Chapter 1
Health Impacts of Cr Contamination in Soil

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Abstract Chromium (Cr) has been widely used for many purposes and products. The elevation of Cr concentration in the environment is mainly related to anthropogenic sources. From a long time ago, chromium trivalent was known as an essential element but in a recent study, chromium can be only acknowledged as a pharmacologically active substance and not an essential substance/element. Under particular conditions, chromium may be oxidized to Cr(III) or Cr(VI) and vice versa. Increased soil Cr content may be hazardous to terrestrial organisms and humans. Chromium is included as a top-priority chemical substance because it may cause toxic, mutagenic and carcinogenic effects on humans. Humans can expose to Cr via direct dermal contact, ingestion of food or accidental ingestion of soil, and inhalation of particulate in the air. Plants exposed to Cr may experience negative impacts on growth, development, and photosynthesis. The excessive deposition of Cr in soil has caused growth retardation and germination issues in a number of food crops, which has significant implications for the food supply chain and raises the probability of serious health effects on humans and animals. Epidemiologic studies have linked chronic and acute dietary Cr exposures with several adverse health effects and symptoms like lung cancer, skin lesions, neurological diseases, and problems in reproductive system. Advanced research strategies and technologies to reduce Cr contamination in the environment and diminish human health risks are needed.

Keywords Chromium · Trace elements · Soil · Health effects · Humans

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1.1 Introduction

Potentially toxic elements (PTEs) contamination in our environment is one of the environmental problems nowadays due to its potential to cause health problems to humans and living organisms, as well as ecological degradation (Tchounwou et al. 2012; Mishra and Bharagava 2016; Ali et al. 2019; Kiran and Sharma 2022; Mitra et al. 2022). This element can become toxic and/or carcinogenic through accumulation in living organisms. One of the PTEs that potentially generate environmental problems is chromium (Cr). The United States Agency for Toxic Substances and Disease Registry ranks this PTE among the most hazardous substances (U.S ATSDR). First found by the scientist named Vauquelin in 1797 in lead ore (crocoite) (Baruthio 1992). Until now, chromium has been widely used for many purposes and products. Chromium (Cr) is naturally found as chromite ore (Cr) in the trivalent form (Cr(III)). Until now, this ore is utilized for manufacturing Cr pigments, chromic acid, dichromates, monochromates, and Cr metal. Cr is mostly utilized in the leather tanning, chrome plating, paint pigment, and wood treatment sectors. The most significant industrial source of chromium in the atmosphere is metallurgical, chemical, and heat-resistant application sectors (ATSDR 2012). Hexavalent chromium (Cr(VI) and trivalent chromium (Cr(III)) are two oxidation states of chromium that occur naturally (Sun and Costa 2022). The toxicity of Cr is based on the states where hexavalent chromium is more hazardous than trivalent chromium (Sun and Costa 2022). A long time ago, several researchers still proposed Cr(III) is commonly used as essential dietary nutrient at low dose (Anderson 1997; Krejpcio 2001; Heimbach and Anderson 2005; Pechova and Pavlata 2007). This statement was based on (1) studies related to low concentration exposure of chromium in rats' diet, (2) studies with total parental nutrition diets given to subjects, (3) studies related to absorption of chromium, however, those evidences are still problematic (Vincent 2017).

The benefit of Cr supplementation is not only for humans but also for animals. There are numerous benefits of Cr, including improved insulin activity (Chen et al. 2017), diminished inflammation and oxidative stress (Preuss et al. 1997; Tuzcu et al. 2011), and reduced body weight and improved blood lipid profile (Nachtigal et al. 2005; Kuryl et al. 2008). Untea et al. (2017) previously demonstrated that chromium picolinate (Cr(pic)) supplementation had effects on fat metabolism and protein, as well as increased amino acids in pork meat. In contrast to animals, the negative effect of Cr occurred to plants due to the accumulation of Cr such as diminished nutrients and the number of tomato fruit (Moral et al. 1995).

In contrast to previous studies, a novel study by Vincent (2017) proposed that chromium can only be included as an active pharmacological substance not a vital element/substance for a living organism. This statement is supported by the European Food Safety Authority (EFSA) (2014) assertion that there is no evidence of the health advantages of chromium consumption in healthy individuals. Other than that, there are no international acceptable plasma Cr values or ranges for the general population (Chen et al. 2017). Meanwhile, prolonged exposure to high levels of Cr can trigger genotoxic and cytotoxic effects, ultimately leading to immune system problems (Shrivastava et al. 2002). Others showed that Cr exposure may limit absorption of Zn or Fe from the gastrointestinal tract which can induce mineral deficiency and anemia (Lukaski 1999). The sixth most abundant element in the earth's crust, Cr, is one of the most dangerous inorganic soil pollutants (ATSDR 2012). Its average concentration is 125 mg/kg. (Sun et al. 2015a). Cr may enter the environment by air, water, soil, and the food chain (Mishra et al. 2019). Soil is one of the environmental media in which inorganic contaminants, such as Cr, can be found. It can serve as both a source and a sink for contaminants in terrestrial ecosystems.

