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Physiological Effects of Cadmium on Plants: A review

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ABSTRACT

Heavy metals are important environmental pollutants and their toxicity is a problem of increasing significance for ecological, evolutionary, nutritional, and environmental reasons. Cadmium contaminated soil ecosystems pose serious threats on the morphological and physiological attributes of the plants. The exudation of secondary metabolites from roots is an effective mechanism adopted by plants to react and modify their environment. Extraction of cadmium and acclimatization in plants depends upon the potential of the plant species and their rhizospheric environment that enables to restrict cadmium entry roots through immobilization or promotes cadmium chelation with ionic species in rhizosphere that influence its solubilization and mobilization. Cadmium inhibits several physiological processes in plants, including seed germination and seedling growth, photosynthesis, antioxidation and affects plant growth and development. Cadmium toxicity in higher plants as well as in the soil - plant system has increased considerably; recently there are many gaps in our knowledge about the basic mechanisms that control cadmium movement and its accumulation in plants. Mechanism of Cadmium uptake by root, translocation, and its deposition within plants; needs more research; furthermore, forms of Cadmium in various staple plant foods need to be identified. We should elaborate to learning about the biochemistry of metal homeostasis factors, physical interaction of transporters, chelators and chaperones. A genetic approach as contrasting to physiological/ biochemical investigations may help understanding the mechanism of metal tolerance. Cadmium is perhaps the metal that has attracted the most attention in soil science and plant nutrition due to its potential toxicity to humans, and its relative mobility in the soil – plant system. Toxic symptoms of cadmium in plants such as, alterations in photosynthesis, stomatal regulation, enzymatic activities, water relation, mineral uptake, protein metabolism, membrane functioning. Summarizing, cadmium absorption and transport in plants, the effects of cadmium on plant growth and development, adaptation mechanisms of plants to cope with cadmium.

Keywords: Cadmium, heavy metals, environmental pollutants, toxicity, contamination, plants

Introduction

Nagajyoti *et al.,* (2010) reported that heavy metals dramatically affect plant growth and development. Some of them are essential for plant growth; such as zinc that is a cofactor for more than 300 plant enzymes Broadley *et al.,* (2007), Zhang and Song, (2018). However, most heavy metals are toxic to plants, such as cadmium. Due to rapid development of industry and manufacturing, large amounts of heavy metal ores have been processed, has gradually increased causing serious environmental pollution, particularly in the soil Seregin *et al.,* (2004), Rai *et al.,* (20016). Heavy metals in the soil are easy absorbed by plant roots from soil and accumulate in aerial parts of plants, earnestly retarding many physiological and molecular processes. Cadmium has been identified as one of the most deleterious heavy metal pollutants due to ubiquitous in the human environment. Chakravarty and Srivastava (1992) stated that cadmium pollution seriously affects plant growth and has become a major environmental problem worldwide. Furthermore, cadmium is listed as a known human carcinogen

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(Class 1) by the International Agency for Research on Cancer IARC, (1993). Toppi and Gabbrielli, (1999), Yi and Wang, (2017) reported that different plant species have shown that cadmium has potential phytotoxicity, which can lead to inhibited the growth yield and even death. Intensive accumulation of cadmium has many harmful effects in plants, such as growth retardation, reducing chlorophyll and carotenoid contents, leaf surface, photosynthesis rate, biomass, water content, and increasing protease activity. Li *et al.,* (1992), Choi *et al.,* (2001) stated that cadmium in plants could bind to proteins, causing denaturation and dysfunction, and leading to growth inhibition Asgher *et al.,* (2015). As a non-redox metal, cadmium can lead to the formation of active oxygen and hydroxyl radicals Sharma and Dietz (2009). Remans *et al.,* (2010) showed that cadmium could also interfere with the capacity of antioxidants in plants and produce oxidative stress through its high binding affinity for oxygen, nitrogen, and sulfur atoms. Remans *et al.,* (2010), Sandalio *et al.,* (2001) reported that cadmium induced oxidative stress in pea (*Pisum sativum*) seedlings by promoting lipid peroxide and oxidized protein accumulation and reducing catalase and SOD activity Sandalio *et al.,* (2001). Plants have evolved various adaptive mechanisms that help them with stand cadmium in the soil, including the regulation of heavy metal ion absorption Clemens *et al.,* (2002), detoxification of metals through chelation, Clemens (2006) and compartmentalization of metal ions into vacuoles and other organelles Fig (1).

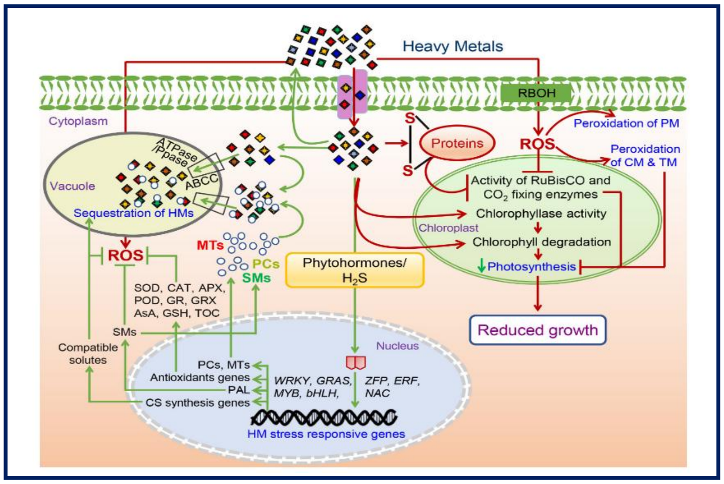

Fig. 1: A putative diagram showing positive and positive molecular responses of the heavy metals (HM) toxicity in the plants. Responses marked with the red color represent negative effects of the HM toxicity while those marked with the green color represent tolerance response to alleviate the HM toxicity. Abbreviations: ROS—reactive oxygen species; SMs—secondary metabolites; CS—compatible solutes; PCs-phytochelatins; MTs—metallothioneins; SOD—superoxide dismutase; CAT—catalase; APX-ascorbate peroxidase; POD—peroxidase; GR—glutathione reductase; GRX—glutaredoxins; AsA—ascorbic acid; GSH—reduced glutathione; TOC—tocopherol; PAL—phenylalanine ammonia lyase; RBOH—respiratory burst oxidase homolog; PM—plasma membrane; CM—chloroplast membrane; TM—thylakoid membrane. After Riyazuddin *et al.,* (2022)

Riyazuddin *et al.,* (2022) reported that heavy metal toxicity has become a global concern in recent years and is imposing a severe threat to the environment and human health. In the case of plants, a higher concentration of heavy metal, above a threshold, adversely affects cellular metabolism because of the generation of reactive oxygen species (ROS) which target the key biological molecules. Moreover, some of them such as mercury and arsenic, among others, can directly alter the protein /enzyme activities by targeting their–SH group to further impede the cellular metabolism. Particularly, inhibition of photosynthesis has been reported under heavy metal toxicity due to trigger the degradation of chlorophyll molecules by enhancing the chlorophyllase activity and by replacing the central Mg ion in the porphyrin ring, which affects overall plant growth and yield. Consequently, plants utilize various strategies to mitigate the negative impact of HM toxicity by limiting the uptake of this heavy metal and their sequestration into the vacuoles with the help of various molecules including proteins such as phytochelatins, metallothionein, compatible solutes, and secondary metabolites. In this comprehensive review, we provided insights towards a wider aspect of heavy metal toxicity, ranging from their negative impact on plant growth to the mechanisms employed by the plants to alleviate the heavy metal toxicity and presented the molecular mechanism of heavy metal toxicity and sequestration in plants.

1. Cadmium sources, contamination of soils and bioavailability

Cadmium with atomic number 48, atomic weight 112.41 and density 8.65 g/cm3 is a silvery bluish-grey metal. It is located at the end of the second row of the transition elements having melting point 320.9 °C and boiling point 765 °C. It belongs to group 12 of the periodic table with electronic configuration of [Kr] 4d10 5 s2. It is soft, malleable, ductile and insoluble in water Asgher *et al.,* (2015). Cadmium exists in $^{+}1$ and $^{+}2$ oxidation states; however, $^{+}2$ oxidation state is the most common. An amorphous substance cadmium oxide (CdO) is formed due to burning of Cd in air. High cadmium levels are positively correlated with excessive industrialization that has led to increased production and consumption of cadmium. Over use of cadmium in electroplating, nickel–cadmium batteries, as pigments for colouring glass and plastic, stabilizers for processing PVC polymers and production of some alloys contribute equally towards its distribution in the environment. Besides, mining activities, inappropriate wastewater irrigational practices, inadequate executions related to waste disposal, high inputs of agricultural fertilizers and industrial and vehicular emissions are the major causes for Cd contamination of agricultural soils Kaplan *et al.,* (2011); Asgher *et al.,* (2015); Khan *et al.,* (2016); Nawab *et al.,* (2016); Khan *et al.,* (2017). Both natural and anthropogenic factors contribute towards enhanced Cd contamination in the environment Chen *et al.,* (2019). Cadmium occurrence in soils ranged from 0.07 to1.1 mg. kg^{-1} soil WHO (2007), although its threshold limit in agricultural soils is nearly 100 mg. kg^{-1} Asgher *et al.,* (2015). According to Gallego *et al.,* (2012), 30,000 tonnes of Cd is added to the environment annually, out of which technogenic activities contribute approximately 13,000 tonnes of Cd annually. During the past decade, undesirable anthropogenic activities have caused the release of Cd at an alarming rate that has reached up to 2.2 × 107 kg throughout the world Costa *et al.,* (2012). Cadmium is considered as the most noxious heavy metal due to its high mobility and toxicity Chen *et al.,* (2015). Rafiq *et al.,* (2014) statistically analysed more than 1.3 × 105 ha Cd-enriched soil area that accounts for 1/5 of the total farmland area. Due to wide distribution and Cd-enriched soils, Rafiq *et al.,* (2014) demonstrated Cd induced grain contamination of approximately 1.2 × 105 kg and induced a reduction in the grain yield by approximately 1010 kg. Based on toxicity and potential for human exposure, Agency for Toxic Substances and Disease Registry (ATSDR) (2017) has ranked cadmium to the seventh position in the priority list of hazardous substances .The fraction of total available of cadmium for plant uptake is a crucial scenario to assess the environmental risk associated with cadmium contamination in soil. Cadmium is mainly present as cadmium ions or found associated as inorganic and organic complexes in the soil solution. The major cadmium uptake in plants occurs through contact with soil porewater, which is the net result of cadmium partitioning between the solid and liquid phases of the soil. Nevertheless, foliar uptake and transfer of cadmium have also been reported in the study of Mombo *et al.,* (2016). Vegetables grown in urban gardens near Pb recycling company showed high Cd and Pb concentrations Mombo *et al.,* (2016). Various chemical reactions such as precipitation/dissolution, adsorption/desorption and cadmium ligand formation influence cadmium partitioning in soil. These dynamic reactions are strongly affected by organic and inorganic ligands Shahid *et al.,* (2014), soil pH Saeki and Kunito (2012), redox conditions Zhang *et al.,* (2012), metal concentration and temperature Silber *et al.,* (2012). In soil systems, Cd partitioning is an important factor in regulating Cd toxicity Rizwan *et al.,* (2017). Shahid *et al.,* (2016) documented that total cadmium concentration in the soil medium does not mandate cadmium solubility, mobility and bioavailability, because the total chemical forms of cadmium are not 100% bioavailable. Moreover, the biogeochemical behavior of cadmium is completely dependent upon the free cadmium ion concentration in the soil medium Shahid *et al.,* (2016). Certain factors such as soil pH, organic matter content, cation exchange capacity and microbial activity of the soil effect cadmium bioavailability Shahid *et al.,* (2016) Fig. (2).

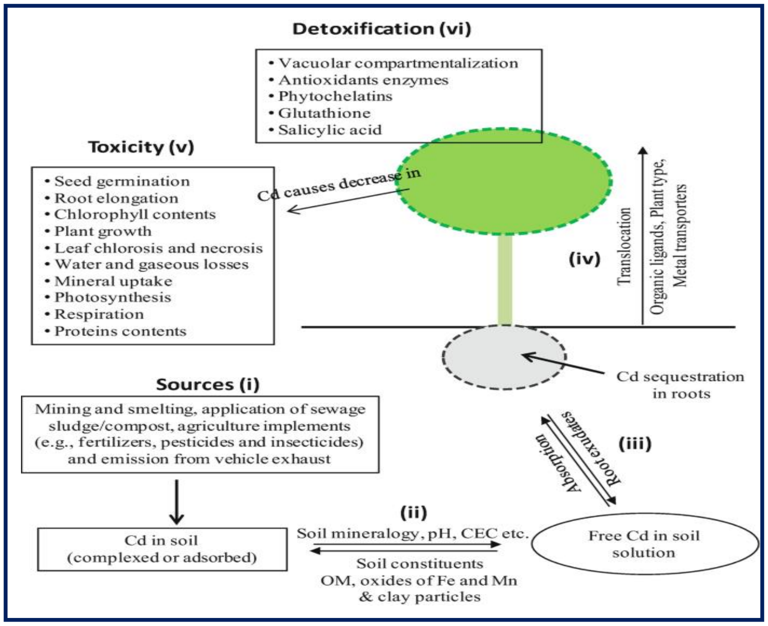

Fig. 2: Biogeochemical behavior of Cd in soil-plant system. (i) Accumulation of Cd in soil from different natural and anthropogenic sources, (ii) effect of soil physic-chemical properties on the complexation, mobility and bioavailability of Cd in soil, (iii) Cd uptake by plants via root transfer and major sequestration (>90 %) in root tissues, (iv) translocation to aerial parts depending on the nature of plant and applied Cd level and (v) toxic effects of Cd to plants and (VI) detoxification mechanisms involving the role of antioxidants, phytochelatins, glutathione and salicylic acid . After Shahid *et al.,* (2016)

Shahid *et al.,* (2016) reported that chemical speciation of cadmium, and its partitioning in soil, is a key factor in controlling both the fate and toxicity of cadmium in the soil-plant system Pizzol *et al.,* (2012); Landrot *et al.,* (2012). It is well known that total soil Cadmium concentrations tend to be a poor proxy for predicting cadmium mobility, solubility, extractability, and bioavailability Udovic and McBride (2012). This is because the total sum of all chemical forms of cadmium is rarely 100 % bioavailable, and the biogeochemical behavior of cadmium depends largely on the free cadmium concentration Dabrin *et al.,* (2012). For these reasons, knowledge of cadmium speciation is considered necessary for informing soil remediation and risk assessment studies Niazi *et al.,* (2011b); Shahid, *et al.,* (2011), (2012a); Bade *et al.,* (2012). Traditionally, analytical techniques used to assess metal speciation in soil and water have included anodic stripping voltammetry, ion selective electrodes, competitive ligand equilibration/adsorptive stripping cathodic voltammetry, and sorption onto C18 columns Cobelo-Garcı´a *et al.,* (2005). However, these techniques are very complex and time consuming. When actual measurements are not feasible, computer speciation models (capable of performing complex calculations) offer a cost-effective alternative Shahid *et al.,* (2012b & 2014b), although site-specific validation is required to confirm the accuracy of the model is output. The most widely used speciation models include: the Windermere Humic Aqueous Model VI (WHAM VI), CHESS, CHEAQS, PHREEQC and VISUAL MINTEQ Tipping, *et al.,* (1998); Parkhurst and Appelo, (1999); Gustafsson, (2008); Antunes and Kreager, (2014); Shahid *et al.,* (2014d). These models offer the advantage of desktop computing and are appropriate for both small and large-scale applications. However, the accuracy of the estimated speciation may vary among models and chosen input values (e.g., cadmium concentration range, DOC concentration and quality, consideration of precipitation reactions).

