

Physiological and Biochemical Responses to Heavy Metals Stress in Plants

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Abstract: Heavy metal (HM) toxicity is a severe abiotic stress that can cause significant harm to plant development and breeding, posing a challenge to sustainable agriculture. Various factors, including cellular toxicity, oxidative stress, osmotic stress, imbalance in the membrane, and metabolic homeostasis cause negative impacts on plant molecular, physiology and biochemistry. Some heavy metals (HMs) are essential micronutrients that play important roles in various plant processes, while excessive amounts can be harmful and have negative impacts on plant growth, metabolism, physiology, and senescence. Phytotoxicity with HMs and the deposition of reactive oxygen species (ROS) and methylglyoxal (MG), can lead to lipid peroxidation, protein oxidation, enzyme inactivation, DNA damage, and harm to other vital components of plant cells. Generally, HM toxicity as environmental stress led to response of plant with different mechanisms, first, the stimulus to external stress, secondly all signals transduction to plant cell and finally it beginning to find appropriate actions to mitigate the adverse stress in terms of physiological, biochemical, and molecular in the cell to survive plant. The purpose of this review is to better understand how plants respond physiologically and biochemically to abiotic HM stress.

1. INTRODUCTION

Heavy metal (HM) is referred to elements with a high atomic weight and a density at least five times greater than that of water (Bindu *et al.*, 2021). HMs are non-biodegradable, meaning they persist in the environment for over 20 years (Hadia-e-Fatima, 2018). Through the environmental stresses, among the most significant stresses having adverse effects on growth and development is HM stress. Additionally, the biochemical and physiological responses of plants are affected by HM toxicity (Hafeez *et al.*, 2023) which can manifest through oxidative damage, ionic imbalance, osmotic stress and metabolic imbalances in cells (Hoque *et al.*, 2021). Certain HMs such as zinc (Zn), iron (Fe), manganese (Mn), copper (Cu), cobalt (Co), molybdenum (Mo), and nickel (Ni) are vital for the growth of a plant but could be toxic if present in excess. On the other hand, cadmium (Cd), lead (Pb), mercury (Hg), and arsenic (As) are severely harmful to plants' growth and not essential to them (Chibuike & Obiora, 2014). Soil contamination by HMs can happen due to natural and anthropogenic activities. The primary

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source of pollution is the parent material, which releases these metals into the soil, both natural and human activities contribute to HM contamination in soil (Choudhary *et al.*, 2022). However, human activities such as mining, industrial processes, fertilizers, pesticides, fossil fuel, sewage irrigation, can release these elements into the environment, leading to pollution of water and soil (Hafeez *et al.*, 2023). Plants are able to absorb HMs from the soil through their roots. This can lead to the depot of HMs in plant tissues, making the plant toxic to animals and humans that consume them (Iqbal *et al.*, 2020).

2. THE EFFECT OF HEAVY METALS ON PLANTS

Various physiological processes in plants, including photosynthesis, seed germination, and the remobilization and accumulation of seed reserves during germination and growth, can be adversely affected by HMs. As a result of these negative effects, the production of crops may be reduced (Shahid *et al.*, 2014). In different regions of the world, HMs have been discovered especially in agriculture fields including Pb, Cd, Ni, Co, Fe, Zn, chromium (Cr), As, silver (Ag), and platinum (Pt) group (Rahman *et al.*, 2023). The primary defense system of plants against high concentrations of these contaminants is the production of ROS. According to Figure 1 showed that the production of ROS by HMs which are the major sites in the chloroplast, peroxisomes, mitochondria, moreover in the cell wall, plasma membrane, and endoplasmic reticulum, they can cause oxidative stress in plants. HM stress leads to stomatal closure, triggers the photorespiratory pathway, increases ROS productions such as hydroxyl radicals (OH^\cdot), superoxide anion radicals (O_2^\cdot), and hydrogen peroxide (H_2O_2), these substances adversely affect the antioxidant system's functionality and hinder the normal operation of electron transport chains in plants. The production of ROS may trigger lipid peroxidation, which further deteriorates the cell membrane integrity and function. (Das & Roychoudhury, 2014; Emamverdian *et al.*, 2015; Kärkönen & Kuchitsu, 2015; Hoque *et al.*, 2021). In addition, ROS, which are detrimental to plant growth and survival, are produced in excess by exposing plants to high concentrations of HMs and can affect the synthesis of secondary metabolites in plants. Secondary metabolites are compounds produced by plants that are not essential for their growth and survival, but play significant roles in the plant's defense mechanisms, attract pollinators, or deter herbivores for instance flavonoids and carotenes can tolerate when they are confronted with metal stress (Khare *et al.*, 2020; Karakas, 2020; Pehlivan Karakas & Bozat, 2020).

Generally, plants produce a variety of secondary metabolites from primary metabolites, such as carbohydrates, lipids, and amino acids, which are divided into different groups according to their chemical makeup and functional groups. Under normal conditions, there is a balance between the production and detoxification of ROS in plants whenever this balance is interrupted, the defense mechanisms of plants against stress situations effect heavily, their chemical composition changes and produces some secondary metabolites, including, phytoalexins, alkaloids, hydrocarbons, terpenes, flavonoids, phenolic chemicals. (Shahid *et al.*, 2014). These chemical compounds play a crucial role in protecting plants from biotic and abiotic stress (Anjitha *et al.*, 2021). It has been noted that the putrescine (Put) level declined in sunflower leaf disks treated with Cd^{2+} or Cu^{2+} when treated with them, sunflower leaf disc demonstrated a discernible reduction in spermidine (Spd) content but no change in spermine (Spm) levels. It has been demonstrated that Cd^{2+} and Cu^{2+} increase the yields of secondary metabolites such as shikonin (Mizukami *et al.*, 1977; Groppa *et al.*, 2003). Vanillic acid accumulated more in *Zea mays* after exposure to metals like Cu, Pb, and Cd (K1sa *et al.*, 2016). The effects of HM toxicity on secondary metabolites and the metal concentration can really vary based on the plant species, the type of metal, and other circumstances. Some of these secondary metabolites, including phenolics and flavonoids, have direct antioxidant properties that can scavenge ROS (Maleki *et al.*, 2017). The impact of arsenic on the synthesis of artemisinin (a sesquiterpenoid) in *Artemisia annua* under stress was studied, upregulation of

