

Chapter 10

Health Risk Linked to Cr Toxicity in Food and Environment



Abhishek Pathak, Varun Asediya, Pranav Anjaria, and Satya Pal Singh

Abstract The increasing prevalence of exposure to high concentrations of chromium in food and the environment has made chromium toxicity a pressing public health issue. This review provides an overview of chromium toxicology, sources of exposure, and strategies for mitigating the associated health risks and consequences. Hexavalent chromium, a toxic form of the metal, has been causally linked to numerous negative health outcomes, including carcinogenicity, genotoxicity, oxidative stress, and inflammation. Exposure to hexavalent chromium primarily occurs through contaminated food and the environment, especially in areas close to industrial sites. Food can become contaminated through soil, water, air, and the use of chromium in food packaging and processing equipment. The highest chromium concentrations have been detected in certain food items such as grains, spices, and meat products. To minimize exposure to chromium toxicity, it is crucial to be aware of the sources of chromium in one's diet and environment. Opting for chromium-free food packaging and limiting consumption of foods with high chromium concentrations can reduce exposure. The government and industry must also take steps to reduce chromium release into the environment and ensure the safety of food and water supplies. In conclusion, this review highlights the significance of comprehending the health risks posed by chromium toxicity and taking necessary precautions to reduce exposure. Further research is necessary to gain a more comprehensive understanding of the toxic effects of chromium and develop effective prevention strategies.

A. Pathak (✉)

Department of Veterinary Pharmacology and Toxicology, Apollo College of Veterinary Medicine, Jaipur, Rajasthan, India
e-mail: drpathak1704@gmail.com

V. Asediya

Animal Nutrition Research Station, AAU, Anand, Gujarat, India

P. Anjaria

Department of Veterinary Public Health and Epidemiology, C. V. Sc & A.H, Kamdhenu University, Anand, Gujarat, India

S. P. Singh

Department of Veterinary Pharmacology and Toxicology, G. B. Pant University of Agriculture and Technology, Pantnagar, Uttarakhand, India

Keywords Chromium toxicity · Environmental toxicant · Genotoxicity · Carcinogenicity · Adsorption and bioremediation

10.1 Introduction

The overexploitation of Earth's natural resources has resulted in the depletion of these finite resources, and the presence of environmental pollutants in the air, soil, water, and food chain is a significant global concern. These pollutants impact ecosystem functions and decrease food and environmental safety. With ongoing urbanization, driven by population migration to urban areas, the discharge of untreated industrial waste into the environment is expected to increase, exacerbating the presence of hazardous inorganic and organic contaminants in aquatic ecosystems, including rivers, lakes, estuaries, and coastal regions.

Humans are exposed to toxic metals, including Chromium(VI) compounds, through various pathways, including skin absorption, ingestion of contaminated soil, or inhalation of air particles. These metals can accumulate in both plants and animals, entering the food chain and posing potential health risks for humans. Approximately 90% of human exposure to hazardous metals is through contaminated food, accounting for 30% of all human cancers globally. Chromium, element 24 on the periodic table, was discovered in 1797 by French scientist Louis Vauquelin and its name is derived from the Greek word "chroma," referring to the distinctive hues present in its compounds. Chromium is a hard, glossy, steely-grey metal with an atomic weight of approximately 52 g/mol and a high melting point, as well as reflective qualities.

The potential health hazards of Chromium (VI) compounds in urban areas have been recognized since the first report of cancer in workers exposed to Chromium over 130 years ago. Subsequent epidemiological studies, particularly in occupational settings, have established a correlation between exposure to Chromium (VI) and specific disease phenotypes, such as bronchogenic carcinoma. Recent studies have implicated Chromium in the development of stomach cancer through various modes of exposure and mechanisms, such as genomic instability or epigenetic alterations, and have associated it with a range of health problems, including respiratory, hepatic, renal, reproductive, and neurological issues. It is important to note that the relationship between human susceptibility and health problems caused by exposure to toxic agents is dependent on individual factors, rather than direct.

10.2 Physiochemical Properties

Chromium, which has an atomic number of 24 and a relative atomic mass of 51.996, exhibits multiple oxidation states, with the most prevalent being +2, +3, and +6. The instability of divalent chromium in air presents difficulties in comprehending its biological implications, necessitating the evaluation of the chemical and biological

properties of its +3 and +6 oxidation states. Hexavalent chromium, in particular, is characterized by its strong oxidizing potential, requiring 1.33 eV of energy to oxidize trivalent chromium to hexavalent chromium. In biological systems, trivalent chromium remains unoxidized, while hexavalent chromium is reduced to an insoluble form upon entering red blood cell membranes. This reduction results in the incorporation of trivalent chromium into cellular components and its subsequent prevention from release from erythrocytes. The most common forms of chromium compounds and their respective applications are illustrated in Fig. 10.1. For more than a century, chromium has been utilized extensively in various industries, primarily in the form of alloys and soluble salts that contain hexavalent chromium ions. Exposure to excessive levels of chromium, commonly encountered in industries such as chromate manufacturing, metal plating, alloy production, and metal welding and forming processes, has been linked to numerous hazardous effects on human health, including irritation, carcinogenicity, and allergenicity. The hexavalent chromium ion has been identified as the primary culprit of these adverse health effects, while trivalent chromium compounds, widely used in certain industrial processes, have only been acknowledged as irritants, but not carcinogens or allergens. The incidence and prevention of dermatitis, asthma, and cancer resulting from chromium exposure have been widely studied.

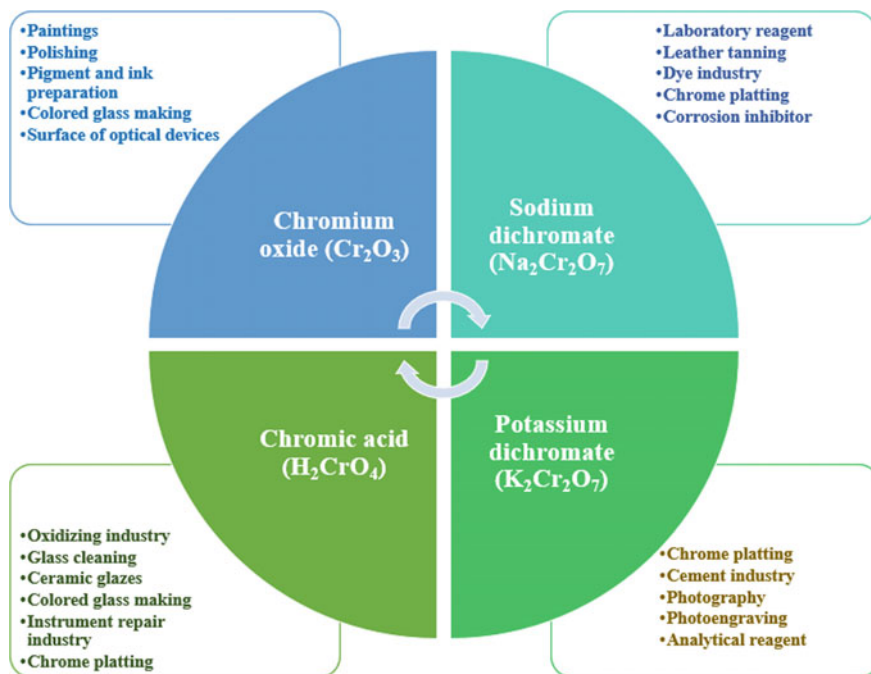


Fig. 10.1 Common forms of chromium and their uses

10.3 Geology of Chromium

Chromium is a transition metal that is widely distributed in the Earth's crust and is found in a variety of mineral forms. Out of the 82 documented mineral species, 23 contain chromium in the hexavalent state (Cr[VI]), which is of great scientific and industrial interest due to its unique properties. The most abundant chromium mineral is chromite (FeCr_2O_4), which is a complex oxide mineral composed of iron, magnesium, aluminum, and chromium in both the trivalent (Cr[III]) and tetravalent (Cr[IV]) states. The chromium content of chromite ranges from 45 to 80% and is the primary source of chromium metal, which is widely used in the production of stainless steel and other alloys. Chromite is also used as a refractory material, due to its high melting point and good thermal stability.

Chromite ore is typically formed through the intrusion and solidification of molten magma, and is typically associated with ultramafic rocks such as peridotites, pyroxenites, and dunites. Chromite deposits can be found in the form of stratiform or podiform deposits, and can contain up to 400 parts per million (ppm) of chromium. Although the occurrence of Cr[VI] in nature is limited, it can be produced through the oxidation of Cr[III] in chromite through interaction with birnessite, a manganese oxide mineral. The presence of Cr[VI] in the environment can pose a risk to human health and the environment, as it is a strong oxidizing agent and has been linked to respiratory problems, skin irritation, cancer, and changes in the composition and function of soil microflora.

Therefore, it is of great importance to carefully manage and control the release of Cr[VI] into the environment, to minimize its harmful effects. Further research is needed to fully understand the geochemistry of chromium minerals and the processes involved in their formation and alteration, in order to optimize the production of chromium and minimize the potential environmental impacts associated with its extraction and use.

10.4 Source of Exposure

The presence of Chromium (III) in the diets of both animals and humans is due to its naturally occurring state in soil and vegetation, as well as its inclusion in animal feed. However, the concentration of Chromium (Cr) may vary based on several factors such as the geology of the area, proximity to industrial operations, and its form of availability. Although Chromium compounds are prevalent in the environment, they are recognized as persistent contaminants as a result of their extensive industrial use during the 21st century. Exposure to Chromium (VI) in humans and animals primarily occurs via inhalation of airborne emissions, including industrial and automotive fumes, cigarette smoke, and other sources. Contamination of water is another avenue of exposure and results from industrial releases and the leaching of wastewater, often due to inadequate waste management practices (Welling et al. 2015). This mode of

exposure is particularly concerning as it affects the entire population through oral consumption of contaminated water, unlike inhalation, which is typically limited to occupational exposure.

Under normal environmental conditions, Chromium(III) exhibits low solubility in water within a pH range of 6–9. The oxidation of Chromium(III) to the hexavalent state (Cr-VI) is often facilitated by catalytic reactions with Mn-bearing minerals, while reduction of hexavalent chromium in the environment is primarily driven by Fe(II) in solution or Fe(II)-bearing minerals, sulfides, and organic matter (Loyaux-Lawniczak et al. 2001). The presence of hexavalent chromium (Cr-VI) in the environment is primarily a result of human activities. The largest contributors to anthropogenic Cr contamination are cement manufacturing and handling practices during construction, accounting for 70% of steel production. The widespread use of chromium sulfate in the tanning industry, with nearly 90% of all leather produced globally containing the compound, is another significant contributor. Occupational exposure to Cr is substantial among workers in over 80 industries, including, but not limited to, welding, electroplating, metal finishing, wood preservation, and the production of textiles, dyes, and pigments (IARC 1990). Human activities result in the release of approximately 75,000 tons of chromium into the environment, of which 33% is the toxic form of Cr-VI, while natural sources account for the remaining 54,000 tons (Kieber et al. 2002). Research has shown that precipitation can effectively remove Cr from the atmosphere due to its high solubility and mobility, leading to leaching into surface water from soil. The estimated atmospheric residence time of Cr is 10 days, and the transmission of Cr through the food chain is depicted in Fig. 10.2.

Approximately 12 billion tons of shipping-grade chromite, a significant portion of the global reserves, can be found in several key locations. The largest concentration of these resources is located in South Africa, accounting for 84% of the total, followed by Zimbabwe with 6%, Kazakhstan with 5%, and India with 2%. The remaining 3% is contributed by countries including Brazil, the United States, Canada, Russia, Finland, and others. India is the world's second-largest producer of chromite ore, further emphasizing the significance of its chromite reserves (Das and Singh 2011).

