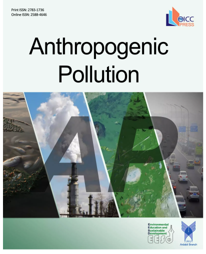

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The relationship between cadmium pollution, soil biology, and Atropa belladonna growth

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Abstract:
Cadmium, a heavy metal, can have devastating effects on the activity and composition of soil organisms. This can lead to environmental pollution which can be detrimental to human health. In order to evaluate the quality of contaminated soils, microbial parameters are used. The Atropa belladonna was used in a factorial experiment to investigate the efficacy of green purification and the role of arbuscular root fungi and growth-promoting bacteria in reducing the effects of cadmium. The experiment included two factors: cadmium at four levels (0, 20, 50 and 100 mg/kg of soil) and microbial inoculation treatment at three levels (control, plant growth promoting rhizobacteria and arbuscular mycorrhizal fungi). The study found that an increase in soil cadmium pollution caused a significant increase in shoot cadmium concentration and metabolic rate. Cadmium also caused a significant decrease in shoot function, microbial biomass carbon, microbial respiration, substrate-stimulated respiration, Plant growth promoting rhizobacteria population and mycorrhizal symbiosis. However, the inoculation of microbial treatments to the soil was found to decrease the inhibition effects of cadmium on the measured indicators. Overall, the results of the study showed that using growth-promoting microorganisms can reduce the adverse effect of cadmium on plant growth and microbial indicators of soil quality in soils contaminated with cadmium. Therefore, the application of growth-promoting microorganisms represents a promising approach for the remediation of cadmium-contaminated soils, as it not only supports plant growth but also enhances the overall quality of soil ecosystems.

Keywords: Atropa belladonna; Cadmium; Environmental pollution; Soil ecosystems

1. Introduction

Cadmium (Cd) is classified as a heavy metal, along with arsenic, mercury, lead, and chromium. It lacks any physiological role and is commonly recognized as a toxic substance (Genchi et al. 2020b; Ardakani et al. 2010). Numerous types of contact with Cd have been demonstrated throughout the previous hundred years, with Cd existing in the surroundings due to various actions carried out by humans. The constant sources of Cd contamination are related to its application in industry as a corrosive reagent, as well as its use as a stabilizer in PVC products, Ni-Cd batteries, and color pigments (Genchi et al. 2020a). House dust in regions with contaminated soil can serve as a possible means of Cd exposure. Cd in the environment comes from human activities, such as copper and nickel production and purification, burning fossil fuels, and the application of phosphate fertilizers (Asif 2018). Cd is a contaminant in non-ferrous metal factories and the reprocessing of electronic waste (Muthumanickam and Saravanathamizhan 2021). Various factors contribute to the rise in Cd levels in natural surroundings, such as forest fires, gradual wear and tear of soil and rocks, and volcanic eruptions (Marlina et al. 2022). Additionally, the extraction of copper, zinc, and lead from mines also releases this metal into the atmosphere, causing soil pollution (Rafiee 2020; Hajjabbari and Fataei 2016). Cd absorption primarily occurs through the respiratory system and, to a lesser degree, through the gastrointestinal tract (Ahmadi and Ghorbanpour 2021). Absorption through the skin is uncommon. Upon entering the body, Cd is carried through the bloodstream by red blood cells and albumin. Eventually, it accumulates in the kidneys, gut, and liver (Genchi et al. 2020b). The body expels Cd gradually through the milk, saliva, urine, and kidneys while breastfeeding (Tan et al. 2022). Exposure to Cd can lead to various adverse effects in humans, including kidney and liver problems, fluid buildup in the lungs, weakened bones, harm to the testicles, and damage to the adrenal glands and blood-producing system (Fu et al. 2023). Furthermore, a connection was noted between indicators of Cd exposure (specifically blood and urine) and the occurrence of peripheral artery disease, coronary heart stroke, disease, and alterations in the lipid profile that promote atherosclerosis (Mekwilai et al. 2023). Cd, apart from its cytotoxic properties which may result in cellular death through apoptosis or necrosis, has been established as a known carcinogen in humans (Fu et al. 2023). There is a correlation between cancer of the lungs, urinary bladder, pancreas, breasts, prostate, and nasopharynx and exposure to Cd in the workplace or environment. Cd-induced apoptosis occurs due to multiple processes, including the production of reactive oxygen species, the buildup of calcium ions, increased expression of caspase-3, reduced levels of bcl-2, and the absence of p-53. In recent studies, the impact of Cd arsenite on the proper folding of newly formed proteins in yeast cells has been established. This interference negatively affects the overall health of the cells and is believed to contribute to a range of medical conditions, including age-related disorders, and neurodegenerative diseases as well as Parkinson's and Alzheimer's diseases. Furthermore, osteoporosis is acknowledged to be associated with exposure to Cd, but the precise mechanisms and crucial levels of exposure remain uncertain. Moreover, research has established a connection between cognitive and kidney development in fetuses and prenatal exposure to Cd (Liu et al. 2019). The function of antioxidant enzymes, including manganese superoxide dismutase, catalase, and copper-zinc superoxide dismutase, may be disrupted by Cd. Zinc-rich metallothionein can act as a scavenger for free radicals. The presence of metallothioneins in cells protects against the harmful effects of Cd, whereas cells lacking the ability to produce metallothioneins are vulnerable to its toxicity (Han et al. 2015). The expression of metallothioneins plays a role in deciding whether Cd-induced toxicity leads to apoptosis or necrosis (Prabu and Shagirtha 2019).

In this comprehensive review article, the purpose is to explore the various aspects related to Cd contamination in soil and its potential impact on human health.

2. Methods

The Atropa belladonna was used in a factorial experiment to investigate the efficacy of green purification and the role of arbuscular root fungi and growth-promoting bacteria in reducing the effects of cadmium (Liu et al. 2019; Tan et al. 2022; Mekwilai et al. 2023). The experiment included two factors: cadmium at four levels (0, 20, 50, and 100 mg/kg of soil) and microbial inoculation treatment at three levels (control, plant growth-promoting rhizobacteria, and arbuscular mycorrhizal fungi).

3. Results and discussion

3.1 Sources of Cd contamination in soil

The contamination of Cd in soil and groundwater is a worldwide phenomenon (Chellaiah 2018). The toxic effects of Cd are well-known, and it remains in the body for an extended period even after being destroyed by living organisms. Anthropogenic sources such as the sewage sludges, combustion emissions, landfills, traffic, incidents, mining, and metal industry contribute to the contamination of Cd in soil and groundwater (Bigalke et al. 2017). Another factor that contributes to the increase of Cd concentration in soil and groundwater is the use of artificial phosphate fertilizers that contain Cd as an unintended component (Kubier et al. 2019). The process of groundwater infiltration has been examined in various nations, including Sweden, the United States, the United Kingdom, Denmark, Canada, Finland, New Zealand, Germany, Norway, and Australia. Studies cited suggested that the introduction of synthetic phosphate fertilizers containing Cd had an impact on soil chemistry by affecting the microbial population and soil biota (Bigalke et al. 2017).

Cd is present in petroleum-derived products as a contaminant (Buekers et al. 2007). It can move into the food web and potentially harm living organisms. Cd can be transferred from various sources, either dispersed or localized. Local authorities include industrial areas, mines, and abandoned mining sites, while distributed sources encompass activities such as waste water reuse, atmospheric processes, and agricultural practices, which contribute to the distribution of Cd in the soil and surrounding environment (Ajami and Fataei 2015). Throughout the world, the primary contributors to the contamination of Cd are landfills, solid municipal waste, and batteries containing Cd-Ni. Cd is primarily employed in Cd-Ni batteries, recognized for their exceptional performance, minimal upkeep requirements, extended lifespan, and impressive resilience to physical and electrical strain. In the European region, solid municipal waste comprises Cd in the range of $0.3-12$ mg kg^{-1}, and leachate (the water drains from landfills) contains Cd in the range of $0.5-3.4$ μg/L (UNEP 2010). Additionally, some products incorporate Cd, such as stabilizers utilized in alloys, coatings, platings, polyvinyl chloride, and pigments. Cd in the soil can be attributed to the leachate produced by compost and sludges, which accounts for approximately $2-5\%$ of its deposition. Sources of leachate can arise from various origins, including atmospheric deposition and farmyard manure, which account for $30-55\%$, $15-50\%$, and 10 – 25% correspondingly, of Cd deposition within the soil. The application of Cd coating offers improved protection against corrosion for automobiles, particularly in environments that are highly prone to corrosion, such as marine and aerospace settings (Zhang et al. 2009). The natural variability of minerals and rocks in soil can lead to increased environmental Cd levels, as opposed to human-caused emissions and actions (Bigalke et al. 2017). Due to the high reactivity of Cd, it is essential to consider soil as a temporary reservoir rather than a permanent sink, as it can rapidly impact the groundwater concentration at different time intervals, such as years (rainy or dry seasons) and decades (during dry or wet years) (during dry or wet years). The potential cause of reduced Cd enrichment in soils could be attributed to the extraction of Cd through crop harvesting (Kubier et al. 2019). Nevertheless, considerable increases in Cd levels have been observed in phosphate fertilizers in countries situated in the eastern Mediterranean region, with reported values as high as 77 mg Cd per kg P_2O_5. Similarly, in European countries, Cd levels in fertilizers have ranged from 36 to 60 mg of Cd per kg P_2O_5 (Six and Smolders 2014). The soil was contaminated with Cd due to leaching of solid waste and atmospheric deposition from zinc smelters, resulting in Cd concentrations of 344 mg kg^{-1} and 74 mg kg^{-1}, respectively. Similarly, the simultaneous occurrence of groundwater contamination from multiple sources and pathways at a specific site can complicate the identification of primary sources of Cd, routes of contamination, and geogenic processes (Zhu et al. 2013).

