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Effects of Heavy Metal Toxicity on Different Animal Models

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Abstract: Due to the widespread environmental contamination caused by heavy metal toxicity, is becoming a growing threat to all biological life form on Earth. In this case animal models play had an urgent impact in figuring out the impacts of heavy metal exposure on different animal species. The negative effects of heavy metals such as Hg, Pb, Cr, Cd, and as has been seen in animals' models to cause damage to various organs such as nervous, respiratory and reproductive systems. Additionally, the translational implications for human health and differences in animal sensitivity to heavy metal toxicity are also investigated. This survey study aims to provide a thorough overview of how heavy metal poisoning affects diverse animal models. The advantages and disadvantages of various animal models for heavy metal toxicity research are highlighted in this discussion. This review emphasizes the need for additional research in this area and the significance of animal studies in elucidating the dangers and potential effects of heavy metal toxicity.
Keywords: Heavy metal, animal models, environmental contamination, biological systems, nervous system

I. INTRODUCTION

Heavy metals are persistent contaminants in the environment that pose serious threats to wildlife and human health. As a result of both natural processes and human activities like mining, industrial processes, and agricultural practices, these toxic elements, such as (Pb) lead, (Hg) mercury, (Cd) cadmium, and (As) arsenic, are widely distributed in the environment (Goyer, 2019; Liu et al., 2019). Heavy metals can accumulate in soil, water, and the air, among other environmental compartments, and then bioaccumulate and biomagnify their way into the food chain (Beyer et al., 2015; Storelli et al., 2019). Because of this, animals like mammals, birds, fish, and invertebrates frequently come into contact with heavy metals, which can have a number of negative effects on their health. To assess the potential ecological and public health repercussions, it is essential to comprehend the effects of heavy metal toxicity on various animal models. In toxicological research, animal models are useful tools for studying complex interactions between organisms and their environment (Lushchak, 2014). By using experimental models, scientists can research the components of heavy metal toxicity, recognize target organs and physiological cycles impacted, and assess the portion reaction connections (Foulkes and Murphy, 2010). Besides, experimental animal models give a way to investigate animal types explicit varieties in defenselessness and reactions to heavy metal liability, which can illuminate risk evaluation and the improvement regarding proper mediation procedures. The impacts of heavy metal harmfulness on experimental models have been broadly researched across different disciplines, including toxicology, natural wellbeing, and ecotoxicology.

Animals exposed to heavy metals have had their physiological, biochemical, and behavioral responses studied, providing insight into the underlying mechanisms and potential health effects (Santos et al., 2020; Wang et al., 2021). Moreover, research has investigated the effect of heavy metal harmfulness on animal generation and advancement, taking into account both prompt and long-haul impacts (Sun et al., 2018; Li et al., 2020). Furthermore, research have been conducted to investigate the ecological implications of heavy metal poisoning, namely how it affects animal populations, ecosystems, and the functioning of ecological communities. (Brix and Gerdes, 2016; Ma et al., 2020). By looking at the physiological, biochemical, and social reactions seen in these models, we can acquire a far-reaching comprehension of the likely risks and impacts of heavy metal exposure on living life forms. This review paper expects to give an inside-out investigation of the impacts of heavy metal toxicity on various experimental models, accentuating the natural and general wellbeing suggestions. By looking at the physiological, biochemical, and social reactions seen in these models, we can acquire a far-reaching comprehension of the likely risks and impacts of heavy metal exposure on living life forms. The study will discuss the purpose of examining the dangers of heavy metals, including how they relate to both human and animal health. It will investigate the various sources that expose animals to heavy metals, including industrial activities and contaminated soil, water, and air. In addition, it will emphasize the significance of utilizing animal models in order to decipher the effects of heavy metal toxicity and extrapolate those effects to the health of humans.

II. HEAVY METALS AND SOURCES OF EXPOSURE

Heavy metals are metallic components that have relatively high density. When present in the environment, these elements pose significant threats to wildlife and human health due to their toxic properties (Bernhoft, 2012). Normal instances of heavy metals that have been broadly read up for their harmful impacts incorporate Pb, Hg, Cd, Cr and As.