10.5 Pharmacokinetics

Chromium (Cr) exists in two stable oxidation states in nature, trivalent chromium (Cr III) and hexavalent chromium (Cr VI) (IARC 1990). The toxicity resulting from exposure to chromium is dependent on various factors, including the chemical form, oxidation state, solubility, and bioavailability of the relevant chromium compounds. Chromium compounds can alter their oxidation state through alkylation and interact with biological molecules upon ingestion. The physiological consequences of exposure to chromium, especially Cr VI, have been shown to impact multiple systems within the human body. This includes the skin, where exposure can lead to allergic reactions, skin rashes, dryness, and swelling (IARC 1990), the respiratory tract,

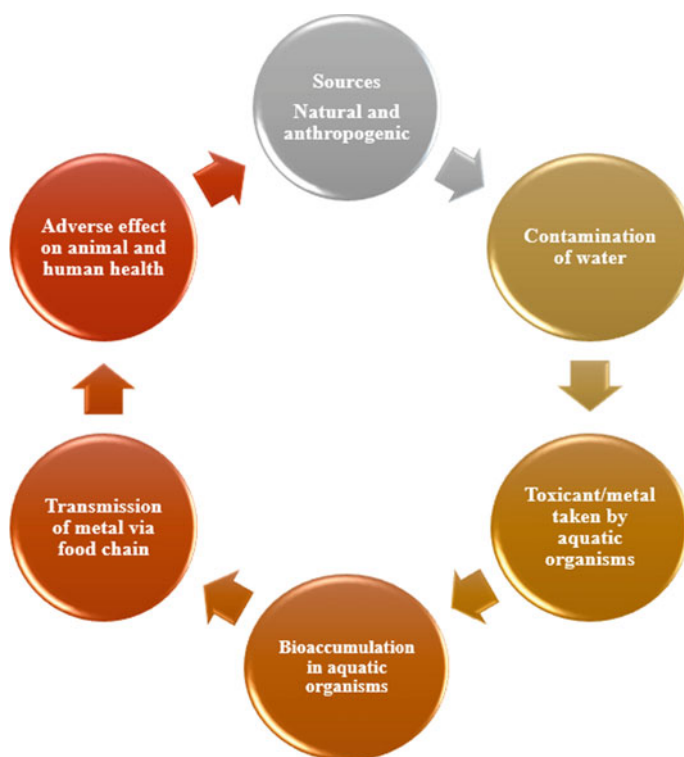


Fig. 10.2 Transmission of chromium via the food chain

which can experience ulceration and perforation of the nasal septum, irritation of the pharynx and larynx, asthmatic bronchitis, nose irritations, nosebleeds, and even lung cancer (IARC 1990), and the gastrointestinal system, causing upset stomachs and ulcers, as well as the renal system (IARC 1990). The mechanisms of Cr III entry into cells have been partially characterized, including slow processes such as passive diffusion or phagocytosis (IARC 1990). Although limited, our understanding of these processes suggests that Cr III exhibits low membrane permeability, is capable of accumulating within cells to levels hundreds of times greater than its extracellular concentration, and therefore presents a high chemical potential for intracellular reactions (Fang et al. 2014). Chromium III transport across the cell membrane may be facilitated by transferrin (Tf), a globulin and main iron III transport protein in the bloodstream, which has been demonstrated to transport various metals, including Cr III, due to its similarities in size and charge to the ferric ion. However, *In-vitro* studies using HepG2 (human hepatoma) cells, which are rich in Tf receptors, suggest that Tf functions as a natural defense against the toxicity and genotoxicity of ingested Cr III by inhibiting its cellular accumulation (Fang et al. 2014). Interferometry studies have indicated that the mechanism of exclusion and efflux of Cr III from cells is due to a lower affinity of cell receptors for Cr III transferrin (Tf) compared to iron III Tf,

which is a critical step in the Tf cycle (Edwards et al. 2020). The debate continues regarding the adequacy or slow rate of release of Cr III from serum Tf to have a physiologically relevant effect. Over 38 variants of the highly polymorphic Tf gene have been identified. Most studies have suggested that Cr VI cannot interact directly with DNA and does not exhibit genotoxic effects under conditions that do not favor reduction (Wakeman et al. 2017). The “uptake-reduction model,” which describes the intracellular reduction and generation of intermediate species, including Cr V and Cr IV, is considered essential in understanding the pathological effects of this element (DeLoughery et al. 2014).

10.6 Mechanism of Toxicity

Extensive research on hexavalent chromium (Cr[VI]) has established that its toxicity surpasses that of trivalent chromium (Cr[III]). The superior toxicity of Cr[VI] can be attributed to its enhanced permeability, enabling its cellular uptake and eventual reduction to Cr[III]. Following intracellular reduction, the occurrence of short-lived pentavalent and tetravalent chromium species is documented, which exhibit dissimilar binding tendencies to cellular components as compared to Cr[III].

The pentavalent form of chromium is stabilized by glutathione and is considered a detoxification process if its reduction occurs away from the site of toxicity or genotoxicity. However, if the reduction takes place within or near the cell nucleus, it may activate Cr and contribute to the initial binding of cellular macromolecules. The intracellular reduction of Cr[VI] is largely dependent on the presence of glutathione and cysteine, although ascorbic acid, microsomes in the presence of NAD/NADH, microsomal cytochrome P450, mitochondria, hemoglobin, and glutathione reductase may also play a role. The mechanism of toxicity of chromium is depicted in Fig. 10.3.

The chromium requirement for humans and animals remains a subject of debate, with some sources positing that it is an essential trace element for insulin-mediated glucose metabolism, while others question its biological or toxicological effects. Despite its poor permeability across cell membranes, Cr[III] is capable of interacting with biomolecules such as DNA. However, at present, there is a lack of conclusive evidence demonstrating the essentiality of Cr in biomolecular or physiological processes (Fig. 10.4).

The transport of Cr[VI] compounds, such as chromate anions, into cells is facilitated through protein channels, driven by both passive diffusion and saturable transport. The anion exchanger 1 (AE1) is the primary carrier responsible for transporting chromate, sulfate, and phosphate ions. In contrast, other proteins do not bind significantly to Cr[VI] under similar conditions. The entry of Cr[III] into the nucleus is hindered by the formation of kinetically inert octahedral complexes.

A minor portion of Cr[VI] may penetrate the nucleus through an active protein transport mechanism that involves histone sequences, lysine- or arginine-rich peptides, or nuclear proteins. Chromatin formation is favored by the association of histones with DNA polyanions, and the reversible binding through electrostatic

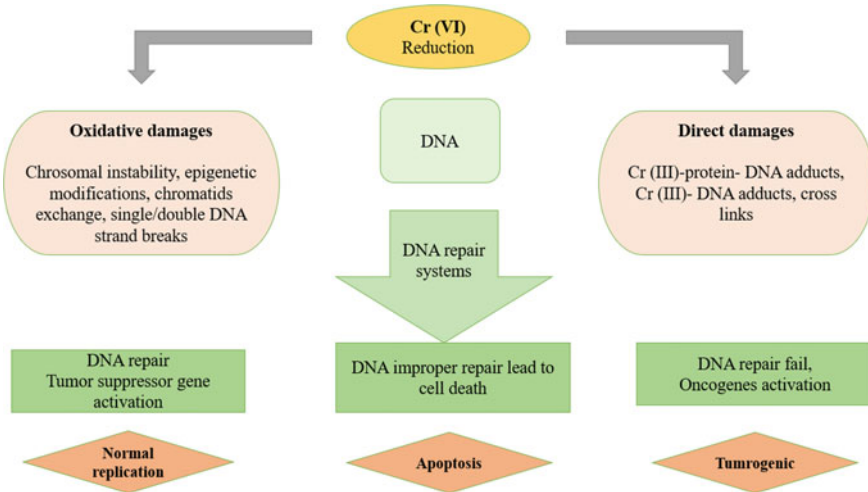


Fig. 10.3 Mechanism of action of chromium toxicity

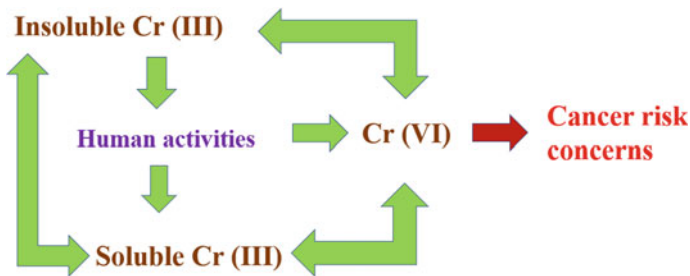


Fig. 10.4 Chromium in drinking water and cancer risk

attraction and hydrogen bonds may contribute to this process. The interaction of Cr[VI] with cytoplasmic elements may also impact the uptake of nuclear protein complexes and subsequent binding, leading to the generation of highly genotoxic Cr[III]-DNA adducts.

10.7 Health Risks Linked with Chromium Exposure in the Food

The bioavailability of chromium in dietary sources has been the focus of extensive research in recent decades. Evidence from studies has revealed that the extent to which chromium is absorbed from food sources is influenced by several factors, including the chemical form in which it exists, the processing and cooking techniques utilized,

as well as the presence of other nutrients, such as ascorbic acid, which can augment its absorption. Furthermore, individual factors such as age, gender, and nutritional status may also impact the bioavailability of chromium from dietary sources. Investigations have established that trivalent chromium in the form of chromium III picolinate or chromium yeast demonstrates greater bioavailability compared to other forms of chromium, such as chromium chloride, which is characterized by low bioavailability. Food sources that are abundant in chromium III picolinate include whole grains, fruits, vegetables, and meats, while chromium yeast is commonly present in beer. The bioavailability of chromium from food sources is dependent on several factors, including the chemical form in which it exists, processing and cooking techniques, and the presence of other nutrients that may influence its absorption. As a result, it is crucial to consume a diverse diet that comprises of chromium-rich food sources to meet the daily recommended intake of chromium.

10.7.1 Absorption of Chromium in the Gut

The absorption of chromium is regulated by various proteins, such as the low molecular weight chromium-binding substance (LMWCr) and glucose tolerance factor (GTF), which enhance its uptake and utilization within the body. Renal excretion of chromium is limited, and its half-life in the body has been estimated to be approximately 20–30 days. The daily requirement of chromium is typically considered to be in the range of 20–35 μg , however, the precise requirement may vary based on factors such as age, sex, health status, and other dietary components. Chronic exposure to elevated levels of chromium, particularly hexavalent chromium (Cr(VI)), can result in toxicity and associated health problems such as skin irritation, respiratory issues, and genotoxicity. Hence, it is essential to maintain a balanced and appropriate intake of chromium to promote optimal health and wellness.

10.7.2 Bioavailability of Chromium in Food

Chromium, a trace mineral, plays a critical role in the regulation of glucose metabolism through its interaction with insulin. The extent to which chromium is absorbed and utilized by the body, known as bioavailability, is subject to a multitude of factors, including the chemical form of chromium in food, processing and preparation methods, and the presence of co-occurring minerals and nutrients. Studies have shown that processing methods, such as refining, milling, and cooking, can result in a substantial reduction of chromium content in food, with the degree of reduction differing among food types. For instance, refined grains, such as white flour and white rice, have been found to have lower chromium levels compared to their whole grain counterparts. The interaction of chromium with other minerals and nutrients also affects its bioavailability. The absorption of chromium may be

hindered by high levels of iron, zinc, and calcium, while its uptake can be facilitated by the presence of ascorbic acid, glucose, and nicotinic acid. In conclusion, to attain sufficient chromium intake, it is recommended to consume a varied diet comprising unprocessed whole foods, and to limit the consumption of refined and processed foods. Furthermore, adequate ascorbic acid intake may enhance the bioavailability and utilization of chromium.

10.7.3 Dietary Sources of Chromium

Chromium is an essential trace mineral that has been demonstrated to play crucial roles in glucose and insulin metabolism, as well as lipid metabolism. The recommended daily intake of chromium for adults is estimated to be in the range of 20–35 μg , although this may vary based on various factors such as age, gender, and overall health status. Dietary sources of chromium include whole grains, fruits, vegetables, animal-derived products, and dairy products. Some foods that have been reported to contain higher concentrations of chromium include whole wheat, beer yeast, potatoes, dairy cheese, and leguminous plants such as beans, lentils, and peanuts. Of the various forms of chromium present in the diet, trivalent chromium (chromium III) is considered the most biologically active and is best absorbed by the body. This form of chromium is present in foods such as brewer's yeast, whole grain bread, and potatoes.