3.2 Uptake of Cd by plants

The plant's reaction to higher concentrations of Cd in the soil differs depending on factors such as the plant variety and species, soil characteristics, and the plant's ability to absorb Cd. Within the facility, efficient transportation of Cd occurs through the utilization of metalloorganic complexes. The accessibility of Cd is reliant on several factors, including pH, temperature, concentration, redox potential, and the presence of different elements in the soil (Hasan et al. 2009). The potential deposition of metals can occur by acidifying the rhizosphere and exuding carboxylase. The processes involved in Cd uptake by plant roots typically involve competition for absorption sites between Cd and other mineral nutrients that share similar chemical properties (Hasan et al. 2009). The substitution of calcium for Cd in minerals occurs because they have the same charge, equal ionic radius, and comparable chemical properties (Prabu and Shagirtha 2019). The levels of Cd in the soil caused a decrease in the concentration of Ca, Mg, and K in lettuce, tomato, maize, and cucumber (Nazar et al. 2012).

In the roots of lettuce, a counteractive association between Zn and Cd and their lively assimilation was observed (Tran and Popova 2013). Similarly, other essential minerals like nitrate do not possess indistinguishable chemical properties from Cd but are influenced by its presence in the soil (Kubier and Pichler 2019). At first, the entry of Cd into the roots of plants causes harm to both the root system and the overall morphology of the plant (Hasan et al. 2007). The regulation of Cd uptake by root cells is influenced by the difference in electrochemical potential between the apoplasts and cytosol of the root. Even at deficient concentrations of Cd, the membrane potential provides enough energy to facilitate the uptake of Cd. The absorption solution exhibits two distinct phases in terms of the roots' ability to absorb Cd. At low levels of Cd activity, there are saturable components that play a role in absorption, while at higher levels of Cd activity, the absorption process becomes linear (Nazar et al. 2012). Cd absorption in roots can happen through inorganic complexes like $Cd^{2+}SO_4$, $CdCl_2$, and $CdCl^+$ or organic forms such as phytometallophore complexes (Kubier et al. 2019). The absorption of zinc in the roots of corn happens easily through phytometallophore complexes. However, the binding sites in the roots' plasma membrane are not specifically made for iron phytometallophores, which allows for the transportation of various metals such as Cd.

Cd uptake is reduced in the presence of Zn under Zn deficiency, as Zn and Cd metals work together. Plants experience an increase in the availability of Cd due to the acidification of the soil, while the excretions from the roots contribute to the enhanced solubility of the element. Cd is commonly encountered in the soil solution as Cd^{2+} and can also exist in the soil solution as Cd-chelates. The absorption pathways to uptake metal ions like Cd include the apoplastic and symplastic routes (Ismael et al. 2019). Water, in conjunction with metal ions, moves within the plant via the apoplastic route, utilizing the unfettered spaces between membranes, which entails passage through intercellular spaces and cell walls. In the process of symplastic absorption, water flows through the symplast, which is made up of cytoplasm and plasmodesmata that have limited connections with the neighboring cell cytoplasm (Lopez and Barclay 2017). The cations gather within the apoplast of the plant roots. This process is controlled by the exchange properties of the cell wall and is influenced by the pH at the beginning stage, like the adsorption of metal ions from the soil solution. As the soil pH increases, the functional groups in the root cell walls, including carboxyl groups, gradually undergo deprotonation. Hence, in the apoplast of the root, there is an electrostatic interaction between metal cations with positive charges and carboxylate groups with negative charges. The initial stage is quick and haphazard, suggesting that it does not require any energy (i.e., it is a passive process). The symplastic pathway functions through metabolic processes and operates at a significantly slower pace compared to the apoplastic pathway (Ismael et al. 2019). However, the significance of each stage differs depending on the type and concentration of the metal and other ions. In the case of Cd, it traverses the apoplastic pathway by crossing the cell membrane of the root cell (Genchi et al. 2020b).

Plants take up Cd through their roots due to its high mobility and assimilation ability. Subsequently, it is transported upwards within the plant through the ascent of sap and, or via transporters in its ionic form, reaching the vascular bundles such as the xylem and phloem. Cd can make its way into the xylem via the symplastic pathway, and it can exist in a higher concentration within the apoplastic way. The transfer of Cd from the vessel components or tracheids of the stele to the plant shoots occurs. Solute transportation occurs through the apoplastic routes, which include the gas spaces and extracellular fluid found both within and inside the cell walls. In the symplastic pathways, the intracellular transfer of water and solutes occurs through tubular channels known as plasmodesmata, enabling transfer between neighboring cells (Song et al. 2017). ATPases that handle metallic elements can transport Cd across membranes and have a notable function in transferring Cd from roots to shoots. Specific integral membrane proteins utilize the energy derived from ATP hydrolysis to facilitate the transport of Cd across membranes. The P1B-ATPases are among the essential ATPases in this process (Ismael et al. 2019). The P1B-ATPases are a specific group within the larger category of P-type ATPases. These proteins are found in various membranes and employ the energy from ATP to transport cations across membranes against their electrochemical gradient. P1B-ATPases play a regulatory role in the efflux of metals from the cytoplasm, contributing to the maintenance of cytoplasmic Cd concentrations. The transportation of Cd to cereal grains might be linked to the transfer of Cd facilitated by the phloem to the crop grain (Guo et al. 2018). The primary means of Cd transfer to the grain is through the phloem. Within the phloem sap, Cd can bind with the 13 kDa-protein and SH-derived compounds. There has been a suggestion of Cd migration from the xylem to the phloem at nodes, and the transfer of Cd through the phloem in the panicle neck suggests variations among genotypes. The findings demonstrate the involvement of transporters located at the nodes, which facilitate the transport of Cd from the phloem to the grain. Irrespective of the Cd's mobility, the concentration of Cd in the roots is higher than that in the aboveground plant tissue (Tran and Popova 2013). Typically, the roots of plants capture Cd particles, with only a small portion being transported to the upper portions of the plant, such as stems, leaves, and reproductive parts. This transport order is observed as grains < fruits < leaves < roots (Prabu and Shagirtha 2019). In the plant species Glycine max L., almost all of the Cd absorbed from the soil is stored in the roots, while a small portion is moved through the vascular bundles to the aboveground parts, such as shoots. It suggests that Cd transportation through the xylem is restricted in many plants, resulting in low concentrations of Cd in fruits, seeds, and shoots, indicating that Cd is not easily transported through the phloem (Ismael et al. 2019). Nevertheless, certain plant species, like tobacco (Nicotiana tabacum L.), exhibit a more extraordinary ability to accumulate metals and consequently get a higher level of Cd in their older leaves than their roots. The transportation of Cd into grains and fruits varies across different cultivars and crops. Cd uptake in various plant parts is influenced by soil characteristics, environmental conditions, agronomic practices, and plant species.

3.3 Human exposure pathways

The initial protection against infection is provided by the nonspecific innate immunity. This system involves the recognition of self and non-self through different immune cells and mechanisms. The natural immune system is characterized by its speed and ability to function without antigen involvement. Studies have demonstrated that Cd exposure can impact various components of this system. There have been multiple investigations that suggest Cd, as a contaminant in the environment, can alter innate immune reactions by affecting the release of chemokines, vulnerability, and gene expression to microbial infections (Razzuoli et al. 2018). Studies have indicated that Cd has the ability to trigger inflammation, although the precise process by which it initiates this response remains unclear. Razzuoli et al. employed porcine epithelial cells to evaluate the impacts of Cd on the expression of genes associated with inflammation (Razzuoli et al. 2018), the release of proteins, and the infectivity within a model of Salmonella typhimurium penetration. According to their findings, it was observed that epithelial cells can absorb Cd in a manner that depends on both time and concentration. This absorption leads to the increased expression of crucial pro-inflammatory chemokines and cytokines (IL-6, IL-8, IL-18), as well as genes encoding transcription factors (MYD88, Nkfb-p65, Nk-fb1). An experiment conducted in a laboratory demonstrated that Cd, when present in non-harmful amounts, can trigger the production of IL-6 and IL-8 in astrocytes. This stimulation occurs in a manner that depends on the dosage and duration through the process of MAPK phosphorylation and NF-jB activation. Importantly, it was observed that the cellular morphology and viability remained unaffected. Elevated concentrations of these inflammatory cytokines instigate the inflammatory response and can be linked to neurodegenerative conditions (Razzuoli et al. 2018). Novel strategies that aim to inhibit the production of IL-6 and IL-8 could be employed to hinder angiogenesis caused by Cd in inflammation and gliomas in the brain (Phuagkhaopong et al. 2017). The activation of CCAAT-enhancer-binding proteins (C/EBP) signaling pathway is suggested to occur due to Cd exposure, which could lead to endoplasmic reticulum (ER) dysfunction and elevated levels of reactive oxygen species (ROS), according to Kim et al. As a result of this activation, changes occur in the expression of multiple genes involved in various processes, such as oxidative stress and inflammatory responses (Phuagkhaopong et al. 2017). Cd induces an increase in the production of ROS, which in turn causes dysfunction in mitochondria and ultimately leads to cell apoptosis.

