

Role of Chromium in Liver Dysfunction and Oxidative Stress

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Abstract:

Chromium is a naturally occurring metal that exists in several oxidation states, of which trivalent chromium [Cr(III)] and hexavalent chromium [Cr(VI)] are the most biologically significant. While Cr(III) is considered an essential trace element involved in carbohydrate, lipid, and protein metabolism, excessive exposure to chromium, particularly Cr(VI), poses serious health risks. Human exposure occurs through industrial activities such as electroplating, leather tanning, stainless steel production, pigment manufacturing, mining, and contaminated water or food sources. Among the various organs affected by chromium toxicity, the liver is highly vulnerable because it serves as the primary site for detoxification and metabolism of toxic substances.

This review paper examines the role of chromium in liver dysfunction and oxidative stress, with a focus on its sources, mechanisms of toxicity, and health consequences. Chromium exposure has been shown to induce the generation of reactive oxygen species (ROS), leading to oxidative stress, lipid peroxidation, mitochondrial dysfunction, DNA damage, inflammation, and apoptosis in hepatic cells. These pathological processes contribute to impaired liver function, hepatocellular injury, altered enzyme activity, and an increased risk of chronic liver diseases. Experimental and epidemiological studies indicate that prolonged exposure to chromium may result in liver fibrosis, hepatic inflammation, and other metabolic abnormalities. The paper further explores the molecular pathways involved in chromium-induced hepatotoxicity and highlights the relationship between oxidative stress and liver dysfunction. Understanding these mechanisms is essential for improving risk assessment, developing preventive strategies, and minimizing the adverse health effects associated with chromium exposure. The study emphasizes the importance of environmental monitoring, occupational safety measures, and public awareness programs to reduce chromium-related health risks and protect liver health.

Keywords: Chromium, Hexavalent Chromium, Liver Dysfunction, Oxidative Stress, Hepatotoxicity, Reactive Oxygen Species, Heavy Metal Toxicity, Liver Injury, Environmental Pollution, Public Health.

Introduction

Chromium is a naturally occurring transition metal widely distributed in the environment and commonly used in various industrial processes. It exists in several oxidation states, among which trivalent chromium [Cr(III)] and hexavalent chromium [Cr(VI)] are the most important from a biological and toxicological perspective. Trivalent chromium is considered an essential trace element that plays a role in glucose metabolism, insulin function, and nutrient utilization. In contrast, hexavalent chromium is highly toxic and has been recognized as a significant environmental and occupational pollutant. Human exposure to chromium occurs through industrial activities such as electroplating, leather tanning, stainless steel

production, pigment manufacturing, welding, mining, and the discharge of industrial effluents into the environment.

The liver is one of the most vital organs in the human body and serves as the primary site for metabolism, detoxification, protein synthesis, and regulation of various biochemical processes. Because the liver receives and processes toxic substances absorbed from the gastrointestinal tract and bloodstream, it is particularly vulnerable to heavy metal toxicity. Following exposure, chromium accumulates in hepatic tissues where it can interfere with normal cellular functions and induce liver injury. The increasing levels of environmental and occupational chromium contamination have raised serious concerns regarding its adverse effects on liver health and overall human well-being.

One of the major mechanisms through which chromium exerts its toxic effects is the induction of oxidative stress. During cellular metabolism, chromium generates excessive reactive oxygen species (ROS) and free radicals that overwhelm the body's antioxidant defense system. This imbalance leads to oxidative damage of lipids, proteins, nucleic acids, and cellular membranes. Oxidative stress further contributes to mitochondrial dysfunction, inflammation, DNA damage, apoptosis, and disruption of normal hepatic metabolism. These pathological changes may result in hepatocellular degeneration, elevated liver enzyme levels, impaired liver function, fibrosis, and increased susceptibility to chronic liver diseases.

Numerous experimental and epidemiological studies have demonstrated a strong association between chromium exposure and liver dysfunction. Research findings indicate that prolonged exposure to chromium can alter antioxidant enzyme activity, disturb cellular signaling pathways, and promote inflammatory responses within liver tissues. Recent advances in molecular toxicology have further revealed that chromium-induced hepatotoxicity involves complex interactions among oxidative stress, genetic damage, immune responses, and metabolic disturbances. These findings have highlighted the need for a comprehensive understanding of chromium toxicity and its impact on liver function.

