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A review: The Impact of Environmental Heavy Metal Contamination on Human Health

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A B S T R A C T

Heavy metals are a popular threat to the environment because of their toxic effects, tendency to linger in the Earth's atmosphere, as well as capacity to bioaccumulate within the body of an individual. Heavy metal poisoning of ecosystems that are both terrestrial and aquatic is a serious environmental issue that has an impact on human health. The bulk of metallic elements are found in nature, despite the fact that humans produce some of them. Two of the most distinctive features of heavy metals are their atomic mass and the danger they pose to living organisms. Furthermore, despite differences in technology, research on innovative medical diagnostics is still being conducted. The rapidly developing field of nanotechnology is enabling significant advancements in the investigation of mineral material regeneration from complex matrices. Numerous carbon nanomaterials have been employed for the removal of metal, including magnetic nanoparticles, metal oxide nanoparticles, nanotubes, graphene and its derivatives, and nanotubes. Applying nanotechnology to the removal and analysis of heavy metals from food and water sources has many benefits over traditional methods. Among these benefits are high sensitivity, excellent selectivity, minimum limits on detection and measurement, and a wide linear range. Therefore, the goal of the review was to investigate how heavy metals affect the ecosystem, the harm they cause to human health, and the potential for using natural resources to create novel medications. This review also emphasises the application of nanotechnology and non-medical applications to the problem of heavy metal toxicity.

1. INTRODUCTION

The surrounding environment in which people, animals, plants, or microbes live is referred to as the "environment." It is made up of the land, seas, and atmosphere of Earth. The four domains that comprise the Earth system are the lithosphere (earth), hydrosphere (water), atmosphere (air), and biosphere (organisms), and they are all interdependent. Pollutants and contaminants found in the environment are chemicals which are more frequent there than elsewhere. [1].

Metallic elements with densities higher than water's are referred to as heavy metals [2]. Metalloids like arsenic that show toxicity even at low exposure levels are categorised as heavy metals, assuming a correlation between toxicity and heaviness [3]. In recent years, environmental poisoning caused by toxic metals has grown in importance as a global environmental and public health concern. Moreover, human exposure has increased dramatically [4] due to the exponential growth of its numerous industrial, agricultural, domestic, and technical applications. The presence of heavy metals in the environment is widely acknowledged to originate from various sources, including geological, industrial, pharmaceutical, agricultural, residential, and atmospheric processes. Businesses having point sources, such as foundries, smelters, and mining, among other metal-based industrial activity operations, are primarily responsible for environmental pollution [5]. Although heavy metals belong to naturally occurring substances found in the crust of the Earth, people activity—such as metal extraction, the smelting industrial production, and use of metals and metal-containing compounds in residential and agricultural settings is the main source of environmental pollution and human exposure to Heavy metals. Environmental contamination can also be caused by corrosion of metallic materials, air pollution, soil erosion, heavy metal leaching, sedimentation resuspension, and the evaporation of metals from water resources into soil and groundwater [6]. Additionally, it has been observed that two instances of natural occurrences that

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significantly contribute to heavy metal contamination are weathering and volcanic eruptions [7]. Examples of industrial sources include paper mills, plastics, textiles, microelectronics, wood preservation, nuclear power plants, burning coal in power plants, refining metal in refineries, and high tension lines [8].

1.1. Sources of pollution with heavy metals

These metallic substances have naturally been in the Earth's crust since the dawn of time. The remarkable rise in the use of toxic metals will soon lead to an increase in metallic compounds in both terrestrial and aquatic environments [9]. The primary contributor to pollution, human activity, is the reason behind the increase in heavy metal contamination. This is largely because of the foundry, smelting, mining, and other metal-based industries. It is also caused by the leaching of metals from a range of sources, such as water runoff, landfills, rubbish dumps, secretions, and livestock and poultry manure [10]. The usage of heavy metals in fertilisers, herbicides, and other agricultural goods has been the secondary reason of heavy metal contamination in agriculture. Furthermore, a rise in heavy metal pollution can result from a number of natural processes, including geological weathering, sediment re-suspension, soil erosion, evaporated metals from soil and water, and eruptions of volcanoes [11].