Some research has shown that Cd exposure may lead to an increase in cyclooxygenase-2 (COX-2), macrophage inflammatory protein (MIP)-2, and prostaglandin E2 (Miyahara et al. 2004). Studies propose that the levels of COX-2 are increased in response to Cd due to the activation of the mitogen-activated protein kinase (MAPK) pathway. The heightened COX-2 levels result in an increased production of the inflammatory mediator PGE2, which can potentially lead to damage to endothelial cells and cell death (Angeli et al. 2013). In a research conducted by Huang et al., it was demonstrated that Cd triggers the activation of phosphatidylinositol 3-kinase (PI3K)/Akt signaling pathway, which leads to the upregulation of COX-2 and macrophage inflammatory protein (MIP-2) in macrophages (Huang et al. 2014).

Cd has been found to trigger the Erk1/2 signaling pathway in airway epithelial cells, according to Cormet-Boyaka et al. This pathway activation results in increased expression of proinflammatory mediators such as IL-8. The researchers proposed that Cd-induced airway inflammation occurs in an NF-j-independent manner and is Erk1/2-dependent (Cormet-Boyaka et al. 2012). The research conducted by Kundu et al. revealed that short-term exposure to low doses of Cd leads to a significant increase in the expression of epidermal growth factor receptor (EGFR), which plays a critical role in upregulating proinflammatory cytokines such as TNF-a, IL-6, and IL-1. Additionally, the overexpression of EGFR can potentially promote oncogenesis, cell proliferation, and survival (Kundu et al. 2011).

While many studies have demonstrated the inflammatory effects of Cd exposure, there have been some findings suggesting that it may also have immunosuppressive and anti-inflammatory properties. For instance, in zebrafish models, high doses of Cd exposure have been shown to down-regulate iNOS and suppress NO production. Nevertheless, lower concentrations of Cd did not impact the expression of iNOS and the production of NO. Furthermore, studies indicate that while the expression of IL-1, TNF-a, and IL-6 increased in the liver, their expression levels were elevated in the spleen. These findings suggest that the effects of Cd exhibit organ-specific characteristics (Guo et al. 2017).

Studies have indicated that Cd exposure can elicit innate immune responses when administered at a concentration of 1 mg/kg. However, it can also impede T-cell reactions and lead to a reduction in respiratory burst stimulation. Interestingly, a lower dose of Cd (0.5 mg/kg) has been shown to enhance respiratory burst activation. The findings of this research propose that increased concentrations of Cd could potentially induce immunosuppressive effects in the spleen of rats. Ultimately, Cd exhibits both pro-inflammatory and anti-inflammatory effects depending on the dosage, duration of exposure, and the type of cells subjected to it (Demenesku et al. 2014).

A different investigation demonstrated that the movement of Trx1 to nuclei, which is redox-active, and its accumulation are crucial in the inflammation and cell death induced by Cd. In current studies, Cd exposure was found to incite the transfer of Trx1 to the nucleus, activating the transcription factor NF-kB. An elevation in the activation of NF-kB led to the augmentation of inflammatory substances, adhesion molecules, and cellular demise. This examination indicated that the interconnection between these signaling routes and provocative sequences is linked to the toxic effects of low doses of Cd (Go et al. 2013).

Toll-like receptors (TLRs) hold significance as receptors of the innate immune system. TLR signaling plays a vital role in activating immune genes needed for combating viral, fungal, and bacterial infections in invertebrates. The impact of Cd toxicity on TLRs and the signaling pathways they are involved in is notable. A recent investigation demonstrated that Cd can potentially influence the gene expression of TLRs and their activation in human epithelial cells. Upon activation of TLR4, lung epithelial cells produce more MUC8 when exposed to inflammatory mediators, such as LPS. An investigation demonstrated that exposure to Cd can activate the TLR4 signaling pathway Erk1/2 and p38 MAPK, resulting in heightened expression of MUC8 in inflamed airways of epithelial cells (Song et al. 2016; Fataei et al. 2013).

Research has shown that the administration of Cd can lead to widespread inflammation and the production of inflammatory cytokines. Consequently, there is a notable rise in CD11b positive neutrophils during the acute phase response. Additionally, polymorphonuclear neutrophils (PMNs) experience an increase in the production of intracellular myeloperoxidase (MPO) as well as nitrogen and reactive oxygen molecules (Djokic et al. 2015; Fataei 2017).

3.4 Cd and mucosal immunity

Extensive investigations have been conducted on the impact of Cd on the immune response of mucosal tissues, particularly within the respiratory and gastrointestinal systems.

Respiratory system

Currently, there is a scarcity of research on the impact of Cd on the immune response of the respiratory mucosa. The inhalation of Cd proves to be highly toxic to the respiratory system. Evidence indicates that immediate exposure to Cd resulted in damage to the lungs, along with inflammation of the bronchial and pulmonary regions, resulting in the recruitment of lymphocytes. Long-term inhalation of Cd negatively affected the respiratory immune system, leading to primary and emphysema lung cancers in rodents. The inflammation and leakage of fluid in the lungs were enhanced due to exposure to Cd. After this exposure, the cells lining the lungs released elevated amounts of inflammatory cytokines, such as MIP-2 and IL-6. Cd was also observed to stimulate the growth of the lung cells. Cd in the body is linked to respiratory problems and a long-term lung condition known as chronic obstructive pulmonary disease (COPD). Research found that elevated levels of Cd in the blood are connected to lung dysfunction and the development of COPD, particularly in males (Oh et al. 2016).

Extensive proof suggests that Cd-induced lung toxicity is facilitated by a Zrt/Irt-like Protein-8 (ZIP8). The expression of ZIP8 transportation proteins is particularly elevated in lung epithelial cells. This specific protein plays a crucial role in enabling the internalization of heavy metals like Cd following inhalation. The expression of ZIP8, which is facilitated by NF-jB, is heightened as a result of exposure to Cd. This increase in ZIP8 leads to the apoptosis of lung cells. By inhibiting NF-jB, the toxicity caused by Cd on cells can be resolved, potentially impacting the presence of ZIP8 (Person et al. 2013).

Research indicates that the element Cd can potentially enhance the likelihood of developing lung cancer. It has been proven that extended periods of exposure to Cd or any Cd-related substance are closely associated with an elevated risk of developing lung cancer. Research has demonstrated that Cd prompted the activation of cyclin D1 and suppressed the expression of P16. Additionally, exposure to Cd resulted in the independent invasion and growth of lung epithelial cells. There appears to be a connection between the development of lung cancer and chronic inflammation brought about by exposure to Cd. In light of this observation, the company of Cd contamination has the potential to convert healthy epithelial cells into cancerous ones (Person et al. 2013).

Gastrointestinal tract

Cd toxicity has a considerable impact on the gastrointestinal tract (GI), which is recognized as the most susceptible area of the body. Inducing intestinal inflammation occurs due to administering Cd orally, which prompts the production of TNF-a. In response, the gut experiences inflammatory reactions, which cause elevated levels of IL-8 and MIP2, as well as the recruitment of neutrophils, a type of inflammatory cell. The presence of Cd in the intestines has detrimental effects on the gut microbiota. Cd diminishes the overall population of microorganisms, including beneficial probiotic bacteria (Ninkov et al. 2015). A study was conducted to examine the impact of Cd on catfish, and the findings revealed that Cd led to the growth of goblet cells and augmentation in mucus production. The accumulation of Cd primarily in enterocytes resulted in dysfunction and eventual death of these cells (Xie et al. 2019). The accumulation and absorption of Cd leads to pathological occurrences such as villi destruction, necrosis of the epithelial cells, and gastritis with blood presence (Ninkov et al. 2015). Besides its direct toxic effects and pathological consequences, Cd can heighten the chances of cancer development by generating ROS. ROS is a crucial factor in promoting inflammation caused by Cd. Increased levels of ROS lead to oxidative stress and consequent DNA harm (Xie et al. 2019). Furthermore, exposure to Cd has been linked to the formation of P53 and the initiation of cell apoptosis in the intestinal epithelium.

Multiple research studies have documented the inflammatory consequences of Cd in the gastrointestinal tract. However, there exist conflicting findings. One study found that in an animal model of colitis induced by TNBS (trinitrobenzenesulfonic acid), prolonged exposure to Cd led to reductions in the levels of specific inflammatory cytokines and genes associated with oxidative stress. These included NO, IL-1, and IL-6. Additionally, it was observed that there was an increase in the levels of the anti-inflammatory cytokine TGF-b. In the given scenario, it appears that a sudden Cd exposure could give rise to manifestations of colitis, whereas prolonged exposure to this metal might possess defensive characteristics in animal models of colitis, thereby alleviating colitis symptoms. Furthermore, research indicated that the concentrations of Cd remained unaltered in cancerous intestinal tissue compared to unaffected samples.