Cr accumulation can easily infiltrate the soil, influencing the soil biota and humans. Nonetheless, the effects of the Cr accumulation in soil on terrestrial organisms are much more extensive because Cr accumulates in the food chain. Food crops are the most important nutrition source for human (Hefferon 2015; Dobermann et al. 2022). The nutritional and toxic substances of food crops will depend on the medium of planting. Plants can absorb Cr concentrated in the soil and accumulate it in the tissues. The accumulation of Cr in soil may contribute to bioaccumulation of Cr in plants. Fruit and vegetable consumption is the primary source of PTE exposure, accounting for 90% of metal intake, with inhalation of contaminated dust and direct skin contact accounting for the remaining 10% (Mawari et al. 2022). Hence, exposure of Cr to humans via ingestion or oral routes is significant for identifying the health risk in the future.

Cr will be absorbed into the body through inhalation, ingestion, and skin contact. Aside from skin contact, the principal routes of Cr exposure in humans are ingestion and inhalation (Langård and Costa 2015). Cr(VI) absorption is quicker than Cr(III) absorption through the digestive and respiration tract. Since food demand is increasing over time, food security and safety issues have become a significant public health concern in terms of human health. Transport of Cr from soil to plant is a crucial stage in the transmission of Cr between trophic levels in our food chain. From pesticide applications, wastewater disposal, sewage sludge applications, industrial effluents, and municipal waste, the food chain is regularly replenished with numerous compounds, including non-essential and essential trace elements such as chromium. Cr may be absorbed into plants from polluted soils and transported up the food chain to animals. Thus, Cr accumulation in soil and its relationship with the food chain are a concern due to human health impacts that may occur in the future. This section explains how soil contamination with Cr will affect human health via the food chain.

1.2 Fate and Source of Chromium in Terrestrial Ecosystems

The trace element such as chromium (Cr) can be found in volcanic dust and rocky soil (Sharma et al. 2020a). Chromium content in rocks is 100 mg/kg on average (Ma and Hooda 2010). Basaltic igneous rocks have an average Cr concentration of 200 mg/kg, ultramafic rocks 1800 mg/kg, sandstone 35 mg/kg, granitic rocks 20 mg/kg, shales and clays 120 mg/kg, and limestone 10 mg/kg (Ma and Hooda 2010). As a consequence of its high redox potential, complex valence shell chemistry, and electron chemistry, chromium may rapidly change from one oxidation phase to another (Prado et al. 2016; Shahid et al. 2017; Sharma et al. 2020b). In nature, Cr exists in multiple oxidation states ranging from valence −2 to +6. (ATSDR 2012; Shahid et al. 2017). The most common and stable oxidation phases of Cr in nature are 0 (elemental metal), +3 (trivalent), and +6 (hexavalent) (ATSDR 2008). Trivalent chromium (Cr(III)) exists as $FeOCr_2O_3$ (chromite), whereas hexavalent chromium (Cr(VI)) exists as CrO_4^{2-} (chromate) or $Cr_2O_7{}^{2-}$ (dichromate), both of which are toxic to organisms (Ertani et al. 2017). Since Cr(III) is highly immobile and has a strong bond with silicates, oxides, and organic matter, thus it is difficult to absorb by plants (Saha et al. 2017). Mobility of Cr is lower than that Cd and Ni. That relative mobility characteristic can be described by transfer coefficient (Sauerbeck 1987). The greater transfer coefficient indicates greater PTE mobility from soil to plant. According to Saha et al. (2017), heavy metals such as Co, Cr, Hg, Pb, Sn, As, Be, and F have low transfer coefficient value (0.01–0.1). Cr(VI) or hexavalent chromium is soluble and toxic to organisms (Astuti et al. 2023). This substance is highly toxic and is only immobile under an alkaline environment in the soil (Shanker et al. 2005; Sun et al. 2015b; Astuti et al. 2023).