genes involved in artemisinin production increased artemisinin accumulation in soil culture and hydroponic systems (Rai *et al.*, 2011). Studying on *Zea mays* leaves exposed to Zn stress showed an increase in anthocyanins, indicating that cyanidin might interact with Zn^{2+} by taking on two electrons and producing a cyanidin-Zn complex (Janeesha *et al.*, 2021). Moreover, phytoalexins are secondary metabolites with antimicrobial properties that plants synthesize in response to fungal attacks. Additionally, they can also be induced by other elicitors. Studies have shown that metal adaptation can affect biotic stress responses in plants and activate defense mechanisms such as the secretion of phytoalexins and phenolic compounds. Studying about *Silene paradoxa* from different soil types including copper mine soil, serpentine soil, and non-contaminated soil, all plants under the different treatments faced a pathogen. The population from the copper mine soil showed an increase in the production of phytoalexins due to the activation of mitogen-activated protein kinase (MAPK) cascades. This activated protective systems, resulting in the production of phytoalexins and other phenolic molecules in the plant (Martellini *et al.*, 2014). In the other hand, in plant biotechnology, nanoparticles can be utilized as efficient abiotic elicitors to stimulate the manufacture of secondary metabolites. They have the ability to boost the emergence of genes that are in the production of secondary metabolites (Hatami *et al.*, 2019), because of elicitation with TiO_2 nanoparticles, *Salvia officinalis* was shown to contain higher levels of monoterpenes, flavonoids, essential oils, and total phenols (Ghorbanpour, 2015) and similar treating *Artemisia* suspension culture with nano-Co resulted in a significant increase in artemisinin production, boosting it by 2.25 times compared to the control (Ghasemi *et al.*, 2015). When exposed to HMs, the photosynthetic system of plants becomes impaired due to interactions with the light-harvesting complex II protein, resulting in changes to its shape. Maleva *et al.*, 2012 and a similar study by (Li *et al.*, 2012) have demonstrated that the level of chlorophyll has decreased by Cu, Mn, Cd, Ni, and Zn in *Elodea densa*.

The photochemical activity of photosystem II (PS II) also decreased as a result, which is responsible for converting light energy into chemical energy and in addition to chlorophyll, carotenoid level decreased as well as the quantum yield of PS II in *Thalassia hemprichii*. In addition to impacting the light-dependent reactions, HMs reduce the assimilation of carbon dioxide (CO_2) by either inhibiting the activity of RUBP carboxylase or by reacting with the thiol group of RUBISCO, an enzyme involved in CO_2 fixation HMs also induce senescence in plants by triggering the production of ethylene, which in turn activates the jasmonic acid signaling pathway (Khare *et al.*, 2020). Plants have various ways of detoxifying metals, including triggering the activity of multiple antioxidants, sequestering and compartmentalizing metals internally, binding them to cell walls, producing osmoprotectants, transporting metal ions, and chelating them with low molecular weight organic acids, within the cell. Additionally, if the concentration of HMs in the soil is with high concentration, they may compete with the transport of essential nutrients, and metal-chelating molecules or rhizosphere microorganisms may be necessary to immobilize the metal ions in the soil to avoid competition for nutrient transport (Yaashikaa *et al.*, 2022). In some cases, HM exposure can induce the production of secondary metabolites that act as defense mechanisms, such as phytochelatins (PCs) and metallothioneins (MTs), which are peptides that chelate and detoxify HMs in cytosol and putting them in the vacuole or another subcellular structure (Clemens, 2001). However, in other cases, HM exposure can lead to a reduction in the synthesis of secondary metabolites, resulting in decreased plant growth, reduced seed production, and decreased resistance to diseases and pests. Abiotic stress signals, such as toxic metals, may trigger genes involved in the biosynthesis of secondary metabolites too (Anjitha *et al.*, 2021; ul Hassan *et al.*, 2019). Two groups of plants can collect toxic HMs known as hyperaccumulators and accumulators (Niu *et al.*, 2021; Pasricha *et al.*, 2021; Sharma and Kumar, 2021) and reported from Brassicaceae and Phyllanthaceae families about 721 species of them recognized as hyperaccumulators plants

(Reeves *et al.*, 2018). Hyperaccumulator plants play an essential role in the remediation of HM-contaminated soil by effectively extracting and mitigating the detrimental impacts of these metals. According to (Shahi, 2002) showed that the affordability of lead phytoextraction is feasible when plants have the capability to accumulate more than 1% of lead (Pb) in their shoots. *Sesbania drummondii*, a leguminous shrub that grows in the wild, has been taken into consideration in this study. Shoot concentrations of *Sesbania* plants grown in modified Hoagland's solution containing 1 g Pb (NO₃)₂/L were > 4% Pb. The absorption was increased by 21% by EDTA (100 M) in the media containing 1 g Pb (NO₃)₂/L. Detailed examination using transmission electron microscopy and X-ray microanalysis revealed the localization of Pb granules in the plasma membrane, cell wall, and vacuoles of root sections.

This study demonstrates that *S. drummondii* prepares the criteria for a hyperaccumulator. However, several methods have been developed for eliminating HMs from polluted soil, utilizing physical, chemical, and biological techniques. The technique of soil replacement as a physical method involves the utilization of uncontaminated soil to substitute the polluted soil, which helps to lower the concentration of pollutants in the soil which is adequate for small-scale soil contamination and also thermal desorption involves heating contaminated soil using methods such as steam, microwave, or infrared radiation. This process converts the pollutants into a volatile form, which can then be collected using a vacuum negative pressure or carrier gas. Ultimately, this method is used to remove HMs from the soil (Haritash, 2023). Chemical methods used for soil remediation, such as soil washing, flushing, solidification/stabilization, vitrification, and electro kinetic remediation. Soil washing, which involves using fresh water, solvents, or other liquids, even gases to wash contaminated soil (Sidhu, 2016). The other method belongs to biological approach includes both microbial remediation and phytoremediation, as well as a combination of both methods (Haritash, 2023). In fact, phytoremediation is an eco-friendly and economical method that involves using plants and their associated microorganisms in the soil to either bind, break down, or store metal contaminants in both soil and water (Pasricha *et al.*, 2021), while microbes are unable to directly break down or eliminate transforming HMs into harmless forms, they can still impact the mobility, bioavailability, and transformation of these metals in the soil by modifying the physical and chemical properties of the pollutants. Several processes lead to the interaction of HMs with microorganisms such as bioaccumulation, bioassimilation, biosorption, biotransformation and bioleaching. During bioaccumulation, solutes are transported through the cell membrane into the cell cytoplasm from outside of the microbial cell, where metals are sequestered. Biotransformation can alter the HM's chemical form through various methods, including methylation/reduction and dealkylation/oxidation, which can change the mobility, toxicity, and bioavailability of the HM (Peng *et al.*, 2018). One of the most significant processes in microbial remediation is biosorption, in which HMs bind to anionic functional groups on the surface of cells and in extracellular polymers. HMs are immobilized because of this binding process, which involves covalent bonding and electrostatic interactions between metal ions and the cell surface (Haritash, 2023).

