Rev. FCA UNCUYO. 2020. 52(1): 391-405. ISSN (en línea) 1853-8665.

Cadmium phytotoxicity: issues, progress, environmental concerns and future perspectives

Fitotoxicidad del cadmio: problemas, avances, preocupaciones ambientales, y perspectivas futuras

Essa Ali [1, 2], Abid Hussain [3], Izhar Ullah [3], Fahad Said Khan [4], Shamaila Kausar [5], Shaikh Abdur Rashid [6], Imran Rabbani [7], Mohammad Imran [8], Kaleem Ullah Kakar [9], Jawad Munawar Shah [10], Ming Cai [1], Lixi Jiang [2], Nazim Hussain [2], Peilong Sun [1*]

Originales: *Recepción:* 02/11/2017 - *Aceptación:* 19/09/2018

INDEX

REVIEW

---

1 Zhejiang University of Technology. Department of Food Science and Technology. China. essaali@upr.edu.pk / * sun_pl@zjut.edu.cn
2 Zhejiang University. College of Agriculture and Biotechnology. Zhejiang Key Laboratory of Crop Gene Resources.
3 The University of Poonch. Department of Pharmacy. Rawalakot. AJ&K.
4 The University of Poonch. Department of Eastern Medicine. Rawalakot. AJ&K.
5 University of Central Punjab. Department of Microbiology. Lahore.
6 Gomal University. Faculty of Pharmacy. DI Khan.
7 Kohat University of Science and Technology. Department of Pharmacy. Kohat.
8 Mohi-ud-din Islamic Institute of Pharmaceutical Sciences. Mohi-ud-din Islamic University. Mir Pur.
9 Department of Biotechnology, Faculty of Life Sciences & Informatics, Balochistan University of Information Technology, Engineering and Management Sciences Quetta.
10 Bahauddin Zakarya University Bahadur sub campus Layyah. College of agriculture.

Abstract

Cadmium, a high toxicity element, is a potential threat to plant and human health, and a dangerous pollutant in the environment. Uptake and accumulation by crops represent the main entry pathway for potentially health-threatening toxic metals into human and animal food. Crops and other plants take up Cd from the soil or water and may distribute it in their roots and shoots. Soil and/or water are usually contaminated with Cd through natural sources, industrial effluent, and anthropogenic activities. In this review, the sources of Cd contamination, evaluation of the phytotoxic effects on plants, and mode of action of Cd toxicity, were summarized. Plant defensive strategies upon excess Cd are also considered in this review. Cd-induced effects include oxidative stress, disintegration of the photosynthetic apparatus, reduction in gas exchange parameters, nutrient imbalance, and subcellular organelle degradation. In addition, Cd severely impairs biomolecules such as DNA, protein, and lipids. Although plants are sessile in nature, they are equipped with certain mechanisms to cope with unfavorable conditions. These mechanisms include synthesis of metal-chelating proteins, expression of enzymatic and non-enzymatic antioxidants, organic acids, and plant root–mycorrhiza association. The built-in system of plant tolerance to Cd can be further enhanced by the application of exogenous organic and inorganic metal sources. This review will broaden the knowledge about the Cd accumulation in plants and the responses to metal exposure, as well as our understanding of metal tolerance and overcoming this serious issue for sustainable agriculture and human health worldwide.

Keywords
Cadmium • antioxidant enzymes • phytochelaton • metal transporters

Resumen

El Cadmio, con su alta tasa de toxicidad, constituye una amenaza potencial para la salud humana y las plantas, es un contaminante peligroso en el medio ambiente. La absorción y acumulación en los cultivos representan la principal vía de entrada de metales tóxicos en alimentos para humanos y animales, potencialmente peligrosos para la salud. Los cultivos y otras plantas absorben Cd del suelo o del agua y pueden distribuirlo en sus raíces y brotes. El suelo y/o el agua se contaminan con Cd generalmente a través de fuentes naturales, efluentes industriales y actividades antropogénicas. En esta revisión, se resumieron las fuentes de contaminación de Cd, la evaluación de los efectos fitotóxicos en las plantas y el modo de acción de la toxicidad. Además, las estrategias de las plantas para protegerse del exceso de Cd. Los efectos inducidos por Cd incluyen el estrés oxidativo, la desintegración del aparato fotosintético, la reducción de los parámetros de intercambio de gases, el desequilibrio de nutrientes y la degradación de los orgánulos subcelulares. Además, el Cd deteriora gravemente las biomoléculas como el ADN, las proteínas y los lípidos. Aunque las plantas son de naturaleza sésil, están equipadas con ciertos mecanismos para hacer frente a condiciones desfavorables. Estos mecanismos incluyen la síntesis de proteínas quelantes de metales, la expresión de antioxidantes enzimáticos y no enzimáticos, ácidos orgánicos y la asociación de la raíz de la planta y la micorriza. El sistema incorporado de tolerancia de plantas al Cd puede mejorarse aún más mediante la aplicación de fuentes orgánicas e inorgánicas de metales exógenos. Esta revisión ampliará el conocimiento sobre la acumulación de Cd en plantas y las respuestas a la exposición a metales, así como la comprensión de la tolerancia al metal y la superación de este grave problema para la agricultura sostenible y la salud humana en todo el mundo.

Palabras clave

Cadmio • enzimas antioxidantes • fitoquelaton • transportadores de metales

Abbreviations

Pn: Photosynthetic rate • Tr: Transpiration rate • Gs: Stomatal conductance • SOD: Superoxide dismutase • CAT: Catalase • APX: Ascorbate peroxidase • POD: Peroxidase • MDA: Malondialdehyde • PCs: phytochelatons

Introduction

Heavy metals are major environmental pollutants given their harmful effects on ecological, evolutionary, nutritional, and environmental ins and outs. A metallic element with a relatively high density (greater than 4 g/cm^3 or at least 5 times greater than water) and is toxic even at a low concentrations, can be categorized as a heavy metal (2, 3, 35).