The presence of Cr(VI) is associated with oxygen as CrO_4^{2-} or chromate and $Cr_2O_7^{2-}$ or dichromate oxyanions (Shanker 2019). Cr in the soil is representing the combination of trivalent chromium Cr(III) and hexavalent chromium Cr(VI) content. Naturally, chromium can transform into different oxidation states. Cr change can occur by reduction, precipitation, oxidation, dissolution, and sorption, among others (Kimbrough et al. 1999). In the soil, hexavalent chromium can change into trivalent chromium and vice versa (Apte et al. 2006). The transformation process of chromium can be influenced by various natural conditions in nature, such as changing of pH, Eh, temperature, and the presence of organic matter, oxygen and manganese oxide (Apte et al. 2006; Ma and Hooda 2010). Dissolved oxygen and manganese oxides are the oxidants in soil that facilitate the transformation of Cr (MnO_2) (Oliveira 2012; Shanker 2019). While Cr reduction can be influenced by the presence of iron, vanadium, sulphydes, and organic matters (Oliveira 2012). When Cr(VI) enters the soil environment with sewage sludge or polluted irrigation water, it rapidly converts to Cr(III) within one or two days in the presence of organic matter and acidic conditions (Saha et al. 2017).

Because trivalent chromium is less mobile than hexavalent chromium, the conversion from Cr(VI) to Cr(III) reduces Cr accumulation in plant tissue. The development of organic compounds in acidic conditions will increase the solubility of Cr(III) (Ma and Hooda 2010). Under aerobic conditions, Cr(III) can be oxidized to Cr(VI), most likely due to the presence of manganese oxide. Due to its high levels in the environment (soil and water) as a result of multiple anthropogenic and natural activities, Cr pollution in the environment has garnered significant attention (Quantin et al. 2008; Ashraf et al. 2017). The accumulation of Cr in plants will affect to plants' growth and photosynthesis process. Exposure to chromium compound is immensely harmful for

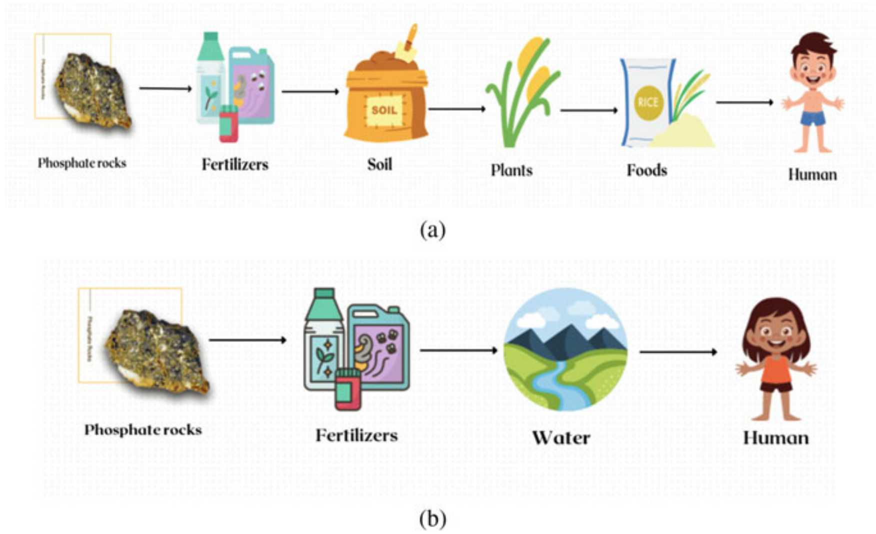

Fig. 1.1 Transfer Cr from fertilizers to human body

various plants. A 100 μM/Kg dry weight of Cr is hazardous to the majority of plant species (Davies et al. 2002). Chromium will enter the environment through surface runoff from industrial and mining areas, the leaching process from landfills, fossil fuel combustion, agricultural activities (e.g., fertilizer and pesticide applications), cement plant emissions, mineral leaching, and waste incineration. Textile industry, leather tanneries, electroplating industries, and steel industries are the common source of Cr (Ali et al. 2019). Fertilizers also contain Cr significantly (Krüger et al. 2017). Phosphate fertilizers derived from phosphate rocks may contribute to the global movement of Cr in the environment and have a substantial impact on the rise in human health risk and ecological risk. There are two major routes for transfer chromium from fertilizers to human (Fig. 1.1).