2. Distribution of cadmium and characterization in soil

Cadmium is obtain from both natural and anthropogenic sources, which natural sources including underlying bedrock or transported parent material such as glacial till and alluvium. Volcanoes and weathering of rocks are considers as natural sources for mobilizations of cadmium from the earth's crust are within the biosphere, several processes can translocate the cadmium.

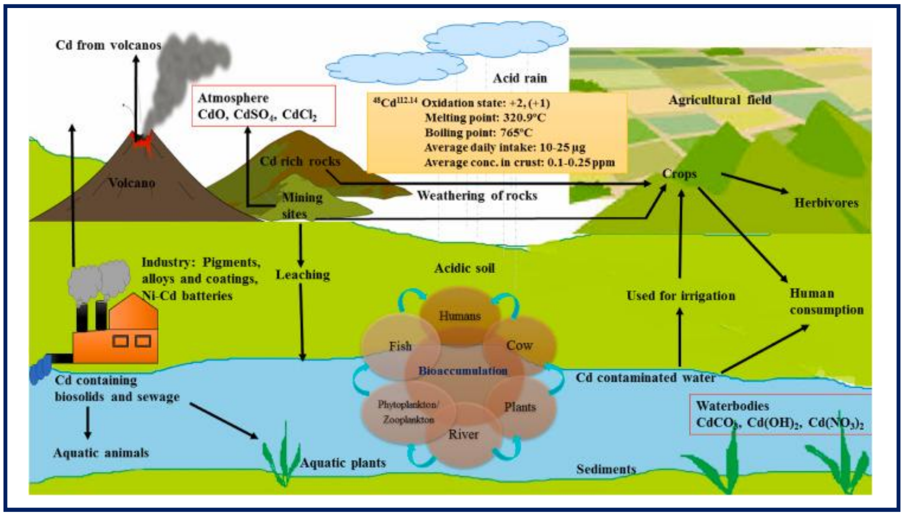

Fig. 3: The anthropogenic and natural sources of Cd together with biogeochemical cycle showing the transportation of Cd in the atmosphere Javed *et al.,* (2019), Kumar *et al.,* (2021)

Kumar *et al.,* (2021) reported that cadmium was discovered as a zinc carbonate impurity belonging to IIB group element. It is a rare earth element with 0.15 mg/kg abundance in Earth's crust and 1.1 $\times 10^{-4}$ mg/L in the sea Hayes, (2016). Cadmium is one of the ubiquitously dispersed noxious and mobile pollutants in soil. It is most commonly present in the +2 oxidation state. Generally, cadmium is soft; therefore, alloying with Zn, it is improved. Annually, ~13,000 tons of cadmium are produced worldwide Orisakwe, (2012) specifically for Ni– Cd batteries, as a chemical stabilizer, pigments, alloying, and coating. It is less soluble in sulphoric and hydrochloric acids and readily in nitric acid. Cadmium salts with strong acids are readily soluble in water. Fig. (3) represents the occurrence of cadmium concentrations in soils, sediments, and water, globally. Consequently, a high amount of cadmium is continuously being released, leading to increased concentration within the environment. Cadmium has a similar ionic radius, chemical nature, and identical charge as calcium. Therefore, it replaces calcium and enters the human body, and is accumulated in various organs at a high level Kubier *et al.,* (2019). Irrigation of agricultural land with contaminated water with cadmium leads to bioaccumulation into the crops. It has been observed that in China, Jamaica, and Korea, the elevated level of cadmium in soil and groundwater leads to enhanced bioaccumulation of cadmium in rice Liu, *et al.,* (2017). Hence, in the human body, cadmium enters mainly via terrestrial route, i.e., consuming vegetables. In 1984, UNEP proposed a regulation for twelve hazardous pollutants globally, amongst which cadmium was placed first. Along with, WHO and IARC have also listed in category one, i.e., a carcinogen Liao *et al.,* (2015). Cadmium is known to have no function in plants, animals, and humans; however, some literature reports essentiality in animals. When cadmium is present in high concentration, severe effects have been observed in digestive and respiratory tracts and predominately accumulates in kidneys with a 10–20 years' biological half-life. Long-term exposure to cadmium leads to irreversible renal effects.

Naturally, a very large amount of cadmium about 25,000 t a year of is released into the environment; half of this is released either into rivers through weathering of rocks or into the air through forest fires and volcanoes. However, the rest is released through human activities, such as electroplating, manufacturing of plastics, mining, paint pigments, alloy preparation, and batteries that contain high amounts of cadmium, composts, or even fertilizers prodution. Even domestic sewage effluents, which contains cadmium, enters rivers and streams and therefore, contaminates other places or accumulates in the sludge. Moradi *et al.,* (2005) reported that addition of cadmium in metal rich sewage sludge might also result in the contamination of groundwater. The average natural abundance of cadmium in the earth's crust has most often been reported from 0.1 to 0.5 ppm, depending on a large number of factors.

Cook and Morrow, (1995) stated that igneous and metamorphic rocks tend to show lower values, from 0.02 to 0.2 ppm, whereas sedimentary rocks have much higher values, from 0.1 to 25 ppm. Fossil fuels contain 0.5 to 1.5 ppm Cd, while phosphate fertilizers contain from 10 to 200 ppm cadmium. According to Wagner, (1993) reported that in non-polluted soil solutions contain cadmium concentrations ranging from 0.04 to 0.32 mM. Soil solutions that have a cadmium concentration varying from 0.32 to about 1 mM can be regarded as polluted to a moderate level. Because cadmium is a naturally occurring component of all soils, all foodstuffs will contain some cadmium and therefore, all humans are exposed to natural levels of cadmium. Mench *et al.,* (1998) reported that leafy vegetables and potato tubers naturally accumulate higher levels of cadmium than fruits and cereals. Moreover, tillage and crop rotation practices similarly have a greater impact on the cadmium content of food than does the concentration of cadmium in soils.

3. Factors affecting cadmium uptake by plants

3.1. Effect of soil pH on Cd bioavailability

Kirkham, (2006) reported that a linear trend between soil pH and cadmium uptake were observed, soil acidity gradually increases the concentration of cadmium in plants, particularly, and soil properties remain unchanged Eriksson, (1989). Singh *et al.,* (1995) reported that soil pH gradually affects the cadmium availability in soil solution but increasing of soil pH does not always reduce cadmium uptake by plants. Christensen, (1984) stated that soil pH is also one of the important factors regulating the extractability of cadmium in soils. Increasing soil pH gradually increases the adsorption of cadmium by soils and furthermore reducing extractability of cadmium. Under field conditions, the uptake of cadmium by plants may be affected by many variable soil and climatic parameters. Adams *et al.,* (2004), Li *et al.,* (2005) observed that total cadmium content in soil and pH were significant factors influencing the cadmium concentration in grain. Chaudri *et al.,* (2007) stated that in field experiments with rice plants grown on the acidic red soil in China, at soil pH of 4.95, cadmium content in grain was 0.36 mg kg^{-1}, while, at pH of 6.54, cadmium content in grain was 0.43 $mg.kg^{-1}$. Factors responsible for cadmium accumulation in wheat grain are cadmium, pH, and organic carbon in soil. Singh and Myhr, (1998) observed that in barley grains, there is no any significant correlation between the extractable cadmium in soil, soil pH, and cadmium accumulation. It is not easy to extrapolate results from greenhouse studies to field conditions. Singh, (1994) stated that in greenhouse experiments application of NPK- fertilizers, gradually increase the concentration of cadmium in crops , but no such increase in cadmium concentration in crops grown under field conditions was found because of long-term application of phosphate fertilizers. The extent of cadmium accumulation also depends on plant genotype Li, *et al.,* (2005). Several researchers consider that uptake of cadmium by plant is active transport, but most directory points to the hypothesis of passive transport. Mengel and Kirkby, (1982) ; Marschner, (1995) reported that active transport always happed across cell membranes depending on metabolic energy (ATP) through carrier theories, via binding sites . Each carrier has the affinity to a certain ion and regulates the content within the plant. However, Larcher, (1995) and Marschner, (1995) stated that passive uptake, is independent of ATP. It is hypothesized that the transport of Cd within the plant occurs in the xylem through water transport upwards in the xylem as described by Greger and Landberg, (1995) Fig. (4). The effects of transpiration on Cd uptake have both been confirmed Hardiman and Jacoby, (1984); Salt, *et al.,* (1995) and not confirmed Perfus-Barbeoch *et al.,* (2002). The uptake of ions takes place in competition with that of elements such as Zn Zhao, *et al.,* (2002), P Dheri *et al.,* (2007), Cl Li *et al.,* (1994), Oporto *et al.,* (2009), Ca Choi and Harada, (2005), and Cu Kudo *et al.,* (2011). Soil, environmental, and management factors impact on the amount of Cd accumulated in plants Hart *et al.,* (1998). Much of the Cd taken up by plants is retained in the roots, but a portion is translocated to the aerial portions of the plant and into the seed. The amount of Cd accumulated and translocated in plants varies with species and with cultivars within species. Shen *et al.,* (2006) reported that mycorrhizal inoculation increased plant growth with enhancement of phosphorous nutrition. Furthermore, may increase plant tolerance to Zn and Cd by a dilution effect.

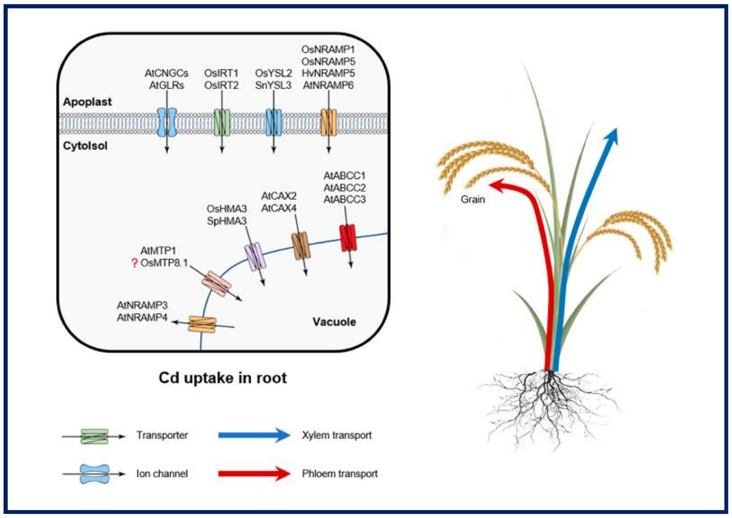

Fig. 4: Illustrates uptake and intracellular compartmentation of cadmium in plant roots. Cd taken up by IRT1/2 (zinc/iron-regulated transporter-like protein), YSL2/3 (yellow stripe-like protein), and NRAMP1/5/6 (natural resistance-associated macrophage protein) transporters that are located at the plasma membrane of the root epidermis. Cd can be also transported into cells through non-selective cation (NSCC) channels such as CNGCs (cyclic nucleotide-gated channels) and GLRs (glutamate receptors). ABCC (ATP-binding cassette transporters), CAX (cation exchanger), HMA3 (metal-transporting ATPases), MTP1 (metal tolerance protein), and NRAMP3/4 mediate Cd transport and sequestration in the vacuole. After Xin *et al.,* (2020)

Yu *et al.,* (2016) reported that pH is a crucial factor for regulating cadmium partitioning and bioavailability. Under varied soil pH, which is known to exist in different chemical forms. Cadmium in soil is found mostly in combined state and about 99% of the total cadmium is coupled with soil colloids. Kabata-Pendias and Sadurski, (2004) reported that Cd in soil occurs in both cationic and anionic forms. Cationic forms include $CdCl^+$, $CdOH^+$, $CdHCO_3^+$, while anionic forms include $CdCl_3^{-}$, Cd $(OH)_3^{-}$, Cd $(HS)_4^{2-}$. It has been estimated that 99% of cadmium is found in free ionic form in the soil solution Kabata-Pendias, (1993). It has been demonstrated that solubility of cadmium in soil solution is greatly influenced by soil acidity. Mineralized soils have pH range from 4.0 to 4.5. A decrease in pH range of up to 0.2 units exhibits 3–5 times increase in labile cadmium pool. An indirect correlation occurs between soil pH and cadmium extraction in plant tissues. At low soil pH, the transformation of cadmium from immobile combined form such as Fe and Mn oxides and carbonates to more phytoavailable and exchangeable form enables free Cd mobility and phytoavailability Qi *et al.,* (2018) Fig. (5).