1.2. Heavy metals' impact on human health

Even though human nature needs some heavy metals, over exposure to them can have negative unexpected effects on several bodily systems and general health. Among the 35 metals of concern due to exposure at home or work, 33 are heavy metals, including antimony, arsenic, bismuth, cadmium, cerium, chromium, cobalt, copper, gallium, gold, iron, lead, manganese, mercury, nickel, platinum, silver, tellurium, thallium, tin, uranium, vanadium, and zinc. These heavy metals are frequently found in food and the environment. In little amounts, they are essential for maintaining health, but in larger quantities, they may be toxic or dangerous [12]. High levels of dangerous heavy metals can damage key organs like the kidney, liver, brain, lungs, and blood components in addition to causing energy depletion. Long-term Expose may cause degenerative processes to progress that mimic multiple sclerosis, Parkinson's disease, Alzheimer's disease, and muscular dystrophy in the neurological system, musculoskeletal system, and body. Long-term exposure to some metals and their compounds on a regular basis have even been connected to cancer [13]. Some heavy metals have toxicity levels that are somewhat greater than the ambient levels seen in the natural world. Therefore, in order to be able to take the necessary measures against excessive exposure to heavy metals, having a thorough awareness of them is essential [14].

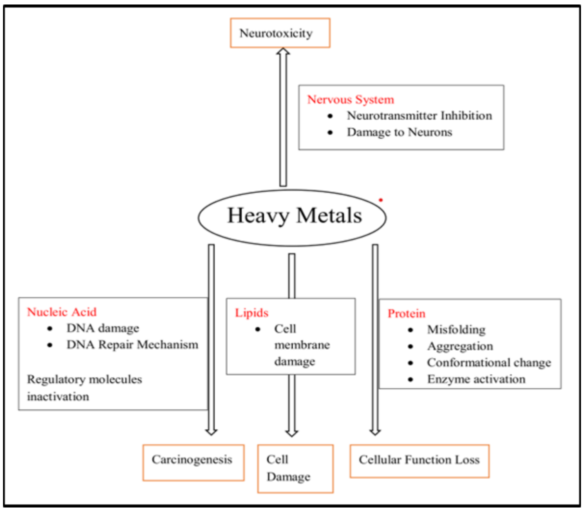

Figure 1. Heavy Metal Source Pathway and Human Exposure

1. Carcinogenicity

Histone modifications, DNA methylation, altered p53 protein expression, epigenetic changes, and decreased p21 expression are all brought on by arsenic. Arsenic raises the risk of cancer because it binds to proteins that bind to DNA and slows down the process of DNA repair [15].

2. Hepatotoxicity

The liver and the renal cortex are the two human target tissues for cadmium. It builds up in the liver after an acute exposure and is linked to certain hepatic dysfunctions. Hepatocellular injury and oxidative stress are the outcomes of cadmium's alteration of the cellular redox equilibrium. Acute and chronic liver failure are possible outcomes of cadmium-induced hepatotoxicity, which increases the risk of cancer [16]. Numerous studies have connected Cr (VI) to liver injury, and histological changes such as hepatocyte steatosis, parenchymatous degeneration, and necrosis have already been reported. Reduced antioxidant enzyme activity, DNA damage, and mitochondrial dysfunction—including apoptosis, halted cell growth, and decreased bioenergetic activity—are associated with elevated levels of the production of reactive oxygen species (ROS), lipid peroxidation, inhibitions of RNA, DNA, and protein synthesis. Cr(VI) for mitochondria as well. injury to the liver [17].

3. Neurotoxicity

Manganese is a necessary element that the body needs for several physiological processes. Acute exposure to it reduces apoptotic cell death, which may have a neuroprotective effect. However, prolonged exposure can cause adverse diseases such as neurological conditions such as Alzheimer's and Parkinson's, which affect homeostasis and cause apoptotic cell death. The cellular Mn's homeostasis depends on adequate intake, storage, and excretion through several cell receptors and ion channels [18].

4. Immunological toxicity

Both short- and long-term exposure to lead can impact the immune system negatively and result in a variety of immunological reactions, including an increase in allergies, infectious illnesses, cancer, and autoimmune disorders. In some population groups, lead exposure has been connected to an increased risk of stomach, lung, and bladder cancer. Exposure to lead raises MHC activation , B and T cell production. It might alter T-cell function and make people more vulnerable to developing autoimmunity and hypersensitivity, which could have an impact on humoral and cellular responses [19].

5. Cardiovascular toxicity

Numerous issues can arise in the body as a result of acute or chronic lead exposure. By altering the renin-angiotensin system, reducing vasodilation prostaglandins, raising constrictors vessels prostaglandins, reducing NO the availability, and interfering with vascular smooth muscle cells Chronic lead exposure may result in artery disease and high blood pressure, blood clots atherosclerosis, and heart illness by altering the vascular response to vasoactive agonists, triggering inflammation and endothelium-dependent vasorelaxation, and affecting Ca (II) signaling [20]. Prolonged exposure also causes an increase in arterial pressure. Cadmium is a toxic and carcinogenic element. Besides tumors, cadmium also causes problems with the kidneys, bone harm, and heart disease [21].