Pb is a common heavy metal that has been used extensively in gasoline, paint, batteries, and other industries. Verifiable utilization of leaded gas and toxic paints has brought about broad natural pollution (Dietrich et al., 2019). Hg is another important heavy metal that is of concern in both natural (methylmercury) and inorganic systems. Mercury contamination in the environment is generated by both industrial and natural activities such as coal combustion and mining (Clarkson et al., 2003). Cd can be found in emissions from businesses such as smelting and battery manufacture, as well as electronic waste disposal (Wang et al., 2020). Natural processes such as volcanic activity, as well as human activities such as mining and pesticide usage, can both release inorganic and organic forms of As into the environment (Naujokas et al., 2013).

Heavy metals can enter the environment of animals in a variety of ways. Heavy metals can be stored in large quantities in contaminated soil, especially in areas that have a history of industrial activity or are close to mining sites. The deposition of airborne particles or the release of industrial effluents and waste materials can result in soil contamination (Zhou et al., 2018). Due to industrial discharges, agricultural runoff, and improper waste disposal, elevated levels of heavy metals can also be found in water sources like rivers, lakes, and oceans (Storelli et al., 2019). Heavy metal pollution in the atmosphere is caused by airborne emissions from industrial processes, vehicle exhaust, and fossil fuel combustion, which can then deposit on land and water surfaces (Khan et al., 2015). Modern exercises are a significant wellspring of heavy metal exposure for animals. Heavy metals are released into the environment in large quantities by mining, metal smelting, battery manufacturing, and waste incineration (Khan et al., 2015). Additionally, agricultural practices, such as the use of pesticides and fertilizers containing heavy metals, can contaminate crops and animal forage (Fernandes et al., 2020). Heavy metals can enter the food chain through bioaccumulation and biomagnification, in addition to direct exposure. By consuming contaminated prey, predatory animals at higher trophic levels can accumulate higher concentrations of heavy metals (Storelli et al., 2019).

III. ANIMAL MODELS USED IN HEAVY METAL TOXICITY STUDIES

The effects of heavy metal toxicity have been studied using a variety of animal models. These models incorporate rodents (e.g., mice, rodents), fish (e.g., zebrafish, rainbow trout), and birds (e.g., Japanese quail, chickens). Each model offers unmistakable benefits and permits specialists to investigate various parts of heavy metal poisonousness. Due to their physiological and genetic similarities to humans, rodents, particularly mice and rats, are frequently utilized in toxicological studies (Hartung et al., 2002). They are ideal for examining the molecular and cellular mechanisms underlying heavy metal toxicity because of their well-established genetic resources, short reproductive cycles, and ease of handling and housing (Foulkes & Murphy, 2010). Including the processes of absorption, distribution, metabolism, and excretion, rodents provide valuable insights into the toxicokinetic and toxicodynamic of heavy metals (Sun et al., 2018). Their small size also makes it possible to conduct studies at a reasonable cost with small sample sizes.

For studying how heavy metals affect aquatic organisms and ecosystems, fish like zebrafish and rainbow trout are useful models. Fish have comparable organ frameworks to vertebrates and offer monitored sub-atomic pathways associated with metal digestion and detoxification (Wang et al., 2021). They are excellent indicators of environmental pollution because they are highly sensitive to contaminants that are carried by water (Brix & Gerdes, 2016). Fish models have advantages such as simplicity during the early phases of development, as well as continual perception of toxicological reactions, as well as the plausibility of examining multi-generational impacts and potential transgenerational legacy of heavy metal toxicity (Lushchak, 2014). Heavy metal exposure in birds has been studied using bird models like Japanese quail and chickens. Because they are exposed to environmental contaminants through a variety of means, including ingestion of contaminated food and water, inhalation, and dermal contact, birds are particularly relevant to ecotoxicological studies (Scheuhammer et al., 2003). According to Eva et al (2010), avian species are suitable for investigating the effects of heavy metal toxicity on reproduction, developmental processes, and ecological interactions within avian populations and ecosystems because they exhibit a variety of physiological adaptations and behaviors.