With rapid industrialization and environmental pollution, chromium contamination has become a growing global health concern. Therefore, investigating the role of chromium in liver dysfunction and oxidative stress is essential for understanding its toxicological effects and developing effective preventive strategies. The present research paper aims to examine the sources of chromium exposure, mechanisms of chromium-induced oxidative stress, its effects on liver function, and the potential approaches for reducing chromium-related health risks. The study may contribute valuable insights to the fields of toxicology, environmental health, and public health management.

S. No.	Aspect	Advanced Facts
1	Chemical Nature	Chromium is a transition metal that exists in several oxidation states, but Cr(III) and Cr(VI) are the most biologically relevant forms.
2	Essential vs Toxic Form	Cr(III) is an essential micronutrient involved in glucose metabolism, whereas Cr(VI) is highly toxic, mutagenic, and carcinogenic.
3	Major Exposure Sources	Electroplating, leather tanning, stainless steel manufacturing, welding, mining, pigments, dyes, and contaminated water sources.
4	Routes of Exposure	Inhalation, ingestion, and dermal absorption are the major pathways through which chromium enters the human body.
5	Environmental Persistence	Chromium remains in soil and water for extended periods and can bioaccumulate in ecosystems.
6	Target Organs	Liver, kidneys, lungs, skin, gastrointestinal tract, and immune system are the primary target organs.

7	Liver Vulnerability	The liver is highly susceptible because it acts as the central organ for detoxification and metabolism of xenobiotics.
8	Cellular Uptake	Cr(VI) easily enters cells through sulfate and phosphate transport channels due to its structural similarity to these ions.
9	Intracellular Reduction	Inside cells, Cr(VI) is reduced to Cr(V), Cr(IV), and finally Cr(III), generating reactive oxygen species (ROS) during the process.
10	Oxidative Stress	Excessive ROS production disrupts the balance between oxidants and antioxidants, leading to oxidative stress.

Review of literature

Several studies conducted in India have highlighted the adverse effects of chromium exposure on liver function and oxidative stress. Sharma et al. (2020) investigated the impact of chromium exposure among industrial workers and found that prolonged exposure significantly increased oxidative stress and elevated liver enzymes such as alanine aminotransferase (ALT) and aspartate aminotransferase (AST), indicating hepatocellular damage. Similarly, Kumar and Singh (2021) examined heavy metal contamination in industrial regions and reported that chromium accumulation in the liver resulted in oxidative stress, inflammation, and cellular injury. Patel et al. (2021) demonstrated through experimental studies that chromium-induced reactive oxygen species (ROS) production causes lipid peroxidation, mitochondrial dysfunction, and structural abnormalities in liver tissues. Verma et al. (2022) further observed that chromium exposure suppresses antioxidant defense mechanisms by reducing the activity of important enzymes such as superoxide dismutase, catalase, and glutathione peroxidase, thereby increasing oxidative damage in hepatic cells. Gupta et al. (2023) studied environmental chromium contamination and concluded that long-term exposure through polluted water and soil contributes to liver dysfunction, metabolic disturbances, and elevated oxidative stress biomarkers. More recently, Sharma and Sharma (2024) assessed chromium toxicity among tannery workers and reported increased inflammatory markers, abnormal liver function tests, and significant oxidative stress, confirming the hepatotoxic nature of chromium compounds. Rodríguez-Mercado and Altamirano-Lozano (2020) reviewed the genotoxic effects of chromium and concluded that chromium-induced oxidative stress contributes to DNA strand breaks, chromosomal abnormalities, and chronic liver diseases. Wang et al. (2022) further reported that chromium activates inflammatory signaling pathways and stimulates the production of pro-inflammatory cytokines, thereby promoting hepatic inflammation and fibrosis. Liu et al. (2023) found that chromium exposure disrupts mitochondrial energy production, resulting in hepatocyte damage and reduced liver function. More recently, Chen et al. (2024) highlighted that oxidative stress, inflammation, apoptosis, and epigenetic alterations are the primary mechanisms involved in chromium-induced liver dysfunction and emphasized the need for effective preventive and therapeutic strategies.

Although various research works have highlighted the biological role of Chromium and its adverse effects on our body, there are certain study areas which need clarity regarding the action of Chromium.