The industrial revolution triggered the regular and uncontrolled release of hazardous materials into the environment as industrial effluents. Therefore, heavy metals, especially Cadmium (Cd), are constantly added into the soil-plant-environment system (36). Over the past decades, Cd has been listed 7th out of 275 compounds in the priority list of hazardous materials (9). Over 2×10^7 acres of farmland in PR China have been contaminated by heavy metals, which is almost one fifth of the total arable farmland area. China suffers a 10,000,000 t loss of crop output per year because of heavy metal pollution (60).

Cd accumulation is an irreversible process; remaining in soil for 15-1100 years (29). In addition, Cd has high plant-soil mobility and easily accumulates in plant tissues. High accumulation of Cd in different tissues of crops, especially edible tissues, reduces growth and quality of crops and poses a danger to the organisms feeding on such crops. Humans are the first victims of Cd toxicity because they are at the top of the food chain (61). A health risk study conducted by Wang (2005), found that the health risk in adults living in Ding Li, Tianjin, China was mainly associated with the intake of Cd through vegetable and fish consumption. Cd causes hepatotoxicity, nephrotoxicity, pulmonotoxicity, neuro-toxicity, bone toxicity, and carcinogenesis in humans. Moreover, Cd is deposited and stored in the human liver ($t_{1/2}$ = 4-19 year) and kidney ($t_{1/2}$ = 6-38 year) (10).

Plants are the main vector of Cd transfer to humans; therefore, extensive studies have been carried out on the effects of Cd on plants including its accumulation and translocation. Though plant responses to Cd stress vary among species and cultivars, the mechanisms of response are almost the same (21).

Effects of Cd on crops include decreased gas exchange (28), photosynthetic pigment degradation (38), deficiency of nutrient elements (19), subcellular changes (58), and modulation of antioxidant enzyme activity (1, 6). Additionally, exposure to Cd results in the inhibition of cell elongation (17), and alterations in root morphological characteristics (28). In brief, Cd contamination in soil and plants has posed a serious issue to sustainable agriculture and human health worldwide (62).

SOURCE OF CONTAMINATION

Cd can be introduced to the environment from different sources ranging from natural to anthropogenic. In China, most areas are contaminated with Cd by mining and smelting operations (25). Water usually contains small amounts of Cd. Seawater has an average Cd concentration of approximately 0.1 mg/L or less, and river water contains dissolved Cd concentrations up to approximately 0.5 mg/L; although higher values have been reported under certain conditions. Atmospheric concentrations of Cd are usually 5 ng/m^3 in rural areas, 5-15 ng/m^3 in urban areas, and up to 60 ng/m^3 in industrial areas (26).

Geologic materials and rock outcropping are the major natural sources of Cd contamination in the environment. According to Climino (1983), 10x10^6 kg of Cd are emitted from Mount Etna every year. Agriculture soil is often contaminated with Cd by the application of different kinds of fertilizers, pesticides, and fungicides. In addition, Cd is introduced to agricultural soil by sewage sludge, animal manure, and limes (63). Nitrate and Phosphate fertilizers are also one of the sources of Cd contamination in the agricultural soil (48). However, , increased Cd accumulation in soil depends on the sources, types, and quantity of the contaminant and the types of agricultural soil.

Heavy metals, particularly Cd, are constantly added to the environment because of industrial revolution and uncontroled release of effluent. These industrial activities include mining, transport of ores, smelting and metal finishing, and recycling of metals. Smelting and castings emit Cd in vapor form that combines with water and gets spread in the environment. In addition, coal-burning power plants, petroleum combustion, nuclear power stations, and high tension lines contribute Cd to the environment (57). Cd is also released as a by-product of Zn, and occasionally Pb, refining (35).

EFFECTS OF CADMIUM TOXICITY IN HIGHER PLANTS

Cd is soluble in water and is highly mobile. Cd-induced toxicity to plants results in physiological to molecular and biochemical changes. Generally, Cd in plants causes leaf rolling and chlorosis and reduces growth of both roots and stems. Some of the effects are described in this study.

Effect of Cd toxicity on Gas exchange in plants

Cd severely decreases gas exchange parameters including photosynthetic rate (Pn), transpiration rate (Tr), and stomatal conductance (g_s). Under severe Cd stress, plants adapt by closing stomata and reducing reduce the uptake of Cd to the upper parts of the plants. Stomatal movements are not directly affected by Cd, but rather due to the strong interference of Cd with K^+, Ca^{+2} and abscisic acid in the guard cells (12). Stomatal closure is followed by a subsequent decrease in Tr and Pn. This phenomenon explains the reduced growth of plants under stress. However, tolerant plants use other strategies to cope with high Cd instead of stomatal closure and reduced Tr.

Effect of Cd toxicity on photosynthetic apparatus and pigments

In the photosynthetic system, photosynthetic pigments are considered indicators of damage induced by environmental stressors (39). In *Brassica napus*, Cd reduced total chlorophyll content and carotenoid content, while increasing non-photochemical quenching (5). The decrease in chlorophyll content is primarily caused by the destruction of chloroplast structures induced by Cd, as well as further inhibition of chlorophyll synthesis and increased degradation (37). Cd also damages the light harvesting complex II (32), and photosystems II and I (51).