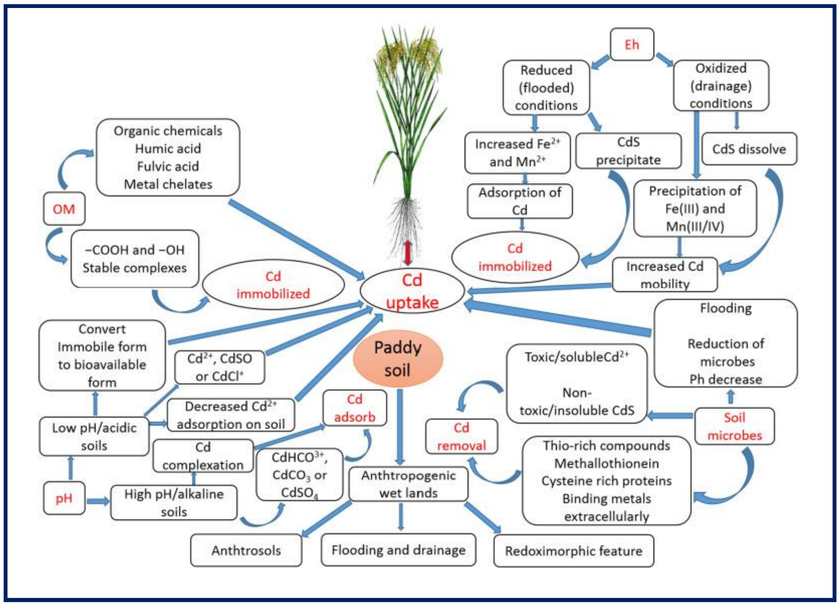

Fig. 5: Illustrates an indirect correlation occurs between soil pH and Cd extraction in plant tissues in paddy soil

Sullivan *et al.,* (2013) reported a negative correlation ($r = -0.55$) between $CaCl_2$ extractable fractions of cadmium with pH particularly, in Elba muck soils of Western New York. The findings probably corroborated with pH 6 that acts as a threshold point for cadmium solubility in soil due to the formation of strong complex with organic matter and adsorption on mineral surfaces Sullivan *et al.,* (2013); Shahid *et al.,* (2016). A positive correlation between the low soil pH with enhanced Cd phytoavailability revealed the possibility of deploying non-conventional techniques such as phytoremediation to ameliorate cadmium uptake by plants from cadmium-contaminated soils Sidhu *et al.,* (2019a). On the contrary, an increase in soil pH enhanced its alkalinity that effects and influences the adsorption of cadmium ions on to the soil particles that in turn subsequently poses negative effect in the uptake of vital nutrients by the plants. Yu *et al.,* (2016) studied 73 pairs of soil and rice samples contaminated with acid mine drainage containing cadmium to assess the effect of soil pH and iron fractions in the bioavailability of Cd in the rice grains. Furthermore, assessment of soil properties for cadmium acquisition in the rice grains revealed that pH of soil imparts a key role in acclimatizing Cd in rice grains, while amorphous iron fractions were considered as the second important factor in contributing Cd bioavailability in the rice grains Yu *et al.,* (2016). Increasing soil pH poses negative effect on the phytoavailability, as Cd precipitation and adsorption onto the soil particles reduce the free Cd availability in the soil solution Meng *et al.,* (2018). In soils with pH > 7.5, cadmium precipitated and adsorbed onto the soil particles remains immobilized. The degree of net charge associated with the solid phase related to the soil pH. In acidic soil solution, protons (H^+) compete with Cd ions for binding sites, which induces Cd desorption from soil particles into the solution. Nevertheless, in the alkaline environment, the solid-phase exchange sites are freely available for binding with cationic metal ions. At high soil pH, Cd hydrolyzed to hydroxy species and is adsorbed readily with the solid phase and influence high-Cd adsorption, making Cd desorption a difficult task in alkaline medium Shahid *et al.,* (2016).

3.2. Bioavailability of cadmium as affected by soil organic matter

Soil organic matter derived from decomposition of plants and animals imparts a consequential role in Cd bioavailability, as it readily forms complex with cadmium in the soil components. Bioavailability of cadmium is directly influenced by humus, and it varies with its concentration, source and various forms such as either suspended or dissolved and other physico-chemical properties Fig. (6). Organic matter is responsible for maintaining high soil pH, and component such as fulvic acid in it is very reactive which helps to maintain high metal bioavailability due to high cation exchange capacity, small size and high oxygen content Shahid *et al.,* (2012). It has been noticed that content of surface organic matter has a direct influence in binding and acclimatizing Cd. Kirkham (2006) documented that soils rich in organic matter had high sorption potential which is about 30 times higher for cadmium compared to mineral soils.

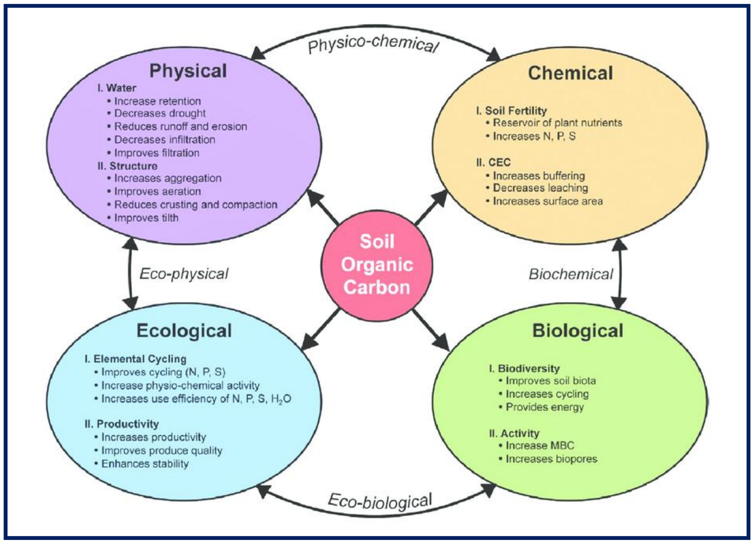

Fig. 6: Illustrates influences of soil organic carbon pool on improvements of soil physical, chemical, biological, and ecological properties. After Rattan (2016).

In a recent finding, Rocco *et al.,* (2018) assessed the potential utilization of organic matter compounds (poultry manure, coal fly ash and biochar) to enhance bioavailability of cadmium in *Zea mays* in two Australian soils with different pH and texture. Rocco *et al.,* (2018) stated that addition of amendments to Kapuda-acid loamy sand though enhanced the soil pH but subsequently reduced the bioavailability of cadmium in *Zea mays*. Addition of biochar to Cd-contaminated soils effectively enhances the soil pH and reduces cadmium bioavailability. The utilization of biochar as organic material reduces cadmium bioavailability in *Lolium multiflorum* by 6–14%, when the plants were grown under Cd-contaminated soils. Furthermore, the application of > 10% biochar dramatically decreased the bioavailability of cadmium in plants through the immobilizing cadmium in soil Xiao *et al.,* (2019). In a similar study, Abbas *et al.,* (2018) reported that application of biochar efficaciously reduces cadmium and salt stress in *Triticum aestivum* by decreasing cadmium bioavailability and promoting plant growth by regulating antioxidant enzyme activities in plants Fig.(7). Likewise, biochar application to soils contaminated with cadmium significantly altered the rhizobacteria communities by stimulating the activities of growth-promoting bacteria in rice plants Wang *et al.,* (2019). The finding revealed that biochar application as organic matter reduced Cd mobilization in soil and hence decreased cadmium bioavailability in rice plants.

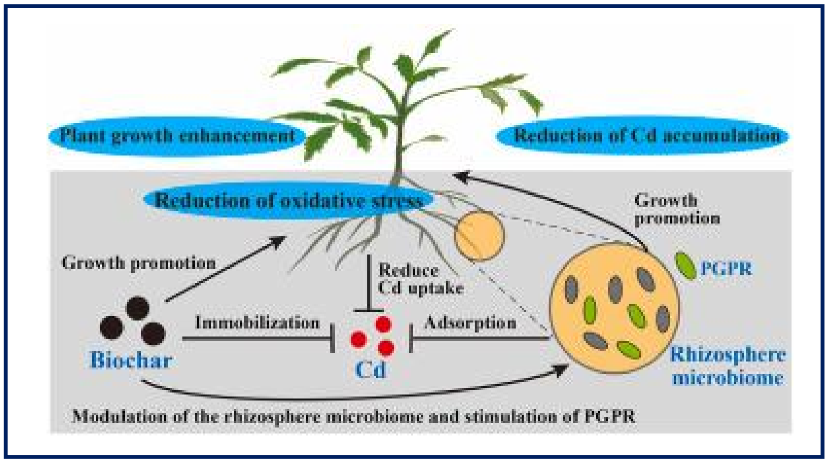

Fig. 7: Illustrates influences of biochar for reducing cadmium uptake by stimulating cadmium-resistant PGPR in tomato rhizosphere. After Zhou *et al.,* (2022)

On the contrary, application of tea waste derived biochar to Cd-contaminated soil sediments enhanced the uptake and accumulation potency of ramie seedlings by altering Cd speciation in soil sediments and by modulating sub-cellular Cd distribution in plant cells Gong *et al.,* (2019) Fig. (8).

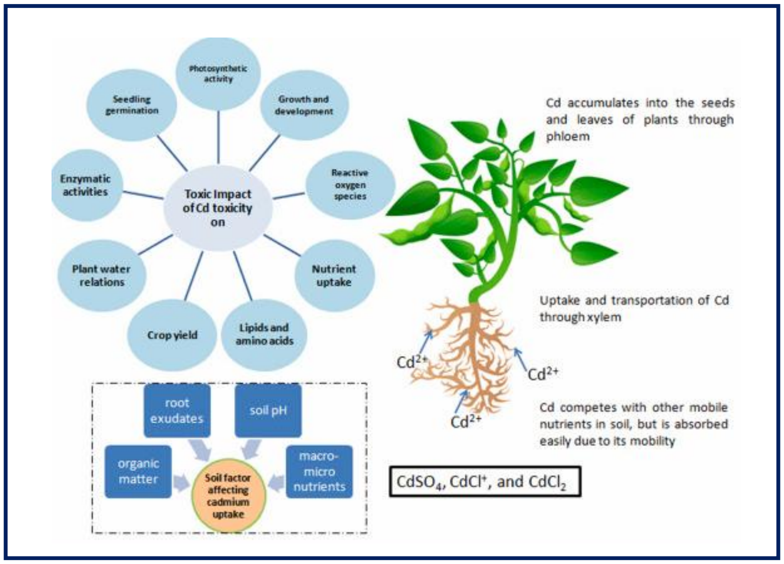

Fig. 8: Cadmium (Cd) absorption, transportation, accumulation, and toxicity in plant species. Root exudates, soil pH, organic matter, and micro- and macro-nutrients in soil are key factors that affect the uptake of Cd in plants. In roots, Cd absorption may occur as inorganic complexes (i.e., $CdSO_4$, CdCl+, and $CdCl_2$). Toxicity of Cd inhibits plant growth and development, thus reducing nutrient and water uptake and ultimately decreasing the photosynthetic rate. Cadmium toxicity disturbs the equilibrium between the synthesis of antioxidants and generation of reactive oxygen species (ROS), and enhances ROS accumulation in plants, which stimulates oxidative stress. Over-accumulation of ROS in plants alters the synthesis of proteins and lipids, affects enzymatic activity that leads to lipid peroxidation, and reduces cell division to negatively impact crop productivity. After Haider *et al.,* (2021)

Yousaf *et al.,* (2016) assessed the potential effect of traditional organic amendments such as press mud, biochar, farm manure, sewage sludge, poultry manure and compost as carbon sources on the bioavailability and uptake of cadmium in *Triticum aestivum*. The results revealed that all the organic amendments significantly increased the organic content of the soil and cadmium uptake in *Triticum aestivum* was enhanced predominantly with the application of sewage sludge, poultry manure and farm manure Yousafm *et al.,* (2016). Amendment of unentrapped inorganic fertilizers such as urea and bio-fertilizers such as *Bacillus subtilis* and *Azotobacter chrocoocum* increased Cd concentration in roots and shoots of *Brassica juncea* and *Ricinus communis* plant species Bauddh and Singh, (2015). The vermicompost as organic fertilizer could bind Cd and promote high biomass production and microbial consortium that ultimately affect the enhanced Cd extraction and growth of both the plant species Bauddh and Singh, (2015).

Additionally, application of vermicompost obtained from pig manure to soils co-contaminated with cadmium and polycyclic aromatic hydrocarbons dramatically enhanced the phytoextraction cadmium efficiency of *Sedum alfredii,* which enhancing root–shoot biomass and growth of the plants that ultimately induce rapid dissemination of polycyclic aromatic hydrocarbons in soil probably due to increased generation of root exudates that subsequently favor the bacterial community structure in the rhizosphere Wang *et al.,* (2012).

3.3. Bioavailability of cadmium as affected by (CEC) cation exchange capacity

Mobility of cadmium in soil and its bioavailability gradually affected by cation exchange capacity of the soil. According to the study by Gusiatin and Klimiuk, (2012), loamy and loamy sand soils in Warmia and Mazury Province, northeastern Poland, slightly bound with the exchangeable of cadmium and acid-soluble fraction having small cadmium concentration associated with organic matter fraction. However, in silt–clay soil, cadmium is bounded with reducible fractions followed by exchangeable acid-soluble fractions Gusiatin and Klimiuk, (2012). Hong *et al.,* (2002) demonstrated the low mobility of Cd due to the strong affinity of Cd with the surface of clay minerals, humus and Fe–Al oxides. Fig. (9).

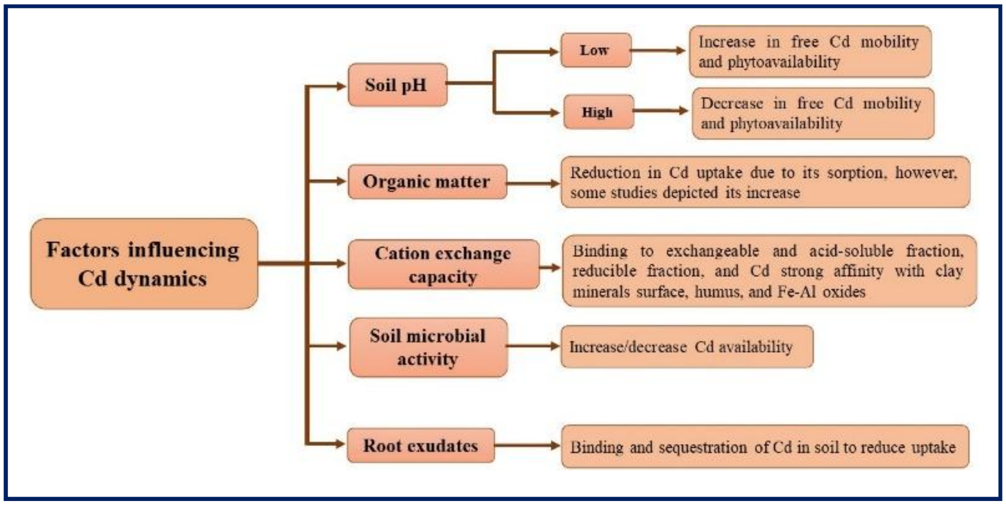

Fig. 9: Factors affecting Cd dynamics in soils. After Shahid, *et al.,* (2016), Zulfiqar, *et al.,* (2022)

The presence of other mineral ions in the soil medium has direct influence on cadmium bioavailability. Which directly correlated with the ionic strength, complexation and competition for soil exchange sites or root surface exchange sites. Moreover, the ionic strength of the growth medium inversely affects Cd- bioavailability. Low ionic strength in the growth medium enhanced the Cd extraction by the plants Gothberg *et al.,* (2004). In another study, Kim *et al.,* (2017) elucidated an increase in soil pH, negative surface charge of the soils treated with combination of both 30 mg.ha^{-1} bottom ash, and animal manure compost ultimately enhanced cadmium adsorption on soil surface and gradually decreased Cd- bioavailability in *Lactuca sativa* plants.