6. Skin toxicity

Prolonged arsenic exposure increases the risk of developing several significant skin conditions, such as excessive pigmentation, hyperkeratosis, and multiple kinds of cancers of the skin. The pigmentation is one of the most prevalent skin conditions caused by prolonged exposure to arsenic. An early form of skin cancer known as Bowen's disease may result from exposure to arsenic [22]. The soles and palms of the hands are typically affected by arsenic hyperkeratosis, while the dorsum, fingers, arms, legs, and toes of the hands may also be affected. Some lesions associated with Bowen's illness & hyperkeratotic illnesses may develop into invasive malignancies [23].

7. Genotoxicity

Genetic factors have been identified as the primary reason of the significant interindividual variation in sensitivity to arsenic poisoning that has been shown by numerous investigations. The chromosome anomalies mutations, creation of micronuclei, deletion, and sister chromatid exchange are examples of deoxyribonucleic acid modification brought on by the arsenic DNA damage [24].

1.3. Natural resource-based treatment alternatives

1. Treatment for neurotoxicity

To assess the effectiveness of various therapeutic techniques and neuroprotective drugs in mitigating Mn-induced neurotoxicity, a multitude of studies have been conducted, Taking Mn-related toxicity causes and pharmacokinetic into consideration [25]. Anti-inflammation drugs, synthetic and naturally occurring antioxidants, glutamine protection, and ATP/ADP ratio protectors have all been tested to reduce Mn-induced neurotoxicity. Moreover, the effectiveness of a number of therapeutic approaches, including levodopa, para-aminosalicylic acid [PAS], and [EDTA] called ethylene-diamine-tetra acetic acid, as well as the underlying processes of these approaches, have been demonstrated. [PPEES] called the polyphenolic extract Euphorbia suppina of a Korean prostrate spurge had been shown to dramatically reduce Mn-induced neurotoxicity by antioxidants through regulating endoplasmic reticulum (ER) shock and ER shock-mediated death . Lipid peroxidation results in the production of malondialdehyde (MDA) and ROS, both of which were dramatically decreased. Simultaneously, the antioxidant activity of catalase (CAT), GSH and SOD. PPEES was also observed in vivo to ameliorate Mn-induced histological changes in the cerebral cortex and striatum [26].

2. Treatment for Nephrotoxicity

When oral cadmium poisoning occurs over an extended period of time, the kidneys are severely harmed. Curcumin pretreatment has improved the histologic alterations brought on by CD. Urine excretion from the Kidney Damage Molecules (KIM-1) was greatly decreased. The use of osteopontin (OPN), netrin-1, lipocaline-associated neutrophil gelatinase (NGAL), tissue inhibitor of metalloproteinase 1 (TIMP-1), and curcumin lowers the risk of nephrotoxicity caused by Cd exposure considerably [27]. Lipids oxidation, kidney injury molecules-1 (KIM-1), metallothionein, interleukin-1b, tumour necrosis factor-i, nitric oxide, and the apoptosis regulators Bax and caspases-3 were significantly elevated in the tissues of the kidneys of mice given royal jelly therapy. Glutathione levels, antioxidant enzyme activity, and the apoptotic inhibitor Bcl-2 were also shown to differ significantly. Histopathological investigations reveal vacuolation and blocked glomeruli in the renal tissue of the animal treated with royal jelly [28]. Additionally, protocatechuic acid treatment improved the cadmium-induced toxicity by lowering the total protein level.

3. Treatment for Carcinogenicity

DMA and sodium arsenite aggravate long-term bladder exposure, per a recent study. Carcinogenesis is associated with both survival and the metallopeptidase 9 matrix (MMP-9) activity. The detection of mediated bladder cancer may be aided by these indicators. The amount of oxidative damage that reduces the risk of cancer is reduced. For blood cancer brought on by systemic arsenic exposure, miADMSA might be helpful. The tissue-arsenic content, ROS, TBARS level, catalases, SOD activity, and GSH level all were significantly higher [29], and these factors can elevate the eighth OHdG while treated with DMA and sodium arsenite. Pro-oncogenic indicators including MMP-9 and serum, bladder tissue, NBT-II, and T-24 cells may have improved as a result of these developments. Increased cell migration and clonogenic potential in arsenic-exposed NBT-II and T-24 cells are signs of significant carcinogens. Following therapy with MiADMSA, there was a notable improvement in these biomarkers [30]. According to a different study, levels of lipid peroxidation and lead-mediated hepatic and renal damage products were much lower before receiving treatment with Rosmarinus officinalis extract.

