium in water supplies is 0.05 mg/L (Benazir et al., 2010). Combustion of oil and coal also release a certain amount of Cr into the environment (ATSDR, 2000).

Absorption and Metabolism-

Chromium and its compounds gets absorbed in human body through the exposure to oral, dermal and inhalation routes. Cr (III) is less absorbed than Cr (VI) and this leads to a difference in their transport methods to cells.

Cr (VI) enters into the cell via a non specific anion channel by facilitated diffusion while Cr (III) enters by passive diffusion or phagocytosis. Human liver, kidney, spleen and bone have more concentration of Cr in comparison to other organs (NTP, 2008). Cr (VI) has the ability to easily penetrate in RBC. Because of its bioavailability Cr (VI) enters into RBC and gets converted into Cr (III) which binds to the cellular components and then it is unable to leave RBC. The structure of cells somewhat resembles to the structure of RBC due to this, Cr (VI) can be easily uptaken by other cells. Also due to oral, intravenous and intra tracheal administration of Cr (VI) its level in tissues increases (Yamaguchi et al., 1983; Edel and Sabbioni, 1985; NTP, 2007).

Absorption of Cr depends on some factors which are particle size, oxidation state and its solubility but majorly on the interaction with biomolecules in lungs. The main reduction of Cr (VI) to Cr (III) takes place in tissue of lungs (U.S. EPA, 1998).

Trivalent chromium [Cr (III)]-
Oral administration of these compounds results in 99% of the dose recovered in faeces and 94% recovered after duodenal administration. In both the cases, only 0.5% was excreted through urine which indicated poor absorption of Cr(III). On inhalation by humans, Cr concentration in urine increases indicating respiratory absorption and by extensive studies we can conclude that Cr (III) has poor absorption (Paine and Dayan, 2001).

Hexavalent chromium [Cr (VI)]-
It is the second stable form of chromium and has a strong oxidizing property. Cr (VI) binds to oxygen and form chromate and dichromate. Cr (VI) has the ability to cross the biological membrane and reacts with proteins and nucleic acid. Through faecal test it is concluded that 10% of the dose is absorbed in gastrointestinal tract. Cr (VI) gets reduced to Cr(III) in lower respiratory tract by pulmonary alveolar macrophages. Cr (VI) enters into blood stream and then taken up by RBC, gets reduced and bound to haemoglobin. Cr (VI) has three half life excretion i.e., 7h, 15-30 days and 3-5 years (Dayan and Payne, 2001).

General pathways for Chromium exposure-
Cr is ubiquitous in nature and ranges in different concentration in environment. Cr (III) is usually present in environment and Cr (VI) is totally produced by human activities. General exposure to Cr (VI) is through emissions from industries. Cr (VI) is used as anticorrosive agent in various cooling system, combustion eg- Cigarette smoke and ash from power plants (OEHHA, 2000).

Mostly, all food materials contain some amount of Cr ranging from 20-500µg/Kg. The highest level of Cr in food founds in meats, mollusks and crustaceans (U.S. EPA, 1985). A worker who works in Cr industries experiences the highest exposures to Cr(VI) and mainly the exposure is through respiratory and dermal routes (NTP, 2008).
The major source for chromium exposure is food. The oral intake for infants of 1 yr is 33-45 µg/day, for children of 11 yr is 123-171 µg/day and for adults it is 246-343 µg/day (Rowbotham et al., 2000).
The most common exposures routes for chromium are as under-

1. Ingestion
2. Dermal contact
3. Inhalation

Human health is adversely affected due to the exposure of chromium and these health effects are categorized in two types, carcinogenic and non-carcinogenic and have three types of exposure duration (Guertin, 2004):

1. Acute (14 days or less)
2. Intermediate (75-364 days)
3. Chronic (365 days or more)

But Unites States Environmental Protection Agency had reported that chromium is carcinogenic only if taken through the route of inhalation.

Human studies-
In humans the oral route exposure to Cr is due to contaminated well water (U.S. EPA, 1998). Certain effects have been reported like mouth ulcers, indigestion, acute tubular necrosis, vomiting, abdominal pain, kidney failure and even death (Beaumont et al., 2008).

Oral Exposure- It has been studied that Cr (III) has an essential role in protein and lipid metabolism but there is one study which has reported that Cr(III) cause oral toxicity in humans (Kusiak et al., 1993). He reported that human mortality gets increased because of stomach cancer in workers (gold miners) in Ontario, Canada. Some other factors are also responsible for stomach cancer including chromium like arsenic, mineral fiber, diesel emission and aluminium powder. According to author stomach cancer is mostly found in the workers of under the age of 60.

Inhalation exposure- Exposure to chromium is majorly due to chromium industries and it includes all mixed exposure of Cr (III) and Cr (VI). Cr (III) is absorbed by the lung tissue during the reduction of Cr (VI) to Cr (III) (O' Flaherty, 1996).