3.4. Bioavailability of cadmium as affected by soil microbial activity

Certain microorganisms develop potential resistance towards cadmium, dominate the rhizospheric conditions and promote the growth of the plants under cadmium stress. To overcome the cadmium stress, the microbes have developed inherent mechanisms to bind free cadmium ions and actively colonize rhizosphere and resistance towards cadmium excess in the soil Fig. (10), availability of cadmium in the soil is enhanced by soil microbes, as the later is highly involved in the subsequent solubilization of cadmium bearing minerals and excretion of chelate-forming organic acids Liu *et al.,* (2020). Cadmium solubilizing microorganisms such as plant growth-promoting bacteria (PGPR) as an amendment in the soil, thus impart a crucial role for increasing cadmium bioavailability Wu *et al.,* (2020). For instance, Li *et al.,* (2019) documented *dsrA* and *soxB* gene and *Thiobacillus* sp. were the dominant bacterial species involved in the effective oxidation of sulphur, assisting the uptake and accumulation of cadmium up to ~ 66%, 46% and 42% in leaves, stems and roots of tobacco plants Fig. (10).

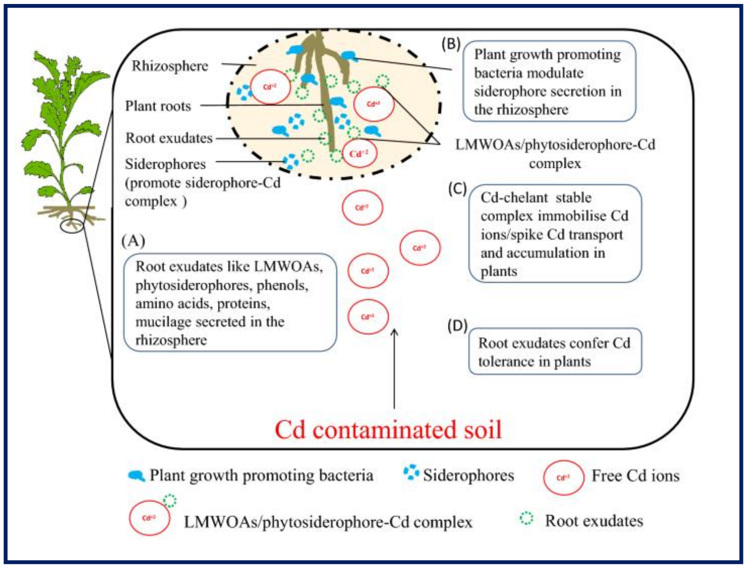

Fig. 10: Illustrates root exudates secreted in the rhizosphere influence Cd tolerance in plants. **(A)** Secretion of root exudates such as low-molecular-weight organic acids, phytosiderophores, phenols, amino acids, proteins, mucilage in the rhizosphere; **(B)** plant growth-promoting bacteria regulate siderophore secretion in the rhizosphere; (**C)** formation of Cd–chelate stable complex can immobilize Cd ions in the rhizosphere or can enhance the transport and accumulation of relatively less toxic Cd ions in the plant tissues; **(D)** secreted exudates induce Cd tolerance in plants. LMWOAs low-molecular-weight organic acids. After Bali, *et al.,* (2020)

On the parallel, a study conducted by Sangthong *et al.,* (2016) postulated the potential of bio augmenting agent *Micrococcus* sp. TISTR2221 to regulate high cadmium uptake in the stem and root part of the *Zea mays* plants grown under high cadmium stress. The above findings support the work conducted by Li *et al.,* (2019) who demonstrated the inoculation of *Lycopersicon esculentum* with arbuscular mycorrhizal fungi (*Funneliformis mosseae*) and Cd-resistant bacteria strain (*Enterobacter* sp. EG 16) enhanced root–shoot biomass along with the increased Cd uptake in the roots of the plants under 50 and 100 mg. kg^{-1} cadmium treatment. Arbuscular mycorrhizal fungi impart a vital role in cadmium mobility in plants. The co-inoculation of *Solanum nigrum* with arbuscular mycorrhizal fungi and earthworms enhanced the plant biomass and acquisition of phosphorus and cadmium in the shoots Wang *et al.,* (2019). The results of their study showed that co-inoculation (arbuscular mycorrhizal Fungi and earthworms) increased cadmium phytoavailability up to 149.3% under 120 mg. kg^{-1} Cd-spiked soils by changing the cadmium chemical fractions Wang *et al.,* (2019). On the contrary, to curb cadmium toxicity in plants, microbes in the form of plant growth-promoting bacteria and arbuscular mycorrhizal fungi impart an active participation in limiting cadmium uptake in roots and its translocation to foliar plant parts. Sharma and Archana, (2016) postulated that plant growth-promoting bacteria are not directly involved in cadmium sequestration but reduce the plant stress based on the plant growth-promoting traits Fig. (11). A significant decline in cadmium phytoavailability was observed by bioaugmentation of soils, employing free and immobilized cadmium-resistant bacteria and fungi in the rhizosphere Sharma and Archana, (2016). Soils inoculated with certain microbes such as *Pseudomonas aeruginosa*, *Burkholderia gladioli* Khanna, *et al.,* (2019); *Cupriavidus* sp. strain ZSK Zeng *et al.,* (2020) and arbuscular mycorrhizal fungi Zhang *et al.,* (2019) have proclaimed decrease cadmium phytoavailability.

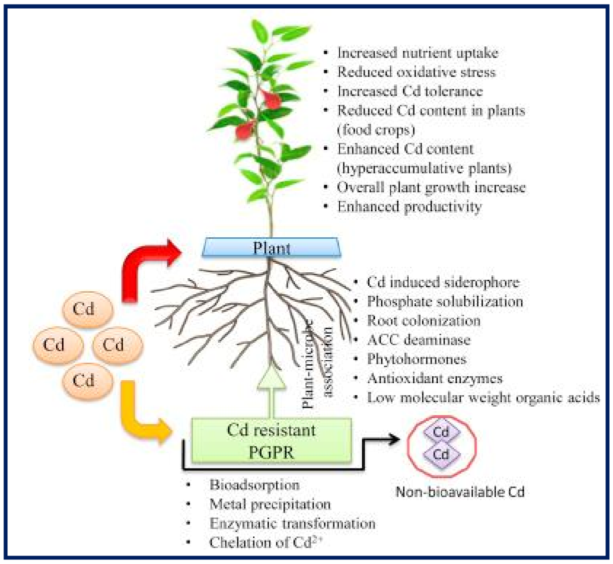

Fig. 11: Illustrates the mechanisms of PGPR in alleviating cadmium stress in plant.
After Kumar and Sukanta, (2022)

The strategies adopted for reducing bioavailability of cadmium in plants depend upon the potency of microbes to transform mobile states of cadmium into inert forms by several mechanisms.

Such as (**a**) reducing Cd- solubility in soil by altering soil pH and metal valency; (**b**) binding or sequestering cadmium with the components present on the cell surface; (**c**) releasing a variety of organic compounds in the rhizosphere that form complex with the Cd ions; and (**d**) formation of insoluble Cd S by releasing H_2S.

The microbes achieve cadmium resistance and decrease the bioavailability of cadmium to plants by biosorption, bioaccumulation, precipitation, complexation and efflux of Cd-ions. In bacterial defense mechanisms, intracellular binding proteins such as metallothioneins (cysteine-rich protein) and metallochaperones function as cytoplasmic Cd-binding proteins that assist in lowering the concentration of free Cd ions within the cytoplasm and hence decrease the bioavailability of cadmium to the plants and promote the number of friendly microbial community in the rhizosphere. In a recent study, Xu *et al.,* (2019) documented a substantial reduction in the bioavailability of cadmium to *Brassica chinensis* when the Cd-contaminated soil was inoculated with *Raoultella* sp. strain X13. The functional trait of X13 strain in releasing indole acetic acid and solubilizing phosphate dramatically improved the growth and production of *Brassica chinensis* plants Xu *et al.,* (2019). The inoculation of Cd-contaminated soil with sulphate-reducing bacteria (SRB-1) strain isolated from metal (loid) contaminated paddy fields significantly reduced the bioavailability of Cd and Pb by 29.5% and 26.2%, respectively, in the rice grains Shan *et al.,* (2019). In a similar work, combined effect of indigenous soil arbuscular mycorrhizal fungi and zeolite addition on Cd uptake in the grains of bread wheat was assessed by Baghaie *et al.,* (2019) who found a noticeable decrease in Cd uptake to the bread wheat grains from 8.9 to 3.3 mg Cd. kg^{-1}, respectively. Additionally, a remarkable increase in growth and phosphorus and nitrogen concentration in plants grown under Cd stress was observed by Baghaie *et al.,* (2019). The reduction in the bioavailability of cadmium to plants by microbes might also be attributed to the Cd immobilization in the soil by forming less soluble organic fractions. This hypothesis is corroborated with the study conducted by Xu *et al.,* (2012), reporting that ~ 8–25% Cd transformation into less bioavailable organic-bound fraction, with the assistance of bacteria. The role of microorganisms in transforming Cd to less soluble organic fractions immobilizes Cd in the soil, decreases its phytoavailability and enables the plants to tolerate and overcome Cd-induced toxicity Fig. (12).

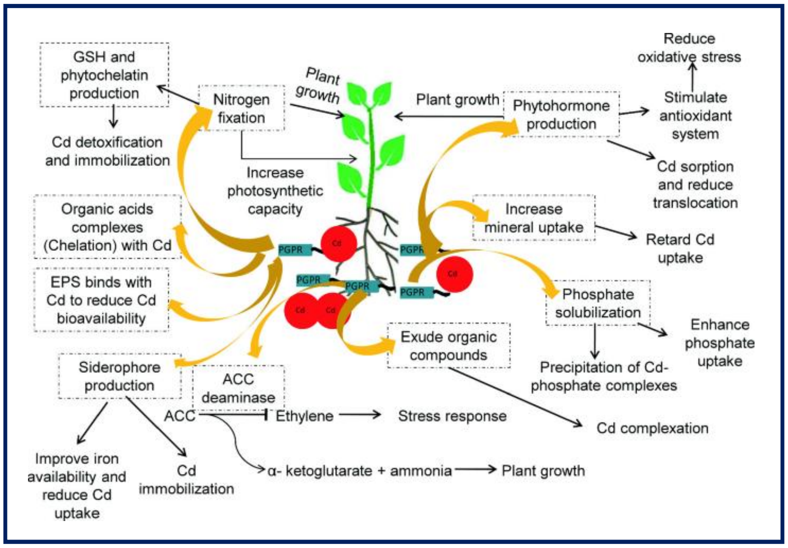

Fig. 12: Illustrates using of PGPR for plant growth and minimization of Cd uptake in edible crops provides an efficient, ecologically sustainable alternative strategy for bioremediation and maintaining food safety. After Pramanik *et al.,* (2018).

Pramanik *et al.,* (2018) reported that Growth-promoting bacterium of plants PGPR is an effective colonizing in roots and enhances the induced and systematic resistance and genetic diversity either directly or indirectly. PGPR is a diverse study; thus, rhizobacteria can be taken into account as a biocontrol for plant growth. Plant growth can be effective directly either while synthesizing a compound by bacterium, i.e., aiding various nutrient uptake from the surrounding environment or plant hormones, or indirectly, reducing the harmful effect of plant pathogens. Bioavailability of cadmium in the rhizospheric region has been the major reason for cadmium toxicity in plants. The use of PGPR strains for plant growth and minimization of cadmium uptake in edible crops provides an efficient, ecologically sustainable alternative strategy for bioremediation and maintaining food safety. However, in non-hyperaccumulator plants, cadmium tolerant PGPR could lower the uptake and distribution of cadmium into the aboveground plant parts; whereas in hyperaccumulator plants, it may facilitate the cadmium uptake and bioaccumulation in the plant. Cadmium resistant PGPR, such as Bacillus sp., Pseudomonas spp., Burkholderia sp., Ochrobactrum, Chryseobacterium sp., Enterobacter sp., Serratia sp., Klebsiella sp., reduce a significant amount of cadmium content in edible crops. PGPR can alleviate cadmium toxicity through several mechanisms, ensuing plant growth. PGPR characters, such as the production of plant growth regulators including IAA, 1-aminocyclopropane-1-carboxylate deaminase (ACCD) production, siderophore production, organic acid secretion, and phosphate solubilization.

3.5. Cadmium absorption and transport in plants

Cadmium exists in the soil in the form of cadmium ions, which are absorbed by plant roots and then accumulated in plant organs, due to their mobility. Lugon-Moulin, *et al.,* (2004) stated that cadmium is transported to the xylem through the root epidermis and root cortex *via* apoplastic and symplastic pathways Fig. (13). Cadmium is readily transported to stems and leaves through xylem, Ni, *et al.,* (2020), Song *et al.,* (2017). Despite plants' ability to absorb Cd ion, cadmium element is not essential to plant metabolism and is considered one of the most hazardous environmental plant poisons. Song *et al.,* (2013), Song *et al.,* (2017) reported that there is no special Cd absorption mechanism by plants. Cadmium-Cd^{2+} is absorbed through metal ion symporters and enters the root epidermis in a chelated form through low-affinity ion channels.