In contrast, hexavalent chromium (chromium VI) is a less biologically active form that is toxic in high doses, and is primarily found in industrial processes and can contaminate food and water sources. It is well established that the bioavailability of chromium from dietary sources can be influenced by a range of factors, including processing and preparation methods, the concurrent presence of other minerals and nutrients, and the chemical form of the chromium. To ensure adequate chromium intake, it is recommended to consume a varied diet that includes a range of chromium-rich foods.

10.7.4 Chromium Levels in Food and Drinking Water

Chromium is found in drinking water in both trivalent (Cr(III)) and hexavalent (Cr(VI)) forms. Cr(III) is considered an essential nutrient with no adverse effects on human health, while Cr(VI) has been identified as a highly toxic substance associated with an increased risk of cancer and other health problems (NTP, 2011). To protect public health, the US Environmental Protection Agency (EPA) has established a Maximum Contaminant Level (MCL) of 100 μg per liter ($\mu\text{g}/\text{L}$) for total chromium in drinking water (EPA 2019). Chronic exposure to elevated levels of Cr(VI) in food and drinking water can pose a significant threat to human health,

with potential consequences including lung cancer, respiratory problems, skin irritation, and allergic reactions (NTP 2011). Long-term exposure to elevated levels of Cr(VI) has also been linked to kidney and liver damage, as well as an increased risk of cardiovascular disease (Schrauzer and Shrestha 2002). Adequate chromium intake, estimated to be between 50 and 200 μg per day, can be obtained through a well-balanced diet. Monitoring the levels of chromium in food and drinking water is crucial in ensuring their safety and mitigating potential health hazards.

10.7.5 Effects of Chromium in Food

The genotoxic potential of chromium represents a significant health concern as research has established that exposure to the element may lead to DNA damage both *In vitro* and *In vivo*, thus increasing the risk of neoplastic transformation (Akerstrom et al. 2013). Moreover, chromium has been implicated in inducing oxidative stress and inflammation, thereby contributing to the progression of chronic diseases, including cardiovascular disease and diabetes (Bhatnagar et al. 2007). The cardiovascular system is also susceptible to the impacts of chromium exposure, as evidenced by the findings of Kaur et al. (2010), which demonstrate an association between high chromium levels and elevated risk of cardiovascular disease, including coronary heart disease, myocardial infarction, and cerebrovascular incidents. Chromium has also been shown to disrupt lipid and glucose metabolism, thus increasing susceptibility to type 2 diabetes (Schneider et al. 2013).

The impact of chromium on the endocrine system has garnered significant attention in the scientific community, with research indicating that chromium can alter insulin sensitivity, potentially contributing to the development of type 2 diabetes (Schneider et al. 2013). Additionally, chromium has been shown to possess estrogenic properties, which can interfere with the normal functioning of the endocrine system and result in reproductive and developmental consequences (Bhatnagar et al. 2007).

10.7.5.1 Effect of Chromium on Liver

Chromium is a trace element that is essential for proper glucose and lipid metabolism. However, excessive exposure to chromium, particularly in its toxic form (chromium VI), can lead to serious health effects, including liver toxicity. Studies have shown that chronic exposure to elevated levels of chromium can cause liver injury, as evidenced by elevated levels of liver enzymes and histopathological alterations. The liver is a critical metabolic organ that is involved in the processing and elimination of toxic substances, and as a result, it is particularly susceptible to chromium toxicity. The mechanism by which chromium toxicity causes liver injury involves the induction of oxidative stress and inflammation.

Oxidative stress is a condition in which there is an imbalance between the production of free radicals and the ability of the body to neutralize them. This can result in cellular damage and contribute to liver injury. Inflammation, on the other hand, is a response to injury or damage that can further contribute to liver injury in the presence of excessive chromium. A study by Eskandari et al. (2020) investigated the toxic effects of chromium on the liver and found that chronic exposure to elevated levels of chromium led to elevated levels of liver enzymes, histopathological alterations, and oxidative stress. Another study by Akinola et al. (2019) similarly found that chromium toxicity induced oxidative stress and inflammation in the liver, ultimately leading to liver damage and increasing the risk of liver disease. The literature supports the idea that chronic exposure to elevated levels of chromium can result in liver injury through the induction of oxidative stress and inflammation. It is important to limit exposure to excessive levels of chromium to prevent adverse health effects, particularly to the liver.

10.7.5.2 Effect of Chromium on Kidney

Studies have shown that chronic exposure to elevated levels of chromium can have a damaging effect on the kidney, leading to renal dysfunction and heightened susceptibility to kidney disease. The nephrotoxic effects of chromium have been linked to oxidative stress and inflammation within the renal tissue, which can result in decreased renal function. A study by Abbas et al. (2018) investigated the nephrotoxic effects of chromium on the kidney and found that exposure to elevated levels of chromium induced oxidative stress and inflammation in renal tissue, leading to decreased renal function and increased susceptibility to kidney disease.

Chromium is eliminated from the body primarily through the kidneys, which makes the kidney particularly vulnerable to the toxic effects of this element. Oxidative stress and inflammation can cause damage to renal tissue and impair renal function, ultimately leading to decreased kidney function and an increased risk of kidney disease. Exposure to elevated levels of chromium can result in renal dysfunction and damage through the induction of oxidative stress and inflammation within the renal tissue. It is important to limit exposure to excessive levels of chromium to prevent adverse health effects, particularly to the kidney.

10.7.5.3 Effect of Chromium on the Cardiovascular System

The cardiovascular system is susceptible to the detrimental effects of chromium toxicity, as demonstrated by the correlations between elevated levels of chromium exposure and increased risk of cardiovascular diseases, including but not limited to atherosclerosis and coronary artery disease (Powers 2009). Furthermore, chromium toxicity has been shown to elevate blood pressure, thereby increasing the likelihood of hypertension (Flynn 2014). Given the crucial role of the cardiovascular system

in facilitating the transport of oxygen and nutrients throughout the organism, it is a vital target for the toxic effects of chromium.

10.7.5.4 Chromium and Carcinogenicity: Possible Link to Cancers

The study conducted by Wang et al. (2012) aimed to assess the relationship between exposure to chromium (VI) in drinking water and colorectal cancer using a mouse model. The findings revealed a heightened incidence and growth of tumors as a result of exposure to chromium. This phenomenon was attributed to the activation of the Wnt/beta-catenin signaling pathway triggered by reactive oxygen species (ROS). Furthermore, it is believed that the interaction between ROS and reactive nitrogen species (RNS) with cellular macromolecules, such as DNA, lipids, and proteins, plays a vital role in cancer toxicity and progression (Aggarwal et al. 2019).

In another investigation by Patlolla et al. (2009), Sprague-Dawley rats were given potassium dichromate through intraperitoneal injection at doses of 2.5, 5.0, 7.5, and 10 mg/kg body weight per day for 5 consecutive days. The results showed a considerable rise in both ROS and malondialdehyde levels in the liver and kidney, as well as a dose-dependent increase in the activities of superoxide dismutase and catalase. Additionally, the study demonstrated a dose- and time-dependent DNA damage 24-, 48-, 72-, and 96 h post-treatment.

Lung cancer

Various studies demonstrated that the genotoxic effects of hexavalent chromium on human lung epithelial cells were investigated. The results showed that exposure to hexavalent chromium caused significant DNA damage and alterations in the p53 and p16 tumor suppressor genes. Additionally, the study found that hexavalent chromium exposure increased oxidative stress, as evidenced by the upregulation of reactive oxygen species and the depletion of antioxidant enzymes. These findings provide further evidence of the carcinogenic potential of hexavalent chromium in the lung and its ability to induce oxidative stress and DNA damage.

Another study by Wang et al. (2019) investigated the effect of hexavalent chromium on lung tumorigenesis in a mouse model. The results revealed that hexavalent chromium exposure significantly enhanced lung tumor formation and growth, as well as the activation of multiple oncogenic pathways, including the epidermal growth factor receptor (EGFR) and phosphoinositide 3-kinase (PI3K) signaling pathways. These findings suggest that hexavalent chromium plays a critical role in the development of lung cancer and highlights the need for increased protective measures for workers exposed to this carcinogenic form of chromium.

Stomach cancer

A study by Chen et al. (2014) showed that chromium (VI) exposure can lead to an increase in oxidative stress and DNA damage in gastric mucosal cells, thereby increasing the risk of stomach cancer development. The findings were supported by subsequent research which showed that hexavalent chromium can trigger oxidative

stress, genomic instability, and inflammation in the stomach, which can result in increased susceptibility to gastric cancer. Moreover, studies have also reported that chromium-induced oxidative stress can affect the normal function of the cell cycle and cause DNA damage, thereby increasing the risk of stomach cancer (Zhou et al. 2017). These findings highlight the importance of limiting exposure to chromium, especially among individuals who are at an elevated risk of stomach cancer.

10.7.6 Interactions with Minerals and Nutrients in Food

Chromium toxicity has been implicated in a wide range of negative health outcomes, including nutritional deficiencies. Elevated levels of chromium have been shown to obstruct the absorption of vital nutrients, such as iron, zinc, and calcium, leading to adverse effects on health and well-being, including anemia, compromised immune function, and impaired bone health. One widely recognized manifestation of chromium toxicity is the association between elevated levels of chromium and decreased absorption of iron, which can result in iron-deficiency anemia. Characterized by a reduced red blood cell count and diminished capacity of the blood to transport oxygen, iron-deficiency anemia is a prevalent issue, particularly among women and children, and has far-reaching impacts on health and well-being.

In addition to its effects on iron absorption, chromium toxicity can also negatively impact the uptake of other crucial minerals, such as zinc. As a vital nutrient, zinc plays a key role in several physiological processes, including immune response, wound healing, and cell division. Zinc deficiency can result in various health problems, including impaired immune function, dermatological issues, and impaired wound healing. Furthermore, chromium toxicity has the potential to affect bone health by interfering with calcium metabolism, a critical component of healthy bones. This can result in decreased bone density and elevated risk of fractures and osteoporosis.

10.8 Health Risks Linked with Chromium Exposure in the Environment

10.8.1 Toxic Effect of Chromium in Human

The International Agency for Research on Cancer (IARC), a subsidiary of the World Health Organization (WHO), has classified hexavalent chromium compounds (Cr(VI)) as Category 1 human carcinogens based on comprehensive epidemiological evidence linking exposure to lung cancer (Seidler et al. 2013). Human exposure to Cr(VI) can result in a plethora of adverse health outcomes, including, but not limited to, skin and nasal irritation, ulcers, eczema, dermatitis, and lung cancer (Focardi et al. 2013). The toxicity of Cr(VI) can arise through multiple mechanisms, including

oxidative protein modifications, DNA mutations, genotoxicity, cytotoxicity, carcinogenicity, and chromosomal damage (Al Osman et al. 2019). Furthermore, high levels of Cr(VI) exposure via inhalation can lead to respiratory issues such as asthma and coughing, as well as anemia, ulcers, and gastrointestinal irritation (Yang et al. 2020). Prolonged exposure to elevated levels of Cr(VI) and related compounds can result in significant health problems.

Studies have indicated a positive correlation between Cr(VI) exposure and the incidence and mortality of several cancers, including lung, bladder, larynx, kidney, testicles, thyroid, and bone (Deng et al. 2019). An ecological study conducted in Greece in 2011 found elevated levels of Cr(IV) in drinking water, with concentrations ranging from 41 to 156 g/L, and an increase in the incidence of genitourinary, lung, and liver cancers among women (Linos et al. 2011). A study conducted in India in 2012 found an increased prevalence of gastrointestinal and dermatological issues in individuals exposed to groundwater contaminated with Cr(VI) (Sharma et al. 2012). The mechanisms underlying Cr toxicity and carcinogenicity include DNA damage, genomic instability, and production of reactive oxygen species (ROS) (Pavesi and Moreira 2020).