Deficiency of nutrient elements under Cd stress

Plants exposed to Cd stress showed disturbances in their macro- and micronutrients homeostasis (46), which indirectly affects the processes where these compounds are involved. Cd stress decreases the absorption of essential nutrient elements such as Ca, Mg, Zn, and Fe (40). As Cd is a non-essential element for plants; it can be transported via other metal transporters such as Ca, Mg, Zn, and Fe. Therefore, as Cd competes with these elements, in excess Cd, the absorption of these nutrients is reduced; causing deficiency of essential elements. In addition, the inhibition of root Fe (III) reductase induced by Cd results in Fe (II) deficiency seriously affecting photosynthesis (4). Finally, reduced Tr under Cd stress could also be a cause of nutrient deficiency in plants given that transpiration is involved in the movement of essential elements to the upper parts of the plant.

Modulation of antioxidant enzymes under Cd stress

Plant cells are equipped with enzymatic machinery (SOD, POD, APX, CAT, GPX, and GR) that actively participate in stress conditions. SOD produces hydrogen peroxide (H_2O_2) from reactive oxygen species (ROS) generated during oxidative stress. H_2O_2 is reduced to water and oxygen by CAT and GPX (in the cytoplasm and other cellular compartments) or APX (in the ascorbate-glutathione cycle) (8).

Cd has inhibitory, as well stimulatory, effects on the activity of these antioxidant enzymes. In *B. napus* leaves, SOD, POD, APX, GR, and GPX showed increased activity, whereas CAT activity decreased (5). In *Helianthus annus* leaves, Cd decreased the activity of superoxide dismutase, catalase, ascorbate peroxidase, glutathione reductase, and dehydroascorbate reductase, whereas lipoxygenase activity and MDA content were increased (20). In *Phaseolus vulgaris* roots and leaves, Cd enhanced GPX and APX activity and lipid peroxidation (15).

Varying responses to Cd-induced oxidative stress are probably related to levels of Cd supplied, duration of treatment, and crop species (44). Modulation of enzyme activities is one of the strategies used by the plants to cope with unfavorable conditions.

Harmful effects of Cd on subcellular organelles

Once Cd enters the cell, it deleteriously affects biomolecules and subcellular organelles. For instance, Cd damaged nucleoli of cells in the root tip of *Allium cepa* (37). Cd also altered the synthesis of RNA and inhibited ribonuclease activity in rice (50). In addition, Cd degrades chloroplasts and mitochondria, compromises the integrity of the plasma membrane (5), and increases the number and size of plastoglobuli (23). The increase in number and size of plastoglobuli under Cd stress is responsible for the synthesis and recycling of lipophilic compounds produced during oxidative metabolism (41). High concentrations of Cd also cause structural changes in the chloroplast through the decrease in photosynthetic activity (14), as previously mentioned.

MECHANISM OF CD PHYTOTOXICITY

Oxidative stress is a disturbance of the cellular redox balance and can lead to disruption of cellular components including proteins, DNA, chloroplast, mitochondria, and cell membrane (figure 1) (56).

Cd is a bivalent heavy metal unable to directly generate free radicals through Fenton and/or Haber Weiss reactions in biological systems under physiological conditions. However, the production of ROS after Cd exposure has been reported in multiple studies (42, 64). Cd indirectly produces cellular ROS by increasing the free Fe-concentration, possibly via replacement in various proteins (18). Free redox-active metals directly enhance the production of $^{\bullet}OH$ (hydroxyl) radicals through the Fenton reaction. Reduction of the oxidized metal ion can be achieved by the Haber-Weiss reaction with superoxide radicals ($O_2^{\bullet-}$) as a substrate.

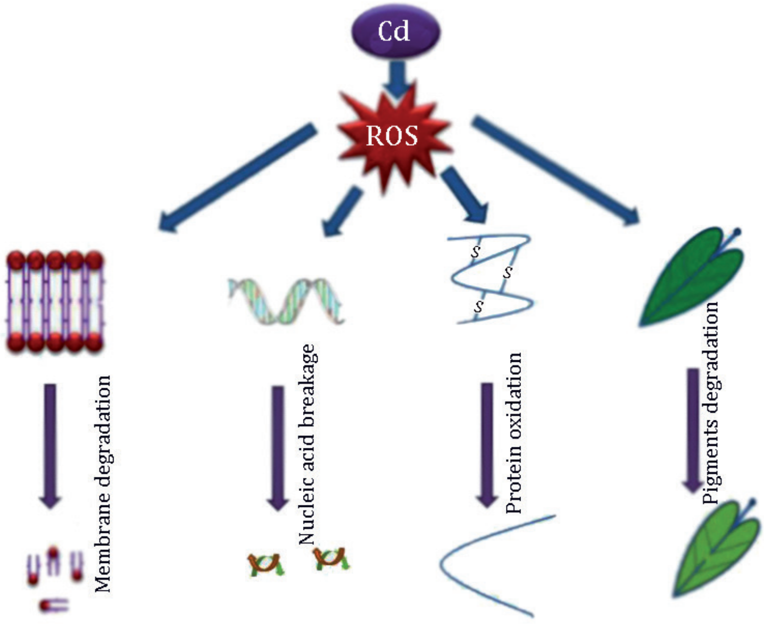

Figure 1. Schematic representation of damage caused by cadmium in plants.

Figura 1. Representación esquemática del daño causado por el cadmio en las plantas.

Other reducing agents, such as ascorbate, can catalyze this reaction. These ROS are responsible for most of the oxidative damage in biological systems. Hydroxyl radicals produced in response to Cd stress can mutate or degrade nucleic acid by adding or removing H^+ from DNA bases or the sugar-phosphate backbone (45). These ROS are responsible for 10^4-10^5 DNA base modifications per cell per day (figure 1, page 396) (7).