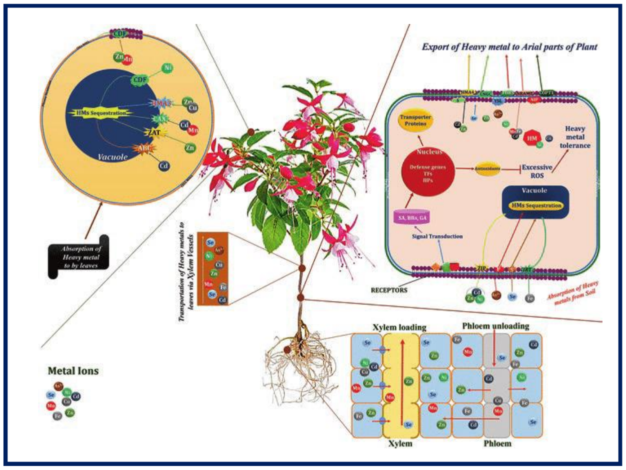

Fig. 13: Illustrates heavy metal uptake and transport in plants through various metal transporters on plasma membrane

The absorption of cadmium by plant roots is usually carried out by transporters and can also absorb other essential elements with chemical properties similar to Cd, such as Fe, Zn, and Mn ions Fig.(14) Morel *et al.,* (2009), Clemens *et al.,* (2013).

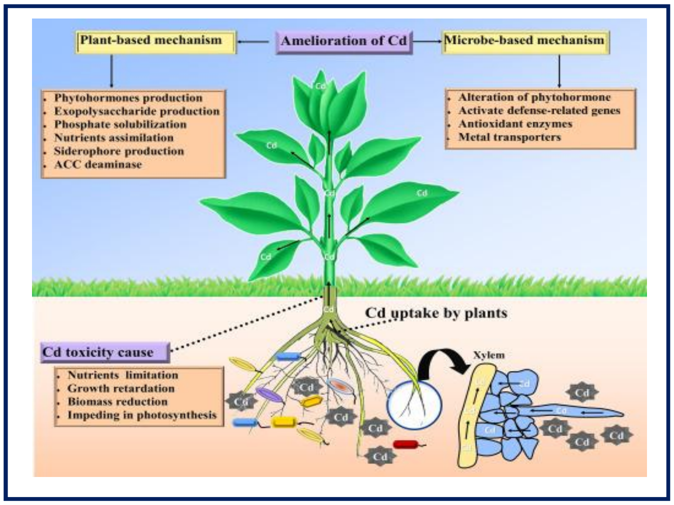

Fig. 14: Illustrates microbe-mitigation of Cadmium Toxicity in Plants. After Shahid *et al.,* (2019)

Shahid *et al.,* (2019) stated that there has been increasing evidence of cadmium (Cd) toxicity and accumulation in various plant parts. Due to its mobile nature, Cd becomes an integral part of the food chain, causing a threat to humans in terms of kidney, liver, and lung diseases. In Cd-prone areas, leaf, stunted growth, and inhibition of photosynthesis are the symptoms displayed by many plants. Microbe-mediated induction of Cd-stress tolerance is associated with various plant-based mechanisms, including alteration of phytohormones levels, modulation of the expression of defense-related proteins, upregulation of antioxidant enzymes, and expression modulation of metal transporters; and microbe-based mechanisms, including production, better nutrient assimilation, production, 1-amino cyclopropane-1-carboxylate (ACC) deaminase activity, production, and so forth. Moreover, the microbes, especially bacteria and fungi, alter the state of toxic metal compounds and trigger the process. Nevertheless, scientists need to explore new mechanisms and microbial signals for Cd-stress alleviation, coupled with increased plant productivity.

In rice (*Oryza sativa*), cadmium is mainly absorbed by OsNRAMP5 (NATURAL RESISTANCEASSOCIATED MACROPHAGE PROTEIN5), which is an important plasma membrane localized transporter for Zn and Cd ions Sasaki *et al.,* (2012). In roots of rice plants, *NRAMP5* is mainly expressed in the root epidermis, the outer layer of the cortex, and the tissues near the xylem Ishikawa *et al.,* (2012) NRAMP5 is the main transporter in rice of Mn and Cd ions Sasaki *et al.,* (2012) Fig.(15). Recent studies have shown that, in the roots of *Sedum alfredii.* Hance, SaZIP4 is responsible for the absorption and transportation of Zn and Cd ions Yang, *et al.,* (2018) OsHMA3 is a tonoplast localized transporter for Zn and Cd ions in the roots of rice (*Oryza sativa*) and limited Cd and Zn in roots and thus Cd and Zn accumulation in aerial parts is low. Overexpression of *OsHMA3* can enhance rice Cd ion tolerance by enhancing vacuolar sequestration of Cd ion in the roots Sasaki *et al.,* (2014) In *A. thaliana*, IRT1 (IRON TRANSPORTER1), has been identified capable of transporting Cd^{2+} in roots. In the absence of iron (the proteins normal substrate) in Arabidopsis IRT1overexpressors, this protein can promote the absorption and accumulation of Cd and Zn ions in the root tissue Vert, *et al.,* (2002), Connolly *et al.,* (2002) IRT1 is involved in Cd^{2+} uptake in root cells Vert *et al.,* (2002), Connolly *et al.,* (2002).

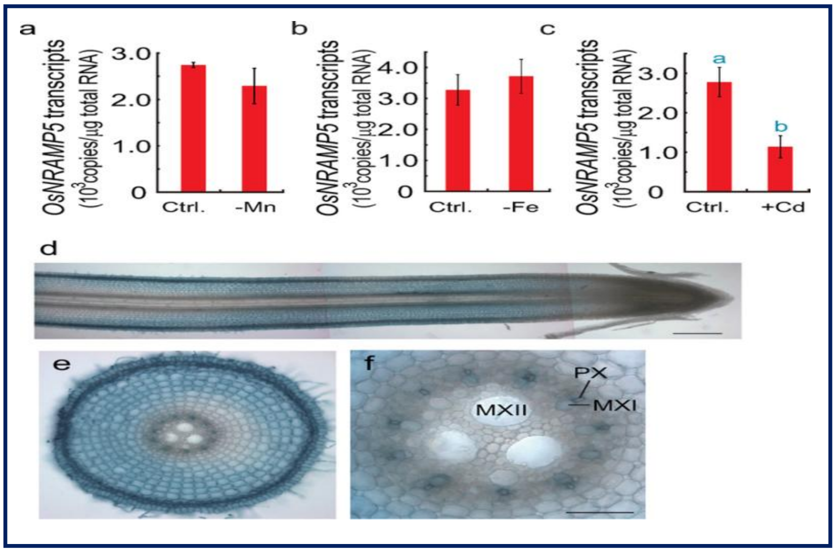

Fig. 15: Illustrates OsNRAMP5 is expressed in rice roots. (a–c) Expression pattern of OsNRAMP5 in rice grown hydroponically under Mn-deficient (-Mn) (a), Fe-deficient conditions (-Fe) (b), and in the presence of 10 µM Cd (+Cd) (c) compared to normal nutrient conditions (Ctrl.). (d–f) OsNRAMP5 promoter GUS analysis in rice roots. Longitudinal section (d). Transverse section (e). Enlargement of part of the stele (f). MXII, metaxylem II; MXI, metaxylem I; PX, protoxylem. Scale bar = 400 µm for (d), and 50 µm for (f). Error bars represent the SD. Columns bars followed by different letters are statistically different according to analysis of variance followed by SNK test (p = 0.0034); n = 3. After Ishimaru *et al.,* (2012)

After Ishimaru *et al.,* (2012), rice plants grown hydroponically in a solution containing 10 mM Cd accumulated less Mn, zinc, and copper in their roots and shoots, while Fe accumulation decreased in the shoots and increased in the roots Fig. (15). Microarray analyses were performed to identify the genes responsible for the changes in metal accumulation. Our results indicate that the ferrous Fe and Cd transporters OsIRT2 and OsNRAMP1, the ferrous Fe- and Mn-NA transporter OsYSL2, and zinc transporter OsZIP3 were induced in the roots of plants exposed to Cd, while OsIRT2, OsZIP2, OsZIP3, OsZIP8, and the ferric Fe-DMA transporter OsYSL15 were induced in the shoots. Among the seven members of the NRAMP family in rice, OsNRAMP140 expression was increased in roots and shoots in the presence of Cd, while OsNRAMP5 (Os07g0257200) expression was decreased in both of these tissues. The root and shoot expression of other OsNRAMP genes did not change significantly. We next characterized OsNRAMP5 to determine its role in Mn, Cd and Fe transport. OsNRAMP5 shares 74.5% homology with OsNRAMP1, and the expression of OsNRAMP5 did not change in response to Mn or Fe deficiency Fig. (15 - a and b), while the expression of OsNRAMP5 decreased in response to the addition of Cd Fig. (15- c). In contrast, OsNRAMP1 expression was upregulated by Mn deficiency in roots and shoots (Supplementary Fig. a and b). In the stele, GUS activity was detected mainly around the xylem (Fig.15 f).

In addition to IRT1, the *NRAMP* (natural resistance-associated macrophage protein) gene family AtNRAMP1, AtNRAMP and AtNRAMP3 all show transport activity to Fe , Mn and Cd ions Curie, *et al.,* (2000), Thomine *et al.,* (2000). Arabidopsis *AtHMA2* and *AtHMA4* (HEAVY METAL ATPase 2 and HEAVY METAL ATPase 4) are mainly responsible for the transfer of Zn and Cd from roots to shoots Hussain *et al.,* (2004) Fig. (16).

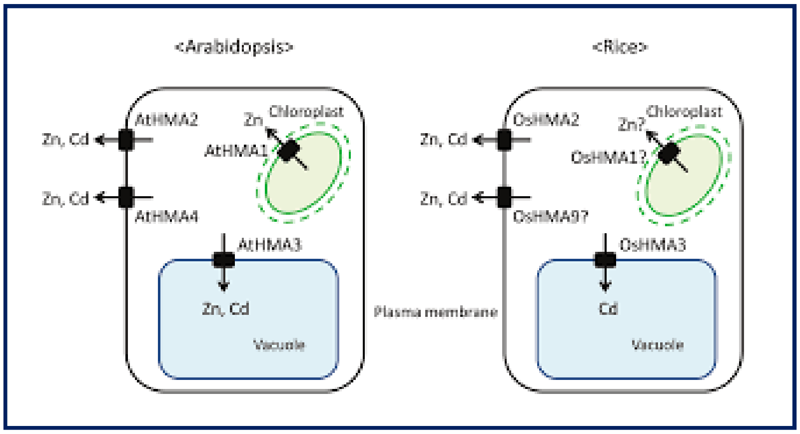

Fig. 16: Predicted subcellular localization and function of HMAs from arabidopsis or rice. AtHMA1 localizes to the chloroplast and exports Zn to the cytoplasm.6 AtHMA2 and AtHMA4 localize to the plasma membrane and transport Zn and Cd out of the cell. Mills *et al.,* (2003), Verret *et al.,* (2005) AtHMA3 localizes to the vacuolar membrane and sequesters Zn and Cd to vacuoles. Gravot, *et al.,* (2004), Morel *et al.,* (2009) OsHMA1 might play a role in Zn efflux from the chloroplast. OsHMA2 localizes to the plasma membrane and transports Zn and Cd out of the cell. Nocito *et al.,* (2011) – Takahashi *et al.,* (2012) OsHMA3 localizes to the vacuolar membrane and sequesters Cd to vacuoles. Ueno *et al.,* (2010), Ueno *et al.,* (2011) - OsHMA9 localizes to the plasma membrane and might transport Zn and Cd. After Takahashi, *et al.,* (2012)

Mutations in or interference with *AtHMA2* or *AtHMA4* greatly reduce the root-to-shoot transport of Cd ions. Wong, *et al.,* (2009), Hermand *et al.,* (2014) and Lekeux, *et al.,* (2015) showed that *HMA4* is mainly expressed in the vascular tissues of roots, leaves, and stems in *Arabidopsis thaliana* Lekeux, *et al.,* (2015) and is responsible for Cd and Zn ions transport from roots to stems. Courbot *et al.,* (2007). Orthologs of *AtHMA2* and *AtHMA4* have already been identified and characterized in rice. OsHMA2 is particularly important for Zn and Cd ions transport to the shoot and for Zn ion distribution to the reproductive tissues Fig. (17). Furthermore, studies have revealed the mechanism of Cadmium uptake via CAL1 (Cd ACCUMULATION In LEAF 1). In this process, CAL1 first binds Cd in the cytoplasm, and then forms a complex that secretes it into the apoplast, especially in xylem parenchyma cells, Luo *et al.,* (2018) which helps load the CAL1–Cd complex into the xylem for transfer to aboveground tissues. Transcriptome sequencing results in rice showed that CAL1 functions in Cd ion detoxification Zhao and Huang, (2018). Most of the Cd ions in leaf tissue is chelated and transported to the extracellular space or to organelles, and a portion of it is detoxified in vacuoles. Cd ions can accumulate in the cellular vacuoles of land plants, which may help protect cells from the toxic effects of Cd ions, Zeng *et al.,* (2010), Ramos *et al.,* (2002).

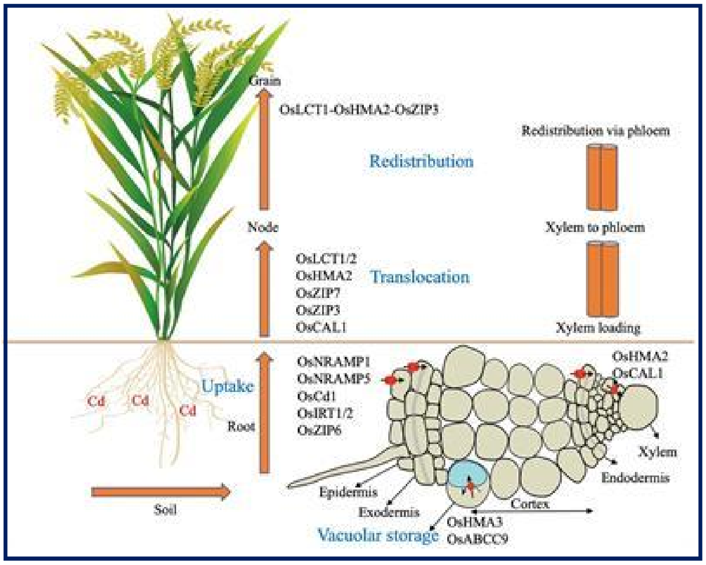

Fig. 17: Illustrates the contribution of genes function in Cd homeostasis. Cd accumulation in plants is first through root absorption, storage in root vacuoles, xylem loading, xylem to phloem transfer and redistribution. Cd is uptake by rice root in soil. OsNramp1, OsNramp5, OsCd1, and OsITR1/2 are suggested to mediate this process. OsHMA3 and OsABCB9 are response for Cd sequestration into vacuoles in root. OsHMA2 and OsCAL1 contributes to the loading process of Cd into xylem in root. OsLCT1/2, OsHMA2, OsZIP3/7 and OsCAL1 are responsible for intravascular Cd transfer at nodes. Co-expression of OsLCT1-OsHMA2-OsZIP3 could reduce the redistribution of Cd in grains. After Ai, *et al.,* (2022)

High concentration of Cd ion can promotes the production of plant chelating peptides, which combine with Cd ion to form a nontoxic chelate that is stored in the vacuole Clemens, (2006). The ability of plants to tolerate Cd^{2+}corresponds with their ability to store Cd^{2+}in vacuoles Ramos *et al.,* (2002).