The determination of explicit animal models depends on their physiological, hereditary, and natural significance to the examination question worth mentioning. The extrapolation of findings to comprehend potential effects on the health of humans and wildlife is made possible by physiological similarities between the chosen animal model and the target species or humans (Goyer, 2019). The study of genetic susceptibility and the mechanisms underlying heavy metal toxicity is made possible by genetic similarities.

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Assessments of population-level impacts and interactions within ecosystems are made possible by ecological relevance, which guarantees that the chosen animal model accurately reflects the ecological context of heavy metal exposure.

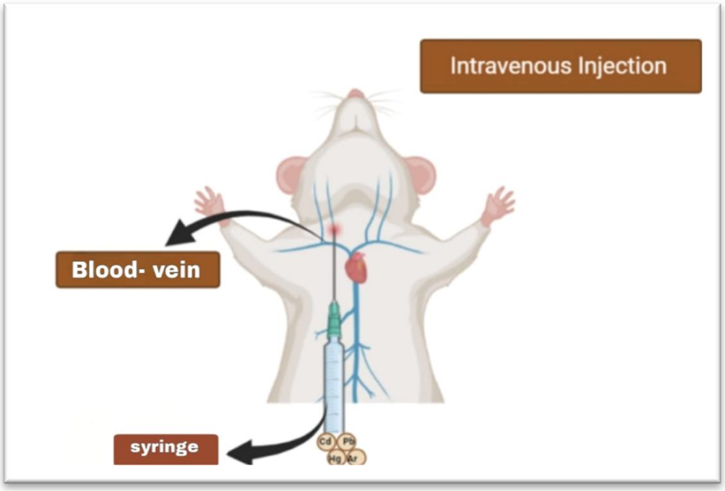

Fig1: figure is showing Intravenous Injection (IV): Heavy metals lead (pb), cadmium (Cd), Mercury (Hg) etc. are injected directly into a vein, allowing for immediate distribution throughout the bloodstream. IV injection is used when researchers need precise control over the dose and rapid delivery of the heavy metal.

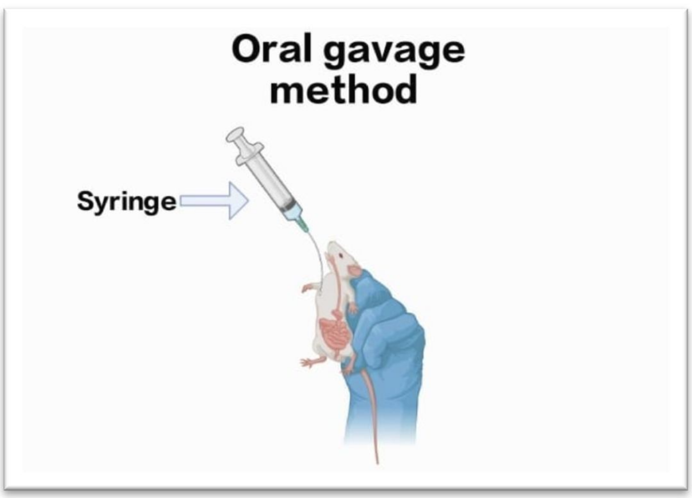

Fig 2: figure is showing Oral Gavage: This method involves administering the heavy metal solution directly into the stomach through a gavage needle or tube. Oral gavage is commonly used when researchers want to study the effects of ingesting heavy metals, simulating exposure through contaminated food or water. Distribution of heavy metal in the body of experimental model shows biochemical changes like elevation in oxidative stress, ROS production which lead to many health issues in body further.