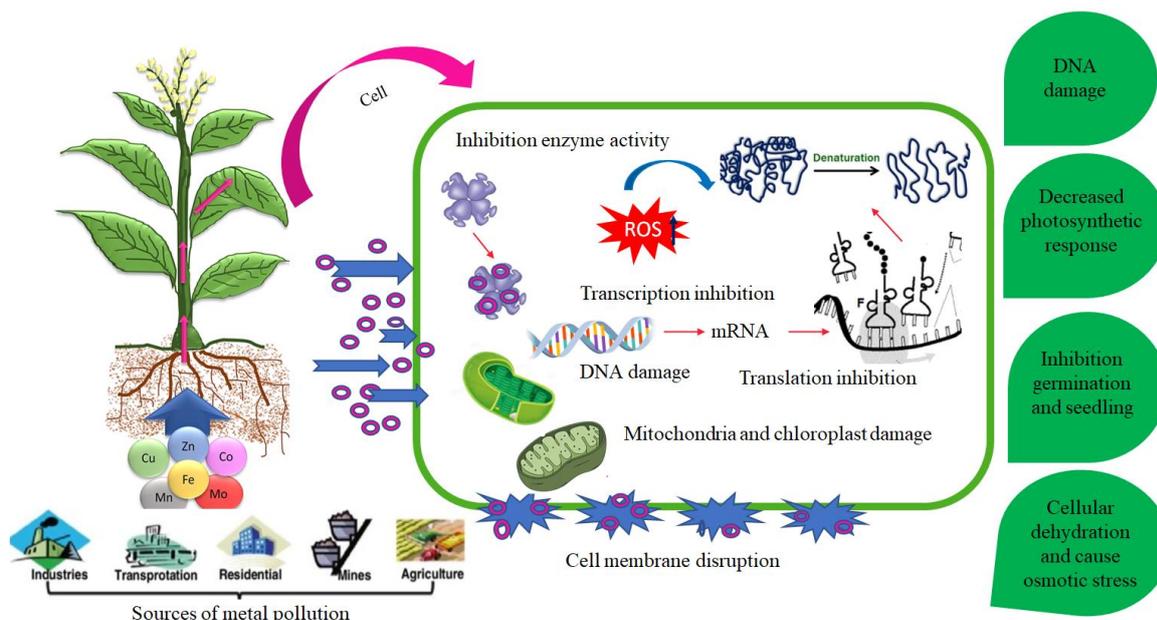


Figure 1. Toxic consequence of entering HM into a cell that led to inhibition of cell division and finally make death of cell.

3. RELATION BETWEEN HM TOXICITY AND OSMOREGULATION

HMs also impact plant water relations and the availability of water in soils, which can lead to decreased water uptake and the onset of various stress conditions. When soils are contaminated with HM, the osmotic potential in the soil decreases relative to the cell sap within the root system. As a result, metal ions can accumulate to levels that severely limit water uptake by plants and cause osmotic disturbances (Rucińska-Sobkowiak, 2016). This can result in stunted root growth, decreased root mass, and reduced root cell elongation, impaired secondary growth and reduced capacity of water uptake by the plant (Mashabela *et al.*, 2023). A research study investigated the effects of combined osmotic stress and exposure to cadmium (Cd^{2+}) on the roots of *Brachypodium* seedlings. The study found that these a few points were responsible for inhibiting seedling growth and causing significant changes in plant physiology and phenotype, such as reduced relative water content, plant height, and primary root length (Chen *et al.*, 2018). In terms of osmoregulation, HMs can cause changes in the water balance of the plant, so that the concentration of solutes in the root cells will be increased. This can lead to dehydration and decreased water uptake by the roots. Moreover, the imbalance in osmotic pressure can lead to oxidative damage, which occurs due to alterations in the electron transport chain and reduced mitochondrial respiration. This results in the overproduction of detrimental free radicals and ROS which damage to various cellular structures, including those involved in transpiration, photosynthesis, and DNA/RNA synthesis, leading to reduced plant growth, development, fertility, or even death (Dumanović *et al.*, 2021). Additionally, the overproduction of ROS can lead to oxidative stress characterized by the loss of cellular membrane construction and function due to lipid peroxidation (Mashabela *et al.*, 2023).

3.1. Plant Response and Adaptation for Tolerance to HM Toxicity Related to Osmotic Condition

Some of the key plant responses and adaptations for tolerance to HM toxicity and osmotic stress include HMs can be sequestered within the plant cell to minimize their toxicity by binding to specific compounds, such as phytochelatins, or by being compartmentalized within the vacuole. Antioxidant defense is another response to HMs that can generate ROS which can cause oxidative damage to plant cells. To counter this, plants have evolved a series of antioxidant