A review of the existing literature indicates that considerable research has been conducted on chromium toxicity and its adverse effects on human health, particularly with regard to oxidative stress and liver dysfunction. Most studies have established that chromium, especially hexavalent chromium [Cr(VI)], can induce oxidative stress, inflammation, DNA damage, mitochondrial dysfunction, and apoptosis, leading to hepatic injury and impaired liver function. However, despite the substantial amount of knowledge available, some important gaps remain in the current research. A majority of the studies have focused on acute or high-dose chromium exposure, whereas the long-term effects of chronic low-dose exposure commonly encountered in environmental and occupational settings have received relatively less attention.

Furthermore, many investigations are based on experimental animal models and in vitro studies, while human-based epidemiological research examining the direct relationship between chromium exposure and liver dysfunction is comparatively limited.

In addition, the precise molecular and cellular mechanisms through which chromium-induced oxidative stress contributes to the progression of chronic liver diseases are not yet fully understood. There is also a lack of comprehensive studies exploring genetic susceptibility and individual variations in response to chromium exposure. Another important limitation is the absence of reliable and sensitive biomarkers for the early detection of chromium-induced liver damage before clinical symptoms become apparent. Most of the previous studies have examined chromium exposure as an isolated factor, whereas real-life environmental conditions often involve simultaneous exposure to many heavy metals and pollutants, which may have synergistic toxic effects on liver function. Moreover, limited research has been conducted on the effectiveness of antioxidant therapies, nutritional interventions, and preventive strategies aimed at reducing chromium-induced oxidative stress and hepatotoxicity.

The literature also reveals lack of longitudinal studies that evaluate the long-term progression of liver dysfunction associated with chronic chromium exposure. Region-specific studies assessing chromium contamination and its health impacts in developing countries are also relatively scarce. Therefore, there is a need for further research to better understand the relationship between chromium exposure, oxidative stress, and liver dysfunction, particularly in human populations. The present study, seeks to address these gaps by providing a comprehensive examination of chromium toxicity, its mechanisms of liver injury, associated oxidative stress pathways, and potential preventive measures. The findings of this study are expected to contribute to the fields of environmental toxicology, hepatology, and public health by enhancing understanding of chromium-induced liver disorders and supporting the development of effective risk reduction strategies.

This review aims to study the effects of Chromium on the biochemistry and pathology of Liver.

1. Identifying the major sources and routes of chromium exposure in humans.
2. To study the accumulation and distribution of chromium in liver tissues.
3. To evaluate the effects of chromium exposure on liver structure and function.
4. To examine the role of chromium in the generation of oxidative stress and reactive oxygen species (ROS).
5. To analyze the molecular and cellular mechanisms involved in chromium-induced hepatotoxicity.
6. To assess the relationship between chromium exposure and alterations in liver function biomarkers such as ALT, AST, ALP, and bilirubin.
7. To examine the impact of chromium exposure on antioxidant defense systems, including superoxide dismutase, catalase, and glutathione.

Analysis of the study

The analysis of the study indicates that chromium exposure, particularly in the form of hexavalent chromium [Cr(VI)], has a significant impact on liver function and is strongly associated with the development of oxidative stress. Chromium enters the human body through contaminated water, food, industrial emissions, occupational exposure, and environmental pollution. Once absorbed, it accumulates in various organs, particularly the liver, where it undergoes metabolic transformations that generate excessive reactive oxygen species (ROS). These free radicals disrupt the balance between oxidants and antioxidants, resulting in oxidative stress, which is considered the primary mechanism underlying chromium-induced hepatotoxicity.

The study further reveals that oxidative stress damages essential cellular components such as lipids, proteins, and nucleic acids, leading to impaired cellular metabolism and structural abnormalities in liver tissues. Elevated levels of liver enzymes, including Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), and Alkaline Phosphatase (ALP), observed in several studies indicate hepatocellular injury and reduced liver function. Chromium exposure also affects mitochondrial activity, reduces energy production, and promotes inflammatory responses that contribute to liver dysfunction. Histopathological investigations have reported degeneration of hepatocytes, cellular necrosis, inflammatory infiltration, and fibrosis in chromium-exposed subjects.

The analysis also highlights that prolonged and repeated exposure to chromium may weaken the body's antioxidant defense system by decreasing the activity of enzymes such as superoxide dismutase, catalase, and glutathione peroxidase. This decrease in antioxidant protection further enhances oxidative damage and increases the susceptibility of liver cells to injury. In addition, chromium-induced DNA damage, apoptosis, and alterations in gene expression have been identified as important factors contributing to chronic liver diseases and potential carcinogenic effects.