Apart from nucleic acid, Cd is believed to oxidize protein as well, , given that most enzymes require a metal as a cofactor for their activities. These cofactors are replaced by Cd ions under Cd stress inhibiting enzymatic activity. These modifications correspond to site-specific processes; with amino acid residues at metal binding sites being specific targets. Therefore, histidine, arginine, lysine, proline, methionine, and cysteine residues are the most common sites of oxidation in proteins. A major consequence of oxygen free radical damage to proteins is making them targets for degradation by proteases (figure 1, page 396) (47).

In addition, ROS produced during Cd stress can compromise the integrity of the plasma membrane by peroxidation of membrane lipids, which can be demonstrated by the increase in MDA content, , being MDA the byproduct of peroxidation of membrane lipids (figure 1, page 396) (49).

In line with the aforementioned, the chloroplast is once more, the candidate target for ROS accumulation in the cell. The chloroplast membrane is rich in polyunsaturated fatty acids such as linoleic and linolenic acids. These fatty acids are very susceptible to oxidation by ROS. After chloroplast degradation, a subsequent obvious decrease in photosynthetic pigments can be observed (figure 1, page 396).

DETOXIFICATION MECHANISM

Reducing Cd absorption from soil

The uptake of hazardous materials can be restricted in plants by the following methods.

The symbiotic relationship between the roots of higher plants and some fungi reduce metal uptake by roots (figure 2, page 398). These fungi secrete metal chelators that bind Cd; thus, making Cd unavailable for the plant (27). Sousa (2012), inoculated *Pinus pinaster* seedlings with *Suillus bovinus*, resulting in seedlings with higher growth parameters, increased Cd tolerance, and low Cd accumulation in the upper parts.

The soil provides a good habitat for fungi and bacteria. Different types of bacterial colonies that chelate metals (especially Cd) are present in the soil (figure 2, page 398). Application of *Pseudomonas aeruginosa* to black gram (*Vigna mungo*) seeds, pumpkin, and mustard seedlings reduced Cd accumulation in the upper parts and enhanced growth. In another study, tomato seedlings were inoculated with *Methylobacterium oryzae* or *Burkholderia sp*., and they restricted the bioavailability of Cd to plants by secreting metal chelators that bind Cd (52). Plant roots constantly secret high and low molecular weight compounds known as root exudates. These exudates, including organic acids, sugars, and polysaccharides, are believed to protect the plants from the harmful effects of Cd and other heavy metals by binding Cd and reducing its bioavailability (figure 2, page 398) (11). These exudates also change the pH of the rhizosphere, inhibiting the uptake of Cd to the root system (13).

The cell wall is composed of suberin and pectin and acts as the first check post for Cd entry; thus, reducing its transport across the cell. Pectin usually binds bivalent ions such as Cd; thus, inhibiting its entry into the cytosol of the cell (figure 2) (33).

The root epidermis provides a reservoir for metal precipitates. Cd is usually restricted as Cd phosphate (Cd-P) precipitate in the root epidermal wall in hyper-accumulator plants (figure 2) (34). Having all these examples in mind, one can conclude that plants have the potential to reduce the bioavailability of Cd by structural modifications and secretions of certain metabolites and defense chemicals.

In brief, plant roots reduce the uptake of Cd by five means:

a) Mycorrhizal association between fungi and roots of higher plants are believed to restrict Cd uptake by the roots. These fungi release metal chelators that form a complex with Cd that cannot be absorbed by plant roots.

b) Soil bacteria, such as *Pseudomonas aeruginosa,* also release some chemicals that bind Cd and inhibit its uptake by roots.

c) Roots release organic acid exudates that bind Cd and inhibit its entry into the root cells.

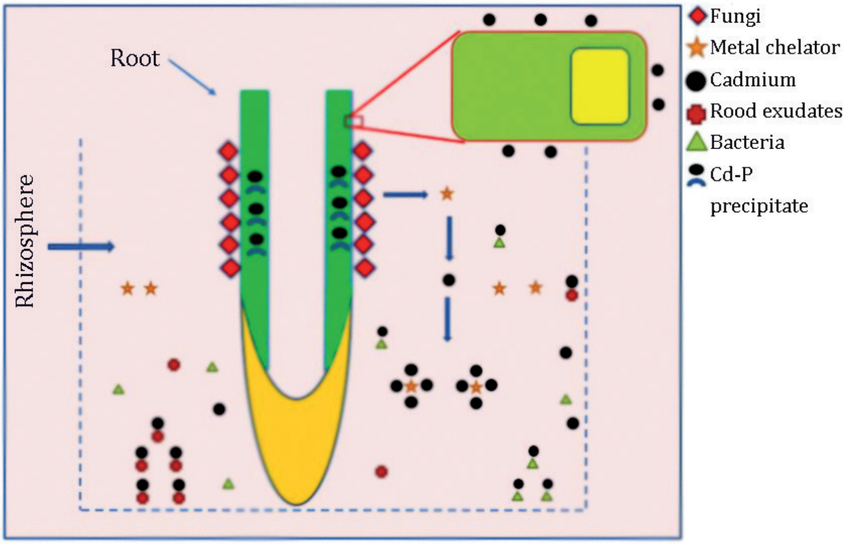

Figure 2. Schematic representation of processes involved in reducing Cd uptake in plant roots.

Figura 2. Representación esquemática de los procesos implicados en la reducción de la absorción de Cd en las raíces de las plantas.

d) d) Suberin and pectin from root cell walls, bind divalent elements such as Cd. This representation is given in the top right portion of the figure.

e) Root epidermis cell wall precipitates Cd in the form of Cd-P and reduces its entry into the cytosol.

Regulation of metal influx to the cytosol

Once Cd breaches the cell wall, it faces the plant cell membrane. Cell membranes are provided with different kinds of metal transporter proteins whose expression are tightly regulated and depend on the quantity and type of metals. These transporters are mostly metal-specific.