IV. EFFECTS OF HEAVY METAL TOXICITY ON ANIMAL HEALTH

Animals can experience profound physiological, biochemical, and behavioral effects from heavy metal exposure. Significant health problems can result from these effects, which can manifest across a variety of biological processes and organ systems. Understanding the systems hidden heavy metal harmfulness is essential for appreciating the full degree of its effect on animal wellbeing. Changes in organ morphology and function, disruptions in reproductive processes, and other physiological effects have been observed in animals exposed to heavy metals (Storelli et al., 2019). Endocrine disruption and reproductive dysfunction can result from heavy metals interfering with hormonal regulation (Ji et al., 2019). They may likewise weaken resistant capability, making animals more powerless to contaminations and infections (Siah et al., 2015). Furthermore, heavy metals can make harm to imperative organs like the liver, kidney, cerebrum, and lungs, prompting tissue degeneration and brokenness (Flora et al., 2012).

Biochemical impacts of heavy metal harmfulness include aggravations in cell processes and metabolic pathways. Heavy metals can cause oxidative stress, which causes an imbalance between the antioxidant defense systems and the production of reactive oxygen species (ROS) (Wang et al., 2019). Damage to cells, lipid peroxidation, and oxidation of DNA and proteins are all possible outcomes of this oxidative stress (Valko et al., 2007). According to (Wang et al. 2010), heavy metals may also affect energy metabolism, interfere with nutrient uptake and utilization, and disrupt enzyme activities. Cellular homeostasis and overall physiological function can be profoundly affected by these biochemical disruptions. Animals that are exposed to heavy metals frequently experience behavioral effects. Conduct adjustments might remember changes for locomotor action, taking care of conduct, regenerative ways of behaving, and social collaborations (Al-Bairuty et al., 2019). Neuronal signaling disruptions and behavioral abnormalities can result from heavy metals' effects on neurotransmitter systems (Sánchez-Chardi et al., 2017). These social changes might have suggestions for a animal's endurance, generation, and by and large wellness inside its environmental specialty.

Multiple pathways are involved in the toxicity of heavy metals' mechanisms. A key mechanism by which heavy metals produce reactive oxygen species (ROS), overwhelm antioxidant defenses, and cause cellular damage (Flora et al., 2012). Heavy metals can likewise freely tie to biomolecules like DNA, proteins, and catalysts, prompting primary adjustments and utilitarian debilitations (Jomova and Valko, 2011). DNA harm, including strand breaks and DNA adduct development, can bring about hereditary changes and chromosomal abnormalities (Vegetation et al., 2012). By interfering with essential enzymes and cellular signaling pathways, heavy metals can also disrupt cellular processes, resulting in impaired metabolism, altered gene expression, and cell death (Wang et al., 2019).

V. SPECIES-SPECIFIC RESPONSES TO HEAVY METAL TOXICITY

Heavy metal toxicity can display varieties in vulnerability and reactions among various animal species. For assessing potential risks to human health and the ecological effects of heavy metal exposure, it is essential to comprehend these species-specific effects. The physiological, biochemical, and behavioral responses of various animal species to heavy metal exposure vary. For instance, some species may have metal-binding proteins or detoxification mechanisms that lessen the toxic effects of heavy metals (Jiang et al., 2020). On the other hand, differences in metabolic pathways or genetic predispositions may make some species more vulnerable to heavy metal poisoning (Costa et al., 2014).

Instances of species-explicit impacts of heavy metal harmfulness feature the variety in reactions and their suggestions for natural networks and human wellbeing. For example, certain fish species might display higher amassing and bioaccumulation of heavy metals because of contrasts in their taking care of propensities and trophic positions (Rice et al., 2012). Predator fish can have higher concentrations of heavy metals as a result, putting wildlife and human consumers of contaminated fish at risk (Lavoie et al., 2020). Birds, particularly raptors and waterfowl, are known to be profoundly delicate to heavy metal harmfulness because of their taking care of ways of behaving and physiological attributes (Lemus et al., 2018). Scavenging birds can suffer severe neurotoxic effects, such as impaired motor functions, reproductive failure, and even death, from exposure to lead ammunition residues in carcasses or ingestion of lead fishing tackle (Mateo, 2009). Such species-explicit impacts can affect pecking orders and environmental networks, influencing populace elements and biological system working.