defense mechanisms such as superoxide dismutase (SOD), catalase (CAT), and ascorbate peroxidase (APX) enzymes activate that help to neutralize ROS and prevent oxidative damage and also, they can activate signaling pathways in the plant, such as the calcium signaling pathway, the ROS signaling pathway, and the abscisic acid (ABA) signaling pathway. These pathways help to coordinate the plant's response to stress. In osmoregulation in response to osmotic stress, plants can adjust the osmotic potential of their cells by regulating the accumulation of solutes such as compatible solutes and proline. This helps to prevent water loss from the cells and maintain turgor pressure. Changes in gene expression, HM toxicity, and osmotic stress can cause changes in gene expression in the plant, leading to the activation of stress-responsive genes that are involved in the defense against HM toxicity and osmoregulation (Mashabela *et al.*, 2023). The recognition of these stimuli initiates a signaling pathway known as mitogen-activated protein kinases (MAPKs), which includes three kinases namely MAPKs, MAPK, and NAPKINs. They are a family of serine/threonine protein kinases that have been shown to play a role in the response to HM toxicity and osmotic stress. (Mashabela *et al.*, 2023). This cascade involves the phosphorylation and activation of several MAPKs, leading to the activation of downstream target proteins that are involved in the plant's response to stress (Cargnello *et al.*, 2011). Additionally, MAPKs have also been shown in the regulation of root plasticity, which is an important mechanism by which plants overcome HM toxicity. For instance, Ye *et al.* (2013) found that Cd exposure activated MPK6 in *Arabidopsis* plants, which in turn activated caspase-3-like enzymes and caused programmed cell death (PCD) as a defense mechanism against stress (Jalmi *et al.*, 2018). Following exposure to Cu and Cd, *Arabidopsis* was used to demonstrate the role of MPK3 in the response to metals (Dos Reis *et al.*, 2018). Exogenous protectants refer to substances that are applied externally to plants to help them overcome the damage caused by HM toxicity. These protectants can be used to mitigate the effects of HM toxicity by either chelating (binding) the HMs to prevent their toxicity or by providing a source of energy and nutrients to the plant. Activation of Ca^{2+} signaling by plants leads to changes in gene expression, accumulating the stress hormone abscisic acid, altering development, and increasing stress tolerance in response to osmotic stress (Chen *et al.*, 2020). Osmotic stress stimulation induces a rapid increase in Ca^{2+} cyst in the roots of *Arabidopsis* seedlings, indicating that cytosolic calcium is implicated in the osmotic stress response (Huang *et al.*, 2017). There are some commonly used exogenous protectants in mitigating HM-induced damages: Chelating agents such as EDTA (Ethylene Diamine Tetra Acetic acid) and citric acid, can be used to chelate HMs, making them less toxic to the plant. By binding HMs, chelating agents prevent their uptake by the plant and reduce their toxicity. Antioxidants, such as ascorbic acid, can help to neutralize ROS generated by HMs and prevent oxidative damage to plant cells. Salicylic acid is a naturally occurring plant hormone that can be applied to induce the expression of stress-responsive genes and enhance the antioxidant defense mechanisms of the plant. Calendula (*Calendula officinalis*) cultivated in calcareous soils enriched with Cd (50-100 mg/kg) did not exhibit any physiological indications of Cd toxicity in plants treated with exogenous citric acid at levels of 0.05 and 0.1 mM (Vega *et al.*, 2022). Citric acid was demonstrated to be a more effective phytoremediation agent in the same study when compared to other chelators as tartaric acid and ethylenediaminetetraacetic acid (EDTA). Additionally, citric acid forestry settings have been used to evaluate -mediated tolerance to HM toxicity (Saffari & Saffari, 2020). For instance, the presence of 20 mM citric acid increased the mobility, bioavailability, and distribution of Cd in the basket willow (*Salix viminalis*), as well as the amount of chlorophyll, the rate of photosynthetic respiration, and other parameters of the plant (Vega *et al.*, 2022). Compatible solutes can accumulate in plant cells to help regulate the osmotic potential of the cells and mitigate the effects of osmotic stress caused by HMs and nutrient sources, such as phosphorous and nitrogen, in a mechanism where molecules of a ligand are attached to ions of the core metal through a coordination bond in a

cyclic or ring structure, a group of low molecular weight chemical molecules provides tolerance to these pollutants (Barceló & Poschenrieder, 1999) such as proteins like phytochelatins (PCs) and metallothioneins (MTs) or amino acids like proline and histidine. The MTs proteins are involved in the uptake and transport of HMs into and within the plant. The addition of MTs considerably raised Cd tolerance and decreased Cd concentration in the leaves of tomatoes (*Solanum lycopersicum* L. cv. Hezuo 903) as demonstrated by decreased growth inhibition, photoinhibition, and electrolyte leakage. MTs decreases Cd uptake and mitigates toxicity in plants (Li *et al.*, 2016). Arnao and Hernández-Ruiz, (2009) shown that melatonin can also be absorbed by the leaves in addition to the roots, as a result, they noticed that incubating *Hordeum vulgare* L. (barley) leaves with rising exogenous melatonin concentrations in the growth medium caused an accumulation of indole in the leaves that were dose-dependent.

4. HM TOXICITY AND PHYTOHORMONES

HM toxicity can significantly alter the hormonal balance of plants, leading to changes in growth, development, and stress responses. Figure 2 showed that hormones play crucial roles in regulating various physiological and biochemical processes in plants, and the effects of HM toxicity on hormones can be diverse and complex. The major phytohormones associated with HM stress are discussed below:

Auxin, a key hormone involved in plant growth and development, is known to be affected by HM toxicity. HMs can disrupt the transport and metabolism of auxin, leading to alterations in the patterns of cell division, elongation, and differentiation. Numerous observations showed that the auxin endogenous status in shoot and root tissues were variably affected, demonstrating both a synergetic and antagonistic relationship between HM stress and auxin level (Yuan & Huang, 2016). Auxin production and signaling are largely dependent on the several auxin-regulatory genes that are increased in response to the harmful effects of HMs, according to several molecular-based studies (Rahman *et al.*, 2023). For instance, Under Cd stress, it was observed that *Arabidopsis* triple mutant (*ddc*) plants demonstrated improved IAA status than wild-type ones. The transcriptomic-based analysis showed that *ddc* mutants mostly decrease the methylation genes (*MES7* and *17*) and auxin biosynthesis genes (*YADOKAR11*; *YDK1*, *GH3.3*, and *GH3.17*). In comparison to Wild - type plants, *ddc* mutants were reported to have an instantaneous overexpression of *IAOX* (indole-3-acetaldoxime), which is connected to auxin biosynthesis genes (*CYP71A13* and *NIT2*). As an alternative, the *AUX/IAA* gene family, which controls the regulation of auxin, was suppressed in *ddc* plants, improving phytohormonal signal transmission and increasing HM resistance (Pacenza *et al.*, 2021).

Abscisic acid (ABA) is another hormone that is involved in regulating plant stress responses. Various plants subjected to HMs have shown elevated endogenous ABA concentrations, including *Helianthus annuus* L., *Lactuca sativa*, *Populus canescens*, *Triticum aestivum*, *Oryza sativa*, *Cucumis sativus*, and *Solanum* (Pacenza *et al.*, 2021). ABA biosynthesis gene *OsNCED4* was shown to be overexpressed in a transcriptomics-based study on Cd-stressed rice, highlighting the critical function of ABA in reducing Cd toxicity (Tandon *et al.*, 2015). Another recent study looked at the role of ABA in protecting Cd-stressed *Sedum alfredi*, and the findings showed that ABA foliar treatment along with Cd improved ABA endogenous status by upregulating the expression of ABA biosynthesis enzymes (*NCED*, *AAO*, and *ZEP*) and downregulating ABA inhibitor (*ABA 8-hydroxylase*) expression. The outcomes of the study showed that ABA is essential for lowering Zn toxicity by altering genes involved in Zn absorption and detoxification (Tao *et al.*, 2021). Critical genes involved in the laboratory's lead (Pb) absorption, transportation, and excretion were increased by ABA when applied topically (Shi *et al.*, 2019). Cytokinin, gibberellins, jasmonic acid and ethylene are other hormones known to be affected by HM toxicity. Cytokinin, for example, plays important roles in regulating cell division and elongation, and exposure to HMs such as cadmium can decrease

their levels, leading to reduced cell division and elongation. that contribute to the developmental alterations brought on by osmotic stress. Due to an increase in JA content in wild type rice compared to a mutant with JA biosynthesis disrupted, it has been demonstrated that intense jasmonates (JA) can make rice more resistant to osmotic stress (Tang *et al.*, 2020).