To date, a specific Cd transporter protein has not been found in plants. Cd chemically resembles Zn; thus, Cd is believed to cross the cell membrane via the ZIP transporter family (ZRT-IRT like protein; zinc-regulated transporter, iron-regulated transporter Protein) (22, 31, 43).

The production of ZIP transporters is inhibited at the transcriptional or posttranscriptional level to inhibit the influx of Cd into the cytosol (figure 3).

Metal chelation

The entry of Cd to the cytosol triggers undesired interactions with biomolecules including DNA and chloroplast among others. Therefore, Cd needs to be chelated in order to inhibit harmful effects to the biomolecules. As previously mentioned, to sequester Cd and/or other heavy metals, plant produce several kinds of metal chelators. These metal chelators inhibit the interaction of Cd with the biomolecules and restrict it to a site, such as the vacuole. These metal chelators are often oligopeptides, amino acids (cystin), organic acids (malic acid), or proteins.

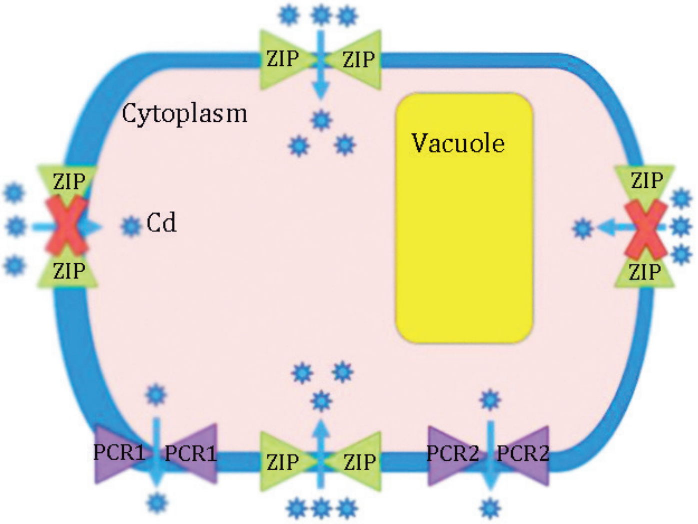

Figure 3. The molecular mechanism of metal homeostasis.

Figura 3. El mecanismo molecular de la homeostasis del metal.

Nicotianamine (NA) and PCs are examples of compounds that form complexes with Cd. Binding strategies are almost the same for most of the chelators, but the transportation sites could be different. Likely, the NA-Cd complex can be transported through the cell membrane by YSL proteins or to the vacuole by ZIF1 proteins (24). The PC-Cd complex can be transported to the vacuole by the two ABCC-type transporters ABCC1 and ABCC2 in *A. thaliana* (figure 4) (54).

Enhancement of Cd efflux

In addition to metal chelation, another strategy used by metal hyper-accumulators and non-hyperaccumulators is metal efflux through the cell membrane. The direction of metal efflux in non-hyperaccumulator plants is towards the soil. By contrast, in hyper-accumulators Cd is loaded into the xylem and transported towards the shoot.

Another way to release these metals from the cells, is by carrying them out via other metal transporters.

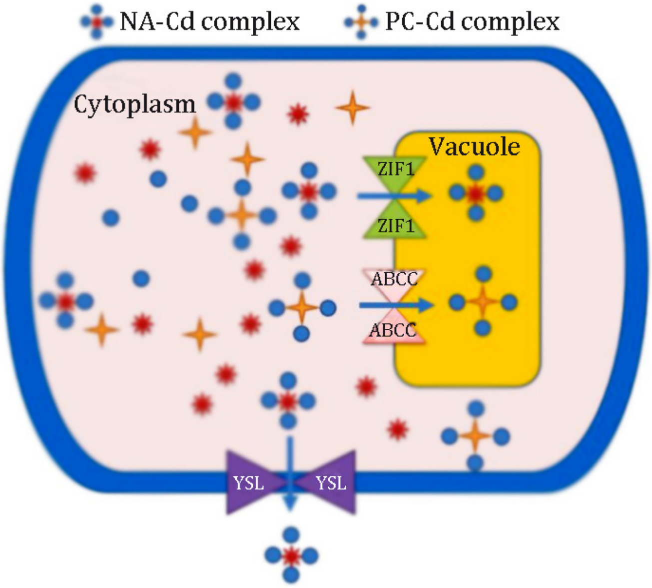

Figure 4. A schematic representation of processes involved in chelation and sequestration of Cd.

Figura 4. Una representación esquemática de los procesos implicados en la quelación y secuestro de Cd.

In *A. thaliana,* two transporters (PCR-1 and PCR-2) are used for the efflux of Cd from the cell (figure 3, page 399) (53). PCR-1 and PCR-2 are, actually, Zn transporters.

Cd sequestration and distribution

The epidermal cell wall and vacuoles are sites of Cd sequestration in case plants are unable to restrict influx or increase efflux of the metal. These organelles are the alternative sites for Cd storage , preventing excess cytoplasmic Cd concentration. In *N. caerulescens*, the Cd-hyper-accumulating ecotype Ganges can significantly store more Cd in the cell walls of epidermal cells than the low Cd-accumulating ecotype Prayon (figure 2, page 398) (30). Sequestration is important to prevent the transport of Cd to the photosynthetic organelles where it can cause serious damage.

SUMMARY AND FUTURE PERSPECTIVES

In summary, Cd is an immense threat not only for crop growth and yield, but for humans as well. Cd induces morphological, physiological, and biochemical responses in plants. Reduced growth, organelle dysfunction, inhibition of photosynthesis, deregulation of membrane metal transporters, modulation of metabolic pathways, and distorted gene expression are some of the Cd-induced impairments.