Cr has been widely used in many industries, primarily in chrome plating, paint pigment, wood treatment, and the leather tanning industry. Thus, anthropogenic sources of Cr have led to widespread pollution in the environment and have elevated biomobility and bioavailability. In addition to human-made sources, natural sources including the weathering of parent rocks also contribute to Cr pollution. Cr occurs naturally as chromite or $FeCr_2O_4$ in serpentine and ultramafic rocks, as well as in other metals including bentorite, $Ca_6(Cr, Al)_2(SO_4)_3$, crocoite, $PbCrO_4$, vauquelinite, $CuPb_2CrO_4PO_4OH$, and tarapacaite, K_2CrO_4 (Babula et al. 2008). Some natural, background, and average Cr concentration are presented in Table 1.1. The levels of Cr in the earth's crust ranges from 0.1 to 0.3 mg/kg (Shahid et al. 2017). In normal settings, Cr content ranges from 10 to 50 mg/kg; however, Cr buildup in agricultural soil can reach as high as 350 mg/kg (Ertani et al. 2017). Pathways of Cr transfer from soil to the human body are shown in Fig. 1.2. Human can expose to Cr through ingestion (food crops and geophagy or pica), direct contact with skin, and inhalation (wind-borne particulate).

Table 1.1 Natural, background, and average Cr concentration in the soil reported by several authors

Parameter	Concentration (mg/kg)	Place	References
Natural concentration	5–3000	India	Shanker et al. (2005), Shanker (2019)
Natural concentration	4.89–106	Korea	Kim et al. (2010)
Natural concentration	2–60	World	World Health Organization (1998)
Natural concentration	10–50	–	Shahid et al. (2017)
Background concentration	50–600	–	Ma and Hooda (2010)
Average concentration	93	Indonesia	Mallongi et al. (2021)
Average concentration	100	Jamaica	Mandal and Voutchkov (2011)
Average concentration	20.71–123.76	Turkey	Isıklı et al. (2003)
Average concentration	59.5	Poland	Kabata-Pendias (2011)
Average concentration	22	Sweden	Eriksson (2001)
Average concentration	58	Japan	Takeda et al. 2004)
Average concentration	25.6	Thailand	Zarcinas et al. (2004)

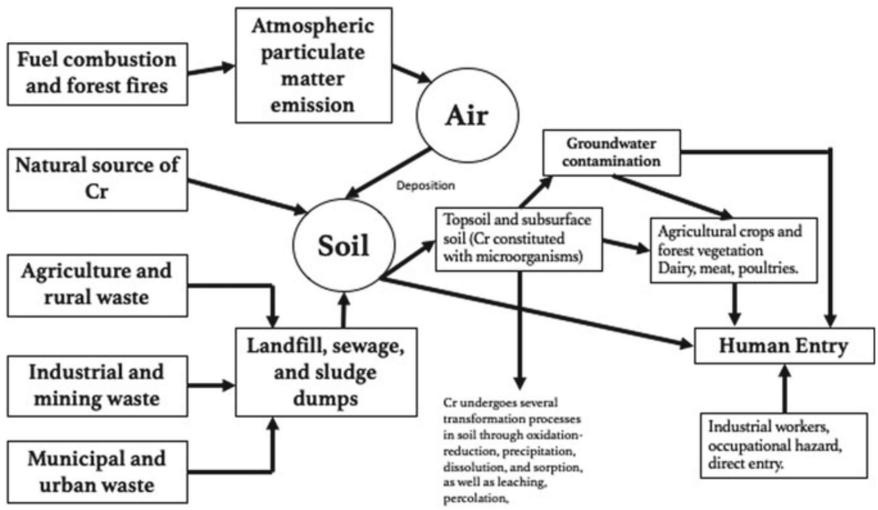

Fig. 1.2 Pathways of Cr transportation from soil to human body

1.3 Chromium in Terrestrial Ecosystems

1.3.1 Chromium Contamination in Plants

Contamination of the environment by Cr has become a major concern. Cr(III) occurs naturally as an essential nutrient in the environment, whereas Cr(VI) is a byproduct of industrial activities. (Sangwan et al. 2014). Low toxicity of Cr(III) associated with its immobility and insolubility. Moreover, both bioavailability as well as biomobility is increased in soil as well as in water. Plants suffer through unstable environmental conditions, biochemical accumulation and production of free radicals as they cannot escape from unfavourable environmental conditions. In hexavalent state, chromium is attributed to the cell impairment and cell damage (Barceloux and Barceloux 1999; Wise et al. 2019; Rauf et al. 2021). In plants, the accumulation of Cr comes from rock weathering, chemical fertilizers, various industrial effluents, fly ash disposal, soil and groundwater contamination. Soil conditions, pesticide residues, water quality, organic matter, pH and geological conditions are potential sources of PTEs (Covarrubias et al. 2018; Mallongi et al. 2019; Astuti et al. 2021a).