4. Impacts of cadmium on some physiological functions

4.1. Seed germination and seedling.

Yin *et al.,* (2018), Wang *et al.,* (2018), reported that seed germination is a critical stage in the plant life cycle, different concentrations of cadmium have different effects on plant seed germination Guo *et al.,* (2012), Song *et al.,* (2012), however, not all species respond the same way to different Cadmium concentrations Yan *et al.,* (2019), Xu *et al.,* (2016). In some cases, low concentrations of cadmium may promote seed germination in some plants, whereas, high concentrations of cadmium can inhibit seed germination. In *Caragana korshinskii*, seed germination is promoted at 10 mg.L^{-1} Cd, and gradually inhibited at higher concentrations 100 mg. L^{-1} Yan, *et al.,* (2019). However, in rapeseed (*Brassica napus*), showed low concentrations of cadmium do not have a significant effect.

Lee *et al.,* (2021) reported that *Arabidopsis thaliana* was used as a model system to assess the toxic effects of cadmium on plant development and growth. cadmium (II) inhibited the germination and growth of *A. thaliana*, and the inhibitory effect was dosage-dependent. The significant decrease of germination rates and root growth of *A. thaliana* was observed from 50 mg/L and 25 mg/L of $CdCl_2$. Although both shoot and Cd (II) suppressed root growths, root developments were more sensitive to Cd (II) than shoot developments, as evidenced by shoot growths observed over 50 mg/L of $CdCl_2$. In the concordance to this result, it was also observed that the expression of DR5::VENUS, a visual marker of auxin response, was dependent on the Cd (II) concentration and was strongly reduced from 5 mg/L of $CdCl_2$. In addition, the *E. coli*-based biosensors were employed to quantify accumulated Cd (II) in plants to understand the correlation between toxic effects and Cd (II) in plants. As a result, it was revealed that 0.012 mg/g and 0.138 mg/g of Cd (II) in dried plants were corresponded to the concentration inhibiting root developments and root growths, respectively. Although it needs further investigations, the findings play a significant role in assessing the toxic effects of Cd (II) based on the relationship between the toxic effects and accumulated Cd (II) concentrations in plants Fig. (18).

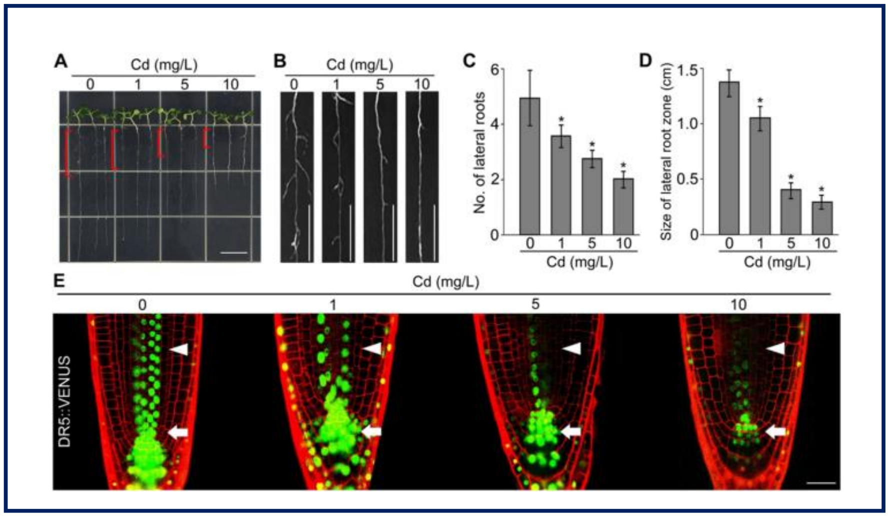

Fig. 18: Illustrates the effect of Cd (II) on lateral root formation. A, B Images showing lateral root formation in the plants grown in the MS solid media with 0, 1, 5, and 10 mg/L of CdCl2 for 2 weeks (A), and their high magnification images (B). Red lines in (A) indicate lateral root forming zones. C, D Quantifications of the number of lateral roots (C) and the size of lateral root forming zone in these plants (D) (n>30). Error bars indicate SD. Asterisks indicate statistically significant differences between the corresponding samples and their control (p value). After Lee, *et al.,* (2021)

Lee *et al.,* (2021) stated that as shown in Fig. (18), lateral root numbers and size of lateral root zone were decreased upon Cd (II) concentration as well as the length of primary roots. This finding led to investigation the level of auxin upon Cd (II) exposure because it is known to regulate root development in plants. The auxin levels in DR5::VENUS plants grown at the same experimental conditions were analyzed, and it clearly decreased at 5 mg.L^{-1} of Cd (II) Fig. (18 - 4E). Compared to control, the localizations and intensity of fluorescence were disrupted and diminished upon Cd (II) exposure. As mentioned above, the adverse effects of Cd (II) on root developments have been intensively studied and the toxic mechanisms had been revealed. Nonetheless, most of studies were focused on the amount of Cd (II) present exterior of plants rather than the amount inside of plants. However, it would be worthy to knowing the correlation between toxic effects and the accumulated Cd (II) in plants. As pointed out, the uptake of heavy metal (loid) is dependent on not only environmental availability but also plant uptake mechanisms. Thus, it is important to quantify accumulated heavy metal (loid), which is the portion causing adverse effects on plants, and to achieve accurate risk assessment. In this regard, we used Cd (II)-specific *E. coli* cell-based bio reporter employing zinc responsive operon (ZnT-operon) reported previously used to analyze the accumulated Cd (II) in Arabidopsis Yoon *et al.,* (2016). As described in “Results” section, the accumulated Cd (II) in plants was proportional to exposed amount of Cd (II), and uptake rates were increased. Additionally, it was noticed that 0.012 mg of Cd (II) per 1 g of dried plants showed the inhibition of root lengths, lateral root formation and size of lateral root forming zone. Although the toxic effects of Cd (II) on plant growth were investigated intensively during past few decades, it had not been revealed the correlation between accumulated Cd (II) and toxic effects. Believing that this study showing the relationship between toxic effects and the amount of accumulated heavy metals would be invaluable to understanding differential toxic effects on different plant species as well as to achieving accurate risk assessments.

Liu, (2016) reported that increasing Cd- concentration inhibits plant growth. At concentration of (1 to 8) mg. Cd L^{-1} has no obvious inhibitory effect on seed germination, high concentration of Cd up to 16 mg. L^{-1} or greater gradually significantly inhibits the germination of tobacco (*Nicotiana tabacum*) seeds Meng *et al.,* (2009). It was noticed that Cd not only affects seed germination, but also affects seedling growth. Cadmium enters the roots of plants, and is transported to the shoots. When cadmium reaches a threshold concentration in plants, it becomes toxic on plant growth and development. Wang and Wang, (2006) reported that, roots are in direct contact with contaminated soil, are most susceptible to poisoning; under cadmium stress, lateral root formation is inhibited and taproots gradually turn brown and decompose. Causing plant chlorosis that delayed both leaf growth, and development Fig. (19).

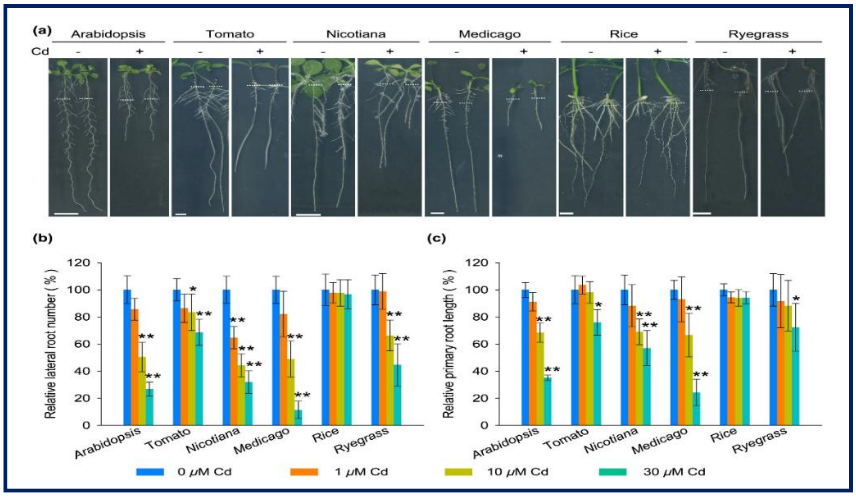

Fig. 19: Illustrates effects of Cd on lateral root formation and primary root elongation in different plant species. (a) Root phenotype of Arabidopsis, tomato, Nicotiana, Medicago, Rice, ryegrass treated under Cd-free or Cd-containing condition. White dashed lines indicate the location of the root tip when the germinated seedlings were transferred to Cd-contained 30 µM or Cd-free agar plates. (b and c) Quantification of relative primary root elongation and lateral root number of different plant species after treated with varying concentrations of Cd for indicated time (see Section 2). Data represent the means ± s.d ($n \geq 10$). Asterisks indicate significant differences compared with Cd-free (*$p < .05$ and **$p < .01$by Student's t test). Cd was used at indicated concentrations. Scale bar, 1 cm. After Xie, *et al.,* (2019)

Xie *et al.,* (2019), reported that A biological clock activated by oscillating signals, known as root clock, has been linked to lateral root (LR) formation and is essential for regular LR spacing along the primary root. However, it remains unclear how this internal mechanism is influenced by environmental factors known to affect the LR pattern. They also report that excessive cadmium (Cd) inhibits LR formation by disrupting the lateral root cap (LRC) -programmed cell death (PCD) -regulated root clock. Cd restricts the frequency of the oscillating signal rather than its amplitude. This could be attributed to the inhibition of meristematic activity by Cd, which resulted in decreased LRC cell number and LRC-PCD frequency Fig. (20). Genetic evidence further showed that LRC cell number is positively correlated with root resistance to Cd.

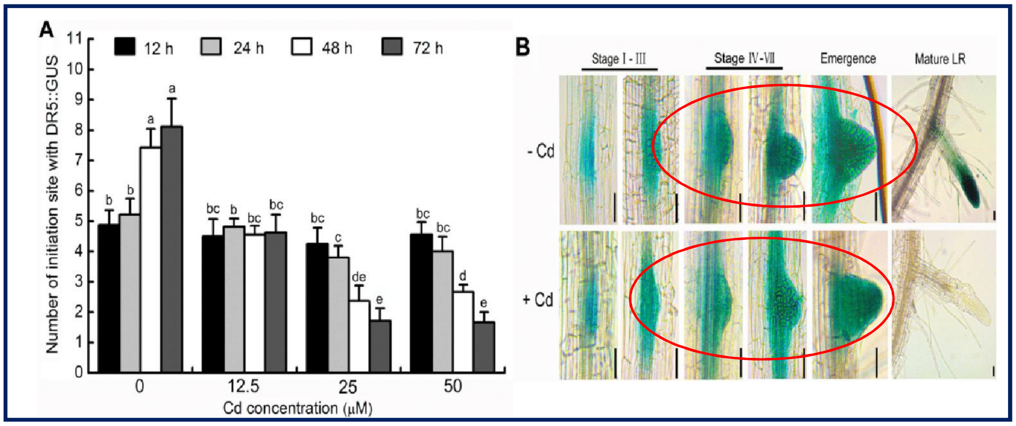

Fig. 20: Illustrates a number of LR initiation sites after 12, 24, 48 and 72 h of Cd treatment. (B) Expression patterns of DR5::GUS in LRP in 5-day-old Arabidopsis DR5::GUS seedlings treated with 50 M Cd for 0, 12, 24 and 48 h. Images shown are representative of each treatment (n = 20). Scale bar = 50 m. Data in A show the mean ± SE (n = 20). The pictures in (B) are representatives of similar results in three independent experiments. Different letters represent significant differences according to Duncan's multiple range tests ($p < 0.05$). After Hu, *et al.,* (2013)

Keller *et al.,* (2005) observed that under cadmium stress, *Nicotiana tabacum* growth was inhibited; symptoms included plant dwarfism, loss of green leaves, leaf detachment, and even death Liu *et al.,* (2015). Moreover, long-term exposure to Cadmium decreases tomato (*Solanum lycopersicum)* yield by reducing the weight and number of fruits Keller *et al.,* (2005), Hediji, *et al.,* (2015).

4.2. Impacts of cadmium on photosynthesis

Many species, such as oilseed rape (*Brassica napus)* Baryla *et al.,* (2001), sunflower (*Helianthus annuus*) Di Cagno *et al.,* (2001), *Thlaspi caerulescens* Kupper *et al.,* (2007), maize, pea and barley Popova *et al.,* (2008), mung bean (*Vigna radiate*) Wahid,*et al.,* (2008), and wheat Moussa and El-Gamal, (2010), showed that photosynthesis was inhibited after both long and short-term Cd exposure. A large number of studies have demonstrated that the primary sites of action of Cd are photosynthetic pigments especially, the biosynthesis of chlorophyll Baszynski *et al.,* (1980) and carotenoids Prasad, (1995). According to Baryla *et al.,* (2001) observed that chlorosis in oilseed rape was not due to a direct interaction of Cd with the chlorophyll biosynthesis pathway and most probably, it was caused by decreasing the density of chloroplast. Cadmium-induced gradually decrements in pigment content and was more powerful at the leaf surface (stomatal guard cells) than it was in the mesophyll. The changing of cell size and reducing stomata density in the epidermis were observed in Cd-treated leaves Fig. (21).