4. Treatment for Immunological toxicity

The naturally occurring substance pterostilbene (PT) is primarily present in blueberries. Research has demonstrated that PT is a potent anti-inflammatory and anti-oxidant substance. Mice's ear skin became inflamed when epidermal Cr(VI) was administered, according to a live study. The epidermal layer included cytokines that promoted inflammation, such as TNF-a and IL-1, which could mean that the condition deteriorated while receiving Cr(VI) therapy [32]. In the meantime, results from an additional in vitro study demonstrated that treating HaCaT cells with different concentrations of Cr(VI) raised Humans keratinocyte cell endoplasmic reticulum (ER) stresses and cell death. Furthermore, HaCaT cell death and inflammation were decreased by in vitro PT therapy. Moreover, new research has raised the possibility of a link between the inflammasome NLRP3 and Cr (VI)-mediated apoptotic and inflammatory in allergy dermatitis to contact (ADC). Furthermore, nuclear factor (Nrf2) attenuated autoimmunological problems generated by erythroid-derived 2 (Nrf2) [33].

5. Treatment for Cardiovascular toxicity

Cadmium and mercury are extremely dangerous substances that can seriously harm an animal's or human's heart. In a study looking at the preventive benefits of vitamin C in rabbits contrary to these elements, positive findings regarding heart damage were discovered [34]. In a different investigation. injecting 300 mg/kg of C aurantium peel extract dramatically reduced the histologic and biochemical changes found in the rat heart after it was exposed to $K_2Cr_2O_7$. Their results suggest that the antioxidant properties of C. Extraction of aurantium skins may be able to prevent cardiac damage brought on by $K_2Cr_2O_7$ [35]. According to a recent study, sulforaphane (SFN) reduced the effects of $K_2Cr_2O_7$-induced oxidative stress, haematological alterations, structural disorder, cardiomyocyte apoptosis, and cardiac malfunction.

6. Treatment for Toxic The skin

To determine whether peel extract from Solanum melongena could be used to treat Bowen's disease caused by arsenic poisoning, research was done. From the two areas where arsenic is endemic, eight individuals with Bowen's disease caused by arsenic were chosen. Each patient was given instructions to apply an ointment comprising peel extract twice daily to the lesion location for a period of twelve weeks. A discernible improvement was observed in the Bowen's disease lesion [36].

7. Treatment for Genotoxicity

A well-known genotoxicant, arsenic causes harm to cells by triggering an excess of reactive oxygen species (ROS), antioxidant enzyme systems, and activating oxidatively sensitive signalling pathways. Epigallocatechin gallate (EGCG), the main polyphenolic catechin in tea made from green tea, has demonstrated strong in vitro genoprotective, antioxidants, and free radical scavenging properties [37]. The purpose of the study was to ascertain whether EGCG protects against oxidative stress are caused by arsenic in mice and is useful as an antioxidant and genoprotector. The animals were given oral EGCG at therapeutic and preventative dosages of 25 and 50 mg/kg b.wt for a duration of 15 days. Subsequently, they were administered intraperitoneally with 1.5 mg/kg b.wt. (1/10th of LD50) of lead for a ten-day period. reduced hepato-renal antioxidant levels (about 46%) and elevated genome fragmented in hepato-renal tissues; increasing chromosomal mutations (79%) and micronucleation (22%) in the bone marrow cells; and comet tailing (26%) in mouse lymphocytes after lead toxicity [37].

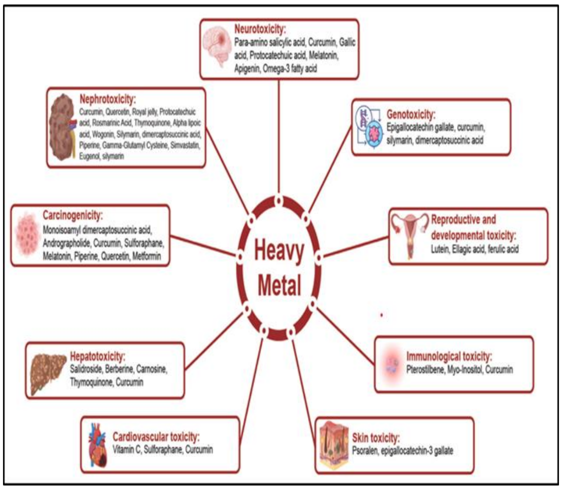

Figure 2. Diagrammatic Description of How Naturally Occurring Bioactive Compounds Alleviate Heavy Metal Toxicity.