The absorption step is the initial interaction between Cr and a plant. Due to the similarities in composition between Cr(VI) and phosphate and sulfate ions, this reaction often occurs in the roots. Through the plasma membrane, root cells will transport phosphate or sulfate ions (de Oliveira et al. 2016; Sharma et al. 2020a). Previous study in *Phaseolus vulgaris* showed the highest bioaccumulation of Cr located in roots (Oruko Ongon'g et al. 2020). Cr(VI) accumulation can reduce the seed germination rate, growth, cell damage, pigment degradation, changes in enzymatic function and nutritional balance. In Fig. 1.3, the uptake of Cr(VI) impairs the beginning of lateral root primordia and influences nutrient absorption.

In developing countries with limited understanding of sustainable agriculture, high levels of Cr in media and crops will become a long-chain problem. Several studies reported the effect of Cr toxicity in plant growth that influences their essential metabolic processes. When there is a deficiency and an increase in the activity of the chlorophyllase enzyme, there is a decrease in the chlorophyll content of plants (Sharma et al. 2020a, b). In agronomic plants, the concentration of Cr in nutrient solution ranges from 0.5 to 5.0 mg/ml and from 5 to 100 mg/g in soil. The typical content of Cr in plants, according to Oliveira, is less than 1 μg/g (Oliveira 2012). Hexavalent chromium can deactivate numerous proteins that bind or displace metal ions from the active core of the protein. In addition, the generation of reactive oxygen species (ROS) during redox processes will activate antioxidant signaling and initiate cellular oxidative stress. This mechanism induces adverse alterations in plant morphology and physiology (Stambulska et al. 2018; DesMarias and Costa 2019; Cooper et al. 2022), caused a stunted growth in shoot and leaf. Edible vegetables with higher Cr(VI) content in the leafy parts of the plant represent a high health risk to consumers, causing harm to children who require primary nutrition from vegetables. Usually vegetables absorb inorganic and organic Cr ions during the growth period which are released through the fertilizers application (Oruko Ongon'g et al. 2020).

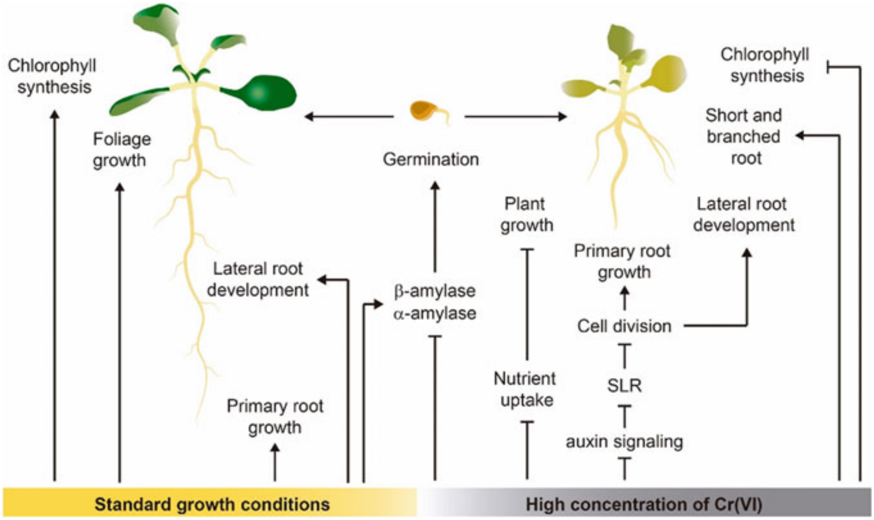

Fig. 1.3 Growth repression imposed by Cr(VI) in plants. Adopted from López-Bucio et al. (2022)

Using the bioaccumulation factor (BAF) index, one may assess the capacity of plants to absorb metals from the soil. This ratio is an assessment for determining metal concentration levels, showing the potential consequences of metal accumulation in the vegetables or fruit that will be consumed by humans or animals (Kováčik et al. 2012). If the BAF value is higher than one, the plant is a hyperaccumulator and phytoremediation actions are needed, whereas a value less than one means the plant is an excluder and not a good candidate for removal due to the low uptake of metal contents. The BAF index is calculated by measuring the concentration of metals in the roots, stems, and leaves of various plant parts (Agarwal et al. 2019; Mishra and Pandey 2019). The formula for calculating BAF showed in Eq. 1.1.

$$\mathrm{BAF} = \frac{\mathrm{Metal\ (plant\ part)}}{\mathrm{Metal\ (substrate)}} \tag{1.1}$$