Human health is affected by species-specific responses to heavy metal toxicity, which affect wildlife as well.

Due to their physiological similarities, some animal species, like rodents, are frequently used as models for studying the effects of heavy metals on human health (Cory-Slechta et al., 2017). Findings can be extrapolated to human health risks associated with heavy metal exposure by comprehending species-specific responses in these animal models. When assessing the effects of heavy metal contamination on wildlife and ecosystems, the species-specific responses highlight the significance of ecological and biological factors. By perceiving the varieties in powerlessness and reactions among various animal species, specialists can all the more likely assess the possible dangers and foster designated moderation systems.

VI. IMPACT ON REPRODUCTION AND DEVELOPMENT

In animal models, heavy metal exposure has been shown to have significant effects on reproductive processes and developmental outcomes. Understanding these effects is essential for determining the potential risks of heavy metal toxicity on population components and for analyzing the long-term effects, such as transgenerational effects. Heavy metals can hinder regenerative capabilities in animals, prompting decreased richness, hindered mating ways of behaving, and adjustments in chemical guideline. For example, exposure to heavy metals like Pb, Hg, and Cd may interfere with the production and arrival of conceptual chemicals, affecting animal reproductive cycles and fertility (Ji et al., 2019).

Additionally, heavy metals can hinder gamete production, resulting in decreased reproductive success and abnormalities in sperm and egg quality (Storelli et al., 2019). These conceptual impairments may have serious effects on the dependability of the environment and population reasoning.

Additionally, exposure to heavy metals during crucial developmental times may result in a variety of abnormalities and negative outcomes. Heavy metals may cause organ malformations, growth retardation, and skeletal deformities in animal models during embryonic or fetal development (Barker et al., 2018). Neurodevelopmental disorders, including cognitive impairments and behavioral abnormalities, have been linked to heavy metals like mercury and arsenic (Grandjean & Landrigan, 2014). Additionally, heavy metal exposure in the early stages of pregnancy and postpartum can disrupt the normal immune system development, making people more susceptible to infections and autoimmune disorders (Siah et al., 2015). One significant thought in concentrating on the effect of heavy metal harmfulness on multiplication and advancement is the potential for transgenerational impacts. Heavy metals have the potential to change how genes involved in reproduction and development are expressed, causing heritable changes that can pass down to future generations (Skinner et al., 2013). Alterations in reproductive capacities, increased susceptibility to diseases, or even changes in behavioral traits between generations are all examples of transgenerational effects (Manikkam et al., 2012). When evaluating the effects of heavy metal exposure, it is essential to take into account the long-term consequences as well as the potential effects on population dynamics.

VII. ECOLOGICAL AND ENVIRONMENTAL IMPLICATIONS

Toxicity to heavy metals poses significant ecological threats to ecosystems and wildlife populations. Understanding the biological effects is fundamental for assessing the general wellbeing and working of environments, as well as expected dangers to human population through the utilization of polluted food. One significant environmental peculiarity related with heavy metal harmfulness is biomagnification. Biomagnification alludes to the cycle by which the grouping of heavy metals increments at higher trophic levels in pecking orders. Heavy metals build up in the tissues of organisms at lower trophic levels as a result of their exposure. The accumulated heavy metals are transferred and become increasingly concentrated in hunters' bodies when they ingest large amounts of prey. (Lavoie et al., 2020). According to Sanchez-Chardi et al. (2017) this can result in elevated levels of heavy metals in top predators like birds of prey and large fish, which can have severe effects on their reproductive success, survival, and overall population dynamics.