Available reports have demonstrated consistent evidence regarding the toxic effects of chromium on liver health. Industrial workers, miners, welders, electroplating workers, and individuals residing near contaminated areas were found to be at greater risk of chromium-induced liver disorders. The severity of liver dysfunction was observed to depend on the concentration of chromium exposure, duration of exposure, nutritional status, age, and individual susceptibility.

Overall, the analysis confirms that chromium is a potent environmental and occupational toxicant capable of causing significant liver damage through oxidative stress-mediated mechanisms. The findings emphasize the importance of environmental monitoring, industrial waste management, occupational safety practices, and antioxidant-based preventive strategies to reduce chromium exposure and protect liver health. Further research is required to identify early biomarkers of chromium-induced liver injury and to develop effective therapeutic interventions for minimizing its adverse health effects.

Aspects of Chromium Toxicity

Chromium occurs widely in nature in various oxidation states ranging from Cr(II), Cr(III), Cr(IV), Cr(V), and Cr(VI) out of which the hexavalent (Cr-VI) Chromium is the most toxic form, which has the ability to cross the Cellular membranes easily through the nonspecific anion transporters. Within the cells hexavalent Chromium gets reduced by reductant compounds into pentavalent (Cr-V), tetravalent (Cr-IV) and trivalent (Cr-III) reactive intermediates along with the generation of Reactive Oxygen Species (ROS).

ROS entities, then induce lipid peroxidation of cellular and subcellular structures, especially the membranes, DNA strand breaks and modification of Bases, all of which eventually lead to the perturbation of normal cellular physiology and generation of toxic effects.

Although the general toxic effects of Chromium noted in the individuals subjected to occupational exposure or environmental sources, ulcerations in the nasal septum, leading to carcinogenesis, apart from increased risk of asthma. Effects on the liver are of special interest, as it is a vital and largest glandular organ of our body and is biochemically active, with considerable powers of Regeneration.

Chromium in its hexavalent state, has been found to exert adverse effects upon hepatocytes due to decrease of cell viability and increase in hypodiploid sub-G1 DNA populations.

The levels of lipid peroxidation in hepatocytes by hexavalent Chromium has been to dose dependent, along with the generation of ROS entities.

Also there are reports that there is a decrease of mitochondrial membrane depolarization due to which normal mitochondrial function is disturbed. Conditions of Oxidative stress can arise which can then lead to Mitochondrial damage.

The cytotoxic effects of Chromium have been found to mediate the eventual apoptosis of Hepatocytes.

Conclusion

The present study concludes that chromium is a significant environmental and occupational pollutant that poses serious risks to liver health through the induction of oxidative stress and hepatotoxicity. Among the different forms of chromium, hexavalent chromium [Cr(VI)] is particularly harmful due to its high toxicity, mobility, and ability to penetrate biological membranes. Human exposure to chromium occurs through contaminated food, water, industrial emissions, occupational activities, and environmental pollution, resulting in its accumulation in various tissues, especially the liver.

The findings of the study demonstrate that chromium-induced oxidative stress is the principal mechanism responsible for liver dysfunction. Excessive production of reactive oxygen species (ROS) and free radicals disrupts the balance between oxidants and antioxidants, leading to lipid peroxidation, protein oxidation, DNA damage, mitochondrial dysfunction, inflammation, and apoptosis. These pathological changes impair normal liver function and contribute to hepatocellular injury, elevated liver enzyme levels, fibrosis, and the development of chronic liver diseases. Furthermore, prolonged exposure to chromium may weaken antioxidant defense systems and increase susceptibility to severe hepatic disorders.

The study also highlights that occupational workers and populations residing in contaminated environments are at a higher risk of chromium-induced liver damage. Factors such as exposure duration, concentration levels, nutritional status, age, and genetic susceptibility influence the severity of toxic effects. Existing scientific evidence consistently supports the association between chromium exposure, oxidative stress, and liver dysfunction, emphasizing the need for effective preventive measures.

In conclusion, chromium contamination represents an important public health concern that requires continuous monitoring and management. Environmental protection measures, strict industrial regulations, occupational safety standards, proper waste disposal practices, and public awareness programmes are essential for minimizing chromium exposure. Additionally, further research is needed to identify sensitive biomarkers of early liver injury, understand long-term health consequences, and develop effective therapeutic strategies to counteract chromium-induced oxidative damage. Overall, reducing chromium exposure is crucial for protecting liver health and promoting environmental and human well-being.

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