According to a study conducted in Bangladesh, the levels of Cr in Spinach, Red Amaranth, Jute Leaf, Bottle Gourd, and Mustard Green surpassed the levels permitted by the Food and Agriculture Organization (FAO) and the Chinese Ministry of Health. This is owing to the accumulation and emission of effluents containing 30–40% Cr in the Buriganga River, which will rise due to the proximity of a battery manufacturing to the river (Miclean et al. 2018; Islam et al. 2020). Similarly, Cr has a high concentration in all parts of the plant as shown in Sidnh and Punjab, India, where increasing the value of BAF (>1) was recorded. In fruit, the high accumulation of Cr found in grapes in Cairo and Fayoum were surpassed the allowable limit of 0.10 mg/kg, which may lead to adverse health effects if consumed for a long time (Amer et al. 2019). Exposure to Cr(VI) reduced the root length and number of root hairs in *Zea mays*. The brown colour of this plant has also been attributed to less cell division (Xu et al. 2020).

Agriculture is the primary source of pollution and Cr presence. Transporting nutrients in agricultural crops will hinder plant growth. Some hyperaccumulating plants are utilized in the bioremediation procedure. Consistent monitoring of water quality, crops, soil, and sophisticated agricultural practices can reduce Cr content (Astuti et al. 2021b; Kapoor et al. 2022; Ali et al. 2022). To prevent the environmental contamination of Cr, the released and discharged of metals from anthropogenic activities must be reduced. Unfortunately, the use of coal and crude oil is one of the main factors for the high accumulation of metals in environmental media, especially in developing countries with low environmental awareness. Contamination of groundwater media is one of the causes of metal contamination, especially Cr, which is generated from agricultural and pond effluents. This element is often found in fly ash from cement dust and fine dust from vehicle exhaust and road surfaces. Government and society must implement cross-sectoral collaboration, communication, and environmental quality management to avoid the onset of Cr (Stambulska et al. 2018; Astuti et al. 2022). An ecofriendly strategy in the agricultural sector is highly desirable. Consumers are advised to clean and separate dirt from fruit or vegetables so that cross contamination can be avoided and the health risk will be lower.

1.3.2 Chromium Contamination in Animals

Trivalent chromium decreases heat stress, which induces lipid peroxidation, and enhances food metabolism and the action of insulin and cortisol hormones in animals, protecting them from the negative effects of heat stress. The minor effect of Cr exposure on rats presented the occurrence of motor coordination dysfunction. It was determined that the brain injury was not very dangerous. However, the detection of time-dependent changes poses a risk of increased server toxicity with prolonged exposure (Hegazy et al. 2021). During its reduction, the toxicity of Cr(VI) releases reactive oxygen species (ROS), which can cause protein, lipid, and DNA protein damage. In chronic animal investigations, the Reference dosage for Cr(III) is 1 mg/kg/d (Barceloux and Barceloux 1999). Based on one year of Sprague-Dawley rat drinking water research, the RfD for Cr(VI) is 5 g/kg/d. In Punjab, Cr levels in soil and forages were related to Cr buildup in the blood plasma of goats and sheep due to feeding practices (Khan et al. 2020).

The index of bioconcentration factor (BCF) is the most important component in determining exposure level. In a separate study on mice, exposure to Cr boosted the activity of the transaminase enzyme in all organs. It began by activating fatty acid synthase activity in hepatic tissue, boosting isocitrate dehydrogenase activity in the liver and skeletal muscle, and changing malate dehydrogenase activity in all tissues (Shil and Pal 2019). As depicted in Fig. 1.4, the presence of Cr in the environment originates from many sources and has detrimental effects on living organisms.

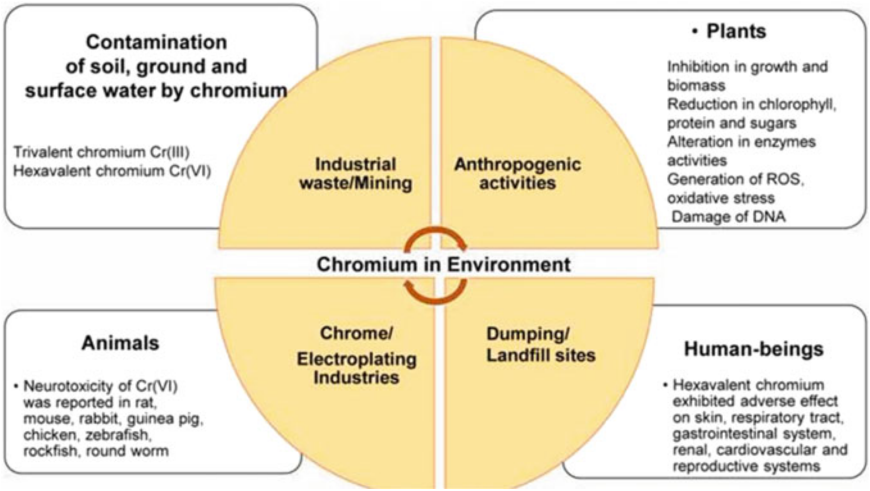

Fig. 1.4 The sources and interaction of Cr in environment. Adopted from Kapoor et al. (2022)