Both Cr(VI) and Cr(III) have the potential to generate ROS (Pavesi and Moreira 2020). Chromium-induced carcinogenicity results in transcriptional regulation disruption and DNA damage. This disruption of chromatin architecture leads to alterations in chromatin accessibility and nucleosomal positions at both local and genome-wide levels. Chromium-induced DNA damage can take various forms, including DNA-Cr-protein crosslinks, DNA inter- and intrastrand crosslinks, single- and double-strand breaks (SSBs and DSBs, respectively), and p53 point mutations (Thompson et al. 2011). The toxicological effects of chromium on humans and animals are depicted in Fig. 10.5.

Numerous In-vitro studies have established the interaction of chromium(III), Cr(III), with nucleic acids (Fang et al. 2014). The formation of binary and ternary DNA adducts has been observed in Cr(III) exposure, with ternary adducts being more toxicologically significant in mammalian cells (Zhitkovich 2005). The four primary ternary adducts identified are Cr(III) ascorbate, Cr(III) cysteine, Cr(III) histidine, and Cr(III) glutathione (Salnikow and Zhitkovich 2008). The presence of DNA-protein crosslinks has also been detected in human lung adenocarcinoma cells (A549) (Macfie et al. 2010). Rapidly dividing cells, such as cancer cells, can exhibit collapse of the replication fork during DNA replication, resulting in cell cycle arrest and activation of the p53 tumor suppressor, leading to apoptosis (Wilhelm et al. 2020).

Studies have established that exposure to hexavalent chromium (Cr(VI)) can induce DNA damage and carcinogenic potential, as demonstrated by the detection of DNA strand breaks (SSBs and DSBs) and protein-chromium (Cr)-DNA crosslinks in liver cells of F344 rats following administration of potassium chromate via drinking water for three weeks (Coogan et al. 1991). The mechanisms behind the carcinogenic effects of Cr(VI) exposure are multifactorial, encompassing factors such as tissue type, cell specificity, concentration of Cr(VI), duration of exposure, and the reactivity of intermediate forms of Cr(V), Cr(IV), and Cr(III) (Ferreira et al. 2019).

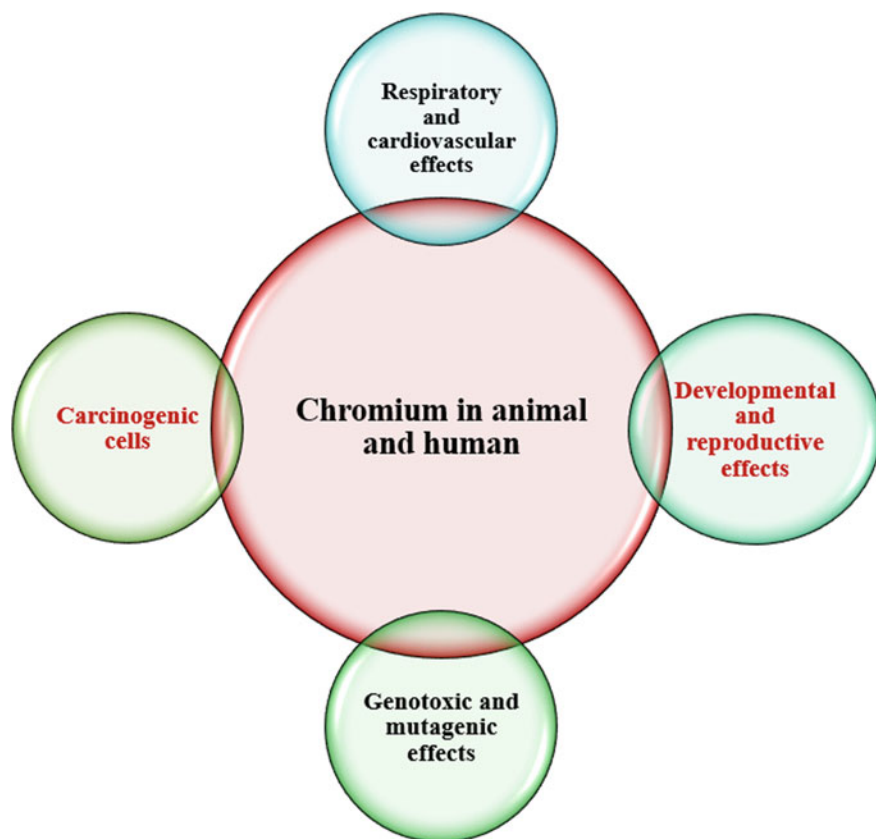


Fig. 10.5 Toxicological effects of chromium on animal and human

Cr(VI) does not bind directly to macromolecules or DNA, but instead forms intermediates with cellular reductants, including Cr(V), Cr(IV), and Cr(III) (Zhitkovich 2005). The intermediates generated during Cr(VI) reduction can trigger Fenton-type reactions in the presence of hydrogen peroxide, resulting in hydroxyl radical formation and oxidative stress (Yao et al. 2008). Additionally, the formation of Cr-Asc (ascorbate), Cr-GSH, and Cr-Cys (cysteine) crosslinks also contributes to oxidative stress (Yao et al. 2008). Cr(VI)-induced oxidative stress targets cells' DNA and lipid contents, causing DNA damage and lipid peroxidation, respectively. This oxidative stress can result in additional cellular harm, cell death through necrosis and apoptosis, and even promote tumor growth and development at low to medium levels of ROS production.

10.8.2 Chromium and Antimicrobial Resistance

The unique characteristics of chromium, particularly its antimicrobial properties, have garnered significant scientific attention. Chromium compounds have been utilized in the medical field for their ability to inhibit the growth of various microorganisms, including bacteria and fungi. However, their use as antimicrobial agent's raises concern about the development of antibiotic resistance, a major public health concern. Antibiotic resistance occurs when microorganisms evolve mechanisms that enable them to withstand the effects of antimicrobial agents, potentially leading to the selection of antibiotic-resistant strains of microorganisms over time. Hexavalent chromium has been demonstrated to possess potent antimicrobial activity against a wide range of microorganisms. However, the challenge of comprehending resistance mechanisms employed by these microorganisms to counteract chromium's antimicrobial properties remains. For instance, studies have shown that bacteria like *Escherichia coli* have evolved mechanisms such as reducing hexavalent chromium to less toxic trivalent chromium or utilizing efflux pumps to pump out chromium ions, leading to reduced toxicity and decreased efficacy of chromium compounds as antimicrobial agents. Furthermore, there is concern regarding the toxic effects of hexavalent chromium on human health, including respiratory problems, skin irritation, and genetic damage due to long-term exposure. The ongoing research and regulatory evaluations surrounding the safety and efficacy of chromium compounds as antimicrobial agents aim to determine the best approach for utilizing their antimicrobial properties while minimizing potential harm to human health and the environment.

10.8.3 Chromium Induced Genotoxicity

Chromium and its various compounds have been extensively studied with regards to their genotoxic effects. A wealth of evidence from a range of genetic tests demonstrates that hexavalent chromium compounds, with varying water solubility, exhibit significant genotoxicity. Chromates, dichromates, and other forms of chromium (VI) such as chromium trioxide, have been found to induce DNA damage, gene mutations, sister chromatid exchanges, chromosomal aberrations, cell transformations, and dominant lethal mutations in various *In vitro* and *In vivo* test systems, including human and animal cells.

In contrast, the genotoxicity of trivalent chromium compounds remains less well understood. While these compounds have been shown to exhibit reactivity with purified DNA and isolated nuclei, few studies using cellular test systems have shown positive results, and these were often observed at high concentrations and under specific conditions. The lack of cellular reducing agents in cell-free systems precludes the reduction of hexavalent chromium to less toxic forms, and the prevalent hypothesis posits that the genotoxicity of hexavalent chromium is due to the highly reactive intermediates generated during cellular reduction, such as Cr(V) and Cr(IV). The role

of cellular reducing agents such as ascorbate and sulfhydryl compounds in reducing Cr(VI) remains unclear, as does the contribution of intermediates such as hydroxyl, cysteinyl, and thionyl radicals to chromium-induced carcinogenesis.

Chromium-mediated reactions have also been shown to generate oxygen-free radicals and activate the transcription factor NF- κ B, which regulates genes involved in inflammation, immunity, and apoptosis. The intricate and complex nature of these mechanisms underscores the ongoing challenge of fully understanding chromium carcinogenicity. Currently, inhaling hexavalent chromium is classified as a known human carcinogen by the International Agency for Research on Cancer (IARC), while the significance of other valence states, the underlying mechanisms, and the impact of solubility remain subjects of ongoing investigation and debate.

10.8.4 Chromium Induced Hepatotoxicity

The carcinogenic properties of chromium (Cr) and its derivatives have far-reaching implications for the environment, industry, and occupational health. Chromium plays a vital role in the metabolic processes of carbohydrates, lipids, and proteins (Zhao et al. 2019). It can enter the bloodstream through various pathways, including the skin, lungs, and perforations, before being eliminated by the liver (Xiao et al. 2012). The reduction of trivalent Cr to tetravalent Cr can generate reactive oxygen species (ROS), leading to oxidative damage and various forms of toxicity, including hepatotoxicity, cardiotoxicity, and gene toxicity (Balakrishnan et al. 2013). High doses of hexavalent Cr have been shown to cause liver damage (Xiao et al. 2012). Accumulation of Cr in the nuclei and mitochondria of cells can result in DNA modifications and changes in cellular regulatory mechanisms (Venter et al. 2015). Histopathological studies have indicated that Cr exposure is associated with nuclear pyknosis, central phlebectasia, and hepatocyte degeneration (Tian et al. 2018).

10.8.5 Effects on Immune Response

The findings of the studies on the effects of hexavalent chromium and other metal elements on cultured human lymphocytes emphasize the criticality of comprehending the toxicity of chromium, particularly hexavalent chromium, in human health. The observed decreases in blastogenesis and immunoglobulin synthesis following chromium uptake by human lymphocytes have far-reaching implications for the immune system and overall health, as the proper functioning of these cells is crucial for maintaining the body's defense against infections and diseases. Extensive research has revealed that exposure to high levels of hexavalent chromium can lead to DNA damage, which in turn increases the likelihood of cell mutations and the development of cancer. Despite these findings, the exact mechanisms by which hexavalent

chromium affects the functioning of human lymphocytes remain unclear and require further investigation.

It is imperative to consider the potential impacts of chromium exposure on vulnerable populations, such as pregnant women, infants, and individuals with pre-existing health conditions, as they may be more susceptible to the toxic effects of chromium. Further research is needed to gain a comprehensive understanding of the potential harm to the health of these populations. The results of the studies on the effects of hexavalent chromium on human lymphocytes highlight the urgency for continued research on the toxicity of chromium and the need for caution in the use and exposure to chromium compounds. These findings have far-reaching implications for public health and inform the development of safe and effective chromium-based products.

10.8.6 Chromium Induced Allergic Reactions

In light of the limited current understanding of chromium-induced allergies, further research is crucial to gain a comprehensive insight into the potential of chromium compounds to elicit allergic responses. A multidisciplinary approach incorporating a thorough understanding of the underlying immune mechanisms, the extent and nature of exposure, and the susceptibility of various populations to chromium-induced allergies is necessary to establish the foundation for the development of effective strategies for the prevention and management of these reactions.

Studies have demonstrated that chromium-based products, such as chromium-plated jewelry, can elicit skin reactions through the process of contact sensitization, whereby the immune system recognizes chromium as a foreign substance and generates an immune response upon subsequent exposures. There is also evidence suggesting that chromium-containing alloys used in dental implants may result in systemic allergic reactions, as a result of the release of chromium ions into the bloodstream. Given the significance of immune responses in the development of allergies, a better understanding of the mechanisms involved in chromium-induced allergies is imperative. This will enable the creation of effective strategies for the prevention and management of these reactions, and ensure the safety and well-being of the public, particularly among susceptible populations such as individuals with pre-existing health conditions or those who are exposed to high levels of chromium.