The microorganisms found in bacteria have a significant impact on the immune system of the mucous membranes. The gut's natural flora is crucial in maintaining the balance and stability of the intestines. These microorganisms help protect against harmful infections and regulate the levels of substances that promote both inflammation and anti-inflammatory responses. Cd has adverse impacts on the microbial balance in the gut. Prolonged intake of Cd can alter the makeup of the intestinal microflora by suppressing the proliferation of specific bacterial communities. Excessive Cd levels lead to a significant decline in the population of various microbial species. The high pH levels present in the small intestine facilitate the accumulation of Cd in that specific area. As a result, the toxic effects of Cd on the size of the bacterial population predominantly occur in the small intestine (Fazeli et al. 2011).

Numerous investigations have indicated that probiotics possess favorable impacts on preserving gastrointestinal equilibrium through the regulation of the host's immune responses. Moreover, evidence has demonstrated that probiotics could potentially provide advantageous effects on the intestinal tract in terms of protecting against Cd contamination (Zhai et al. 2015). Recent research has proven the effectiveness of Lactobacillus as a prominent probiotic in binding with Cd, thereby diminishing the accumulation of this harmful heavy metal in the gastrointestinal tract. The probiotic has also shown remarkable antioxidant properties and the ability to reduce the cytotoxic effects of Cd. Lactobacillus improved the survival rate of cells that make up the outer layer of organs and reduced the levels of molecules that cause inflammation and attract immune cells. Furthermore, research has indicated that using Lactobacillus as a treatment had positive outcomes in repairing liver tissue that had been harmed by exposure to Cd (Zhai et al. 2014).

The presence of Cd pollution hurts the production of mucosal immunoglobulin. Research has demonstrated that the accumulation of Cd in the gastrointestinal tract leads to a significant decrease in the secretion of IgA. Additionally, it was proven that Cd uptake in the intestines led to an elevation in the permeability of the epithelial layer, resulting in the activation of inflammatory reactions. The occurrence of inflammatory mediators triggers the death of epithelial cells and disrupts the integrity of the epithelial barrier. When tight junctions are damaged, the absorption of Cd increases, leading to the onset of inflammation.

3.5 Health effects of Cd exposure

The release of Cd into the environment is a common occurrence due to various industrial and household activities, as it is a prevalent heavy metal contaminant (Zhang et al. 2017). Cd is highly poisonous and can be present in water sources, land, and the atmosphere due to its extensive utilization in various industries (such as mining, leather tanning, battery production, petrochemicals, etc.), vehicle fuel, tires, and phosphate fertilizers. These factors contribute to its introduction into the environment (Zhang et al. 2017).

The presence of Cd contamination poses a significant health concern beyond occupational settings as it can accumulate in grains and various parts of vegetables. Consequently, it can infiltrate the human food chain. The inhalation of

Cd through smoking contaminated tobacco leaves is a potential contributor to its presence in the human respiratory system. Cd can accumulate in the liver and kidneys, as well as replace calcium in bones. It can lead to various health problems, including multiple cancers, osteoporosis, cardiovascular diseases, hepatotoxicity, genotoxicity, renal dysfunction, osteomalacia, and kidney damage. Additionally, Cd is classified as a human carcinogen of group 1 because it is suspected of causing cancer (Zhou et al. 2022). Research indicates that Cd functions as an endocrine disruptor, potentially leading to hormone-related tumors in the urinary and respiratory systems. There are conflicting research findings regarding the correlation between occupational exposure to Cd and the development of various cancers, including prostate cancer, pancreas, endometrial, breast, and kidney (Hartwig 2010). The precise mechanism of Cd's interaction within the body remains uncertain. Despite not playing a significant role in diseases through weak binding to DNA, which lacks mutagenic solid properties, Cd exposure can still impact specific genes and induce disease development through transcriptional processes. DNA methylation, for instance, can inhibit the tumor suppressor RASAL1 and the renal fibrosis inhibitor KLOTHO, potentially leading to kidney damage. Exposure to Cd has been linked to increased activity of the DNMT3b enzyme and malignant transformation of the prostate in humans (Jiang et al. 2008). Exposure to Cd can lead to hypermethylation, which can prevent gene transcription related to various cellular processes such as apoptosis, cell cycle regulation, proliferation, and DNA repair. Additionally, it can also exacerbate diseases and affect the activity of antioxidant enzymes.

The effects of Cd on the human body are influenced by several factors such as the pathway, amount, and duration of absorption. Consequently, Cd can result in both acute and chronic toxic effects. While acute toxicity of Cd is not prevalent in numerous nations, immediate exposure to Cd can result in symptoms such as acute pulmonary edema, pneumonitis, chest pain, loss of consciousness, and abdominal pain (Theron et al. 2012). Cd can cause long-term harm to individuals who are exposed to it for an extended period, resulting in renal tubular dysfunction and pulmonary disease (Theron et al. 2012). The buildup of Cd in the kidney can lead to calcium loss and the onset of osteoporosis through tubular dysfunction and urinary excretion (Lv et al. 2017).

The presence of heavy metals, like Cd, in the environment significantly affects the immune responses of the host. Exposure to Cd toxicity can lead to a suppression of immune reactions, particularly in cases of iron-deficiency anemia, which in turn impacts the body's ability to combat infectious diseases. Cd functions in contrast to zinc by competing for cell surface binding sites. The excessive accumulation of Cd hinders zinc's ability to bind to carrier molecules and disrupts the absorption of zinc. The dysfunction of various immune cells, such as macrophages and neutrophils, is caused by Cd contamination, which results in the loss of zinc absorption (Theron et al. 2012).

3.6 Factors influencing Cd bioavailability

The availability of Cd is influenced by various factors such as plant age, root exudates, micro and macronutrients, organic matter, plant genotypes, and soil pH. However, soil pH is considered the primary factor that affects the availability of Cd. There is a negative correlation between soil pH and Cd uptake. Decreasing soil pH leads to increased Cd concentration in plants. The availability of Cd in the soil solution is affected by the pH of the soil. However, an increase in soil pH does not necessarily restrict the absorption of Cd by plants. The extractability of Cd in soils is regulated by soil pH, while plant uptake of Cd is influenced by various environmental factors such as climate and soil conditions (Kim et al. 2009). Li et al. (Li et al. 2019) found that the level of Cd in rice grain was affected by soil pH, with a pH of 4.95 resulting in 0.36 mg kg^{-1} of Cd and a pH of 6.54 resulting in 0.43 mg kg^{-1} of Cd in China. The accumulation of Cd in a grain of wheat (Triticum aestivum L.) is influenced by soil factors such as organic carbon, pH, and Cd concentration (Fataei 2016).

The presence of Cd in plants is influenced by their genetic makeup (Z et al. 2018). The introduction of mycorrhizal fungi enhanced the absorption of P. It promoted the growth of the Jamaican nettle tree (Trema micrantha L.), consequently improving its resistance to Cd using a dilution effect (Nazar et al. 2012). The presence of organic matter in soil impacts the availability of Cd in soil due to its ability to hold onto metal components. In forest soils with organic composition, organic matter acts as the primary substance for absorbing metals. Cd sorption in Canadian forest soils was significantly greater when organic matter was present compared to soils with no organic matter, with a 30-fold increase (Kubier et al. 2019). Various organic amendments, including bio-solid waste, crop residue, farmyard manure, and compost, effectively decrease Cd availability to plants, even in soils with high Cd pollution levels (Sohail et al. 2019).

The precense of other ions in the soil affects the availability of Cd through ionic strength, complexation, and competition for root or soil exchange sites (Song et al. 2016). The quality and availability of Cd are inversely affected by the ionic activity of the growth medium, meaning that lower ionic pressure leads to higher metal content in plants. Cd is known to form complexes with chloride ions, which increase the solubility and accessibility of Cd. Cations like calcium (Ca), magnesium (Mg), zinc (Zn), and manganese (Mn) compete with Cd for binding sites in the soil and plant uptake. Moreover, root exudates play a significant role in modifying the soil's Cd availability. Root exudates are substances produced by plants during photosynthesis and are made up of various organic compounds such as polysaccharides, amino acids, peptides, proteins, and sugars. These compounds are released into the soil through the plant's roots (Zulfiqar et al. 2019). Root secretions can capture and attach Cd within the soil, safeguarding plant roots against Cd toxicity in the soil. Furthermore, root secretions reduce the absorption of Cd in plants while enhancing uptake of vital nutrients by plants (Person et al. 2013).

3.7 Geographic distribution of Cd-contaminated soil

Joint FAO/WHO Expert Committee on Food Additives (JECFA) and European Food Safety Authority (EFSA) suggest acceptable thresholds for evaluating the dietary exposure to Cd in varying nations. Various methods, such as Total Diet Studies (TDS), replicative diet analysis, and dietary assessment, have been employed to gauge the levels of dietary exposure among diverse populations across the globe. A recent study conducted in the United States found that the average daily intake of dietary Cd was estimated to be around 4.6 lg/day. The comparison was conducted between NHANES 2007 – 2012 data on food intake over a two-day period and the Food and Drug Administration (FDA)'s TDS 2006 – 2013 data on the concentration of Cd in food, leading to the aforementioned estimation (Kim et al. 2018). According to Health Canada's 2007 data, it was determined that the average daily intake of Cd in the Canadian diet is estimated to be 13.2 micrograms per day (Zhao et al. 2023). The reason for the lower estimated intake of dietary Cd in the US population compared to Canada may be due to the implementation of new legislation in specific US states restricting the amount of Cd in phosphate fertilizers, resulting in lower Cd concentrations in the US food supply.