A study in crucian carp (*Carassius auratus*) reported the higher uptake rate for Cr(VI) in fish head comparing to fish muscle. Dynamic processes of metals play an important role during uptake, distribution and elimination. In aquatic exposure, the first organ to acquire Cr is the gills (VI). After absorption, Cr(VI) can be transported to various tissues, including the liver, kidney, and intestines, before being deposited in muscle (Mohamed et al. 2020; Yin et al. 2021; Astuti et al. 2022). As a vital organ for storage and detoxification, liver Cr levels are usually elevated after purification. The fish's head may act as a short-term buffer for Cr^{6+}, which is possibly connected with the high lead bone. The antioxidant responses of S. Schlegelii were affected by dietary Cr exposure. The expression of metallothionein (MT) in crustacea or aquatic animals is a sensitive biomarker for assessing the toxic effects of metal exposure, including Cr(VI). The gene expression of MT was significantly increased about 120 ascorbic acids (AsA) (Mohamed et al. 2020).

1.3.3 Chromium in the Human Body

Inducing severe clinical symptoms, allergies, and chronic diseases, Cr-contaminated foods and other exposures may pose concerns to human health. The previous study found the association of Cr(VI) with allergies and skin problems in human, specifically in workers (Bregnbak et al. 2016; Chou et al. 2016; Rauf et al. 2020a). Redness, itching, and inflammation of the skin were observed among industrial employees exposed to Cr in the cement manufacturing region of Taiwan. Additionally, some workers are diagnosed with dermatitis, ulcers, eczema, and an elevated risk of skin cancer (Wang et al. 2011; Chou et al. 2016). Workers exposed to Cr usually work in the electroplating, coating and printing process sectors. Apart from skin, workers also experience increased lung cancer due to the daily inhalation of Cr(VI). According to the Agency for Toxic Substances and Disease Registry (ATSDR), chromate tank employees in a chrome plating factory with inadequate ventilation reported the neurological effects of breathed Cr(VI) (ATSDR 2012). Cr(III) is absorbed orally at 1%, whereas Cr(VI) is absorbed primarily by intestinal bacteria in the duodenum.

a. **Absorption**

According to a number of studies, Cr(VI) compounds are more quickly absorbed in the lungs than Cr(III) compounds, due in part to their ability to penetrate cell membranes. Short-term exposure of 0.005–0.23 mg Cr(III) lignosulfonate dust to workers is still detectable in their urine at the end of their shift. Previous research in rats exposed to Cr demonstrated that particle size is the primary determinant of pulmonary clearance in both valence states, with Cr(VI) being more mobile and rapidly delivered to the circulation than Cr(III) (ATSDR 2012). Children are exposed to Cr when they eat food or drink water. Adults are exposed to Cr when they smoke cigarettes, use agricultural fertilizers, or eat food.

The entry of Cr into the body is associated with environmental conditions of air, soil and groundwater. Farmers who work around 3–6 h and above every day will be exposed to Cr through dermal exposure due to contact with agricultural soil (Rauf et al. 2020b; Motas et al. 2021; Ali et al. 2022). In addition, dermal contact with chromium can occur when bathing, although the risk is very small and negligible (Mallongi et al. 2022). Within a few hours, the body absorbs about 5% of the Cr(III) chloride. Several studies demonstrated the poor water solubility of chromates through the gastrointestinal tract, whereas more water-soluble chromates are absorbed into the blood (ATSDR 2016). Previous research has shown that ingesting Cr(VI) compounds causes nasal and pharyngeal discomfort in humans. Symptoms may include a runny nose, sneezing, coughing, itching, and a burning sensation. Exposure to low concentrations of Cr does not cause adverse effects directly in workers, but some of them will experience allergies when inhaling Cr compounds, which are associated with asthma characteristics like wheezing and shortness of breath. Maximum hexavalent chromium absorption was detected at 6 h, with a reduction at 72 h (Alvarez et al. 2021).