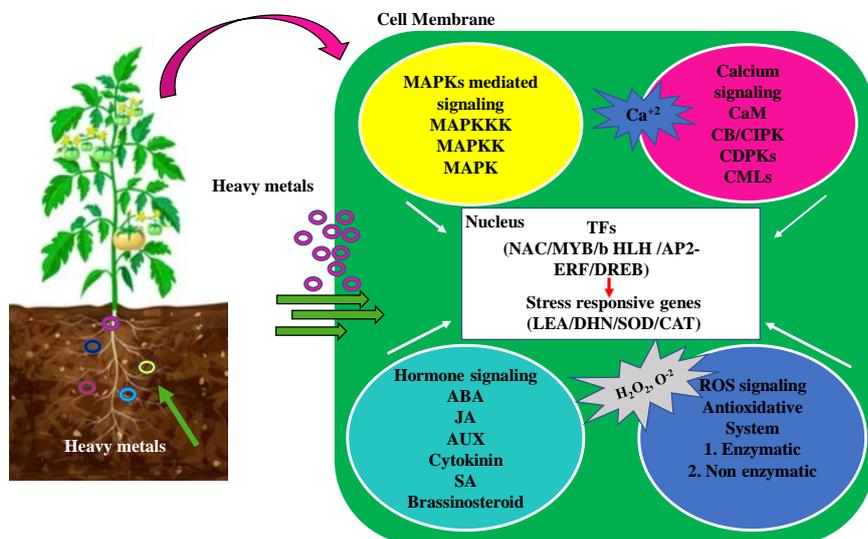


Figure 2. HM stress signaling cascade in plants that mediate signal transduction to improve genes of expression to stress response.

5. MACRO AND MICRONUTRIENT OF METAL-BASED FOR PLANTS

The function of important enzymes and the control of metabolic processes including redox homeostasis, metabolism, DNA synthesis, and photosynthesis depend on proper levels of metal-based micro and macro nutrients like Cu, Zn, Co, Ni, Fe, Cr, Mn, I, and Se. However, HMs in excess show toxicities that can be dangerous. For convenience, some recent study about reaction of plants against HM is given in Table 1.

5.1. Zinc Effects on Plants

Zinc is an essential micronutrient for plants, playing a crucial role in various plant processes, such as growth and development, photosynthesis, and defense mechanisms. However, when present in large quantities, zinc can harm plants and have negative impacts. At low concentrations, zinc is involved in the activation of several enzymes and transcription factors, which regulate plant growth and development. Zinc also plays a role in the regulation of the hormone auxin, which is involved in the control of cell elongation and division (Broadley *et al.*, 2007). According to Tsonev and Cebola Lidon (2012) Zn concentrations in unpolluted soils are normally lower than 125 ppm, and in plants growing in these soils, this metal concentration varies between 0.02-0.04 mg/g dry weight. The bioavailability of Zn in soil solution increases at low pH, while organic ligands and hardness cations such as Ca²⁺ decrease Zn availability (Pedler *et al.*, 2004). At higher concentrations, zinc can become toxic to plants and lead to various physiological and biochemical changes. For example, high levels of zinc can lead to oxidative stress, which can cause damage to cellular membranes and result in the accumulation of reactive oxygen species. Additionally, zinc toxicity can also disrupt the plant's ion balance, leading to changes in osmotic potential and water uptake. Zinc and cadmium's phytotoxicity are observed in plant species such *Phaseolus vulgaris*, *Brassica juncea* and tobacco (Cakmak & Marschner, 1993; Prasad & Hagemeyer, 1999), which exhibit reduced growth, metabolism, and oxidative damage (Tkalec *et al.*, 2014).

Table 1. Tolerance of plant growth reaction to HMs/metalloids in soil.

Plant	Heavy metal	Plant response and related parameter	References
<i>Sedum hybridum</i> 'Immergrunchen'	Cd	Higher concentrations (200 mg/kg) significantly damaged the plant.	Guan <i>et al.</i> , 2022
<i>Althaea rosea</i> <i>Abutilon theophrasti</i>	Cd	The root, shoot, and plant height of both plants were significantly impacted by cadmium stress. Tolerance Index (TI) was 1.	Wu <i>et al.</i> , 2018
<i>Helianthus annuus</i>	Pb	Without significantly affecting the production of biomass, the plant demonstrated considerable metal accumulation capability at all concentrations (0-250 mg/kg).	Al-Jobori and Kadhim, 2019
<i>Lavandula angustifolia</i>	Ni	Plant grew well up to 40 mg/kg Ni of soil	Barouchas <i>et al.</i> , 2019
<i>Zinnia elegans</i>	Cr	The plant grew up to a Cr stress of 50 mg/kg.	Panda <i>et al.</i> , 2020
<i>Hydrangea</i>	Pb	Under any Pb treatments (0-1600 mg/ kg), no apparent evidence of heavy metal toxicity was seen in the plant.	Ma <i>et al.</i> , 2022
<i>Euphorbia pulcherrima</i>	Hg, Zn, As, Pb, Cr, Cu	Zn, Pb, and Cu were significantly accumulated in the roots of the plant, while Hg was removed and transported in the leaves. Additionally, the plant was discovered to be tolerant to As and Cr.	Xiao <i>et al.</i> , 2021
<i>Mirabilis jalapa</i>	Cd	The plant effectively eliminated Cd, As, and Pb from contaminated soil without facing with any negative consequences from phytotoxins.	Li <i>et al.</i> , 2022
<i>Pteris cretica</i> , <i>Spinacia oleracea</i>	As	The significant effect of 100 mg/kg as treatment on the analyzed parameters such as chlorosis, growth process inhibition, oxidative stress. <i>S. oleracea</i> is an As-root excluder while <i>P. cretica</i> is an As-hyperaccumulator.	Zemanová <i>et al.</i> , 2021
Cherry radish (<i>Raphanus sativus</i> var. <i>sativus</i> Per s. 'Viola')	As	The metabolism of free amino acids (AAs), phytohormones, and antioxidative metabolites changed as a result of the rising As content in tubers and rising soil pollution. The majority of the changes were seen in environments with significant As pollution (20 and 100 mg/kg).	Pavlíková <i>et al.</i> , 2023
<i>Pleiblastus pygmaeus</i>	As	Due to the high production of reactive oxygen species (ROS) components and induction of cell membrane peroxidation, at 150 and 250 M, the plant growth was considerably affected.	Emamverdian <i>et al.</i> , 2023
<i>Eucalyptus nitens</i>	As	Roots can accumulate to levels ranging between 69.8 and 133 µg/g for plants treated with 100 and 200 µg/mL As and leaves between 9.48 µg/g (200 As) and 15.9 µg/g (100 As) without apparent morphological damage and toxicity symptoms. The As effects on the uptake and translocation of Ca, Fe, K, and Zn revealed two contrasting interferences.	Ramalho <i>et al.</i> , 2023
<i>Arabidopsis thaliana</i>	Al	Growth inhibition, ROS increase, lipid peroxidation	Kochian <i>et al.</i> , 2015