10.8.7 Skin Allergy

The relationship between exposure to chromium compounds and the incidence of contact dermatitis has been extensively documented in the scientific literature. Notably, a decrease in the prevalence of this condition in Scandinavia can be attributed to reduced exposure to chrome-plated objects. However, the underlying mechanisms by which chromium induces sensitization and elicits a skin reaction, particularly

at low levels of exposure, remain poorly understood. The observation of cross-reactivity among sensitized individuals and the results of lymphocyte transformation and migration inhibition tests provide evidence that trivalent chromium compounds serve as the underlying allergens for adverse skin reactions. Furthermore, oral ingestion of hexavalent chromium salts has been shown to induce sensitization, suggesting that hexavalent chromium can enter the body and trigger a systemic immune response.

Clinically, chromium-induced contact dermatitis is characterized by a delayed hypersensitivity response, which progresses over time and is evidenced by histological findings on biopsy. However, the minimum duration and amount of exposure required for sensitization remain unclear and require further investigation. While the evidence linking chromium exposure, particularly hexavalent chromium, to contact dermatitis is substantial, many questions about the underlying mechanisms and risk factors associated with this condition remain unanswered. Further research is needed to advance our understanding of chromium-induced contact dermatitis and to develop effective strategies for its prevention and management.

10.8.8 Effects on Macrophages

Inhaling chromium compounds can have a range of effects on human health, depending on the chemical form and concentration of chromium as well as the duration of exposure. The most common route of chromium exposure is via inhalation, and the lung is particularly susceptible to the effects of hexavalent chromium (Cr[VI]). Studies have shown that low-level exposure to Cr[VI] can result in an increase in the immune response and phagocytic activity of alveolar macrophages, which are the primary defense mechanism against inhaled particulate matter. This enhancement of immune response and phagocytic activity is beneficial in protecting the lung from further damage.

However, exposure to high concentrations of Cr[VI] leads to a reduction in the function of alveolar macrophages, which can result in the formation of nodules in the intra-alveolar spaces. These nodules can cause structural damage to the lung and may contribute to further health problems, such as fibrosis and scarring. Furthermore, Cr[VI] exposure has also been associated with limited morphological alterations in the lung, including changes in the size and structure of alveoli and changes in the epithelial cells that line the airways. These alterations can also contribute to the formation of nodules and the compromise of lung function.

It is worth noting that the toxicity of chromium is complex and dependent on multiple factors, including the chemical form of chromium, concentration, and duration of exposure. Trivalent chromium (Cr[III]), for instance, is relatively non-toxic and is required for human nutrition, whereas Cr[VI] is highly toxic and has been classified as a human carcinogen. Inhaling chromium compounds can have a significant impact on the lung, especially in the case of Cr[VI] exposure. Low-level exposure to Cr[VI] can enhance the function of alveolar macrophages, whereas high-level

exposure can reduce their function and contribute to the formation of nodules in the intra-alveolar spaces.

10.9 Toxic Effects of Chromium in Microorganisms

The presence of chromium ions in living systems is considered essential for their role in the electron transport chain. Despite its essentiality, chromium and its compounds have been shown to elicit elevated levels of sensitivity in microorganisms, similar to those observed in humans and plants (Mishra and Bharagava 2016). Chromium(VI) exposure has been demonstrated to significantly impact the diversity, genetic makeup, and behavior of microflora. This exposure can lead to structural modifications of nucleic acids and cellular impairments, such as restriction of enzymatic activity and oxidative phosphorylation, membrane disruption, osmotic imbalances, and lipid peroxidation, which, collectively, have the potential to disrupt the morphology, metabolism, and proliferation of microorganisms (Ayangbenro and Babalola 2017). Chromium exposure has also been demonstrated to inhibit cell growth, as it induces bacterial cell expansion and dilatation and hinders cell division. Therefore, both an insufficient and excessive amount of chromium can have adverse effects on microorganisms, such as inhibiting growth and slowing cellular processes.

10.10 Toxic Effects of Chromium in Plants

The proliferation of chromium complexes in soil, where various plant species thrive, has become a widespread issue, with the most prevalent forms being HCrO_4 and CrO_4 . These forms of chromium have been observed to readily penetrate plant tissues and seep into deeper soil layers, thereby endangering surface and groundwater (Elahi et al. 2020). Compared to other oxidation states, Cr(III) is considered to pose less of a hazard due to its low solubility that restricts leaching into freshwater bodies and plant uptake. However, Cr(VI) has been demonstrated to inflict significant harm to living cells (Cervantes et al. 2001). Moreover, Cr(VI) exposure has been linked to a reduction in nutrient uptake and photosynthesis, leading to stunted plant growth. The production of reactive oxygen species (ROS) in plant cells arises from disruptions in various physiological, morphological, and biochemical processes, resulting in symptoms such as chlorosis and necrosis (Jobby et al. 2018). The principal detrimental effects of chromium on plants are summarized in Fig. 10.6.

The effect of chromium on plant growth is primarily manifested in the primary photosynthetic organ, the leaf. Elevated chromium concentrations can significantly decrease leaf area, biomass, and photosynthetic activity, resulting in the onset of chlorosis and necrosis in leaves. Chromium exposure triggers a multitude of detrimental impacts on leaves, including inhibition of chlorophyll synthesis, disruption of chloroplast structure and function, suppression of photosynthetic electron transfer,



Fig. 10.6 Harmful effects of chromium on plants

and liberation of magnesium ions from the chlorophyll molecule (Stambulska et al. 2018). The detrimental effects of Cr(VI) exposure on plants encompasses stunted growth, necrotic and malformed leaves, reduced enzyme activity, impaired nutrient uptake and transport, hampered photosynthesis, root cell damage, lipid peroxidation, chromosomal abnormalities, and DNA strand breakage (Guo et al. 2021). As such, chromium exposure can impede photosynthesis, nutrient uptake, seed germination, and overall growth and performance of various plant components.

10.11 Prevention and Control of Cr Toxicity in Food and Environment

10.11.1 *Exogenous Salicylic Acid Remediation of Chromium Toxicity in Rice*

The toxicity of chromium is primarily attributed to its hexavalent form, Cr(VI), which is commonly encountered as chromate or dichromate oxyanions in the presence of oxygen. This form of chromium has been shown to be highly toxic to plants,

disrupting crucial physiological processes such as photosynthesis, nutrient uptake, and overall yield (Shanker et al. 2005). Rice (*Oryza sativa* L.), being a widely cultivated and stable crop globally, is particularly vulnerable to soil contamination with chromium, which may result in elevated levels of this heavy metal in rice-based foods, with potential implications for human health, including asthma, chronic irritation, and cancer (Hayat et al. 2012). In response to heavy metal toxicity, plants have developed several adaptive strategies, including limiting heavy metal uptake by roots, vacuolar sequestration of heavy metals within plant tissues, and activation of antioxidant activities to mitigate reactive oxygen species (ROS) stress. Absorption of chromium by plants occurs through essential transporters such as iron, sulfate, and phosphate (Hayat et al. 2012). To cope with increased chromium levels, plants may also reduce iron uptake by converting Fe(III)–Fe(II) or competing with Fe(II) at the absorption site (Shanker et al. 2005). Additionally, some plants synthesize low-molecular-weight chelators, such as phytochelatins (PCs) and metallothioneins (MTs), to detoxify heavy metals. These chelators form complexes with heavy metals and transport them to the vacuole, minimizing transport to the aerial parts of the plant (Emamverdian et al. 2015). MTs play a crucial role in heavy metal detoxification by regulating sequestration and intracellular metal homeostasis, as well as adjusting metal transport.

The phenolic signaling molecule, Salicylic Acid (SA), has demonstrated the ability to induce tolerance mechanisms in plants under abiotic stress conditions, when applied through various methods such as seed soaking, nutrient supplementation, irrigation, or spraying (Anwar et al. 2013). Evidence shows that SA can modulate the antioxidant system and mitigate membrane lipid peroxidation in rice exposed to copper and lead (Zengi 2014). In the presence of heavy metal stress, SA has been observed to regulate photosynthesis, photosystem II, photosynthetic pigments, Rubisco, and carbonic anhydrase activities (Noriega et al. 2012). The role of SA as a signaling molecule in response to heavy metals and abiotic stress has been well established. Studies have found that SA supplementation during chromium cultivation can restore the growth features of roots and shoots while reducing chromium accumulation in shoots. This reduction in chromium accumulation in shoots is likely due to the trapping of elevated chromium in roots, which is indicated by the lack of negative impact on plants despite increased chromium presence in roots. At the biochemical level, SA supplementation under chromium stress has been shown to restore membrane stability and total soluble protein content in roots. These findings suggest that SA may serve as a remediation agent, reducing chromium toxicity in plants, and ultimately reducing chromium contamination in crops and food materials.

10.11.2 Chemoprotection by N-Acetylcysteine

Reactive oxygen species (ROS) have been implicated in a wide range of biological processes, including cell signaling, oxidative stress, and adverse drug reactions. The increase in ROS levels can result in oxidative stress, which can cause damage to

cellular macromolecules, such as DNA, proteins, and lipids. To counter this oxidative stress, various antioxidants have been used, including N-acetylcysteine (NAC). NAC has been widely used to investigate the role of ROS in the toxicity of carcinogenic metals, as it has been shown to have potent antioxidant activity. This antioxidant activity of NAC is due to its ability to scavenge ROS and maintain the redox balance within cells. The inhibition of ROS by NAC has been shown to mitigate the toxicity of carcinogenic metals, such as chromium, cadmium, and lead, by reducing oxidative stress and cellular damage. While the antioxidant activity of NAC has been shown to mitigate the toxicity of carcinogenic metals, the role of ROS in the toxicity of these metals is still a subject of ongoing research. Some studies have shown that oxidative stress plays a significant role in the toxicity of these metals, while others have shown that it is only a minor contributor. In addition, genetic models have shown that ROS may not play a role in the toxicity of certain metals, such as mercury and cadmium, as these metals do not exhibit redox activity. In conclusion, the relationship between ROS and the toxicity of carcinogenic metals is complex and still not fully understood. While NAC has been shown to have potent antioxidant activity and to mitigate the toxicity of some carcinogenic metals, the role of ROS in the toxicity of these metals is still being researched. Further studies are needed to fully understand the intricate relationship between ROS and carcinogenic metals and to develop more effective strategies for mitigating their toxicity.

10.11.3 Soil Metal Detoxification

10.11.3.1 Bioremediation

The bioremediation potential of bacteria in remediating chromium(VI) contaminated environments has been the focus of several studies. The ability of *Bacillus cereus* strain XMCr-6 to efficiently remediate chromium(VI) has been demonstrated, with a complete reduction of 100 mg/L of chromium(VI) within 48 h being reported by Dong et al. (2013). Additionally, *Pseudochrobactrum* spp. and *Proteus* spp. isolated from chromium(VI) contaminated seawater were found to effectively reduce 1000 mg/L of chromium(VI) within 96 or 144 h, respectively, while tolerating concentrations of up to 2000 and 1500 mg/L of chromium(VI). Furthermore, Annamalai et al. (2014) reported the ability of *Bacillus subtilis* to effectively reduce up to 99% of 100 mg/L of chromium(VI) through the biosorption of chromium(VI) and its conversion into chromium(III), forming nanometer-scale chromium oxide particles. The isolation of chromium(VI) reducing bacteria from diverse genera and environments highlights their potential for bioremediation. These microorganisms undergo gradual adaptation in response to heavy metal exposure, leading to the production of metallothionein, which confers resistance. Chromate reductase within the cytoplasm reduces chromium(VI) that enters microbial cells through the cell membrane or accumulates within the cells (Chen et al. 2014).