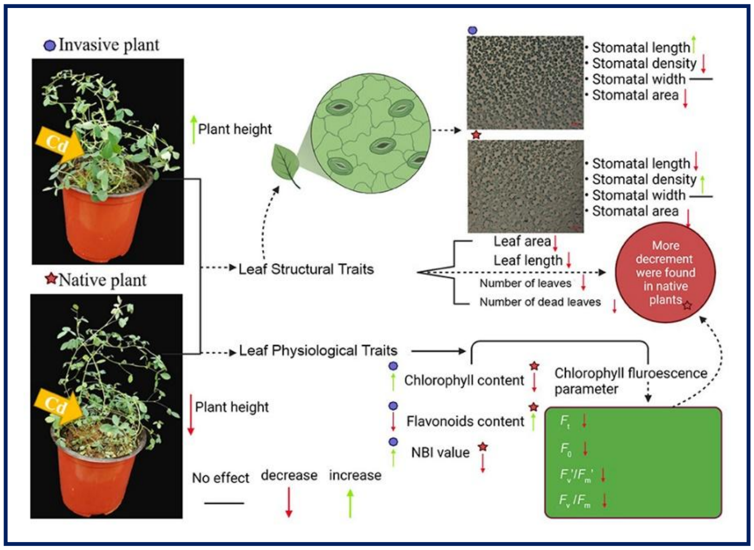

Fig. 21: Illustrates the higher structural and physiological leaf traits in invasive than in native plants. After Ilyas *et al.,* (2022)

Thus, Cd might interfere directly with chloroplast replication and cell division in the leaf. Stomatal conductance was strongly reduced by Cd. Cadmium ions are known to affect the structure and function of chloroplasts in many plant species such as *Triticum aestivum* Atal, *et al.,* (1991), *Beta vulgaris* Greger and Ogren, (1991), *Vigna radiata* Keshan and Mukherji, (1992) *Spinacea oleracea* Sersen and Kral'ova, (2001) and *Phaseolus vulgaris* Padmaja *et al.,* (1990) Fig. (22).

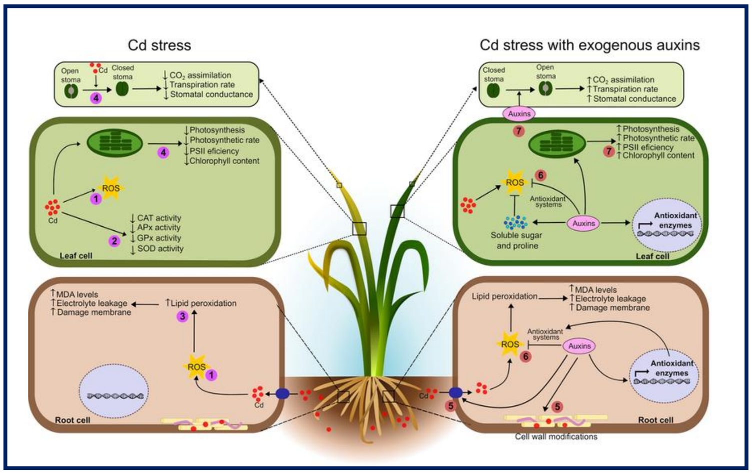

Fig. 22: Illustrates Cd effects in exposed plants and possible mechanisms of auxins to alleviate cadmium stress. In roots exposed to Cd, its entry into the cell increases the generation of ROS (1) and decreases the activity of antioxidant enzymes (2), the ROS produces oxidation of membrane lipids, thereby increasing MDA levels and electrolyte leakage (3). In leaves, Cd decreases photosynthesis by interfering with Chl levels, PSII efficiency, and CO_2 assimilation (4). Regarding auxin application in Cd-exposed plants, auxins regulate the entry of Cd into the cell, either by immobilizing it to the cell wall and/or by reducing its transport to the cytosol (5). In addition, auxins reduce Cd oxidative damage in plant roots by modifying the activity of antioxidant enzymes and the production of compounds including soluble sugars, and proline (6). While in the leaves, auxin application promotes photosynthesis, increases PSII efficiency, Chl content, and stomatal opening (7)

The main target of the influence of cadmium are two key enzymes of CO_2 fixation: such as ribulose-1,5-bisphosphate carboxylase (RuBPCase) and phosphoenolpyruvate carboxylase (PEPCase). Results showed that Cd ions lower the activity of RuBPCase and damage its structure by substituting for Mg ions, which are important cofactors of carboxylation reactions and Cd can shift RuBPCase activity towards oxygenation reactions Siedlecka *et al.,* (1998). Stiborova, (1988) and Malik *et al.,* (1992) reported that cadmium caused an irreversible dissociation of the large and small subunits of RuBPCase, thus leading to total inhibition of the enzyme. Furthermore, Clijsters and Assche, (1985) reported that negative effects of cadmium on the photosynthetic carboxylation, reactions PSII electron transport and especially oxygen evolving complex were found to be very sensitive. The mechanism of cadmium inhibition due to that the water-oxidizing complex (OEC) of PS2 is affected by Cd by replacing the Cd ion in Ca / Mn clusters constituting the oxygen-evolving centres Sigfridsson, *et al.,* (2004), or modifications in the Qb-binding site Geiken *et al.,* (1998) .

In addition cadmium produces alterations in the functionality of membranes by inducing changes in their lipid and fatty acid composition Ouariti *et al.,* (1997); Popova, *et al.,* (2009).

Cadmium disturbs homeostasis of several essential metal ions, especially of Fe. Causing and inducing a moderate to strong deficiency of Fe in leaves plant. Fodor *et al.,* (1996&2005) stated that cadmium has been shown to inhibit Fe uptake even in the presence of chelating agents. Iron deficiency, induced or accompanied by cadmium, significantly altered the photosynthetic apparatus in cucumber Fodor *et al.,* (1996) and poplar Solti *et al.,* (2008) plants. The presence of Fe lowers the damaging impact of cadmium stress. This protection might stem from the competition of Fe with Cd for intake and availability of sufficient amount of Fe for assemblage of Fe-S clusters Qureshi *et al.,* (2010). Roth, *et al.,* (2006) reported that adequate amount of Fe tends to diminish cadmium impacts on photosynthesis and reduces Cd accumulation in leaves. Iron supply during cadmium exposure helps plants to minimize the cadmium -stress symptoms. However, a high concentration of cadmium causes a devastating and nonspecific destruction of all multiprotein complexes (MPC) subunits related to all four photosynthetic complexes, despite the presence of Fe. This nonspecific damage to photosystems and other MPCs is ascribed to ROS production at large, recorded during Fe sufficiency, Fe deficiency, and Cd treatments Qureshi *et al.,* (2010). The over-production of ROS destroys most proteins at random and forces the cell to strengthen its tolerance mechanisms at the cost of growth Bashir, *et al.,* (2013). Eventually, the cell slips into early irreversible senescence Pietrini *et al.,* (2003), as it was observed in the Cd-treated Arabidopsis Sarry *et al.,* (2006), spinach Timperio *et al.,* (2007), Indian mustard Qureshi *et al.* (2010), and sugar beet Basa *et al.,* (2014). In the absence of Fe, Cd caused a strong damage to the entire photosynthetic apparatus and only a small amount of antenna proteins and some ATPase subunits were retained Qureshi, *et al.,* (2010). One of the possible reasons of stress aggravation might be the reduced amount of xanthophylls, a well-known antioxidant Timperio *et al.,* (2007). Changes in the monomertrimer equilibrium of major PSII antenna suggest that Fe deficiency also decreases the content of violaxanthin, which represents the first adaptive adjustment to Fe deficiency and has a role in light-dissipation mechanisms. When violaxanthin starts to recover, a de novo formation of Lhcb and Lhca takes place Timperio *et al.,* (2007). Therefore, both the level of ROS produced by Fe deficiency or due to Cd stress goes beyond the quenching capacity of xanthophyll pigments due to their relatively low content and the ROS start to attack all proteins of MPC complexes of photosynthetic apparatus. Exceptionally, proteins that are the most abundant and hydrophobic in nature might survive this devastating attack of ROS Qureshi *et al.,* (2010). It has been suggested that Cd stress induces Fe deficiency in leaves, which strongly affects photosynthesis Siedlecka and Krupa, (1999), Larabi *et al.,* (2002), Qureshi *et al.,* (2010), Basa *et al.,* (2014) Fig. (23) & (24)

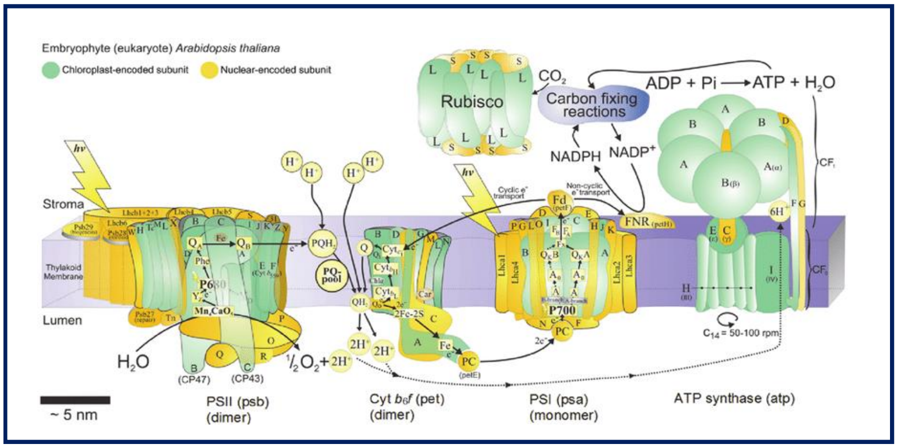

Fig. 23: Illustrates a major proteins and protein complexes of the chloroplast of Arabidopsis thaliana. Photosystem II (PSII); cytochrome b6f (Cyt b6f); photosystem I (PSI); ATP synthase; and Rubisco. Subunits are given single-letter names, omitting the three-letter prefix that denotes the complex of which each forms a part: psa – photosystem I; psb – photosystem II; pet (photosynthetic electron transport) – cytochrome b6f complex and secondary electron carriers; atp – ATP synthase; and rbc – Rubisco. Polypeptide subunits encoded in the chloroplast are marked in green, while those in the nucleus are shown in yellow. After Allen, *et al.,* (2011), Bashir *et al.,* (2015).

During the period of cadmium exposure, losses to thylakoid MPCs and photosynthetic activity are closely related to availability of Fe Sárvári *et al.,* (1999), Shao *et al.,* (2006), Solti *et al.,* (2008), Qureshi *et al.,* (2010), López-Millán *et al.,* (2013) and Basa *et al.,* (2014). Cadmium severely impairs Fe supply in leaves, inhibiting enzymatic steps in Chl biosynthesis Larbi, *et al.,* (2002), (2006), including the production and function of Chl a oxygenase Tanaka *et al.,* (1998). Complexes containing PSI and LHCII during both cadmium treatment and Fe deficiency are more prone to damage Andaluz, *et al.,* (2006), Timperio *et al.,* (2007), and Basa *et al.,* (2014). PSI and LHCII, being the most abundant thylakoid complexes, are strongly influenced by the decrease in leaf Chl. In addition, PSI complexes contain a high amount of Fe in the form of Fe-S centres (12 Fe per PSI unit), which are structurally important for stabilization of the complexes Amann *et al.,* (2004). A decrease for LHCs may be due to Fe deficiency-induced loss of stabilizing Chls Hoober *et al.,* (2007), suppressed expression of lhc genes Tziveleka, *et al.,* (1999), Fusco, *et al.,* (2005), and/or acclimation tendency towards a decreased antenna size Timperio *et al.,* (2007), Laganowsky *et al.,* (2009).

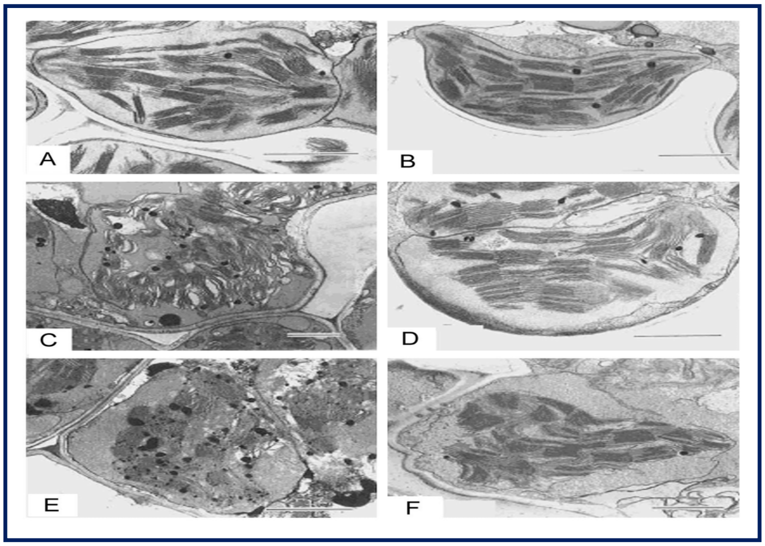

Fig. 24: Illustrates ultrastructure of a chloroplast in the cells of control plants (A), plants treated with 500 µM SA alone (B), plants treated with Cd (C-400 µM, D-1000 µM), plants treated with Cd (E-400 µM, F-for 1000 µM) after pretreatment with SA (500 µM). After Moussa and. El-Gamal, (2010)