According to a report from the EFSA, it was found that European countries have an average daily intake of Cd in adults ranging from 12.9 to 19.1 mg, assuming an average body weight of 60 kg (Authority 2012). In terms of adults with high exposure levels (such as those in the 95th percentile), their daily consumption of Cd through diet can vary from 21.2 to 41.2 milligrams per day (Authority 2012). For adults, the food Cd concentration and the consumption data were compared at the individual level to determine these estimates. To determine the parameters, we made use of consumption information taken from the EFSA Comprehensive European Food Consumption Database. This database contains data on over 67,000 populations residing in 22 Member States. Additionally, we incorporated food Cd concentrations obtained by the EFSA between 2003 and 2011. Spain had the most significant intake of dietary Cd among the European countries at 19.1 mg/day, while Italy followed closely at 18.9 mg/day. Ireland had an input of 16.9 mg/day, and Germany had the lowest intake at 12.9 mg/day.

Different or greater levels of Cd consumption have been documented in Asian nations. In the case of South Korea, an approximation of 14.5 micrograms of Cd per day as part of the diet was calculated based on the information regarding food consumption obtained from the Korean Nutrition Survey and the Cd concentration from the Korean Food and Drug Administration (Kim and Wolt 2008). From 2016 to 2019, the 6th TDS in China encompassed 24 provinces and involved around 86% of the population. According to a study by Zhao et al. (Zhao et al. 2022), the estimated daily intake of dietary Cd averaged 17.3 lg/day. According to a study conducted between 2001 and 2005, Japanese women aged 20 to 74 had an average daily intake of 26.4 micrograms of dietary Cd. From 2008 through 2009 in Bangladesh, the average daily intake of Cd in the diet was measured to be 34.6 micrograms.

According to the information provided earlier, the average daily intake of Cd through diet in most countries (ranging from 4.6 to 19.1 μg per day) was within the limits established by EFSA and JECFA. However, in Japan and Bangladesh, the dietary Cd intake (ranging from 26.4 to 34.6 μg per day) was lower than JECFA's limit of 50 μg per day but higher than EFSA's limit of 21.4 μg per day. The amounts of Cd consumed by individuals with prominent exposure, such as those within the 95th percentile, were found to be in the range of $21.2 - 41.2$ lg/day, which approached or slightly surpassed the established limit determined by EFSA. Hence, for these individuals, there is virtually no room for additional means of Cd exposure if the acceptable intake level determined by EFSA is not surpassed (Zhao et al. 2023).

Moreover, mounting proof indicates that long-term exposure to Cd at concentrations below the limits established by EFSA or JECFA might still heighten the likelihood of developing cancer in the uterus, urinary bladder, and mammary glands (Zhao et al. 2023). According to the findings of the Swedish Mammography Cohort, the risk of endometrial cancer was 2.9 times higher in postmenopausal women who consumed more than 15 lg/day of Cd through their diet compared to those who consumed less than 15 lg/day. In a study, it was found that individuals who consumed more than 16 lg/day of dietary Cd had a considerably greater chance of developing invasive breast cancer compared to those who consumed less than 13 lg/day of Cd. The rate ratio, after considering other relevant factors, was calculated as 1.27 with a 95% confidence interval of $1.07 - 1.50$. The study included a total of 55,987 participants (Julin et al. 2012). The investigations pose an inquiry as to whether the existing regulations set by EFSA and JECFA can sufficiently safeguard individuals against potential health hazards resulting from the consumption of dietary Cd. It is because these thresholds are primarily designed to shield against the non-cancerous repercussions of Cd intake.

To evaluate the potential of Cd as a carcinogen for humans, researchers have calculated the excess lifetime cancer risk (ELCR), which represents the additional likelihood of an individual developing cancer throughout their lifetime due to exposure to Cd in their diet. Yuan et al. (Yuan et al. 2014) conducted a comprehensive evaluation of the potential health risks associated with consuming dietary Cd among adults residing in all 31 provinces of China in 2014. The researchers discovered that despite the mean intake of dietary Cd being lower than the JECFA limit, the risk of developing cancer for the adult population in the southern region exceeded the safe level. Therefore, it is uncertain if the established JECFA threshold provides adequate protection against potential cancer-causing impacts.

3.8 Regulatory measures and guidelines

Given the escalation in the utilization of Cd in industrialized nations and the rising levels of this substance in the environment (Satarug et al. 2013), it is presently not feasible to further restrict the overall population's exposure to this harmful metal. Consequently, recent efforts have been increasingly directed towards implementing measures to diminish the absorption of Cd from a contaminated diet and prevent adverse impacts resulting from exposure. Exploring efficient approaches to safeguard the body against the harmful effects of heavy metals is a significant area of focus in modern toxicology. It is particularly crucial, given that there is currently no established method for effectively removing Cd from the body, leading to a lack of specific treatment for Cd poisoning (Arjaghi et al. 2021). Over the past few years, an increasing focus has been placed on the potential utilization of naturally derived biologically active substances found predominantly in diverse plants and certain animals (Mezynska and Brzóska 2018).

These substances are being explored as a preventive measure against the detrimental health consequences associated with exposure to different heavy metals, including Cd. Among the constituents of this category are L-carnitine, carotenes, certain vitamins, taurine, both large and small minerals, polyphenols, and coenzyme Q10 (Abdel-Hady and Abdel-Rahman 2011). Polyphenols are a group of antioxidants that are found in various plant-based foods such as vegetables, fruits, and spices. They are also present in popular beverages like cocoa, wine, tea, and coffee (Mezynska and Brzóska 2018).

Polyphenols exert their protective influence through their potent antioxidant characteristics and their capacity to bind Cd^{2+} ions (Brzóska et al. 2016a). Polyphenolic compounds can reduce the absorption of toxic Cd^{2+} ions from the gastrointestinal tract due to their ability to bind with hydroxyl groups and increase intestinal MT expression (Brzóska et al. 2016b; Brzoska et al. 2015). Supplementation using polyphenols serves to hinder the excessive accumulation of Cd in the body, both by inhibiting its absorption through the gastrointestinal tract and by promoting its excretion through urine (Brzoska et al. 2015; Brzóska et al. 2016b). The diminished presence of Cd in bodily fluids and organs leads to a reduction in its harmful effects, which include oxidative stress and related outcomes.

There is a shortage of epidemiological information on using polyphenolic compounds to prevent Cd accumulation and toxicity in the human body. Although there are only a limited number of experiments conducted in animal models that reflect a lifetime human exposure to this toxic metal, a range of experimental studies suggests that plant extracts containing polyphenols can protect the body from Cd exposure (Six and Smolders 2014; Lakshmi et al. 2014). Additional research using animal models is required to explore potential solutions for mitigating the impacts of low-level Cd exposure. The favorable outcomes of in vivo experiments provide a solid foundation for conducting epidemiological studies to assess the effectiveness of polyphenolic compounds in preventing and treating illnesses caused by environmental exposure to this foreign substance.

There is existing knowledge that a rise in polyphenol intake can lower the likelihood of various illnesses such as certain cancers, obesity, type 2 diabetes, and cardiovascular diseases (resserra-Rimbau et al., 2014). Cd represents a significant risk factor in the development of these conditions. Notably, individuals who consume an average daily intake of approximately 1235 ± 199 mg of polyphenols exhibit a 46% lower risk of cardiovascular disease compared to those consuming around 483 ± 108 mg per day. According to the research conducted by Henning et al., it has been demonstrated that male individuals diagnosed with prostate cancer who consume green tea for 33 days (equivalent to an intake of 1.010 mg of polyphenols per day) experience noticeable reductions in nuclear NF-κB levels in tissues post-radical prostatectomy (Henning et al. 2015). Additionally, their urine shows lower levels of 8-hydroxy-2′-deoxyguanosine (8-OHdG), a primary marker of oxidative DNA damage, while the concentration of prostate-specific antigen (PSA) in their serum decreases. This effect is not observed in individuals who do not consume green tea (Henning et al. 2015). Considering the information presented, it appears feasible that products containing high levels of polyphenols may have a safeguarding effect on individuals who are exposed to Cd.