However, plants launch a range of defensive mechanisms to cope with the adverse effects of Cd including reduced uptake from the soil, binding of the absorbed Cd to the epidermis of cell walls, sequestration by the vacuole, and detoxification by metal chelators (organic acids, phytochelatins, and metallothioneins).

In the past few decades, tremendous progress has been reached regarding the molecular mechanisms of plant tolerance to toxic non-essential metals such as Cd. Some literature on the entrance pathway of Cd is also available.

However, a detailed and quantitative understanding of Cd accumulation in plants is lacking. Moreover, finding the associated genes is also important because low Cd content of edible plant parts might be one important target for future crop breeding programs.

Towards this end, breeding and selection of plants showing reduced ability to accumulate Cd in the cells and tissues, and/or its efficient binding, complexation, and compartmentation, along with strategies like seed and foliar application of osmo-protectants, mineral nutrients, and plant-growth regulators, are among the important strategies for mitigating Cd toxicity in plants in the future.

REFERENCES

1. Ahmad, P.; Nabi, G.; Ashraf, M. 2011. Cadmium-induced oxidative damage in mustard (*Brassica juncea* L.) Czern & Coss.] plants can be alleviated by salicylic acid. South African Journal of Botany. 77: 36-44.
2. Alcalá Jáuregui, J.; Rodríguez Ortiz, J. C.; Hernández Montoya, A.; Filippini, M. F.; Martinez Carretero, E.; Díaz Flores, P. E.; Rojas Velázquez, A. N.; Rodríguez-Fuentes, H.; Beltrán Morales, F. A. 2018. Heavy metals in atmospheric dust deposited in leaves of *Acacia farnesiana (Fabaceae)* and *Prosopis laevigata (Fabaceae)*. Revista de la Facultad de Ciencias Agrarias. Universidad Nacional de Cuyo. Mendoza. Argentina. 50(2): 173-185.

3. Alcalá Jáuregui , J.; Rodríguez Ortíz, J. C.; Hernández Montoya, A.; Filippini, M. F.; Martínez Carretero, E.; Diaz Flores, P. E. 2018. Capacity of two vegetative species of heavy metal accumulation. Revista de la Facultad de Ciencias Agrarias. Universidad Nacional de Cuyo. Mendoza. Argentina. 50(1): 123-139.
4. Alcantara, E.; Romera, F. J.; Canete, M.; De La Guardia, M. D. 1994. Effects of heavy metals on both induction and function of root Fe (III) reductase in Fe-deficient cucumber (*Cucumis sativus L.)* plants. Journal of Experimental Botany. 45: 1893-1898.
5. Ali, E.; Maodzeka, A.; Hussain, N.; Shamsi, I. H.; Jiang, L. 2015. The alleviation of cadmium toxicity in oilseed rape (*Brassica napus*) by the application of salicylic acid. Plant Growth Regulation. 75: 641-655.
6. Ali, E.; Hussain, N.; Shamsi, I. H.; Jabeen, Z.; Siddiqui, M. H.; Jiang, L. 2018. Role of jasmonic acid in improving tolerance of rapeseed (*Brassica napus* L.) to Cd toxicity. Journal of Zhejiang University Science B. 19: 130-146.
7. Ames, B. A.; Shingenaga, M. K.; Park, E. M. 1991. Oxidative damage and repair: chemical, biological and medical aspects. In: Elmsford (ed) Pergamon Press. New York. 181-187.
8. Asada, K. 1994. Production and action of active oxygen species in photosynthetic tissue. In: Foyer CH, Mullineaux PM (eds) Causes of photo-oxidative stress and amelioration of defense system in plants. CRC Press. Boca Raton. 77-104.
9. ATSDR. 2008. Draft toxicological profile for cadmium. US Department of Health and Human Services. Atlanta.
10. ATSDR. 2012. Toxicological profile for cadmium. US Department of Health and Human Services, Atlanta.
11. Bais, H. P.; Weir, T. L.; Perry, L. G.; Gilroy, S.; Vivanco, J. M. 2006. The role of root exudates in rhizosphere interactions with plants and other organisms. Annual Review of Plant Biology. 57: 233-266.
12. Barcelo, J.; Poschenrieder, C. 1990 Plant water relations as affected by heavy metal stress: a review. Journal of Plant Nutrition. 13: 1-37.
13. Bertrand, M.; Poirier, I. 2005. Photosynthetic organisms and excess of metals. Photosynthetica. 43: 345-353.
14. Carginale, V.; Sorbo, S.; Capasso, C.; Trinchella, F.; Cafiero, G.; Basile, A. 2004. Accumulation, localization, and toxic effects of cadmium in the liverwort. Protoplasma. 223: 53-61.
15. Chaoui, A.; Mazhoudi, S.; Ghorbal, M. H.; El Ferjani, E. 1997. Cadmium and zinc induction of lipid peroxidation and effects on antioxidant enzyme activities in bean (*Phaseolus vulgaris* L.). Plant Science. 127: 139-147.
16. Climino, G.; Ziino, M. 1983. Heavy metal pollution part VII emissions from Etna volcanic. Geophysical Research Letter. 10: 31-38.
17. Di Toppi, L. S.; Gabbrielli, R. 1999. Response to cadmium in higher plants. Environmental and Experimental Botany. 41: 105-130.
18. Dorta, D. J.; Leite, S.; DeMarco, K. C. 2003. A proposed sequence of events for cadmium-induced mitochondrial impairment. Journal of Inorganic Biochemestry. 97: 251-257.
19. Feng, R. W.; Wei, C. Y.; Tu, S. X.; Ding, Y. Z.; Song, Z. G. 2013b. A dual role of Se on Cd toxicity: evidences from the uptake of Cd and some essential elements and the growth responses in paddy rice. Biological Trace Element Research. 151: 113-121.
20. Gallego, S. M.; Benavides, M. P.; Tomaro, M. L. 1996. Effect of heavy metal ion excess on sunflower leaves: evidence for involvement of oxidative stress. Plant Science. 121: 151-159.
21. Grant, C. A.; Clarke, J. M.; Duguid, S.; Chaney, R. L. 2008. Selection and breeding of plant cultivars to minimize cadmium accumulation. Science of the Total Environment. 390: 301-310.
22. Guerinot, M. L. 2000. The ZIP family of metal transporters. Biochimica et Biophysica Acta (BBA)-Biomembranes. 1465: 190-198.
23. Hakmaoui, A.; Ater, M.; Boka, K.; Baron, M. 2007. Copper and cadmium tolerance, uptake and effect on chloroplast ultrastructure. Studies on *Salix purpurea* and *Phragmites australis*. Zeitschrift für Naturforschung C. 62: 417-426.