In United States, six chromium industries are examined and 23 people are studied. It has been reported that 14 of the workers worked there for 2-7 hr/day with the continuous handling of chromic acid, due to which Cr (VI) is generated in range of 0.12-5.6 mg/m^3. These workers suffered from many problems like perforated septum, nasal tissue damage, inflamed mucosa, nosebleed and ulcerated septum. And the remaining 9 workers reported only inflamed mucosa because they do not handle chromium directly (Bloomfield and Blum, 1928). In recent studies it has been cleared that Cr is responsible for asthma, wheezing, coughing and other respiratory problems (Langard, 1980).

Animal studies-

It has been reported that if Cr (VI) is given to rats and mice in drinking water then it shows the ability to cross the placenta and can easily reach to foetal tissue (Junaid et al., 1996; Elsaieed and Nada, 2002).

Some experiments have been done by NTP in 2008 that if Cr is given through drinking water in rats and mice different effects are seen which includes cellular infilteration in the liver, pancreatic and small intestine. In addition, there are clear evidences of carcinogenic activity in both the sexes of rats and mice. In mice skin tumors are reported due to the presence of Cr (VI) in drinking water along with small intestine carcinogenicity and oral cavity carcinogenicity was observed in rats (Costa and Klein, 2006).

It has been reported that if a hairless mice is exposed to UV light then skin tumors starts appearing but if Cr is given to them in drinking water with UV light then these tumors gets increased. If $K_2Cr_2O_7$ is present in drinking water then it increases the number of UV induced skin tumors and so it supports the concern of health problems for human exposure to Cr in drinking water (Davidson et al., 2004).

Toxic effects-

Dermal exposure- workers which were exposed to Cr containing material were reported to have chronic ulcers of the skin and irritative dermatitis. Chromates and Cr (III) which is released from alloys and Cr plated objects are responsible for dermatitis.

Respiratory exposure- due to the exposure to respiratory tract it causes irritation in workers who worked in chromate and Cr (VI) producing industries. It has been reported that it cause ulceration and perforation of the nasal system.

International agency for research on cancer had reported sinonasal cancer due to Cr. Workers who were in contact with Cr (VI) was reported to Rhinitis bronchospasm and pneumonia. It also leads to lung cancer. It has been confirmed by doing experiments on animals that Cr(VI) is toxic by inhalation but not by ingestion or skin contact.
Animal studies on mice had revealed that if mice are treated with Cr(VI) then it develops lung tumors from exposure to 4.3 mg/m3 of Cr(VI) (Nethesheim et al., 1971, ATSDR, 2000). If chromium is taken up by oral route then it gets 100% reduced in the gut. This shows that Cr(VI) is not toxic if ingested. It is only toxic if taken through inhalation.

Mechanism of chromium toxicity-

It ia already reported that Cr(VI) is more toxic than Cr(III). Cr(VI) enters more readily into the cell in comparison to Cr(III) but it also gets reduced to Cr(III) ultimately after entering into the cells. By the help of carboxylate, sulphate and phosphate carrier system Cr(VI) was transported through mammalian cell membrane.

When Cr(VI) gets reduced intracellular some short lived species also generates like pentavalent and tetravalent species with affinities for cellular components but differ from trivalent chromium. Cr(V) is stabilized by glutathione.

If Cr(VI) reduction takes place at a distance from the target cell. But if it occurs near to the target site then it will activate Cr. Once they all gets absorbed, Cr compounds occurs as Cr(III). Most important co-factors in intracellular reduction of Cr(VI) are glutathione and cysteine.