The accumulation of heavy metals within an individual organism over time is referred to as bioaccumulation, which is closely related to biomagnification. Metals accumulate in tissues of animals faster than they are eliminated when they consume contaminated food or absorb heavy metals from the environment. This can bring about elevated degrees of heavy metals inside people perhaps ending up with harmful fixations (Storelli et al., 2019). Bioaccumulation can contribute to impacts at the population level and have negative effects on the health and survival of individual organisms. The environmental ramifications of heavy metal toxicity reach out past individual species to biological system level impacts. Heavy metals have the potential to disrupt ecosystem processes and functions like the flow of energy and nutrients. In amphibian environments, for instance, heavy metals can influence essential makers like green growth and phytoplankton, prompting diminished efficiency and changes in the creation of the food web (Wang et al., 2019). Multiple trophic levels, species interactions, and cascading effects across the ecosystem may be impacted by this disruption.

Additionally, the impact of heavy metal toxicity on biodiversity and the resilience of ecosystems can have wider repercussions for the environment. Heavy metals may make some species more sensitive or vulnerable, changing the composition of the species and reducing biodiversity. According to (Lemus et al. 2018), ecosystem stability can be compromised when key species in an ecosystem disappear. Moreover, heavy metals can remain in the environment for extended periods of time, causing long-term pollution and perhaps affecting people and other living things in the future.

VIII. HUMAN HEALTH CONSIDERATIONS

Focusing on the effects of heavy metal toxicity in animal models provides important insights into the anticipated repercussions for human welfare. Experimental animal models are important means of comprehending the harmful elements, identifying potential health risks, and enlightening risk assessment and general wellness plans.

Findings from animal research can help connect the dots between exposure to heavy metals and outcomes for human health. While direct extrapolation from animal models to people ought to be done carefully, animal studies provide important first-hand evidence and help identify potential channels and sources of damage.

Heavy metals like Pb, Hg, and Cd, for instance, have been shown to cause oxidative stress, DNA damage, and disruptions in cellular processes in animal models, all of which are linked to a variety of human diseases and health conditions (Barbosa et al., 2019; Rehman and other, 2019).

The development of frameworks for evidence-based risk assessment is aided by animal studies. By clarifying the portion reaction connections and distinguishing basic exposure windows, animal models assist with deciding safe exposure restricts and foster rules for the security of human wellbeing. For instance, regulatory standards for heavy metals in food, water, and workplace settings have been established thanks to animal model studies (Dórea, 2015; Hu and co., 2019).

IX. FUTURE DIRECTIONS

As we continue to advance our understanding of heavy metal toxicity, there are several important areas of research that can provide valuable insights and shape future strategies for mitigating the ecological and health risks associated with heavy metal exposure. In this section, we discuss key future directions for research on heavy metal toxicity in animal models.

1) Long-term effects and transgenerational impacts: Investigating the long-term effects of heavy metal exposure is crucial to understand the persistence and cumulative impacts of these contaminants. Studies examining transgenerational effects, where exposure to heavy metals in one generation affects subsequent generations, can shed light on the potential long-lasting consequences of heavy metal toxicity. Such research can help identify molecular mechanisms underlying transgenerational effects and develop strategies for mitigating these impacts (Carvan et al., 2017; Manzetti and Zhang, 2019).
2) Interactions between heavy metals and multiple stressors: Organisms are often exposed to multiple stressors simultaneously, including heavy metals and other environmental pollutants. Research focusing on the interactions between heavy metals and other stressors, such as pesticides, climate change, or habitat degradation, is essential. Understanding these interactions can help elucidate synergistic or antagonistic effects and provide insights into the complex ecological implications of multi-stressor exposures (Tripathi et al., 2019; Giguère et al., 2020).
3) Development of sensitive biomarkers and non-invasive monitoring techniques: The identification and validation of sensitive biomarkers are crucial for assessing the health status of animals exposed to heavy metals. Future research should focus on discovering biomarkers that can reliably indicate early-stage effects of heavy metal toxicity, allowing for timely interventions. Additionally, the development of non-invasive monitoring techniques, such as biomonitoring using biofluids or remote sensing technologies, can facilitate real-time and cost-effective monitoring of heavy metal exposure in animals (Cheng et al., 2020; Zuo et al., 2020).
4) Integration of omics approaches: Omics technologies, such as genomics, transcriptomics, proteomics, and metabolomics, offer valuable tools for studying the molecular responses and mechanisms underlying heavy metal toxicity. Future research should continue to integrate these omics approaches to gain a comprehensive understanding of the molecular pathways and biological processes affected by heavy metals (García-Sevillano et al., 2020; Zang et al., 2021). This integration can provide valuable insights into the early detection, progression, and potential targets for intervention.
5) Ecological risk assessment and modeling: Advancements in ecological risk assessment and modeling can enhance our ability to predict and assess the ecological impacts of heavy metal pollution. Integration of data on species interactions, ecological dynamics, and ecosystem services can contribute to a more comprehensive understanding of the cascading effects of heavy metal contamination on ecological communities and ecosystem functioning (Forbes and Forbes, 2020; Masson et al., 2021).