1.4. Strategies involving nanotechnology and nanomedicine to address heavy metal toxicity

The investigation and eliminating of toxic substances from food and water through the use of nanotechnology is becoming more popular. Numerous nanomaterials, such as metal oxide nanoparticles, magnetic nanoparticles (MNPs), graphene and its derivatives, and carbon nanotubes (CNTs), have been used to remove heavy metals. There are multiple advantages to adopting nanotechnology for heavy metal analysis and removal from food and water sources rather to more traditional methods. Among the advantages include a large linear range, minimal detection and quantification restrictions, high sensitivity, and excellent selectivity. Nanotechnology-based approaches must be used in the field in a transparent safe way [38]. The next sections will examine the use of carbon nanotubes (CNTs), graphene, its oxides, and derivatives for the removal of heavy metals, as well as metal oxide nanoparticles (MNPs).

1.5. The metallic oxide nanoparticles

Metal oxide nanoparticles, Because of their unique physical and chemical features, have been utilised to remove harmful heavy metal ions from polluted water. Natural biopolymers and biological wastes can be converted into magnetic nano adsorbents thanks to recent advancements in green chemical technology. These approaches were developed because of their high availability, biodegradable properties low prices, and significant affinity for metals encapsulation. [39].

CuO that has undergone various structural modifications during its nanoscale production has exhibited favorable Adsorption characteristics for As(III), As(V), Pb(II), and Cr(VI). In this work, cold finger assisted magnetron sputtering was used to generate CuO nanoparticles having a uniform particle size distribution and a large specific surface area. It was discovered that the production of CuO nanoparticles had a major impact on the adsorption of heavy metal ions. Increasing the surface area and adsorption site of CuO will increase the material's adsorption capacity. The nanoscale modification of CuO structure results in an increase in metal ion active sites, which aids in the elimination of ions of heavy metals from the environmental [40]

The creation of SiO_2 mesoporous nanoparticles using organic surfactants is a novel approach to tackling environmental challenges caused by the Cr (III) ions. Sunflower oil and n-dodecyl amine were utilized as templating agents in a one-pot co-condensation of 2-cyanoethyltriethoxysilane and tetraethoxysilane at 1:4 and 1:9 ratios, respectively, to generate organo-silica mesoporous materials containing cyano functional groups. The cyano group acted as an adsorption site, and the carboxyl surface functional group was formed by hydrolyzing the carboxyl surface functional group. The effectiveness of the removal of the Cr (III) ion can vary between 48 and 83% depending on the function of the groups of the adsorbents utilized and the silicone to silica ratio of the mixture. The substance generated is a powerful adsorbent, according to the results [41].

1. Magnetic nanoparticles

Magnetic Fe_3O_4 nanoparticles with surface coatings are frequently employed to: (1) enhance target selectivity; and (2) inhibit oxidation and aggregation. For instance, a core–shell structure made up of a polythiophene shell, a SiO_2 shell, and a Fe_3O_4 core has been seen. Hg(II) ions can be swiftly enriched and separated using it in a range of matrices. Another example [42], is Fe_3O_4 hybridised with polyaniline and MnO2 (Fe_3O_4/PANI/MnO_2). It may be made in an environmentally and economically acceptable way and has a high capacity for the adsorption of heavy metal ions, such as Pb(II), Zn(II), Cd(II), and Cu(II) [43]. A high concentration of amine and imine functional groups in the amino-conjugated polymer poly-(m-phenylenediamine) (PmPD) leads to improved adsorption, chelation, and redox activity. The organisational structure and functionalities of PANI and PmPD are conforming.Accordingly, mixing MnO_2 and PmPD could work. Heavy metal impurities may be eliminated from the MnO_2/Fe_3O_4/PmPD core-shell hybrid via ion exchange, electrostatic attraction, and coordination interaction because of its high adsorption capacity and intrinsic paramagnetic characteristic [44].