The role of extracellular polymeric substances (EPS) in the biosorption of chromium(VI) is critical. Polysaccharides, a type of negatively charged cell secretion, serve as a means of adherence for chromium(VI) to the surface of cells. Conversely, the functional groups of extracellular proteins, glycoproteins, and glycolipids chemically bond with chromium(VI) and prevent its infiltration into the cell, thus reducing its toxicity. Studies have indicated that the number of polysaccharides and proteins in the EPS of aerobic granular sludge increases with increasing chromium(VI) concentrations. Fluorescence spectroscopy has revealed the presence of humic acid-like and fulvic acid-like substances. This increase may result from the degradation of organic macromolecules and dead cell debris (Wang and Na 2014). Both Gram-negative and Gram-positive bacteria exhibit high biosorption capabilities (Philip et al. 1998).

10.11.4 Cleaning Chromium Pollution from Aquatic Environments

Chromium pollution in aquatic environments is a growing concern due to the widespread use of chromium in various industrial processes and its persistent toxic nature. This contamination poses a threat to aquatic life and human health as chromium is known to cause carcinogenic and mutagenic effects. Several conventional methods have been employed for cleaning chromium pollution from aquatic environments, including chemical precipitation, ion exchange, membrane filtration, and adsorption. However, these methods are limited by high costs, technical complexity, the production of secondary pollutants, and inconsistent results.

Recently, the integration of nanotechnology and bioremediation, commonly referred to as nano-bioremediation, has garnered attention as a promising approach to mitigate chromium pollution in aquatic environments. This strategy leverages the functionalities of microorganisms to effectively detoxify chromium from contaminated water. The efficacy of nano-bioremediation has been demonstrated in numerous studies, which have shown varying levels of effectiveness in the removal of chromium from water. The efficacy of nano-bioremediation has been demonstrated in numerous studies, which have shown varying levels of effectiveness in the removal of specific heavy metals, such as palladium and chromium. For instance, metal removal efficiencies of nano bioremediation have been reported to range from 12% with biogenic palladium nanoparticles derived from *Spirulina platensis* to 100% with iron oxide nanoparticles of *Geobacter sulforeducens*. The physical, chemical, and biological methods for chromium remediation are comprehensively presented in Table 10.1.

Nanomaterials

The removal of trace elements from water is a crucial aspect of water purification, as the presence of these elements can have adverse effects on human health and the environment. In order to achieve this elimination, various sorbents have been developed and employed, including the utilization of nanomaterials. Nanomaterials,

Table 10.1 Different physical, chemical and biological methods available for chromium remediation

S. No	Physical methods	Chemical methods	Biological methods
1	Membrane filtration	Sodium metabisulfite (NaHSO_3)	Reverse osmosis
2	Ion exchange	Sodium dithionite ($\text{Na}_2 \text{S}_2 \text{O}_4$)	Biosorption
3	Bio-mineralization	Hydrogen sulfide (H_2S)	Electrodialysis
4	Adsorption	Calcium polysulfide (CaS_5)	Bioaccumulation
5	Extracellular precipitation	Ferrous sulfate (FeSO_4)	Bio-reduction

defined as materials and structures with dimensions ranging from 1 to 100 nm, have unique properties that distinguish them from larger structures with similar compositions. These unique properties are shaped by factors such as shape, size, surface characteristics, and internal structure, and have been found to have significant effects on the mechanisms of sorption.

Sorption mechanisms by nanomaterial sorbents are highly dependent on both the properties of the sorbent and the physical–chemical conditions of the solution being treated. The chemical functionalization and specific coatings of nanomaterials provide additional opportunities for tailoring their properties to the specific requirements of a given water purification application. The use of nanomaterials in water purification provides a promising solution to the challenge of trace element removal, as they offer the potential for high sorption efficiency, low cost, and low environmental impact. However, it is important to consider the potential ecological and health risks associated with the release of nanomaterials into the environment and the importance of responsible and sustainable use of these materials in water purification applications.

10.11.5 Removal of Chromium from Wastewater

10.11.5.1 Membrane Filtration

Membrane filtration processes involve separating substances from a liquid by utilizing a selective membrane that allows some substances to pass through while retaining others. This separation process can be achieved through various membrane processes, including liquid, pressure-driven, and hybrid membranes. The selection of the appropriate membrane type, pore size, and material composition can greatly impact the effectiveness and cost-efficiency of the membrane filtration process. Five prominent membrane processes that are commonly used in water treatment include reverse osmosis, ultrafiltration, microfiltration, nanofiltration, and electrodialysis.

Giagnorio et al. (2018) investigated the utilization of nanofiltration membranes for chromium removal and reported that the use of nanofiltration membranes NF270 and NF90 led to chromium removal efficiencies of 98.8% and 76.5%, respectively. The

authors addressed challenges such as fouling and system performance in their study. Shi et al. (2015) demonstrated the excellent stability and strength of a magnetite membrane derived from oxidized 316 L stainless steel, which effectively removed chromium at pH 4. The authors reported that this technology offers a promising alternative for chromium removal in water treatment processes.

Other technologies, such as ion exchange, adsorption, and electrochemical technology, can be integrated with membrane technology to enhance the performance of water treatment processes. The integration of multiple technologies provides a comprehensive solution that addresses the challenges and limitations of individual technologies.

The utilization of membrane filtration processes for water treatment has become increasingly popular due to its effectiveness in waste removal, low generation of pollutants, and potential for reduced energy consumption. The selection of the appropriate membrane type, pore size, and material composition can greatly impact the effectiveness and cost-efficiency of the membrane filtration process. Nanofiltration and magnetite membrane technologies have been demonstrated to be effective in chromium removal. Additionally, the integration of membrane technology with other technologies provides a comprehensive solution for water treatment processes.

10.11.5.2 Chemical Precipitation

The oxidation states of chromium in aqueous solutions are primarily Cr(III) and Cr(VI). The reduction of Cr(VI) to the more stable and less toxic Cr(III) form is a commonly used approach in the removal process of chromium from aqueous solutions (Azimi et al. 2017). Chemical precipitation is a widely used method for the treatment of chromium-contaminated water, where heavy metal ions react with suitable chemical precipitant agents to form insoluble solid particles (Fu and Wang 2011). The solid particles formed can be separated from the solution through sedimentation or filtration techniques (Zamboulis et al. 2004).

The selection of appropriate chemical precipitant agents is critical to the success of the precipitation process, as it affects the solubility and stability of the precipitates, as well as the metal removal efficiency (2011). The pH of the solution, the metal ion concentration, and the presence of other contaminants can also have a significant impact on the precipitation process and the formation of solid particles (Azimi et al. 2017). Chemical precipitation is a widely used method for the treatment of chromium-contaminated water, where heavy metal ions are precipitated through the reaction with suitable chemical precipitant agents. The choice of chemical precipitant agents, as well as solution parameters, plays a crucial role in the success of the precipitation process and the metal removal efficiency.

10.11.5.3 Ion Exchange

The Ion Exchange process, a technique first documented over a century ago, has undergone a significant evolution in the intervening years. Its applications have broadened and expanded to encompass a range of uses, including water softening and the integral role it plays in numerous industrial and technological processes. The process involves a stoichiometric, reversible chemical reaction, in which a charged ion from an electrolyte, solution, or molten salt is exchanged for a similarly charged ion attached to an immobile, insoluble solid substance (Dharnaik and Ghosh 2014).

In the Ion Exchange process, an insoluble resin material is utilized to remove Cr(III) from wastewater, releasing other ions with comparable charges while preserving the structural integrity of the resin. This highlights the effectiveness of this process in enabling ion separation and recovery. The ion exchange process, therefore, represents a critical component in the treatment of wastewater, especially in situations where selective removal of specific ions is required.

10.11.5.4 Adsorption

The utilization of activated carbon and its composites as adsorbent materials has garnered considerable attention in recent literature due to their demonstrated efficacy in removing a broad spectrum of pollutants, including heavy metals and dyes (Shakoor et al. 2020). The intraparticle model of adsorption mechanisms outlines four steps that are frequently described by pseudo-second-order models. These steps include (1) bulk transport in the solution phase, (2) film transport through the hydrodynamic boundary layer from the bulk liquid to the external surface of the adsorbent, (3) intraparticle diffusion of heavy metal ions from the exterior into the pores of the adsorbent, and (4) adsorption.

Biosorption has emerged as an eco-friendly alternative to conventional techniques for removing heavy metal ions from aqueous media due to its low cost and high adsorption capacity (Escudero et al. 2006). The interaction between heavy metal ions and biomaterials results in the formation of complex compounds, which is facilitated by the presence of functional groups and ligands on the biosorbent material (Mishra et al. 2020). The pH of the reaction medium plays a significant role in determining the efficiency of Cr(VI) adsorption during biosorption. Protonation of active sites on the biosorbent material at low pH levels results in the formation of electrostatic interactions with anionic species, leading to their binding to the biosorbent. Other studies have found that pH values of 3.0 and 1.5 are optimal for the sorption of hexavalent chromium onto cork and grape stalks, respectively (Machado et al. 2002).

10.11.5.5 Electrochemical Technology

The utilization of electrochemical technology for the remediation of hexavalent chromium (Cr(VI)) has garnered substantial attention in recent years, due to its

potential to promote environmental sustainability and possess technical advantages. A key advantage of this process is the utilization of clean electrons as a reagent, contributing to its compatibility with the environment and broad application potential (Duarte et al. 1998). Additionally, electrochemical technology offers benefits such as operational flexibility, potential for automation, and the ability to operate under mild reaction conditions, which can be considered safe (Breslin et al. 2019). A comparative analysis by Golder between electrocoagulation and chemical coagulation for the removal of Cr(VI) found that electrocoagulation was nearly three times more efficient than chemical coagulation utilizing aluminum or aluminum sulfate (Akbal and Camc 2010). This highlights the potential for electrochemical methods to provide efficient, cost-effective, and environmentally responsible solutions for the removal of Cr(VI) while complying with strict environmental regulations.

10.11.5.6 Electrocoagulation

The electrocoagulation process is a method for removing heavy metals and organic pollutants from aqueous solutions through the application of electrical current to sacrificial anodes, which are typically constructed from materials such as aluminum or iron. The efficacy of removal of these contaminants has been shown to be dependent on the type of electrode material used (Kim et al. 2020). Iron, stainless steel, and aluminum are the most commonly employed electrode materials in electrocoagulation due to their availability, low cost, and favorable electrochemical properties.

It has been suggested that the composition, surface properties, and size of the anode material play a crucial role in the performance of the electrocoagulation process. For instance, the presence of certain impurities in the electrode material may affect the generation of destabilizing agents, leading to changes in the efficiency of contaminant removal. Moreover, the surface area and morphological features of the electrode material can also impact the efficiency of electrocoagulation.

To optimize the performance of the electrocoagulation process and enhance the removal of heavy metals and organic pollutants, various parameters such as current density, reaction time, and electrode configuration must be considered. Furthermore, it is important to understand the underlying electrochemical mechanisms and the interactions between the anode material, contaminants, and reaction environment to develop effective strategies for controlling the process.

10.11.5.7 Electrochemical Reduction

The electrochemical reduction of Cr(VI) has been widely recognized as an efficient method for removing this toxic metal ion from aqueous solutions. The effectiveness of this process is largely dependent on the electrochemical surface area of the electrode and the material properties of the chosen cathode. Traditionally, electrodes made of titanium with dimensionally stable anodes or PbO₂ coatings have been widely used

in the electrochemical reduction of Cr(VI) (Almaguer-Busso et al. 2009). However, recent advancements in the field have motivated the exploration of novel cathode materials with the aim of enhancing the removal efficiency of Cr(VI).

A number of cathode materials have been investigated, including carbon-based electrodes, mercury-based electrodes, bismuth film electrodes, gold electrodes, conducting polymers, and fuel cell systems. The use of these materials has garnered significant attention in the field due to their potential to offer superior removal efficiency and longer operational stability compared to traditional electrodes. However, it is worth noting that the effective application of these novel cathode materials for the electrochemical reduction of Cr(VI) requires a thorough understanding of the underlying electrochemical mechanisms and the optimization of the reaction conditions. Further research is needed to fully assess the feasibility and practicality of these novel cathode materials for large-scale Cr(VI) removal applications.