Mode of Action (MOA) and effects of Chromium

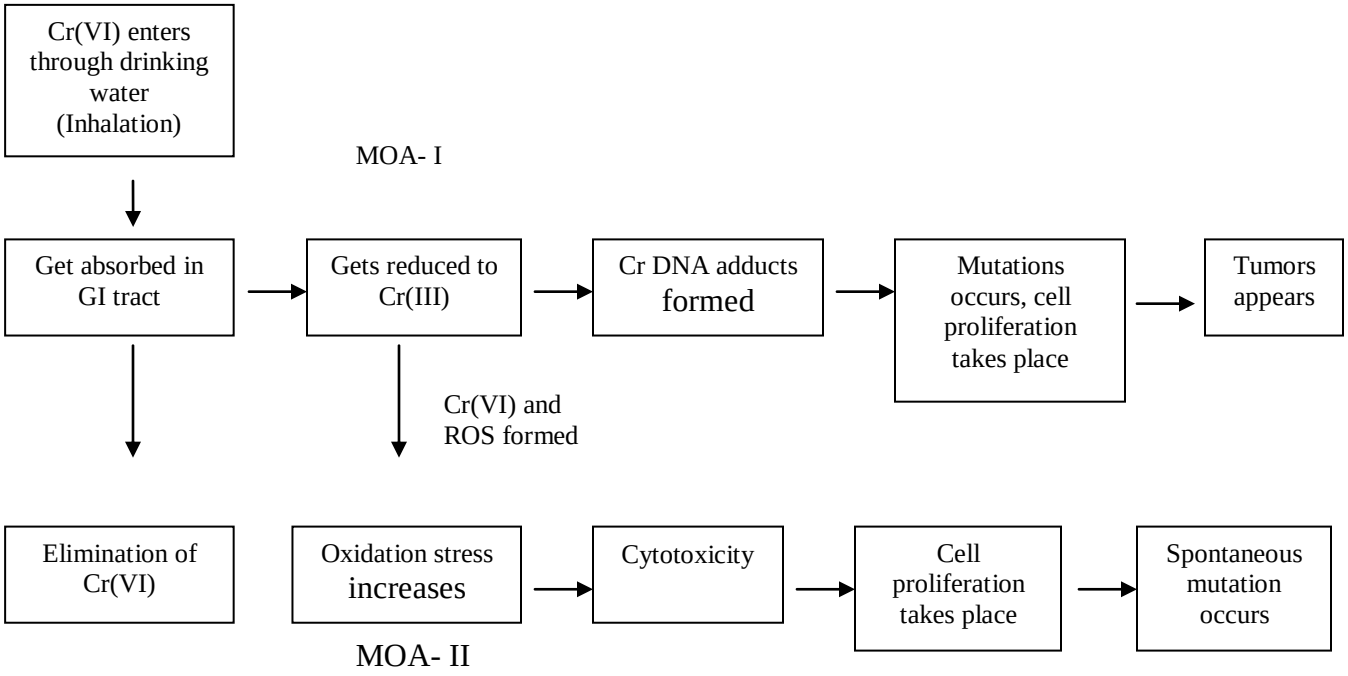

Figure I: MOA- I (McCaroll et al., 2010); MOA- II (Thompson et al., 2011)

Cr(VI) toxicity is based on an oxidative impairment of DNA (Cohen et al., 1993). It has been reported that due to the intermediate form Cr(V) which was produced from the reduction of Cr(VI) to Cr(III) is responsible for genotoxicity (Stearns et al., 1995). While extracellular reduction of Cr(VI) to Cr(III) has been reported as a protective reaction (De Flora et al., 1989). The main reduction process takes place in lungs and stomach during a NAD(P)H- dependent ascorbate which convert Cr(VI) to Cr(III). Due to the inhalation of chromium anatomical changes occurs in lungs, kidney and liver. After inhalation of chromium perforation of nose septum takes place and the lungs gets affected with hyperaemia and erosion (Lee et al., 2002).

This Cr(III) which gets produced during the intracellular reduction of Cr(VI) gets binds to DNA and form Cr(III)-DNA adduct and it's also responsible for the cross linkage of DNA and protein which leads to mutagenesis (Costa et al., 1997).

Allergy to chromium-

Cr(VI) compounds due to their solubility and reactivity causes sensitization and allergic reaction. Due to the tetravalent form of CrO_7 contact dermatitis is reported.

- Skin allergy- Cr(VI) is an extremely sensitized agent. Workers who worked in Cr salt industries were exposed to Cr and they were reported to have contact dermatitis and it becomes a serious problem in industries. A very high proportion of population which comes in contact with Cr compounds shows a positive result of skin patches which becomes a serious issue.
- Respiratory system- People who came in contact or get exposed to welding fumes from stainless steel are reported to have Asthma. It is caused by Cr(VI) compounds. The maximum amount of Cr(VI) which gets inhaled by air is 0.02µg/m3.

Autoimmunity- many of the reports have mentioned that due to the exposure to Cr and its compounds anti-DNA antibodies are formed but the relationship between them is still unclear. Many of the diseases are caused due to the exposure to Cr like hepatitis and renal damage and cancers.

Specific investigation-

Due to an allergy, keratinocytes are the first cells who get exposed to allergen. Then they activate Antigen Presenting Cells and produce cytokines due to which the immune system gets activated. If dichromates are treated for up to 48h then it may leads to the increased production of TNFα and some heat shocked proteins which latter cause toxicity.

Conclusion-

There has been a vast study on chromium and its effects on human health. It has been concluded that chromium is responsible for the toxic effects in humans and it cause allergenicity and carcinogenicity in humans and in animals also. Hexavalent chromium is mainly responsible for all carcinogenic activity in comparison to trivalent chromium. With all the toxic effects there are clear evident of asthmatic responses sometimes with respiratory exposures. It is responsible for dermatitis allergy; perforation in nasal septum and some cases of lung cancer is also evident. Due to the exposure to chromium some genetic alteration also takes place which is harmful for human health. It has been stated earlier that in mice excess of chromium cause patches on skin and lung cancer. But there is still no clear evidence of activity of chromium ions as an allergen to humans.

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