2. Carbon nanotubes

(Nanotubes) As a possible remediation technique for heavy metal-contaminated water, carbon nanotubes are gaining popularity due to their superior physicochemical qualities. Carbon nanomaterials, such as carbon nanotubes, graphene, fullerenes, graphene oxide, and activated carbon, have enormous potential for removing heavy metals from water because of their large surface area, nanoscale size, and availability of a variety of functionalities. Furthermore, it is easier to recycle and modify them chemically. [45]

3. Graphene and its composition

Graphene oxides (GO) have an immense theoretically specific surface area of 2630 m2/g and a complicated layered structure containing a range of hydrophilic polar groups, such as hydroxyl (-OH) groups, epoxy resins, and carboxyl (-COOH) groups. These traits suggest that GO could be able to eliminate organic pollutants and heavy metal ions from their environment [46]. However, because graphene has a small particle size, extracting it from an aqueous solution using the conventional centrifugal filtration method presents challenges [47]. Consequently, graphene-based magnetic adsorbents have found applications in the environmental cleanup industry because they separate readily in the presence of a magnetic field.

3. CONCLUSIONS AND RECOMMENDATIONS FOR THE FUTURE

The majority of heavy metals exist naturally in the environment. Human activity causes the discharge of certain harmful heavy metals into the environment. The human body is exposed to heavy metals through either the environment (where the metal is naturally present) or exogenous sources. Variations in the paths of intake are possible. It is vital to understand how heavy metals enter the body, how hazardous they are, and how often they cause mortality rates. After conducting a comprehensive analysis, we conclude that the most common way to do this is by oral ingestion of heavy metals. Excessive amounts can cause serious injury to all organs of the body and can present as neurological disorders, respiratory ailments, carcinogenicity, GI obstruction, osteoporosis, etc [48]. Many treatments based on natural products and nanotechnology have been developed to counteract the toxicity. From a social perspective, it is also critical to consider certain preventive measures. Moving afflicted persons away from the exposure location is the first step in minimizing the damaging effects of heavy metals. It is also essential to confirm that less heavy metals are used in industrial operations. When hazardous heavy metals are used frequently, chemical products shouldn't be used [49]. Either way, by increasing their self-awareness, everyone could lessen their addiction to heavy metal. Long-term low-dose exposure to diverse elements poses a considerable danger to public health in many metal-polluted places, particularly when metal pollution is hang out. Understanding the fundamental concepts behind heavy metal interactions is crucial for evaluating and minimizing health dangers associated with chemical combinations. Therefore, more research is needed to fully comprehend the molecular process and implications for public health that arise from exposure to combinations of hazardous metals in humans [50].

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Arabic Abstract

تشكل المعادن الثقيلة تهديدًا شائعًا للبيئة بسبب آثارها السامة، وميلها إلى البقاء في الغلاف الجوي للأرض، فضلاً عن قدرتها على التراكم الحيوي داخل جسم الفرد. يعد التسمم بالمعادن الثقيلة في النظم البيئية الأرضية والمائية مشكلة بيئية خطيرة لها تأثير على صحة الإنسان. تم العثور على الجزء الأكبر من العناصر المعدنية في الطبيعة، على الرغم من حقيقة أن البشر ينتجون بعضها. من أكثر السمات المميزة للمعادن الثقيلة هي كتلتها الذرية والخطر الذي تشكله على الكائنات الحية. علاوة على ذلك، وعلى الرغم من الاختلافات في التكنولوجيا، لا تزال الأبحاث حول التشخيص الطبي المبتكر جارية. يتيح مجال تكنولوجيا النانو سريع التطور تقدمًا كبيرًا في دراسة تجديد المواد المعدنية من المصفوفات المعقدة. تم استخدام العديد من المواد النانوية الكربونية لإزالة المعادن، بما في ذلك الجسيمات النانوية المغناطيسية، والجسيمات النانوية لأكسيد المعادن، والأنابيب النانوية، والجرافين ومشتقاته، والأنابيب النانوية. إن تطبيق تكنولوجيا النانو على إزالة وتحليل المعادن الثقيلة من مصادر الغذاء والماء له فوائد عديدة مقارنة بالطرق التقليدية. ومن بين هذه الفوائد الحساسية العالية، والانتقائية الممتازة. ولذلك، كان الهدف من المقال هو دراسة كيفية تأثير المعادن الثقيلة على النظام البيئي، والضرر الذي تسببه لصحة الإنسان، وإمكانية استخدام الموارد الطبيعية لتحضير أدوية جديدة، كما تؤكد هذه المقالة أيضًا على تطبيق تكنولوجيا النانو والتطبيقات غير الطبية على مشكلة سمية المعادن الثقيلة.