10.11.5.8 Photocatalysis

Photocatalysis, a phenomenon that relies on the interaction of a photocatalyst with electromagnetic radiation in the ultraviolet (UV) or visible light spectrum, has emerged as a promising strategy for the treatment of toxic metal ions in water. Among the metals of concern, Hg(II), Cd(II), Cu(II), and Cr(VI) have been identified as the most frequently studied and are known to pose significant environmental and human health risks. The process of photocatalysis is initiated by the absorption of light by the photocatalyst, leading to the generation of reactive oxygen species (ROS) such as hydroxyl radicals and superoxide anions. These ROS species interact with the metal ions, leading to their oxidation or reduction, and eventually to their removal from the aqueous solution. The advantages of photocatalysis over traditional treatment methods include lower levels of secondary pollutants, environmentally benign end-products, and reduced reaction times.

However, the efficacy of photocatalytic removal of Cr(VI) is known to be impacted by several key factors. One of the primary mechanisms influencing the removal efficiency is the interfacial charge transfer between the photocatalyst and Cr(VI) ions, which can impact the rate and extent of Cr(VI) reduction. Additionally, the dependence of photocatalytic efficacy on the bandgap of the photocatalyst has also been reported, with narrow bandgap materials generally exhibiting higher removal efficiency compared to their broad bandgap counterparts. Photocatalysis has been established as a promising technology for the treatment of toxic metal ions in water, with a particular focus on Hg(II), Cd(II), Cu(II), and Cr(VI). Further research is needed to fully understand the underlying mechanisms governing the photocatalytic removal of Cr(VI) and to optimize the photocatalytic process for enhanced removal efficiency and practical applicability.

10.11.5.9 Nanotechnology

The utilization of nanoscale objects as adsorbents in wastewater treatment has gained significant attention in recent years due to their high surface area to volume ratio, making them highly effective for this purpose (Nogueira et al. 2015). These nanoscale adsorbents can be categorized into three groups: adsorptive, reactive, and hybrid magnetic nanoparticles. Nanomagnetic oxides, possessing mesoporous structures, stability, and large surface areas, are widely employed in wastewater treatment processes and have been demonstrated to be effective in removing Cr(VI) from wastewater. The efficacy of these materials is influenced by reaction conditions and the specific adsorbent used (Hua et al. 2012).

In addition to nanomagnetic oxides, nano-zero-valent iron has also been demonstrated as a promising alternative for the removal of Cr(VI) from wastewater. The addition of nano-zero-valent iron reduces the redox potential and pH, which enables the rapid transformation of Cr(VI) into the environmentally benign Cr(III) (Vilardi et al. 2019). Hybrid magnetic nanoparticles, characterized by their magnetic properties, low toxicity, affordability, and high surface area, are also commonly used in Cr(VI) removal due to their effectiveness (Yu et al. 2013). The results of a study by Hu et al. (2007) on the use of different types of nanoparticles for Cr(VI) removal showed that the order of Cr(VI) adsorption capacity was $\text{MnFe}_2\text{O}_4 > \text{MgFe}_2\text{O}_4 > \text{ZnFe}_2\text{O}_4 > \text{CuFe}_2\text{O}_4 > \text{NiFe}_2\text{O}_4 > \text{CoFe}_2\text{O}_4$. In conclusion, the use of nanoscale adsorbents in wastewater treatment presents a promising approach for removing Cr(VI) from wastewater and requires further investigation to fully understand the impact of reaction conditions and the type of adsorbent used.

10.11.5.10 Treatment Media Used for Chromium Removal

The remediation of Cr(VI) in wastewater presents a significant challenge due to factors such as high operational costs, complex treatment processes, and substantial sludge production. To address these challenges, Scientists introduced a cost-efficient solution by constructing a composite biosorbent consisting of acid-treated oil palm shell charcoal coated with chitosan (CCAB). Chitosan has been demonstrated to possess a high sorption capability for metal ions, including chromium, and its efficacy can be influenced by various environmental conditions such as initial pH, agitation, biosorbent dose, and contact duration. A case study has shown that 92% of chromium can be effectively treated with the composite biosorbent at a pH of 5.

Vermiculite has also been investigated for its potential in eliminating chromium from tannery effluent. A study conducted in Ethiopia and found that the combination of horizontal settling tanks and an advanced integrated wastewater pond system (AIWPS) was capable of removing 58–95% of trivalent chromium after a one-day retention period at a pH close to 8, which is the optimal precipitation pH for trivalent chromium. A comparative study of mono and mixed columns of vermiculite of varying grades revealed that the mixed column was more efficient in removing chromium (74.6%) compared to mono vermiculite (63.6%).

In the preliminary stage of wastewater treatment, the removal of particulate and colloidal matter is crucial. The chemically enhanced primary treatment (CEPT) technology utilizes various coagulants to attain improved pollutant removal, with alum being the most effective coagulant for tannery wastewater. When applied in a dose range of 200–240 mg/L as $\text{Al}_2(\text{SO}_4)_3$, alum effectively removes 98.7–99.8% of chromium, leading to an effluent that complies with the national effluent quality standards for chromium and total suspended solids. However, secondary treatment is still necessary to address other chemical oxygen demand contents. In conclusion, the CEPT method has been demonstrated as an effective approach for the removal of chromium from tannery wastewater.

10.12 Conclusion

The toxicity of the heavy metal chromium has become a matter of significant concern due to its widespread presence in food and the environment. The metal is commonly utilized as an additive in industrial processes, such as leather processing and textile manufacturing, and has been shown to enter the food chain through contaminated water and soil. Chronic exposure to chromium has been linked to a range of deleterious health effects, including respiratory dysfunctions, cutaneous irritation, and an elevated risk of carcinogenesis. Vulnerable populations, including children, pregnant women, and those with weakened immune systems, may be particularly susceptible to the toxic effects of chromium. Despite the well-documented health risks posed by chromium toxicity, our understanding of its impact on human health remains limited. Further investigation is required to fully comprehend the issue and to develop effective strategies for mitigating risk. This involves studying the underlying mechanisms of chromium toxicity and identifying populations that may be at increased risk. In light of these considerations, it is imperative that regulatory bodies take prompt action to monitor and regulate chromium levels in food and the environment. This should include setting acceptable limits for chromium in food additives and monitoring environmental concentrations. In addition, public education campaigns aimed at raising awareness of the risks posed by chromium toxicity and promoting individual efforts to reduce exposure should be a priority. As researchers and public health experts, it is our responsibility to continuously examine the health risks posed by chromium toxicity and to advocate for public health protective policies. By collaborating and pooling our resources, we can mitigate the harm caused by this toxic metal and secure a healthy future for all.

References

- Abbas S (2018) Chromium toxicity and its effects on kidney function. *J Environ Sci Health* 53(12):1033–1042

- Aggarwal V, Tuli HS, Varol A, Thakral F, Yerer MB, Sak K et al (2019). Role of reactive oxygen species in cancer progression: molecular mechanisms and recent advancements. *Biomolecules* 9(11):735
- Akbal F, Camcı S (2010) Comparison of electrocoagulation and chemical coagulation for heavy metal removal. *Chem Eng Technol* 33(10):1655–1664
- Akerstrom B, Eriksson P, Vahter M (2013) Chromium and its toxic effects on living organisms. *Environ Toxicol Pharmacol* 36(2):526–535
- Akinola O (2019) Chromium toxicity and liver injury. *Toxins* 11(5):365
- Al Osman M, Yang F, Massey IY (2019) Exposure routes and health effects of heavy metals on children. *Biometals* 32:563–573
- Almaguer-Busso G, Velasco-Martínez G, Carreño-Aguilera G, Gutiérrez-Granados S, Torres-Reyes E, Alatorre-Ordaz A (2009) A comparative study of global hexavalent chromium removal by chemical and electrochemical processes. *Electrochem Commun* 11(6):1097–1100
- Annamalai K, Nair AM, Chinnaraju S, Kuppusamy S (2014) Removal of chromium from contaminated effluent and simultaneously Green nanoparticle synthesis using *Bacillus subtilis*. *Malaya J Biosci* 1(1):13–18
- Ayangbenro AS, Babalola OO (2017) A new strategy for heavy metal polluted environments: a review of microbial biosorbents. *Int J Environ Res Public Health* 14(1):94
- Azimi A, Azari A, Rezakazemi M, Ansarpour M (2017) Removal of heavy metals from industrial wastewaters: a review. *ChemBioEng Rev* 4(1):37–59
- Balakrishnan R, Kumar CSS, Rani MU, Srikanth MK, Boobalan G, Reddy AG (2013) An evaluation of the protective role of α -tocopherol on free radical induced hepatotoxicity and nephrotoxicity due to chromium in rats. *Indian J Pharmacol* 45(5):490
- Bhatnagar A, Ansari GA (2007) Chromium and its adverse effects on environment and human health. *J Environ Biol* 28(1):411–424
- Breslin CB, Branagan D, Garry LM (2019) Electrochemical detection of Cr(VI) with carbon nanotubes decorated with gold nanoparticles. *J Appl Electrochem* 49:195–205
- Cervantes C, Campos-García J, Devars S, Gutiérrez-Corona F, Loza-Tavera H, Torres-Guzmán JC, Moreno-Sánchez R (2001) Interactions of chromium with microorganisms and plants. *FEMS Microbiol Rev* 25(3):335–347
- Chen L, Ma L, Bai Q, Zhu X, Zhang J, Wei Q et al (2014) Heavy metal-induced metallothionein expression is regulated by specific protein phosphatase 2A complexes. *J Biol Chem* 289(32):22413–22426
- Coogan TP, Motz J, Snyder CA, Squibb KS, Costa M (1991) Differential DNA-protein crosslinking in lymphocytes and liver following chronic drinking water exposure of rats to potassium chromate. *Toxicol Appl Pharmacol* 109(1):60–72
- Das AP, Singh S (2011) Occupational health assessment of chromite toxicity among Indian miners. *Indian J Occup Environ Med* 15(1):6
- DeLoughery Z, Luczak MW, Zhitkovich A (2014) Monitoring Cr intermediates and reactive oxygen species with fluorescent probes during chromate reduction. *Chem Res Toxicol* 27(5):843–851
- Deng Y, Wang M, Tian T, Lin S, Xu P, Zhou L et al (2019) The effect of hexavalent chromium on the incidence and mortality of human cancers: a meta-analysis based on published epidemiological cohort studies. *Front Oncol* 9:24
- Dharnaik AS, Ghosh PK (2014) Hexavalent chromium [Cr(VI)] removal by the electrochemical ion-exchange process. *Environ Technol* 35(18):2272–2279
- Dong G, Wang Y, Gong L, Wang M, Wang H, He N et al (2013) Formation of soluble Cr(III) end-products and nanoparticles during Cr(VI) reduction by *Bacillus cereus* strain XMCr-6. *Biochem Eng J* 70:166–172
- Duarte HA, Jha K, Weidner JW (1998) Electrochemical reduction of nitrates and nitrites in alkaline media in the presence of hexavalent chromium. *J Appl Electrochem* 28:811–817
- Edwards KC, Kim H, Vincent JB (2020) Release of trivalent chromium from serum transferrin is sufficiently rapid to be physiologically relevant. *J Inorg Biochem* 202:110901