Phaseolus vulgaris and *pea* plants have demonstrated that Cd and Zn change the catalytic efficiency of enzymes (Romero-Puertas *et al.*, 2004; Somashekaraiah *et al.*, 1992; van Assche & Clijsters, 1983) reported zinc levels in polluted soil have been measured to be between 150 and 300 mg/kg (de Vries &., 2007; Warne *et al.*, 2008). The toxicity of zinc to plants limits the growth of roots and shoots (Malik *et al.*, 2011). Zinc toxicity can also cause the yellowing of young leaves, which can spread to old leaves after long-term exposure to high concentrations

of zinc in the soil (Ebbs & Kochian, 1997). The toxicity of zinc to plants restricts the growth of roots and shoots and can also result in young leaves getting yellow, which spreads to older leaves with prolonged exposure to excessive concentrations of zinc in the soil (Ebbs & Kochian., 1997; Malik *et al.*, 2011). However, hydrated Zn^{2+} and Fe^{2+} ions have equal radii, the chlorosis may be caused in part by an induced iron deficit (Marschner, 1986). Additionally, excessive zinc can cause plant shoots to be deficient in copper and manganese. The emergence of a purplish red color in leaves, which is attributed to phosphorus insufficiency, is another typical result of Zn toxicity (Lee *et al.*, 1996).

5.2. Cadmium Effects on Plants

The amount of cadmium (Cd) in agricultural fields should not exceed 100 mg/kg (Salt *et al.*, 1995) because this may damage plants and induce symptoms including chlorosis, growth inhibition, blackening of the root tip, and death (Guo *et al.*, 2008; Mohanpuria *et al.*, 2007). According to studies, Cd affects the way plants absorb, transport, and use a variety of nutrients, including water, Ca, Mg, P, and K. It also decreases the absorption and transport of nitrate from the root to the bud, which inhibits the function of nitrate reductase in the bud (Hernandez *et al.*, 1996). Although it has been observed that Cd interacts with water balance, the toxicity of this metal will impact the permeability of the plasma membrane, resulting in a decrease in water content (Costa & Morel, 1994). Additionally, causes changes in chloroplast metabolism due to the inhibition of chlorophyll biosynthesis and decreased activity of CO_2 fixation enzymes, as well as changes in membrane function by inducing lipid peroxidation (Fodor *et al.*, 1995; Raziuddin *et al.*, 2011). Cd accumulation in the tobacco plant was demonstrated to enhance oxidative damage and reduce catalase and superoxide dismutase activity (Islam *et al.*, 2009). Noticed in previous research, various HM-stressed plants were found to have decreased mitosis content, which led to accelerated root development. For instance, disrupting the extracellular matrix's (ECM) normal function led to an overproduction of H_2O_2 (up to 116%), which consequently led to a 77% reduction in the roots of wheat plants grown in a 200 M Cd hazardous environment (Howladar *et al.*, 2018). In other study showed that seeds of sweet basil (*Ocimum basilicum* L.) treated to various amounts of cadmium also had lower germination rates (Fattahi *et al.*, 2019). Moreover, *Coriandrum sativum* seed germination was significantly inhibited by soil with a Cd concentration of 50 mg/kg (Sardar *et al.*, 2022). Pollution with cadmium significantly decreased the amounts of N, Ca, Mg, and P in the roots and shoots of alfalfa (Zhang *et al.*, 2019). Cd toxicity reduced the amounts of Cu, Mg, Fe, and K in *Trifolium repens* L. plant shoots, but significantly increased the Ca content. However, when compared to control plants, Cd stress significantly decreased the Ca, Mg, and Fe levels in roots while increasing the concentration of K and Cu (Hafeez *et al.*, 2023). In finding of (El Rasafi *et al.*, 2020) while increasing intercellular CO_2 concentration, cadmium stress dramatically decreased net photosynthetic ratio, stomatal conductance, transpiration ratio, chlorophyll a, b, and total chlorophyll content. Similar to this, (Kaya *et al.*, 2020) observed that under 0.10 mM Cd stress, wheat plants significantly reduced their chlorophyll a, b concentration as well as their photosystem II (Fv/Fm) maximal photochemical efficiency. When compared to their respective control plants, Rahul and Sharma (2022) reported that Cd stress (500 M) caused H_2O_2 and MDA content to accumulate more in castor (*Ricinus communis*) genotypes S1 and S2, whereas a nonsignificant change was seen in genotypes T1 and T2.

5.3. Chromium Effects on Plants

Germination is the first physiological activity in plants, the rate of seed germination in a medium containing chromium could demonstrate a plant's resistance to such a metal (Peralta *et al.*, 2001). while according to (Rout *et al.*, 2000) revealed that the germination rate of barnyard grass (*Echinochloa colona*) seedlings declined to 25% after adding 20 ppm Cr. Hexavalent chromium, present in the soil in high concentrations (500 ppm), can cause kidney

bean (*Phaseolus vulgaris*) germination rates to drop by 48% (Dreyer Parr & Taylor, 1982). In addition, (Peralta *et al.*, 2001) investigated the germination and growth of alfalfa seeds (*Medicago sativa* cv. Malone) increased by 40 ppm Cr (VI) in a contaminated environment. Other research showed that with 20 and 80 ppm Cr, respectively, sugarcane bud germination was reduced by 32-57% (Jain *et al.*, 2000). It is possible that Cr Amylase activity's inhibitory effect and subsequent sugar transfer to the embryonic axis are the causes of the lower seed germination under Cr stress (Zeid, 2001). Alternatively, protease activity rises with the Cr treatment, which may possibly be a factor in the decreased germination of Cr-treated seeds (Zeid, 2001). HMs in trees and crops have a well-documented effect on root formation (Tang *et al.*, 2020). According to (Prasad *et al.*, 2001) Cd and Pb were the most toxic to new root primordia in *Salix viminalis*, whereas Cr had the most significant impact on root length. Cr stress is one of the most significant elements influencing the generation of plant-related pigments like anthocyanin and chlorophyll during photosynthesis. It has been demonstrated that chromium in the radish plant interferes with nutrient translocations and metabolic activity (Tiwari *et al.*, 2013). Boonyapookana *et al.*, (2002) presented changes in the metabolic pool to induce the production of biochemically related metabolites, which may provide tolerance or resistance to Cr stress with phytochelatins and histidine, act as a direct reaction to Cr stress, or produce other metabolites such as glutathione and ascorbic acid that may harm the plants. Additionally, studies on transgenic *Arabidopsis thaliana* seedlings revealed that Cr increases the expression of the low phosphate (Pi) inducible reporter genes AtPT1 and AtPT2, which are both involved in photosynthesis. The outcome showed that seedlings exposed to Cr had primary-root development 60% reduced. Root growth fully resumed because of increased Pi supply to the seedlings, which also resulted in a reduction in Cr content. Moreover, alterations in the amounts of auxin-inducing genes and auxin transporters expressed by MPK6 are associated with changes in the differentiation of root meristems caused by low phosphorus levels (López-Bucio *et al.*, 2014). Therefore, Supplements containing Pi and sulfate can be utilized in management plans for Cr-contaminated soil.