A multitude of experimental investigations suggests that the inclusion of bioelements, vitamins, carotenoids, and coenzyme Q10 in one's diet may have a significant impact in protecting against the negative consequences of Cd exposure (Abdel-Hady and Abdel-Rahman 2011). Certain epidemiological studies also provide evidence for the beneficial impact of bioelements and the heightened toxicity of Cd when there is a deficiency of these elements in the human body. A study involving 16 girls between the ages of 9 and 20 found that taking magnesium pidolate supplements (2×140 mg per day) for six months resulted in a decrease in Cd levels in their hair. Before the supplementation, Cd levels ranged from 0.03 to 0.10 μg/g dry hair weight, which decreased to 0.01 to 0.03 μg/g dry hair weight after the supplementation. This suggests that magnesium supplementation may help reduce Cd exposure. In a study conducted by Lin et al. (Lin et al., 2014), it was found that individuals with low levels of zinc in their serum are at a greater risk of kidney damage caused by Cd compared to those with high levels of zinc in their serum. The cutoff values for low and high levels of zinc in men were $\geq$ 74, 60, and 61 μg Zn/dL, and for women were $\geq$ 70, 66, and 59 μg Zn/dL in morning fasting, morning non-fasting, and afternoon urine, respectively. Bioelements such as iron, calcium, magnesium, manganese, selenium, and zinc possess the capacity to decrease the absorption of Cd from the gastrointestinal tract and its accumulation within the body. In addition, some of these elements are components of antioxidative enzymes such as Se-GPx, Fe-CAT, Mn-SOD, and CuZn-SOD, which support the enzymatic antioxidative barrier and development of oxidative stress and protect against Cd-induced weakening of antioxidative potential (Rogalska et al. 2011). The antioxidative properties of vitamins C and E, carotenoids, and coenzyme Q10 are primarily responsible for their protective effects (Abdel-Hady and Abdel-Rahman 2011; El-Missiry and Shalaby 2000). Furthermore, in experimental trials involving animal subjects, various substances, such as synthetic antioxidants and certain animal-derived compounds like L-carnitine, Haruan fish extract, and taurine, have displayed a beneficial impact when exposed to Cd.

3.9 Remediation strategies for Cd-contaminated soil

Defense mechanisms of Cd toxicity in plants

There are two contrasting approaches when it comes to Cd toxicity in plants, which are avoidance and tolerance (Tran and Popova 2013). The strategy of prevention involves restricting the absorption of Cd into the botanical organism (Liu et al. 2015). Plants utilize a mechanism of endurance that involves the retention and buildup of Cd through the attachment to peptides, proteins, and amino acids. Plants have developed various pathways to deal with the presence of Cd, which are connected to specific molecules involved in stress signaling. These include nitric oxide, ethylene, salicylic acid, humic acid, methyl jasmonate, and jasmonic acid (Shahid et al. 2014). Signaling molecules related to stress are activated when exposed to Cd, aiding in the cellular response to reduce the harmful effects of this element (Popova et al. 2012). Despite the presence of elevated levels of Cd in the soil, many plants can flourish and yield crops without significant detriment. Certain plants experiencing damage from the toxicity of Cd display a remarkable capacity for tolerating the adverse effects on their tissues and organelles (Shahid et al. 2014). Approaches aimed at managing the toxic effects of Cd include the processes of Cd distribution and uptake, commonly referred to as hyperaccumulation. Likewise, alternative plants have enhanced their antioxidant activity to safeguard their tissues and cells against Cd-induced destruction caused by ROS (Zhao et al. 2012).

Phytotoxicity effects are not observed in hyperaccumulating plants, as mentioned by Lata et al. (Lata et al. 2019). Up until 2011, around 450 angiosperm species were identified as hyperaccumulators of metals, and constant discoveries of new plants with potential for hyperaccumulation are being made. Detoxification processes help hyperaccumulating plants minimize the detrimental impact of high metal concentrations. Different mechanisms rely on the subdivision of cells and the use of chelation methods (Lata et al. 2019). The principal way in which plants absorb Cd is through transporters for zinc, manganese, iron, and calcium. In non-hyperaccumulating plants, the uptake of Cd is not particular (Lu et al. 2009). In maize, the absorption of Cd on the root apoplast might act as the primary factor influencing the plant's uptake of this metal from the ground. However, the findings on rice were contradictory (Lu et al. 2009). The transportation of metals, like Cd, from the roots to the shoots in plants that accumulate them differs from the process observed in plants that do not accumulate metals. The described strategy effectively preserves most of the metal ions extracted from the soil and sequesters them within the root cells, where they are rendered harmless through storage or chelation in the vacuoles. These toxins are rapidly transported to the aboveground portions of the plant through the xylem conduit, facilitated by the xylem (Liu et al. 2018). Several characteristics of the tonoplast of root cells aid in the rapid removal of metal ions from vacuoles. Histidine, a type of free amino acid, is involved in the accumulation of trace metals by forming stable compounds with divalent cations (Hassan and Aarts 2011). One method used by hyperaccumulating plants to deal with trace metal ions such as Cd is through sequestration, detoxification, and storage in their shoots (Lata et al. 2019). The primary sites of metal sequestration and detoxification are the cuticles, trichomes, and epidermis, which are least affected by photosynthetic activity (Hasan et al. 2009). Subordinate cells and guard cells of stomata are not affected by metals, which helps protect the functioning stomatal cells from the harmful effects of Cd ions (Sohail et al. 2019). One important strategy used by plants to detoxify trace metal ions involves the synthesis of specific low molecular weight chelators. These chelators prevent the attachment of metals to proteins that are vital for physiological functions and facilitate their movement into cell vacuoles (Ahmad et al. 2015).

Plant growth regulators

Different methods can cause plants to become more resistant to stress (Hasan et al. 2019). Studies have also demonstrated that applying plant growth regulators externally can enhance plants' resistance to various stresses. The role of plant growth regulators is pivotal in upholding the physical characteristics, blossoming, closing of stomata, and overall development of plants, as per the physiological function of plants (Sharma et al. 2020). Plants use various mechanisms to manage their growth and development. For example, in pulses, certain factors such as cell growth, nodule formation, and seedling germination are regulated. Similarly, in cereals, the stem diameter, dry biomass, leaf area, and overall growth of plants can be enhanced by applying plant growth regulators externally (Hasan et al. 2019). Furthermore, the external administration of plant growth regulators restrained the production of reactive oxygen species, hydrogen peroxide, and malondialdehyde levels while enhancing the effectiveness of antioxidant enzymes (such as catalase, peroxidase, and superoxide dismutase), proline concentration, and the expression of heat-shock proteins in plant organisms.

The investigation of salicylic acid's reaction to Cd and other metal stresses is a recently explored topic in the realm of crop physiology. Applying salicylic acid to maize seeds has resulted in alterations to the physiological procedures related to plant development, growth, and the photosynthetic system. At the early stages of growth, salicylic acid may have a positive impact on plants by helping them counteract the harmful effects of Cd toxicity (Ahmad et al. 2011). Salicylic acid may influence the production of specific proteins and defense-related enzymes in plants, allowing them to adapt and reduce the adverse effects of Cd toxicity. Preconditioning maize and pea plants with salicylic acid has been found to protect against the accumulation of damage caused by Cd toxicity in the rhizosphere (Popova et al. 2012). The application of salicylic acid before exposure to Cd has resulted in enhanced photosynthetic activity and growth in plants, as well as reduced Cd levels in the roots. The presence of salicylic acid in plants induces a protective reaction against stress and decreases the oxidative harm resulting from Cd exposure (Ahmad et al. 2011). Krantev et al. (Krantev et al. 2008) demonstrated that pre-treating plants with salicylic acid resulted in decreased proline and MDA levels, as well as reduced electrolyte leakage when compared to plants subjected to high Cd concentrations. The reason for this is the favorable impact of salicylic acid on the stability of the cell membrane by increasing the amount of lipids present, leading to alterations in the fatty acids' makeup, and controlling the functioning of the antioxidant system (Tran and Popova 2013).

The addition of abscisic acid (ABA) from an external source reduced the rate of water loss in seedlings, decreased the amount of Cd present, and enhanced the ability of rice seedlings to withstand Cd stres. Shahid et al. (Shahid et al. 2014) discovered that gibberellins, which are a different type of plant hormone, also play a role in enabling plants to develop resilience against Cd stress. Utilization of 10 mg m^{-3} of gibberellins resulted in a reduction of the damaging impact caused by Cd toxicity on the aerial parts of soybean plants and the physiological functions of the roots. Nitric oxide (NO) is an unbound radical compound that interacts with molecules of oxygen, thereby regulating the distribution of oxygen in plant tissues. Nitric oxide serves as a signaling molecule, functioning to trigger cellular defense responses under various stress circumstances (Tran and Popova 2013). In crops like sunflower, soybean, pea, and wheat, nitric oxide plays a crucial role in reducing the harmful effects of Cd toxicity (Singh et al. 2008). Various other substances such as humic acid, melatonin, brassinosteroids, jasmonates, paclobutrazol, and daminozide, are extensively employed worldwide to decrease the negative impacts of Cd on cultivated plants (Hasan et al. 2019).

3.10 Bioremediation

The presence of microorganisms like fungi, bacteria, and algae has the potential to contribute to the reduction of organic and metal pollutants present in various environments (Parthipan et al. 2017). In particular, Bacillus species have been found to effectively counteract the toxicity of several pollutants, including Ar, Cd, Ni, Fe, Cr, Cu, Pb, and U, in agricultural soils affected by contamination or in industrial wastewater (Radhakrishnan et al. 2017). Pseudomonas strains have proven to be highly effective in the removal of various pollutants such as nickel, lead, copper, chromium, and Cd (Chellaiah 2018). Nevertheless, the bacterial remediation process can come to a halt when the bacteria are depleted of their food reserves (Parthipan et al. 2017). To ensure that these microorganisms are able to obtain the most optimal food source found in soil, which is the root exudates, a technique was created to isolate the microorganisms. This technique, developed by Kuiper et al. (Kuiper et al. 2004) and Radhakrishnan et al. (Radhakrishnan et al. 2017), incorporates two significant qualities: the ability to break down specific pollutants and establish influential colonization within the roots (Imam et al. 2016). Organic acids, alcohols, and sugars released by plant roots provide nourishment for soil microorganisms, promoting their vitality and development. Some of these root exudates can also act as signals, guiding the movement of microbes. Moreover, plant roots contribute to the loosening of the rhizosphere and enhance water transport, facilitating the establishment of microbial communities.