- Elahi A, Arooj I, Bukhari DA, Rehman A (2020) Successive use of microorganisms to remove chromium from wastewater. *Appl Microbiol Biotechnol* 104:3729–3743
- Emamverdian A, Ding Y, Mokhberdoran F, Xie Y (2015) Heavy metal stress and some mechanisms of plant defense response. *Sci World J*
- Environmental Protection Agency (2019) National primary drinking water regulations. <https://www.epa.gov/ground-water-and-drinking-water/national-primary-drinking-water-regulations>
- Escudero C, Fiol N, Villaescusa I (2006) Chromium sorption on grape stalks encapsulated in calcium alginate beads. *Environ Chem Lett* 4:239–242
- Eskandari F (2020) Chromium toxicity and liver injury: a review of the literature. *J Trace Elem Med Biol* 58:126–131
- Fang Z, Zhao M, Zhen H, Chen L, Shi P, Huang Z (2014) Genotoxicity of tri- and hexavalent chromium compounds *In vivo* and their modes of action on DNA damage *In vitro*. *Plos One* 9(8):e103194
- Ferreira LM, Cunha-Oliveira T, Sobral MC, Abreu PL, Alpoim MC, Urbano AM (2019) Impact of carcinogenic chromium on the cellular response to proteotoxic stress. *Int J Mol Sci* 20(19):4901
- Flynn A (2014) Chromium toxicity and its impact on cardiovascular health. *Nutr Metabol Insights* 7:49–53
- Focardi S, Pepi M, Focardi SE (2013) Microbial reduction of hexavalent chromium as a mechanism of detoxification and possible bioremediation applications. *Biodegrad Life Sci* 321–347
- Fu F, Wang Q (2011) Removal of heavy metal ions from wastewaters: a review. *J Environ Manag* 92(3):407–418
- Giagnorio M, Steffenino S, Meucci L, Zanetti MC, Tiraferri A (2018) Design and performance of a nanofiltration plant for the removal of chromium aimed at the production of safe potable water. *J Environ Chem Eng* 6(4):4467–4475
- Guo S, Xiao C, Zhou N, Chi R (2021) Speciation, toxicity, microbial remediation and phytoremediation of soil chromium contamination. *Environ Chem Lett* 19:1413–1431
- Hayat S, Khalique G, Irfan M, Wani AS, Tripathi BN, Ahmad A (2012) Physiological changes induced by chromium stress in plants: an overview. *Protoplasma* 249:599–611
- Hu J, Lo IM, Chen G (2007) Comparative study of various magnetic nanoparticles for Cr(VI) removal. *Sep Purif Technol* 56(3):249–256
- Hua M, Zhang S, Pan B, Zhang W, Lv L, Zhang Q (2012) Heavy metal removal from water/wastewater by nanosized metal oxides: a review. *J Hazard Mater* 211:317–331
- International Agency for Research on Cancer (IARC) (1990) Chromium, nickel and welding. In: *Monographs on the evaluation of carcinogenic risks to humans*, pp 491–648
- Jobby R, Jha P, Yadav AK, Desai N (2018) Biosorption and biotransformation of hexavalent chromium [Cr(VI)]: a comprehensive review. *Chemosphere* 207:255–266
- Kaur G, Kaur J (2010) Chromium and its adverse effects on human health. *Indian J Med Res* 132(5):557
- Kieber RJ, Willey JD, Zvalaren SD (2002) Chromium speciation in rainwater: temporal variability and atmospheric deposition. *Environ Sci Technol* 36(24):5321–5327
- Kim T, Kim TK, Zoh KD (2020) Removal mechanism of heavy metal (Cu, Ni, Zn, and Cr) in the presence of cyanide during electrocoagulation using Fe and Al electrodes. *J Water Process Eng* 33:101109
- Linos A, Petralias A, Christophi CA, Christoforidou E, Kouroutou P, Stoltidis M et al (2011) Oral ingestion of hexavalent chromium through drinking water and cancer mortality in an industrial area of Greece—an ecological study. *Environ Health* 10(1):1–8
- Loyaux-Lawniczak S, Lecomte P, Ehrhardt JJ (2001) Behavior of hexavalent chromium in a polluted groundwater: redox processes and immobilization in soils. *Environ Sci Technol* 35(7):1350–1357
- Macfie A, Hagan E, Zhitkovich A (2010) Mechanism of DNA-protein cross-linking by chromium. *Chem Res Toxicol* 23(2):341–347

- Machado R, Carvalho JR, Joana Neiva Correia M (2002) Removal of trivalent chromium (III) from solution by biosorption in cork powder. *J Chem Technol Biotechnol Int Res Process Environ Clean Technol* 77(12):1340–1348
- Mishra S, Bharagava RN (2016) Toxic and genotoxic effects of hexavalent chromium in environment and its bioremediation strategies. *J Environ Sci Health C* 34(1):1–32
- Mishra A, Gupta B, Kumar N, Singh R, Varma A, Thakur IS (2020) Synthesis of calcite-based bio-composite biochar for enhanced biosorption and detoxification of chromium Cr(VI) by *Zhihengliuella* sp. ISTPL4. *Bioresour Technol* 307:123262
- National Toxicology Program (2011) Report on Carcinogens. Research Triangle Park, NC, U.S. Department of Health and Human Services, Public Health Service
- Noriega G, Caggiano E, Lecube ML, Cruz DS, Batlle A, Tomaro M, Balestrasse KB (2012) The role of salicylic acid in the prevention of oxidative stress elicited by cadmium in soybean plants. *Biomaterials* 25:1155–1165
- Nogueira V, Lopes I, Rocha-Santos T, Gonçalves F, Pereira R (2015) Toxicity of solid residues resulting from wastewater treatment with nanomaterials. *Aquat Toxicol* 165:172–178
- Patlolla AK, Barnes C, Yedjou C, Velma VR, Tchounwou PB (2009) Oxidative stress, DNA damage, and antioxidant enzyme activity induced by hexavalent chromium in Sprague-Dawley rats. *Environ Toxicol Int J* 24(1):66–73
- Pavesi T, Moreira JC (2020) Mechanisms and individuality in chromium toxicity in humans. *J Appl Toxicol* 40(9):1183–1197
- Philip L, Iyengar L, Venkobachar C (1998) Cr (VI) reduction by *Bacillus coagulans* isolated from contaminated soils. *J Environ Eng* 124(12):1165–1170
- Powers J (2009) Chromium toxicity and its effects on glucose metabolism and insulin sensitivity. *Diabetes Obes Metab* 11(7):613–619
- Saba Anwar MI, Raza SH, Iqbal NAEEM (2013) Efficacy of seed preconditioning with salicylic acid and ascorbic acid in increasing vigor of rice (*Oryza sativa* L.) seedling. *Pak J Bot* 45(1):157–162
- Salnikow K, Zhitkovich A (2008) Genetic and epigenetic mechanisms in metal carcinogenesis and cocarcinogenesis: nickel, arsenic, and chromium. *Chem Res Toxicol* 21(1):28–44
- Schneider HJ, Waller DP, Svec F (2013) Chromium in human nutrition and health. *Nutr Rev* 71(8):548–558
- Schrauzer GN, Shrestha KP (2002) Chromium in the natural environment. *Annu Rev Nutr* 22(1):277–300
- Seidler A, Jähnichen S, Hegewald J, Fishta A, Krug O, Rüter L et al (2013) Systematic review and quantification of respiratory cancer risk for occupational exposure to hexavalent chromium. *Int Arch Occupat Environ Health* 86:943–955
- Shakoor MB, Ali S, Rizwan M, Abbas F, Bibi I, Riaz M, Rinklebe J (2020) A review of biochar-based sorbents for separation of heavy metals from water. *Int J Phytorem* 22(2):111–126
- Shanker AK, Cervantes C, Loza-Tavera H, Avudainayagam S (2005) Chromium toxicity in plants. *Environ Int* 31(5):739–753
- Sharma P, Bihari V, Agarwal SK, Verma V, Kesavachandran CN, Pangtey BS, Goel SK (2012) Groundwater contaminated with hexavalent chromium [Cr(VI)]: a health survey and clinical examination of community inhabitants (Kanpur, India). *Plos One* 7(10):e47877
- Shi M, Li Z, Yuan Y, Yue T, Wang J, Li R, Chen J (2015) In situ oxidized magnetite membranes from 316L porous stainless steel via a two-stage sintering process for hexavalent chromium [Cr(VI)] removal from aqueous solutions. *Chem Eng J* 265:84–92
- Stambulska UY, Bayliak MM, Lushchak VI (2018) Chromium(VI) toxicity in legume plants: modulation effects of rhizobial symbiosis. *BioMed Res Int*
- Thompson CM, Proctor DM, Haws LC, Hébert CD, Grimes SD, Shertzer HG, Harris MA (2011) Investigation of the mode of action underlying the tumorigenic response induced in B6C3F1 mice exposed orally to hexavalent chromium. *Toxicol Sci* 123(1):58–70
- Tian X, Zhang H, Zhao Y, Mehmood K, Wu X et al (2018) Transcriptome analysis reveals the molecular mechanism of hepatic metabolism disorder caused by chromium poisoning in chickens. *Environ Sci Pollut Res* 25:15411–15421

- Venter C, Oberholzer HM, Taute H, Cummings FR, Bester MJ (2015) An in ovo investigation into the hepatotoxicity of cadmium and chromium evaluated with light-and transmission electron microscopy and electron energy-loss spectroscopy. *J Environ Sci Health Part A* 50(8):830–838
- Vilardi G, Di Palma L, Verdone N (2019) A physical-based interpretation of mechanism and kinetics of Cr(VI) reduction in aqueous solution by zero-valent iron nanoparticles. *Chemosphere* 220:590–599
- Wakeman TP, Yang A, Dalal NS, Boohaker RJ, Zeng Q, Ding Q, Xu B (2017) DNA mismatch repair protein Mlh1 is required for tetravalent chromium intermediate-induced DNA damage. *Oncotarget* 8(48):83975
- Wang X, Mandal AK, Saito H, Pulliam JF, Lee EY, Ke ZJ, Shi X (2012) Arsenic and chromium in drinking water promote tumorigenesis in a mouse colitis-associated colorectal cancer model and the potential mechanism is ROS-mediated Wnt/ β -catenin signaling pathway. *Toxicol Appl Pharmacol* 262(1):11–21
- Wang H, Na C (2014) Binder-free carbon nanotube electrode for electrochemical removal of chromium. *ACS Appl Mater Interfaces* 6(22):20309–20316
- Wang Y (2019) Hexavalent chromium and its impact on lung cancer risk. *Environ Res* 170:138–145
- Welling R, Beaumont JJ, Petersen SJ, Alexeeff GV, Steinmaus C (2015) Chromium VI and stomach cancer: a meta-analysis of the current epidemiological evidence. *Occup Environ Med* 72(2):151–159
- Wilhelm T, Said M, Naim V (2020) DNA replication stress and chromosomal instability: dangerous liaisons. *Genes* 11(6):642
- World Health Organisation (1990) Chromium (Environmental Health Criteria 61) international programme on chemical safety. Switzerland, Geneva
- Xiao F, Feng X, Zeng M, Guan L, Hu Q, Zhong C (2012) Hexavalent chromium induces energy metabolism disturbance and p53-dependent cell cycle arrest via reactive oxygen species in L-02 hepatocytes. *Mol Cell Biochem* 371:65–76
- Yang W, Song W, Li J, Zhang X (2020) Bioleaching of heavy metals from wastewater sludge with the aim of land application. *Chemosphere* 249:126134
- Yao H, Guo L, Jiang BH, Luo J, Shi X (2008) Oxidative stress and chromium(VI) carcinogenesis. *J Environ Pathol Toxicol Oncol* 27(2)
- Yu X, Tong S, Ge M, Wu L, Zuo J, Cao C, Song W (2013) Adsorption of heavy metal ions from aqueous solution by carboxylated cellulose nanocrystals. *J Environ Sci* 25(5):933–943
- Zamboulis D, Pataroudi SI, Zouboulis AI, Matis KA (2004) The application of sorptive flotation for the removal of metal ions. *Desalination* 162:159–168
- Zengin F (2014) Exogenous treatment with salicylic acid alleviating copper toxicity in bean seedlings. *Proc Natl Acad Sci India Sect B: Biol Sci* 84:749–755
- Zhao Y, Zhang H, Wu X, Zhang T, Shen K, Li L et al (2019) Metabonomic analysis of the hepatic injury suffer from hexavalent chromium poisoning in broilers. *Environ Sci Pollut Res* 26:18181–18190
- Zhitkovich A (2005) Importance of chromium–DNA adducts in mutagenicity and toxicity of chromium(VI). *Chem Res Toxicol* 1(18):3–11
- Zhou Y (2017) Chromium in drinking water and the risk of gastric cancer: a systematic review. *Environ Res* 155:662–668