5.4. Lead Effects on Plants

It is known that lead (Pb) has negative impacts on a plant's morphology, growth, and photosynthetic activities. In addition, Pb stress causes plants to do oxidative damage to proteins, lipids, and nucleic acids when too many very damaging ROS build up (Shahzad *et al.*, 2018). Pb also prevents the germination of *Spartina alterniflora* and Hefei pine seeds (Nakos, 1979). There is a hypothesis that germination inhibition may result from lead interfering with essential enzymes. It is also noteworthy, Pb severely hampered root and stem elongation, as well as leaf expansion, in *Allium* species (Gruenhage & Jaeger, 1985) as well as in barley (Juwarkar & Shende, 1986). When maize plants were seedlings, they significantly reduced the fresh and dry weight of their branches and roots when exposed to Pb toxicity. The morphological properties of maize seedling root tissues changed as a result of Pb stress because roots are more sensitive to metal stressors. These alterations demonstrated increased central cylinder diameter, cortex thickness, and endodermis thickness to 20%, 19%, and 53%, respectively. However, Pb toxicity did not cause changes in the diameters of the metaxylem and protoxylem. (Zanganeh *et al.*, 2021). Additionally, 100-200 ppm of Pb distributed to potted sugar beet plants resulted in chlorosis and decreased development (Hewitt, 1953). Similarly, low lead concentrations of 5 ppm severely inhibited lettuce and carrot root growth (Baker, 1972). The inhibitory effect of Pb²⁺ may derive from changes in the metabolic pathways that impact on growth and development (Sharma & Dubey, 2005). High amounts of Pb can also conflict with enzyme function, disrupt water balance, change membrane permeability, and ultimately interfere with mineral nutrition (Sharma & Dubey, 2005; Sinha *et al.*, 1988). Lead also has an effect on the process of photosynthesis by slowing down the activity of aminolevulinic acid dehydratase (ALAD) (Cenkci *et al.*, 2010). According to a study by (Zhu *et al.*, 2009) lead

hyperaccumulation in *Brassica* species caused a reduction in growth. In a recent investigation, it was found that coriander plants (*Coriandrum sativum* L.) cultivated in soil contaminated with Pb (at levels of 0, 500, 1000, and 1500 mg/kg of soil) demonstrated a marked increase in MDA content, with the highest concentration recorded at 1000 mg/kg Pb, followed by a decrease at higher levels. Additionally, flavonoids were found to be higher under Pb stress at the 1500 mg/kg Pb concentration. The study revealed that the enzymatic activities of SOD and POD exhibited a significant increase when exposed to 1000 mg/kg of Pb but decreased at 1500 mg/kg Pb. Conversely, CAT activity increased at 500 mg/kg Pb but declined at higher concentrations. Additionally, a decrease of 15% in vitamin C content was observed under 1500 mg/kg Pb. On the other hand, at 500 mg/kg Pb, there was a noteworthy increase of 93% in anthocyanin, which a higher concentration of Pb decreased when compared to witness group (Fatemi *et al.*, 2021).

5.5. Arsenic Effects on Plants

Arsenic (As) toxicity can interfere with the normal functioning of plant cells by disrupting the normal flow of ions and other essential nutrients. At higher concentrations, As can cause oxidative stress, leading to the formation of reactive oxygen species and the subsequent damage of cellular elements like lipids, proteins, and DNA (Gunes *et al.*, 2009). As toxicity can also interfere with the normal functioning of the plant's hormonal balance, leading to changes in growth and development. Three primary forms of this metal can be found in soils and water, namely arsenite [As (III)] and arsenate [As (V)], with the latter being the most prevalent form in soil (Garg & Singla, 2011). Additionally, there are methylated versions of this metal, including monomethylarsinic acid (MMA) and dimethylarsinic acid (DMA) (Angulo-Bejarano *et al.*, 2021). Plant species absorb As by utilizing phosphate transporters and nodulin 26-like intrinsic aquaporin (NIP) channels (Pommerrenig *et al.*, 2020). As a result, arsenic can disrupt many metabolic pathways in plants, leading to diminished germination, growth, development and crop production. Studies have found that As can affect starch metabolism enzymes, resulting in decreased seed germination (Zia *et al.*, 2017). As is an analog of P that competes for the same uptake carriers in the root plasmalemma of plants. Interestingly, in the *Holcus lanatus* L. plant, the short-term uptake kinetics of the high-affinity arsenate transport system were examined in excised roots of arsenate-tolerant and non-tolerant genotypes, it showed that there is a single gene encoding suppressed P/As transport as an arsenate-tolerant (Meharg & Macnair, 1992). The lack of induction of the synthesis of the arsenate (phosphate) carrier may be the cause of the low rate of arsenate uptake across a wide range of different root phosphate statuses. On the other hand, several research (Barker, 1972) showed that arsenate effects on carrots, lettuce, spinach, and sunflowers resulted in a loss in growth, an increase in the generation of stress biomarkers, and a decrease in photosynthetic pigments (Bergqvist *et al.*, 2014; Yadav *et al.*, 2014). A recent study by Wu *et al.* (2020) revealed that the exposure of rice plants to As resulted in a notable decline in seed germination percentage. The impact of arsenic stress on plants has been found to have a negative effect on their photosynthetic pigments, as reported by (Bali & Sidhu, 2021) For instance, a important reduction was observed in the content of Chl a, Chl b, and Chl a/b ratio in wheat plants. Additionally, As was discovered to have an adverse effect on various gas exchange attributes in wheat plants, including transpiration and photosynthetic rates, and water use efficiency, and internal CO₂ concentration decline in Rubisco activity and the maximum efficiency of photosystem (PS) II in rice plants under As stress (Ali & Perveen, 2020; Khan *et al.*, 2021).