24. Haydon, M. J.; Kawachi, M.; Wirtz, M.; Hillmer, S.; Hell, R.; Kramer, U. 2012. Vacuolar nicotian amine has critical and distinct roles under iron deficiency and for zinc sequestration in Arabidopsis. The Plant Cell. 24: 724-737.
25. Herawati, N.; Suzuki, S.; Hayashi, K.; Rivai, I. F.; Koyoma, H. 2000. Cadmium, copper and zinc levels in rice and soil of Japan, Indonesia and China by soil type. Bulletin of Environmental Contamination and Toxicology. 64: 33-39.
26. Jensen, A.; Bro-Rasmussen, F. 1992 Environmental cadmium in Europe. Reviews of Environmental Contamination and Toxicology. 125: 101-181.
27. Jentschke, G.; Godbold, D. 2000. Metal toxicity and ectomycorrhizas. Physiologia Plantaram. 109: 107-116.
28. Jia, Y.; Tang, S. R.; Ju, X. H.; Shu, L. N.; Tu, S. X.; Feng, R. W.; Giusti, L. 2011. Effects of elevated CO_2 levels on root morphological traitsand Cd uptakes of two Lolium species under Cd stress. Journal of Zhejiang University Science B. 12: 313-325.
29. KabataPendias, A.; Pendias, H. 1992. Trace Elements in Soils and Plants. 2nd ed. Baton Rouge: CRC Press. Fl.
30. Kim, D. Y.; Bovet, L.; Maeshima, M.; Martinoia, E.; Lee, Y. 2007. The ABC transporter AtPDR8 is a cadmium extrusion pump conferring heavy metal resistance. Plant Journal. 50: 207-218.
31. Korshunova, Y. O.; Eide. D.; Gregg, C. W.; Lou Guerinot, M.; Pakrasi, H. B. 1999. The IRT1 protein from *Arabidopsis thaliana* is a metal transporter with a broad substrate range. Plant Molecular Biology. 40: 37-44.
32. Krupa, Z. 1988. Cadmium-induced changes in the composition and structure of the light-harvesting complex II in radish cotyledons. Physiologia Plantaram. 73: 518-524.
33. Krzesłowska, M. 2011. The cell wall in plant cell response to trace metals: polysaccharide remodeling and its role in defense strategy. Acta Physiologia Plantarum. 33: 35-51.
34. Kupper, H.; Lombi, E.; Zhao, F. J.; McGrath, S. P. 2000. Cellular compartmentation of cadmium and zinc in relation to other elements in the hyperaccumulator *Arabidopsis halleri*. Planta. 212: 75-84.
35. Lenntech Water Treatment and Air Purification. 2004. Water treatment. Lenntech, Rotterdam seweg, Netherlands.
36. Lima, A. I. G.; Pereira, S. I. A.; de Almeida, P.; Figueira, E. M.; Caldeira, G. C. N.; de Matos Caldeira, H. D. Q. 2006. Cadmium detoxification in roots of *Pisum sativum* seedlings: relationship between toxicity levels, thiol pool alterations and growth. Environmental and Experimental Botany. 55: 149-162.
37. Liu, D.; Jiang, W.; Wang, W.; Zhai, L. 1995. Evaluation of metal ion toxicity on root tip cells by the Allium test. Israelian Journal Plant Science. 43: 125-133.
38. López-Millán, A. F.; Sagardoy, R.; Solanas, M.; Abadıa, A.; Abadıa, J. 2009. Cadmium toxicity in tomato (*Lycopersicon esculentum*) plants grown in hydroponics. Environmental and Experimental Botany. 65: 376-385.
39. Maxwell, K.; Johnson, G. N. 2000. Chlorophyll fluorescence-a practical guide. Journal of Experimental Botany. 51: 659-668.
40. Metwally, A.; Finkermeier, I.; Georgi, M.; Dietz, K. J. 2003. Salicylic acid alleviates the cadmium toxicity in barley seedlings. Plant Physiology. 132: 272-281.
41. Olmos, E.; Kiddle, G.; Pellny, T. K.; Kumar, S.; Foyer, C. H. 2006. Modulation of plant morphology, root architecture, and cell structure by low vitamin C in *Arabidopsis thaliana*. Journal of Experimental Botany. 57: 1645-1655.
42. Pathak, N.; Khandelwal, S. 2006. Oxidative stress and apoptotic changes in murine splenocytes exposed to cadmium. Toxicology. 220: 26-36.
43. Pence, N. S.; Larsen, P. B.; Ebbs, S. D.; Letham, D. L. D.; Lasat, M. M.; Garvin, D. F.; Eide, D.; Kochian, L. V. 2000. The molecular physiology of heavy metal transport in the Zn/Cd hyperaccumulator *Thlaspi caerulescens*. Proceedings of the National Academy of Sciences. 97: 4956.