Different ways in which microorganisms exhibit resistance to Cd have been demonstrated, such as the deposition of toxic metals in the cell wall, modifications of harmful substances, confinement/accumulation, and changes in the complex formed by the plasma and cell wall membrane. Bacterial cells can be exposed to Cd through various mechanisms involving the absorption of divalent cations like Mn^{2+} or Zn^{2+}, amplification of genes, active elimination of Cd, and enhanced transcription of metallothionein genes. Microbes offer a cost-effective and efficient way to remediate metals due to their ability to recover metals, regenerate bio-sorbents, and their high capacity (Chellaiah 2018). Various aerobic bacteria, such as Mycobacterium, Sphingomonas, Pseudomonas diminuta, Pseudomonas putida, and Rhodococcus, participate in metal bioremediation (Lata et al. 2019; Mehrzad et al. 2015). According to a study conducted by Imam et al. (Imam et al. 2016), Saccharomyces cerevisiae and Bacillus subtilis were able to remove 69.56% and 75.76% of Cd from contaminated soil after being inoculated for 5 days. In terms of enhancing plant growth and reducing Cd toxicity, Bacillus subtilis L. has the ability to improve water absorption and decrease electrolyte leakage (Ahmad et al. 2014). Meanwhile, Bacillus licheniformis L. has been found to enhance Cd distribution and accumulation in plants in soils contaminated with trace metals, ultimately reducing the level of toxic metals in the soil (Radhakrishnan et al. 2017).

The bacterium Pseudomonas aeruginosa produces antibiotic resistance against several types of antibiotics including cephalexin, erythromycin, streptomycin, amoxicillin, and penicillin. This resistance is beneficial in aiding the development of resistance against Cd in contaminated soil (Nath et al. 2014). Numerous other types of microorganisms, including Pseudomonas spp., Bacillus spp., Flavobacterium spp., Rhodococcus spp., Mycobacterium spp., Variovorax spp., Psychrobacter spp., and Achromobacter spp., contribute to the process of soil bioremediation. These particular species have been shown to aid in the removal of harmful metals from the soil. The application of Bacillus siamensis L. in soil contaminated with Cd leads to a notable enhancement in the harmful effects of Cd by reducing the MDA concentration and enhancing the CAT and SOD levels in wheat (Awan et al. 2020). Furthermore, the application of Bacillus siamensis L. enhanced the stability of the membrane, the production of amino acids, the accumulation of soluble sugars, the efficiency of photosynthesis, and the overall yield of wheat plants experiencing Cd-induced stress conditions (Awan et al. 2020). In addition to bacteria, fungi possess a multitude of characteristics and exhibit vast potential for application in agriculture, as they can remediate Cd by 94% and other soil contaminants including various metals. The symbiotic association between mycorrhizae and plants can potentially reduce the transfer of pollutants to plants by acting as a preventative barrier, which can effectively bind metals to fungal hyphae (Zhang et al. 2019). Vesicular structures, reproductive units, mycelia located outside the root, and mycelia located within the root of fungi have a crucial function in the sequestration of pollutants and accumulation of metals (Wang et al. 2016). Furthermore, plants inoculated with arbuscular mycorrhizal fungi can synthesize chelating compounds for complexing Cd, including metallothioneins, phytochelatins, and glutathione. Glomalin, synthesized by the mycelia of arbuscular mycorrhizal fungi, possesses the ability to bind a greater number of metals and plays a significant role in immobilizing trace metals and facilitating the adaptation of their respective host plants to inherently stressful environments (Zhang et al. 2019).

Certain types of fungi, such as Trichoderma spp. and Piriformospora indica, are highly adaptable to soils with elevated levels of pollutants, showcasing their versatility. These fungi are acknowledged for their role as promoters of plant growth and agents of biological control (Yaghoubian et al. 2019). Evidence suggests that Trichoderma strains with metal tolerance can exert a significant influence on the bioaccumulation of Cd and other pollutants (Sahu et al. 2012). A specific Trichoderma species, Trichoderma simmonsii L. (UTFC 10063), demonstrates the ability to mitigate Cd toxicity by 46.1% and exhibits the potential for bioaccumulation of Cd (Yaghoubian et al. 2019). A strain of Aspergillus niger, specifically Aspergillus niger L., effectively eliminated 84% of Cd ions from the soil (Júnior et al. 2003). Research indicates that Trichoderma atroviride L. has an impact on the translocation and uptake of Ni, Zn, and Cd in rapeseed plants. Additional fungal strains, such as Trichoderma mutant L. (Wang et al. 2009), Talamyces emersonii L., Bsaidiomycetes (Wang and Zhou 2005), as well as Trichoderma asperellum L., Trichoderma harzianum L., and Trichoderma tomentosum L., contribute to the remediation of Cd pollution in agricultural soils (Yaghoubian et al. 2019). It is crucial to conduct ongoing investigations into fungi, bacteria, and other microorganisms that can control environmental pollution in contaminated soil through mechanisms such as phytobial, bioaccumulation, biosorption, and biovolatilization remediation.

3.11 Mineral nutrition in minimizing Cd toxicity

The utilization of plant nutrients for reducing the harmful effects of Cd in plants is deemed a cost-efficient, productive, and time-efficient method for averting food pollution caused by Cd (Nazar et al. 2012). The provision of adequate and suitable amounts of vital nutrients at the correct time is crucial for enhancing the development of plants. To achieve the best crop yield, farmers add nutrients to the soil, and proper management of these nutrients is necessary to counteract the harmful effects of Cd. This can be achieved by understanding how plant nutrients interact with Cd in the soil (Nazar et al. 2012). It is important to note that many essential plant nutrients have a direct and indirect effect on the availability of Cd and its toxicity in soil (Zhang et al. 2019). Indirect consequences encompass maximizing the solubility of Cd in soil by impeding various mechanisms, such as releasing Cd in the reproductive components, desorption and dissolution, collaboration among plant nutrients and Cd for different membrane carriers, and promoting the accumulation of Cd in the grain and fruit of plants (Ahmad et al. 2015).

The alleviation of plant physiological stress and improvement of productivity are indirect ways to dilute the concentration of Cd. Utilization of N and specific additional elements in excessive quantities can result in soil acidification, thereby amplifying the solubility and accessibility of harmful metals such as Cd in the soil (NING et al. 2017). Likewise, the presence of various phosphorous-related Cd minerals may impact the solubility of Cd through the process of Cd precipitation, which is dependent on the configuration of P within the soil. Pertinent alterations in the inorganic composition have been documented to decrease the bioavailability of Cd in cultivatable soils through the application of P fertilizers. The presence of fertilizers determines the chemical form of Cd, thereby impacting its movement toward the roots and integration into the rhizosphere. The introduction of fertilizers likewise impacts the nutrient composition within the root development, rhizosphere, and overall plant growth, consequently altering the uptake, storage, and accessibility of different plant components (Wang et al. 2018). Within the soil-plant ecosystem, the bioavailability and function of Cd are greatly influenced by plant nutrients (Zhang et al. 2016).

Adding selenium (Se) in low amounts to polluted soil can enhance plant development and mitigate the impact of Cd stress (Gao et al. 2018). The mechanism behind this phenomenon involves Se shifting its binding from low-molecular-mass proteins to high-molecular-mass proteins and forming complexes with Cd. The existence of selenium in the soil reduces the accessibility of Cd, leading to its entrapment in insoluble complexes. By administering 2 μM sodium selenate (Na_2SeO_4), the effects of 600 μM Cd chloride ($CdCl_2$) on chloroplast function and ultrastructure in mustard plants are diminished through alterations in the activities of antioxidant enzymes, such as CAT, POD, SOD, APX, and glutathione peroxidase (Nazar et al. 2012). Selenium served as a counteracting agent for the nutrient enhancements resulting from Cd toxicity in wheat and rapeseed plants, while also reducing lipid peroxidation and promoting the integrity of the cell membrane (Wu et al. 2017). Likewise, the presence of silicon (Si) had a significant impact on Cd absorption, photosynthetic activity, and plant growth (Gao et al. 2018). In plants subjected to 2.5 μM Cd treatment, the introduction of 0.6 mM Si after 20 days resulted in an enhancement of chlorophyll fluorescence, while the application of 0.2 mM Si significantly improved photochemical quenching, indicating an increase in light utilization efficiency (Nazar et al. 2012). The utilization of 1.5 mM Si greatly diminished the uptake and transportation of Cd from roots to shoots, thereby mitigating Cd toxicity in Chinese cabbage (Brassica chinensis L.) cultivated hydroponically with 0.5 mg/L of Cd. This was achieved by elevating the activities of APX and catalase (Wu et al. 2017).