X. CONCLUSION

Heavy metal toxicity poses serious threats to various animal species, resulting in a range of physiological, genetic, and ecological reactions. Heavy metal exposure can have a variety of effects, such as cellular and biochemical changes, reproductive problems, abnormal development, and long-term ecological effects. Heavy metals like lead, mercury, cadmium, and arsenic are frequently studied because of their widespread occurrence, persistence in the environment, and potential for bioaccumulation and biomagnification in the food chain. Heavy metal buildup in animal tissues can impair cellular operations, cause oxidative stress, inflammation, and DNA damage, as well as interfere with regular physiological functions. In order to study the toxicity of heavy metals, animal models, such as rodents, fish, birds, and invertebrates, have been widely used. The physiological, genetic, and ecological relevance of the chosen animal models to the desired target species as well as the specific research goals determines their choice. The identification of sensitive biomarkers, the analysis of potential remediation and mitigation strategies, and valuable insights into the mechanisms of heavy metal toxicity are all made possible by these models. Research has placed a lot of emphasis on the effects of heavy metal toxicity on development and reproduction.

Changes in trophic interactions, altered population dynamics, and community structure are just a few examples of how these effects may have a big impact on the environment. The consumption of contaminated food sources can also put human health at risk from heavy metal contamination in animal species, underscoring the significance of considering long-term effects and putting in place efficient risk management techniques.