6. THE MECHANISM OF TOXIC HMs ACTIVITY IN PLANT CELLS

The toxicity of HMs has manifested in many ways when they are accumulated in plant cells (Figure 3). Plants have developed different mechanisms to maintain a balance, including ROS signaling, an upregulated antioxidant defense system, biosynthesis of root exudates, binding of HM to the cell wall, sequestration, and compartmentation. Higher plant species detoxify metal-

triggered ROS through the activation of enzymatic antioxidant systems, such as SOD, POD, CAT, and non-enzymatic antioxidants such as phenolic compounds (Xu *et al.*, 2020; Pehlivan Karakas *et al.*, 2022). In addition, MTs, low molecular weight, and cysteine-rich metal binding proteins play a significant biochemical and physiological role in metal homeostasis and protect plants from oxidative damage through ROS scavenging and sequestration of HM (Chaudhary *et al.*, 2018). Moreover, plants also activate chaperones that protect and repair proteins and assist MTs in the sequestration and detoxification of metal ions (Haap *et al.*, 2016). Two types of HMs include redox such as Co, Cu, Fe, and Cr, and elements containing Al, Zn, and Cd, which belong to inactive redox groups. The capability of HMs to form strong chemical bonds with oxygen, nitrogen, and sulfur atoms is another significant mechanism of HM toxicity. The free formation enthalpy of HM products and their poorly soluble ligands are connected to this binding affinity. These properties allow HMs to bind to cysteine residues and thereby inactivate enzymes. The oxidation and cross-linking of protein thiols, the suppression of essential membrane proteins like H⁺-ATPase, or modifications in the composition and fluidity of membrane lipids are other ways that HMs affect membranes (Meharg & Macnair, 1992). According to previous studies, there are three potential causes of HM toxicity, HMs target structural, catalytic, and transport sites of the cell through direct interaction with proteins because of their propensities for thionyl-, histidyl-, and carboxyl groups. On the other hand, stimulation of ROS, MG is produced through auto-oxidation and the Fenton reaction. In addition, the antioxidant defense system and glyoxalase system modification also showed displacement of essential metal ions from specific binding sites, leading to the function change (Sharma and Dietz, 2009).

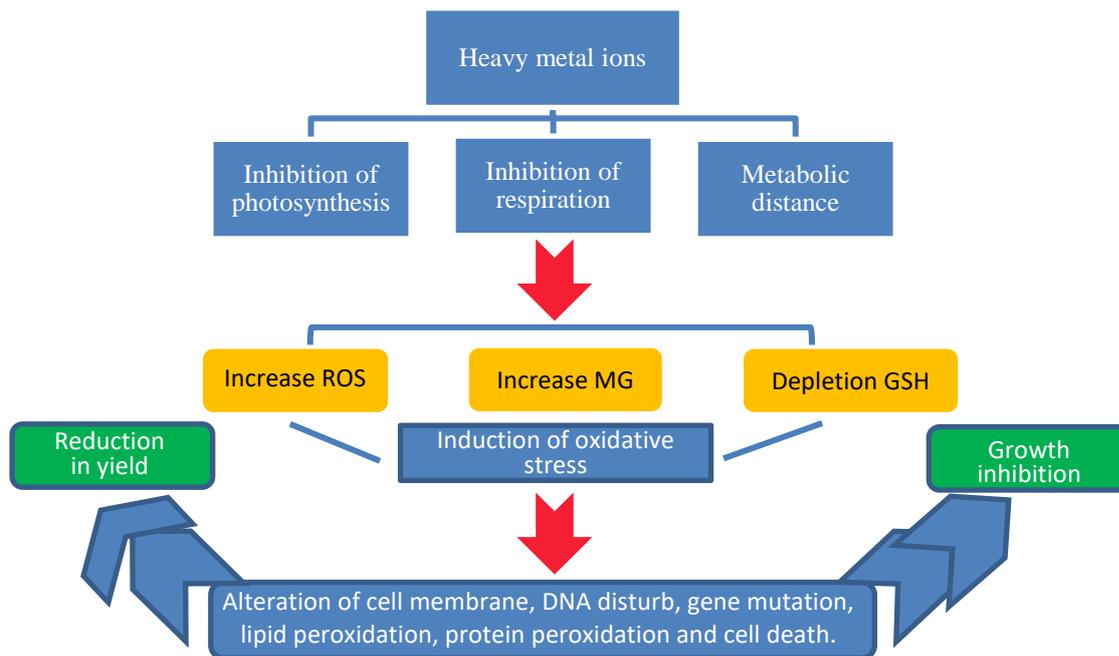


Figure 3. In response to HM stress the potential processes of ROS-induced damage in vulnerable plants.

7. CONCLUSION

HM toxicity is a significant challenge for plants because numerous human activities result in the excessive release of HMs into the environment, creating a significant risk to environmental integrity and agricultural productivity indeed, it poses a risk to the protection of the food chain. Due to the struggle with HM toxicity problem, plants have evolved several mechanisms for detoxification, defense, and adaptation. These mechanisms involve changes at the molecular, biochemical, and physiological levels, including, metal transporters, activate enzymatic and

non-enzymatic antioxidants, and produce phytohormones led to the boost antioxidative defense system by activating some biosynthetic genes. Furthermore, the most important mechanisms responsible for phytohormone induced HM toxicity tolerance in plants contain upregulated glutathione (GSH) biosynthesis genes, osmoregulation, and modulation of metal transporter gene. In recent decades, much progress has been made in understanding the molecular mechanisms underlying HM stress tolerance in plants. By using omics-based approaches and biotechnology, researchers have been able to identify novel genes, metabolic pathways, and signaling networks involved in HM stress tolerance in plants. Future advances in plant science, biotechnology, and genomics are anticipated to deepen the comprehension of the mechanisms underlying the ability of plants to withstand HM stress. In pollution regions of HM, finding new strategies for improving HM stress tolerance in agriculture would lead to increased food security and sustainability. The development of efficient, low-cost technologies for detoxifying HMs from contaminated soils will also be critical for the long-term health of the environment and the populations that depend on it.

Declaration of Conflicting Interests and Ethics

The authors declare no conflict of interest. This research study complies with research and publishing ethics. The scientific and legal responsibility for manuscripts published in IJSM belongs to the authors.

Authorship Contribution Statement

Sarah Jorjani: Investigation, Visualization, Writing – original draft. Fatma Pehlivan Karakaş: Supervision, Methodology, Software, Formal Analysis, Validation, and Writing – review and editing.

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