3.12 Phytoremediation

The strategy of phytoremediation, which aims at the degradation of contaminants in polluted areas, relies on biochemical, physical, and chemical interactions. This evolving approach involves mineralizing pollutants (Zulfiqar et al. 2012). Exist of several pathways associated with phytoremediation (Lata et al. 2019). The effectiveness of these processes is highly dependent on the nature of the pollutants, as different pollutants require specific mechanisms for remediation. Metals like Cd are eliminated through extraction as a remediation method, whereas other pollutants such as hydrocarbons and chlorinated compounds, are addressed through volatilization, degradation, and rhizoremediation (Kuiper et al. 2004; Fataei et al. 2015).

Phytoremediation plants exhibit characteristics like fast growth, extensive and densely-rooted systems, substantial biomass output, and a high bioaccumulation coefficient. When considering the selection of a plant for phytoremediation, various factors must be taken into consideration. These include the nature of the plant's root system (tap or fibrous), which depends on the rate of the plant's growth when exposed to the pollutant, the extent of damage caused to the plant by the pollutant, the toxicity level of the pollutant, and the duration required to attain the desired level of remediation.

Certain plant species like Indian goosegrass (Eleusine indica L.), chickweed (Ageratum conyzoides L.), and asthma-plant (Euphorbia hirta L.) have demonstrated their ability to decrease Cd levels in soil, achieving reductions of 58.8%, 52.2%, and 51.8%, respectively (Lata et al. 2019). Reducing Cd toxicity by plants depends on various factors such as soil pH, nutrient concentrations, soil temperature, and concentration of Cd toxicity in the soil (Radziemska et al. 2017). Plants involved in phytoremediation belong to diverse families such as Brassicaceae, Cunouniaceae, Caryophyllaceae, Lamiaceae, Euphorbioceae, Febaceae, Cyperaceae, Asteraceae, Violaceae, and Poaceae. Phytoremediation encompasses a range of mechanisms including phyto-volatilization, phyto-stabilization, rhizo-filtration, and phyto-extraction (Lata et al. 2019). Phyto-remediation encompasses various methods plants utilize to eliminate Cd pollution from soil or water, regardless of whether the concentrations are low or high (Chen et al. 2015). The toxins can be moved from the roots to the shoots and leaves of a plant, and this depends on the plant's ability (Khandare and Govindwar 2015). When rapeseed phyto-extracts are used, the phyto-extraction of Cd has been proven to decrease Cd levels in soil by 60% compared to the control. In wetlands or wastewater steams, plants can remove trace metals like Cd from aqueous solutions through rhizo-filtration (Mahajan and Kaushal 2018). For a plant to be suitable for rhizofiltration, it needs to have a root system that is long, hairy, and has a significant surface area since the roots filter pollutants from aqueous solutions (Khaokaew and Landrot 2015).

Sunflower and rapeseed are types of plants that are well-suited for the process of rhizo-filtration, which is an effective method for remediating Cd pollution (Z et al. 2018). Phyto-stabilization is a technique where plants are used to immobilize pollutants in soil, thereby transforming them from a toxic state to a less harmful form and preventing their migration (Mahajan and Kaushal 2018). In phyto-stabilization, specific plants with the ability to thrive in contaminated areas are utilized. These plants help immobilize metals in the soil through processes such as metal precipitation, complexation, reduction, or adsorption. This method does not require soil removal or the disposal of polluted biomass. Phyto-stabilization is an efficient technique that can be applied to soil with a dense texture and a significant amount of organic matter (Zhang et al. 2018). Phyto-volatilization, on the other hand, involves the use of plants to convert toxic pollutants into less harmful volatile substances through the process of plant-related transpiration (Song et al. 2017). Additionally, plants can volatilize pollutants such as Hg, As, and Se.

3.13 Chemical methods

The electroplating industry has traditionally utilized barium acetate to cause the coagulation of Cd in chemical processes (Rao et al. 2010). In soil, the precipitation of Cd ions can be achieved through the addition of magnesium hydroxide, calcium hydroxide, and sodium hydroxide. To extract Cd ions from aqueous solutions, alternative chemical methods such as cementation are effective (Rao et al. 2010; Ku et al. 2002). Different extracts like phosphorous-based extract, Cyanex 301, and aqueous nitrogen-donor extract can be utilized for Cd extraction. The excessive use of solvent in the extraction stripping phase is the primary reason for failure during the process (Rao et al. 2010). Therefore, it is not recommended to employ these methods when the metal removal concentration is extremely low (Mahajan and Kaushal 2018).

3.14 Biochar

The inclusion of biochar in agricultural soils contaminated with Cd has become significantly important in recent times (Zhang et al. 2019). Biochar is an organic substance with a porous carbon structure that occurs naturally through the pyrolysis of organic manure and crop residues in the absence of oxygen (Ding et al. 2016). By incorporating biochar, the presence and harmful effects of Cd in plants can be reduced, thus reducing its accumulation and toxicity (Shaaban et al. 2018). The adsorption ability of Cd in contaminated agricultural soils is regulated by various factors such as biochar parameters (e.g., pyrolysis temperature, pyrolysis retention time, feedstock type) and physiochemical biochar properties (e.g., surface area, pore space, and surface charge) (Yuan et al. 2019; Bashir et al. 2018). Chen et al. (Chen et al. 2015) demonstrated that urban sewage sludge-derived biochar significantly enhances Cd removal with an increase in the rate of biochar, leading to improved efficiency. The increase in removal ability corresponds to a value of approximately 42.80 mg g^{-1}. The metalloid reduction potency of biochar derived from legumes was found to be greater than that of biochar derived from non-legumes (Wang et al. 2012). Biochar made from sugarcane (Saccharum officinarum L.)

resulted in a 56% reduction in Cd absorption by plants compared to the untreated group.

3.15 Organic manure and compost

Organic soil amendments, such as farmyard manures, are widely used due to their accessibility and efficacy (Shan et al., 2016). These manures have been shown to enhance soil structure and fertility, thereby improving crop production (Radhakrishnan et al. 2017). Additionally, farmyard manure contains essential components like humic acid and fulvic acid, which can have an influential effect on the physic-chemical properties of the soil and can also aid in transforming pollutants in polluted soils (Sohail et al. 2019). Fulvic acid and humic acid contain functional groups, such as carboxyl and phenolic-OH groups. These groups can interact with pollutants and form high metal complexes. As a result, they have a significant influence on the transport, bioavailability, and solubility of metals in soils (Zhang et al. 2009). Differences exist in the literature regarding the impact of applying livestock/farmyard manure on the movement and solubility of Cd (Shahid et al. 2014). The incorporation of organic waste derived from livestock, specifically enriched with P, can bind to Cd and reduce its mobility within the soil (Sohail et al. 2019; Wei et al. 2014). Additionally, it is important to pour soluble Cd through the production of PO_4^{2-}, HPO_4^{2-}, or H_2PO^{4-} (Ullah et al., 2017). The utilization of composted swine manure in soils with high calcium content can have a significant impact on reducing the absorption of Cd in the tissues of radish plants.

The proportion of fulvic acid to humic acid is a crucial determinant of the solubility of Cd in polluted soils, and the ratio is significantly affected by organic modifications (Sohail et al. 2019). On one hand, crop residues and fresh manures exhibit a lower proportion of humic acid to fulvic acid, while on the other hand, aged manures and composted residues have a higher concentration of both fulvic and humic acids (Ahmad et al. 2015). In a laboratory study, the application of poultry and cattle manure had a positive impact on the development and yield of rice and reduced the amount of Cd present in the rice tissues when compared to a control group that did not receive any treatment. Other research studies have also demonstrated similar outcomes for crops like okra (Abelmoschus esculentus L.) and maize. The concentration of chloride and dissolved organic carbon (DOC) present in cattle urine helps to immobilize Cd by forming Cd-DOC complexes and soluble Cd-chloride (Gray et al. 2017; Ajorlo et al. 2010). When soil treated with sheep manure is used for cultivating alfalfa, it significantly decreases the mobility of Cd, reducing it by 57% in comparison to a control scenario (Elouear et al. 2016). During a 4-year trial in the field, researchers discovered that incorporating swine manure into soil contaminated with Cd resulted in a noticeable decrease in Cd levels in rice's stem, leaf, and grain. Specifically, the Cd content was reduced by 44% in the stem, 36.4% in the leaf, and 37.5% in the grain, when compared to a control group (Xie et al. 2015). The solubilization of Cd is increased by the presence of organic acids generated during decomposition. However, it is also crucial to take into account other factors such as the soil matrix's physicochemical properties, the impact of roots in the micro-environment of the rhizosphere, and the interactions among microbial populations.

4. Conclusion

In conclusion, the contamination of Cd is a pressing issue that affects numerous life forms and ecosystems. The improper handling and disposal of Cd-containing waste contribute to its presence in food, soil, smoke, water, and air, posing a significant threat to the environment and human health. The negative impacts of Cd are evident in microfaunal abundance, biogeochemical cycles, enzymatic activities, water uptake in plants, photosynthesis, root elongation, nutrient uptake, and overall food safety. The accumulation of Cd in the body can lead to severe impairments in various systems and even induce carcinogenic effects. However, there are mitigation techniques available to reduce Cd accumulation in plants. Moving forward, it is crucial to conduct further research on the molecular mechanisms of Cd translocation, considering the routes, doses, time of exposure, and specific tissues or cells that exhibit toxicological responses. Large-scale experimental studies can help address knowledge gaps and inform remediation measures to tackle the multifaceted toxicity of this heavy metal.

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