44. Pichorner, H.; Korori, S. A. A.; Thur, A.; Ebermann, R. 1993. The two and the four electron transfer to molecular oxygen mediated by plant peroxidase in the presence of thiols. In: Welinder KG, Rasmussen SK, Penel C, Greppin H. (Eds.), Plant Peroxidases: Biochemistry and Physiology. University of Geneva. 131-136.
45. Pryor, W. A. 1988. Why is the hydroxyl radical the only radical that commonly adds to DNA? hypothesis: it is a rare combination of high electrophilicity, high thermo chemical reactivity, and a mode of production that occurs near DNA. Free Radical Biology and Medicine. 4: 219-223.
46. Ramos, I.; Esteban, E.; Lucena, J. J.; Garate, A. 2002. Cadmium uptake and subcellular distribution in plants of *Lactuca sativa* sp. Cd, Mn interaction. Plant Science. 162: 761-767.
47. Roseman, I. E.; Levine, R. L. 1987. Purification of a protease from *Ochelichia coli* with specificity for oxidized glutamine synthetase. Journal of biological chemistry. 262: 2101-2110.
48. Ross, S. M. 1994. Toxic metals in soil-plant systems. Wiley. Chichester. p. 469.
49. Scholz, R. W.; Graham, K. S.; Wynn, M. K. 1990. Interaction of glutathione and a-tocopherol in the inhibition of lipid peroxidation of rat liver microsomes. In: Eddy CC, Hamilton GA, Madyastha KM (eds) Biological oxidation systems. Academic Press. San Diego. 841-867.
50. Shah, K.; Dubey, R. S. 1998. Effect of cadmium on proline accumulation and ribonuclease activity in rice seedlings: role of proline as a possible enzyme protectant. Biologia Plantaram. 40: 121-130.
51. Siedlecka, A.; Krupa, Z. 1996. Interaction between cadmium and iron and its effects on photosynthetic capacity of primary leaves of *Phaseolus vulgaris*. Plant Physiology and Biochemistry. 34: 833-841.
52. Sinha, S.; Mukherjee, S. K. 2008. Cadmium-induced siderophore production by a high Cd-resistant bacterial strain relieved Cd toxicity in plants through root colonization. Current Microbiology. 56: 55-60.
53. Song, W. Y.; Martinoia, E.; Lee, J.; Kim, D.; Kim, D. Y.; Vogt, E.; Shim, D.; Choi, K. S.; Hwang, I.; Lee, Y. 2004. A novel family of cys-rich membrane proteins mediates cadmium resistance in Arabidopsis. Plant Physiology. 135: 1027.
54. Song, W. Y.; Park, J.; Mendoza-Cózatl, D. G.; Suter-Grotemeyer, M.; Shim, D.; Ho¨rtensteiner, S.; Geisler, M.; Weder, B.; Rea, P. A.; Rentsch, D. 2010. Arsenic tolerance in Arabidopsis is mediated by two ABCC-type phytochelatin transporters. Proceedings of the National Academy of Sciences. 107: 21187-21192.
55. Sousa, N. R.; Ramos, M. A.; Marques, A. P. G. C.; Castro, P. M. L. 2012. The effect of ectomycorrhizal fungi forming symbiosis with *Pinus pinaster* seedlings exposed to cadmium. Science of Total Environment. 414: 63-67.
56. Thévenod, F. 2009. Cadmium and cellular signaling cascades: to be or not to be? Toxicology and Applied Pharmacology. 238: 221-239.
57. Verkleji, J. A. S. 1993. The effects of heavy metals stress on higher plants and their use as bio monitors. In: Markert B (ed) Plant as bio-indicators: indicators of heavy metals in the terrestrial environment. VCH. New York. 415-424.
58. Wang, F.; Chen, F.; Cai, Y.; Zhang, G.; Wu, F. 2011. Modulation of exogenous glutathione in ultrastructure and photosynthetic performance against Cd stress in the two barley genotypes differing in Cd tolerance. Biological Trace Element Research. 144: 1275-1288.
59. Wang, X. L.; Sato, T.; Xing, B. S.; Tao, S. 2005. Health risks of heavy metals to the general public in Tianjin, China via consumption of vegetables and fish. Science of Total Environment. 350: 28-37.
60. Wang, X. L.; Ma, X. Q. 2008. Advance in the research of phytoremediation in heavy metal contaminated soils. Subtrop. Agriculture Research. 4: 44-49.
61. Wenzel, W. W.; Unterbrunner, R.; Sommer, P.; Sacco, P. 2003. Chelate-assisted phytoextraction using canola (*Brassica napus* L.) in outdoors pot and lysimeter experiments. Plant Soil. 249: 83-96.
62. Wu, F. B.; Dong, J.; Qian, Q. Q.; Zhang, G. P. 2005a. Subcellular distribution and chemical form of Cd and Cd-Zn interaction in different barley genotypes. Chemosphere. 60: 1437-1446.

63. Yanqun, Z.; Yuan, L.; Jianjun, C.; Haiyan, C.; Li, Q.; Schratz, C. 2005. Hyper accumulation of Pb, Zn and Cd in herbaceous grown on lead-zinc mining area in Yunnan, China. Environ International. 31: 755-762.

64. Zhou, Y. J.; Zhang, S. P.; Liu, C. W. 2009. The protection of selenium on ROS-mediated apoptosis by mitochondria dysfunction in cadmium-induced LLC-PK1 cells. Toxicology in Vitro. 23: 288-294.

Acknowledgements

Key Project of Research and Development Plan of Zhejiang (2018C02SA780973), Natural 323 Science Foundation of China (31401506).