b. **Distribution**

The circulation of Cr(III) in the human body is affected by age, gender, and occupation. Cr may be transferred to fetuses while breast-feeding. A previous study found the association of woman worker and the breast milk quality in Murcia Region (Spain) (Motas et al. 2021). The highest levels of Cr and Mn were detected in the breast milk of women living near an agricultural region. Continuous exposure from infant's daily consumption and children age increase the intake of heavy metals and higher than those recommended. The distribution of Cr through the blood will carry over to the organs and affect the liver and kidney. Transferrin is responsible for Cr(III) transport and metabolism as a serum protein. It has the same size and charge as ferric ions (Edwards et al. 2020). The generation of free radicals can damage the protein molecules, lipids and nucleic acids. The molecular mechanism includes mutation of bases, strand breakage, DNA aberrations, RNA polymerase activity, and alterations in gene expression (Kapoor et al. 2022).

c. **Metabolism**

Cr(III) absorption into cells is 500 times lower than Cr(VI), and only 5% of Cr is absorbed by the body. In chromium-treated cell membranes, chromium increases the activity of insulin receptor tyrosine kinase. If chromium is transported to tissues, it could bond with both large and small molecules. An animal study showed the metabolic fate of $CrCl_3$ and CrO_4^{2-} collected from rat liver and their blood after the oral intake. Significant results of Cr(III) were observed in rat blood which has high binding activity for transferrin in plasma, whereas Cr(VI) is permeable to red blood cells and bound to hemoglobin. Bands from different chromium sources significantly differ in the cytosol of hepatocytes, Cr of $CrCl_3$ is an example of a primary bond with a high molecular weight protein (Feng 2007).

d. **Elimination**

Mutagenic carcinogens are strongly linked to DNA-reactive mutagenic mechanisms in Cr's chronic and carcinogenic effects (VI). In animal and human, elimination of Cr in the body can occur in urinary and sweat events. The nature of heavy metals, which makes decomposition difficult and time-consuming, will cause Cr to accumulate in the body for quite some time. Specific decomposition will be left in the body, especially Cr ions with a fairly high mobility in blood cells. This was proven through the previous studies on workers who were exposed to Cr and could still excrete it several hours later at work hours (Kapoor et al. 2022).

1.4 Effects of Chromium Exposure on Human Health

As an element with a high level of toxicity that is categorized as a heavy metal, Cr has a strong correlation with chronic diseases and is associated with bad environmental conditions. Consumed fruit or vegetables will accumulate Cr in the human body. Poor waste management, residual fertilizer carried by water into rice fields, and dry deposition of vehicle-generated particle dust on plant leaves would enhance the Cr accumulation in the soil. The use of fertilizers containing many trace metals will raise the risk of carcinogenic and non-carcinogenic substances, especially when consumed daily. Several cases of Cr exposure that disrupt the food supply chain and human health are presented in Table 1.2.

Based on the list of disease in Table 1.1, the carcinogenic effects in the form of cancer and skin disorders in workers dominate the negative effects of Cr exposure. As a result of consuming agricultural goods or coming into contact with high Cr levels, agricultural and industrial workers are exposed to adverse long-term impacts and perhaps elevated carcinogenic hazards that pose a future cancer hazard. Women and children are vulnerable populations due to their physical condition and higher

Table 1.2 Diseases and cases related to Cr exposure in human

S. No	Diseases	Symptoms	Country/locations	References
1	Dermatitis and eczema in cement workers	Itching, burning sensation and redness	Taiwan	Chou et al. (2016)
2	Psoriasis	Redness, itching and rash on the skin. High levels of Cr and other metals in scalp hair, blood and urine	Pakistan	Afridi et al. (2011)
3	Neuropsychological problems	Poor performance test, reaction and lower IQ	Spain	Caparros-Gonzalez et al. (2019)
4	Occupational contact dermatitis	Irritation and allergies from wet cement, skin permeation that causes sensation	Australia	Wong et al. (2015)
5	Chromium allergy	Itching, redness and chromium allergies	Denmark	Thyssen et al. (2009)
6	Kidney injury	Higher plasma blood and urinary chromium	Mexico	Cárdenas-gonzález et al. (2016)
7	Lung cancer	Small cell lung and breathing problem	Slovakia	Halasova et al. (2010)
8	Lung injury and cancer development	Suffering to breath and lung injury	USA	Beaver et al. (2009)
9	Cancer and non-cancer effects	Learning disabilities, decrease intelligence and growth disturbance	Poland	Mainka and Fantke (2022)
10	Tumor	Unstable metabolism and genomic instability	–	Wang et al. (2019)
11	Allergic contact dermatitis and irritant contact dermatitis	Psychosomatic condition, physical trauma, redness	–	Packham (2007)

intake of heavy metals, especially Cr (Glorennec et al. 2012; Caparros-Gonzalez et al. 2019; Motas et al. 2021).

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