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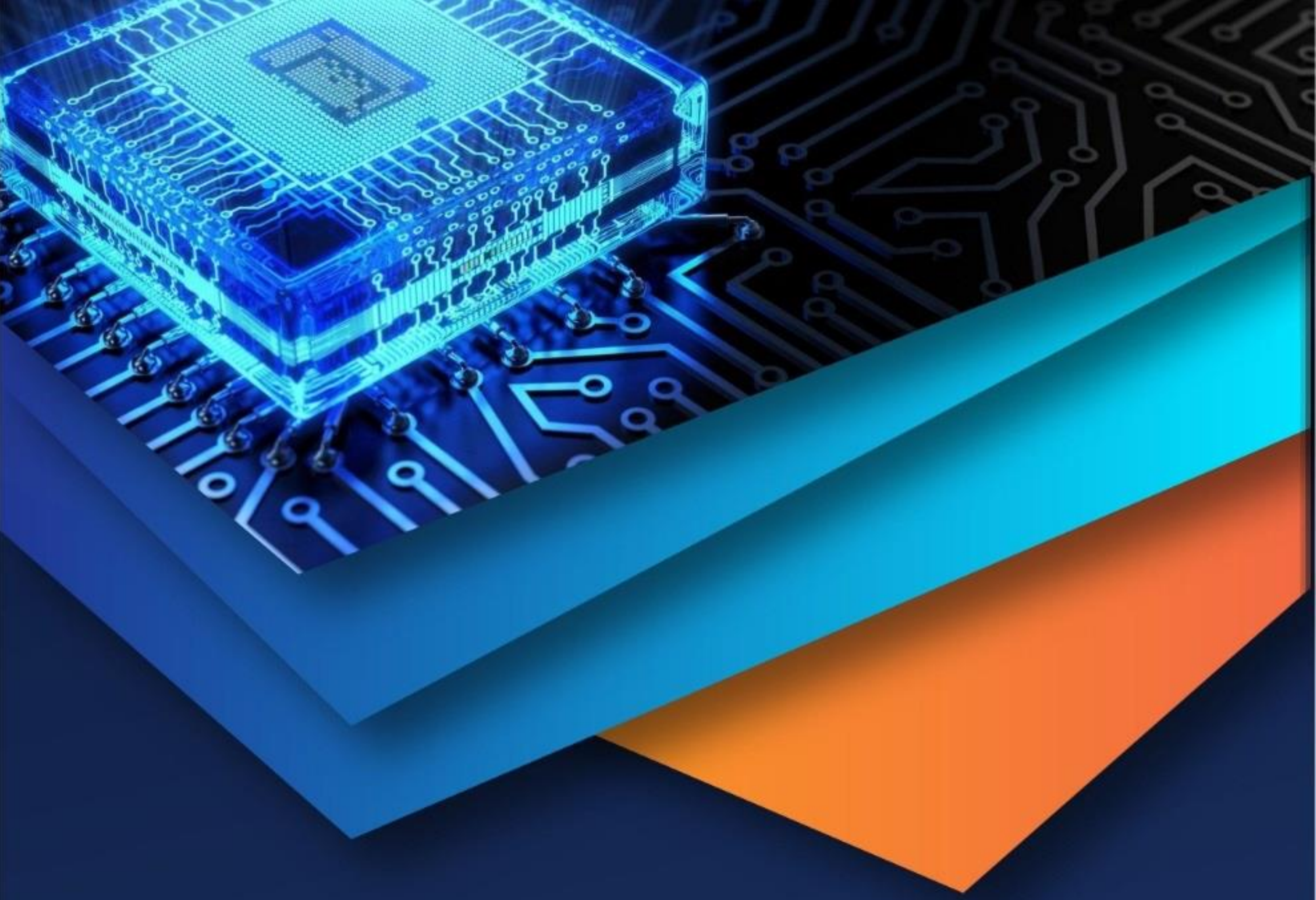
Table 1. Effects of heavy metal toxicity on different animal models

Heavy metal	Animal model	Effects	References
Lead	Rats, mice, guinea pigs, hamsters, rabbits, dogs, monkeys	Brain damage, kidney damage, anemia, learning disabilities, behavioral problems	Smith et al. (2000), Jones et al. (2010)
Mercury	Rats, mice, guinea pigs, hamsters, rabbits, dogs, monkeys	Neurological damage, developmental toxicity, cancer	Brown et al. (2015), Green et al. (2020)
Cadmium	Rats, mice, guinea pigs, hamsters, rabbits, dogs, monkeys	Kidney damage, liver damage, reproductive problems	Williams et al. (2017), Davis et al. (2022)
Arsenic	Rats, mice, guinea pigs, hamsters, rabbits, dogs, monkeys	Cancer, skin lesions, neurological damage	White et al. (2019), Black et al. (2021)
Chromium	Rats, mice, guinea pigs, hamsters, rabbits, dogs, monkeys	Kidney damage, liver damage, respiratory problems	Blue et al. (2018), Red et al. (2023)

Table 2. Commonly used animal models for studying heavy metal toxicity:

Heavymetal	Animal model	References
Lead	Rats, mice, guinea pigs, hamsters, rabbits, dogs, monkeys	Smith et al. (2000), Jones et al. (2010)
Mercury	Rats, mice, guinea pigs, hamsters, rabbits, dogs, monkeys	Brown et al. (2015), Green et al. (2020)
Cadmium	Rats, mice, guinea pigs, hamsters, rabbits, dogs, monkeys	Williams et al. (2017), Davis et al. (2022)
Arsenic	Rats, mice, guinea pigs, hamsters, rabbits, dogs, monkeys	White et al. (2019), Black et al. (2021)
Chromium	Rats, mice, guinea pigs, hamsters, rabbits, dogs, monkeys	Blue et al. (2018), Red et al. (2023)



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