PSI super complexes are likely to represent NAD (P)H dehydrogenase-PSI(NDH-PSI) super complexes participating in cyclic electron flow Peng *et al.,* (2008), Xu *et al.,* (2014). Thus, the higher proportion of PSI super complexes under Cd-induced Fe deficiency may be a sign of a higher contribution of cyclic electron flow to the excess light-energy-quenching processes Basa *et al.,* (2014). In the case of extremely Fe-deficient thylakoids, an increase in a proportion of the membrane-bound FNR was noticed Benz *et al.,* (2010) together with an increased abundance of ATP synthase and a higher stability of Cyt b6f dimers Basa *et al.,* (2014). Iron deficiency enhanced the amount of Lhcb1 and Lhcb2 proteins of spinach leaves Timperio *et al.,* (2007) besides causing posttranslational modifications of PsaH2 protein, which is involved in the binding of Lhcb proteins to PSI in Arabidopsis Laganowsky *et al.,* (2009) contributing to the light-harvesting efficiency of PSI participating in the cyclic flow of electrons. Basa *et al.,* (2014) did not find a higher proportion of PSI super complexes or an increased abundance of membrane-bound FNR, ATP synthase, and higher stability of Cyt b6f dimers in thylakoids of Cd treated plants, which suggests that cyclic electron flow is not relevant as a protective mechanism under Cd stress. These authors correlated PSII organizational changes to Cd-induced Fe deficiency. However, PSII super complexes, differing for trimer and/or being in different oligomerization state, were the most sensitive to both Cd treatment and extreme Fe deficiency. This may be related to high sensitivity of Lhcb4 and Lhcb6 to the Fe deficiency Timperio *et al.,* (2007), since these connecting antennae are essential for the formation of super- and mega-complexes Dekker and Boekema, (2005). An in vivo study has demonstrated that Fe deficiency causes monomerization of PSI trimer and reduces the capacity for state transitions Ivanov *et al.,* (2006). Ivanov *et al.,* (2007) showed that induction of CP43 during Fe deficiency is accompanied by a significant increase in the relative abundance of all carotenoids. The amount of CP43-less PSII core, considered as intermediate in the PSII regeneration cycle is usually less reduced than that of the other PSII forms due to slow regeneration of PSII Geiken *et al.,* (1998). In moderately Fe-deficient thylakoids, however, the abundance of CP43-less PSII core is greater than in other PSII forms. An increase for components, suggesting a higher rate of PSII repair, was also observed in Brassica juncea (Indian mustard), which is a hyperaccumulator under both Fe deficiency and Cd treatment Qureshi *et al.,* (2010). Therefore, plants grown even under moderate concentrations of Fe may have enough opportunity for repairing the damaged PSII, which is not otherwise possible under strong Fe deprivation or Cd stress. The most obvious change in the organization of complexes, i.e., increased Lhc monomer to trimer ratio in the thylakoids from stressed plants Basa *et al.,* (2014), was shown earlier in Cd-treated Indian mustard Qureshi *et al.,* (2010) and Fe-deficient sugar beet and spinach Andaluz *et al.,* (2006), Timperio *et al.,* (2007). It has been demonstrated that light energy can be quenched more easily when absorbed by the monomeric Lhcs than by the trimeric form Garab *et al.,* (2002); this might be due to changed Lhcb isoforms, hence influencing the organization of both PSII super complexes Damkjær *et al.,* (2009) and LHCII Caffarri, *et al.,* (2005). Transcriptome data of Fe-deficient barley plants showed that expression of two of the lhcb1 genes was upregulated with a concomitant increase of monomeric Lhcb1 proteins Saito, *et al.,* (2010). Distinct changes in Lhcbs were found in some other species, thus suggesting that acclimation may be species-specific Andaluz *et al.,* (2006), Timperio *et al.,* (2007), and Laganowsky *et al.,* (2009). It is hypothesized that the organizational changes in the LHC antennae in sugar beet under both Cd stress and Fe deficiency could cause reduction in the proportion of absorbed energy reaching the reaction centre, thus limiting the degradation of photosynthetic components caused by photo inhibitory processes. Carotenoid content and composition also contribute to the protection of photosynthetic apparatus against excess light, particularly in severely Fe-deficient plants, where high amounts of zeaxanthin accumulate in the thylakoids Morales *et al.,* (1990), Quílez *et al.,* (1992). In the Chl b and xanthophyll biosynthesis mutants, xanthophylls were either bound loosely to the complexes or occurred as free pigments Dall'Osto *et al.,* (2010). The dynamics among the various biochemical, molecular, and proteomic players ultimately

Photosynthesis is essential for the survival of all green plants Hussain and Ashraf, (2017), Gu, *et al.,* (2020). Li and Yu, (2018), Janeczko *et al.,* (2005) reported that this process includes absorption, transmission, and transformation of light energy and carbon dioxide (CO_2) fixation, which mainly occurs in the chloroplasts of leaves. Gu *et al.,* (2020) stated that because of affecting the morphology of chloroplasts, chlorophyll biosynthesis, and enzyme activity, Cd stress has dramatic effects on photosynthesis. Under Cd stress, the number and size of chloroplasts were significantly reduced and the ultrastructure of chloroplasts was distorted. Cadmium stress also alters thylakoid shape, resulting in thylakoid swelling Ying *et al.,* (2010), increased starch granule content, and plastid accumulation in the leaves. These symptoms have been observed in multiple species, including tartary buckwheat (*Fagopyrum tataricu*), barley (*Hordeum vulgare*), and brassica (*Brassica campestris*) I V S and Ivanov, (2001), Krantev *et al.,* (2008). As observed for seed germination, different Cd concentrations cause various degrees of damage to chloroplasts. In, *Zea mays* treated with a low Cd concentration 5 mg. Cd L^{-1} had sparse grana lamellae and reduced layers of grana lamellae in chloroplast. However, at high concentrations (50 mg.L^{-1} Cd), the chloroplasts membrane system began to collapse, the chloroplasts contracted and a large number of vesicles appeared. Indicating that Cd destroys the structure of chloroplasts and impairs chloroplast function Krantev *et al.,* (2008). Cadmium also affects the levels of chlorophyll in plants Wang *et al.,* (2013). The chlorophyll content in maize plants was reduced by around 20% and 50% when treated with 2 and 5 mg.L^{-1} Cd respectively Somashekaraiah *et al.,* (1992). On one hand, a cadmium-induced reduction of chlorophyll content is a result of competitive inhibition of the absorption of Cu, Mn, Fe and Zn ions, which are essential for chlorophyll biosynthesis. Barcelo and Poschenrieder, (1990) stated that, the dysfunction of the enzyme protein involved in chlorophyll synthesis induced by cadmium ion stress is a mechanism responses for decreasing the chlorophyll content. Under cadmium stress, Cd ions can enter mesophyll cells through channel proteins (e.g., Fe^{2+} and Zn^{2+} channel proteins), inhibiting the absorption of other ions Melis, (2009), Somashekaraiah, *et al.,* (2010) point out, Cd in the cells interacts with sulfhydryl-rich regions of enzymes involved in chlorophyll biosynthesis, causing conformational changes and inhibiting enzyme activity reported by Neelima *et al.,* (1993). Furthermore, Cd inhibits photosynthesis by inducing stomatal closure. In response to Cd stress, plants close their stomata, thereby reducing the transpirational pull from the roots, and hence reducing the degree of Cd poisoning. Baszynski *et al.,* (1980) stated that decreasing in stomatal conductance could indirectly affect the photosynthesis. Exposure of Cd significantly reduces the stomatal conductance of cucumber (Cucumis sativus) cotyledons, resulting in decreasing in CO_2 fixation pointed out by Li and Yu, (2018), Janeczko *et al.,* (2005). Popova *et al.,* (2009) reported that in early studies indicated that cadmium can inhibit the oxidizing side of photosystem Ⅱ(PS Ⅱ) and lead to uncoupling of electron transport in the chloroplasts . Muhammad *et al.,* (2021) reported that photosynthesis sustains plant life on earth and is indispensable for plant growth and development. Factors such as unfavorable environmental conditions, stress regulatory networks, and plant biochemical processes limit the photosynthetic efficiency of plants and thereby threaten food security worldwide. Although numerous physiological approaches have been used to assess the performance of key photosynthetic components and their stress responses, though, these approaches are not extensive enough and do not favor strategic improvement of photosynthesis under abiotic stresses. The decline in photosynthetic capacity of plants due to these stresses is directly associated with reduction in yield. Therefore, a detailed information of the plant responses and better understanding of the photosynthetic machinery could help in developing new crop plants with higher yield even under stressed environments. They also reported that soil contamination with heavy metals such as cadmium (Cd), copper (Cu), zinc (Zn), nickel (Ni), cobalt (Co), chromium (Cr), lead (Pb), and arsenic (As) is generally caused by the application of phosphate-rich fertilizers, sewage sludge, industrial waste, wind-blown dust, incinerator emissions, traffic, volcanoes, and hard water practices Bagur *et al.,* (2009); Ghori *et al.,* (2019). Heavy metal pollution considerably inhibits plant growth by causing Chl degradation, DNA and protein damage as well as enzymatic inhibition Fig. (25).

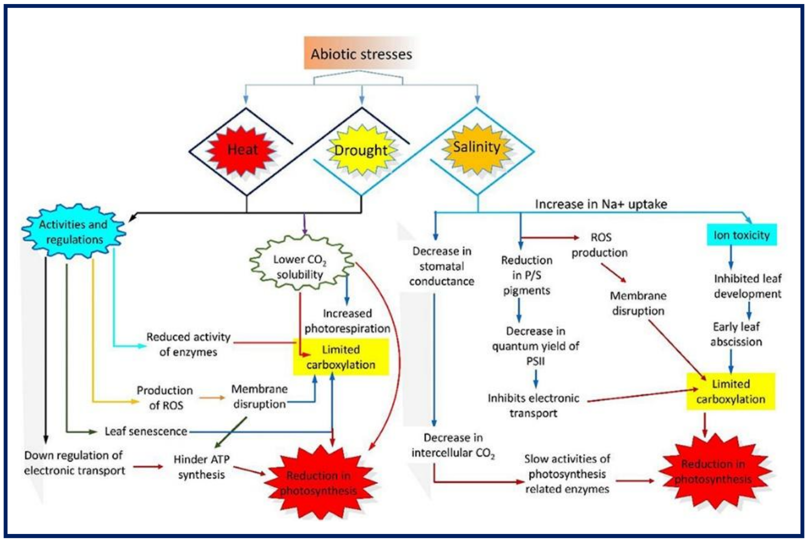

Fig. 25: Schematic representation of the photosynthesis performance under abiotic stresses (heat, drought, and salinity). Drought and heat stress down-regulate enzymatic activity and electron transport chain (ETC) and cause membrane rupture, low CO_2 solubility, leaf senescence, and reactive oxygen species (ROS) production. On the other hand, salinity causes ion toxicity, membrane disruption, reduced stomatal conductance, lower quantum yield of PSII, slow electron transport, and reduced activity of photosynthesis related enzymes. After Muhammad, *et al.,* (2021)

Metal ion toxicity causes DNA damage and/or impairs DNA repair mechanisms, disrupts membrane functional integrity, affects enzymatic activity, and perturbs protein function Tamás, *et al.,* (2014), Fig. (26)

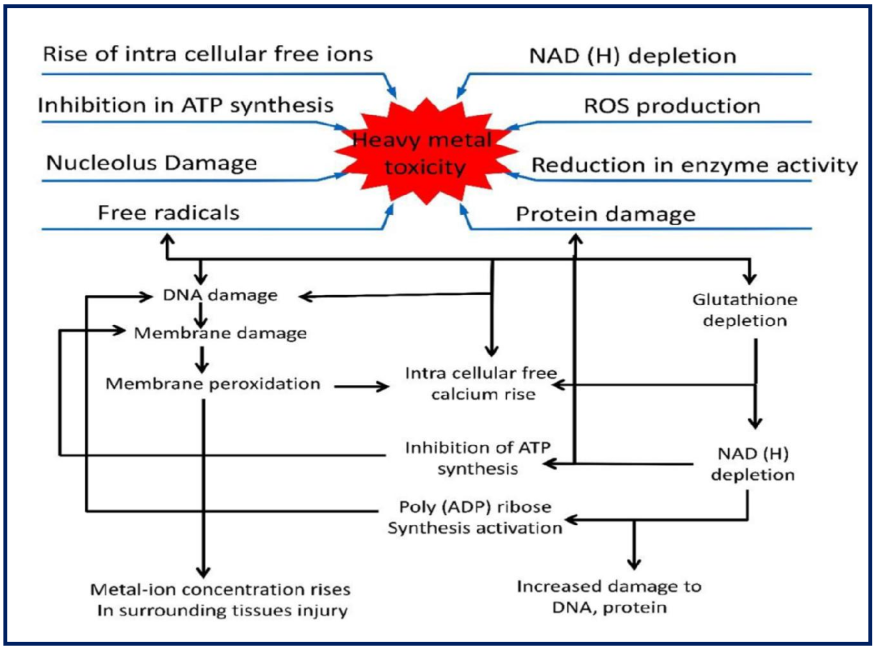

Fig. 26: Diagram showing the general and specific effects of heavy metals on plants. Heavy metals affect ROS production, inhibit ATP synthesis and damage DNA and proteins. The damage to DNA and proteins is shown separately. Free radicals damage DNA and cause membrane peroxidation when metal ions surround the site of tissue injury, causing ATP inhibition, and NADH depletion. After Muhammad *et al.,* (2021)

Light harvesting complex II (LHCII) is the basic pigment protein complex of PSII, which harvests light energy and converts it into chemical energy. This protein complex plays a protective role by dissipating excess light energy and efficiently channelize excitation energy Barros *et al.,* (2009). Cd stress affects the LHCII Parmar *et al.,* (2013). In rye (Secale cereale), cadmium stress reduced the dissipation of excitation energy, indicating that Cd stress either altered the quenching center (QC) or interfered with energy transfer between proteins and pigments Janik *et al.,* (2010). Ahmed and Tajmir-Riahi, (1993) confirmed changes in LHCII by Pb, where imperfect assembly of its components triggered disintegration Ahmed and Tajmir–Riahi, (1993). Plants grown in metal contaminated soils exhibit leaf chlorosis due to the reduced chloroplast size Shahzad *et al.,* (2016& 2017). When coupled with other environmental stresses, heavy metal pollution causes more severe damage Srivastava *et al.,* (2012); Kumar *et al.,* (2019); Sharma *et al.,* (2020). Abiotic stresses like heavy metals induce excessive accumulation of ROS and cause oxidative stress in plants Li *et al.,* (2016). Interestingly, metallothioneins (MTs) have been proposed an alternative tool by which plants protect themselves from stress-induced oxidative damage Yu *et al.,* (2019). Hassinen *et al.,* (2011) reported the role of MTs in abiotic stress tolerance as ROS scavengers, though the mechanisms through which MTs mediate ROS homeostasis remain unclear Hassinen, *et al.,* (2011). Moreover, heavy metal stress considerably alters the biological, biochemical and metabolic processes of plants Anjum, *et al.,* (2015), (2016 a, b, c), Handa *et al.,* (2018); Shahzad *et al.,* (2018a); Khanna *et al.,* (2019) and Kohli *et al.,* (2020). Rascio and Navari-Izzo, (2011); Guo *et al.,* (2016&2017 b) reported that alteration at the cellular and molecular levels causes severe damage thus, blocking the functional group and active site of enzymes, thereby disrupting membrane stability and transcriptional regulation Fig.(27)

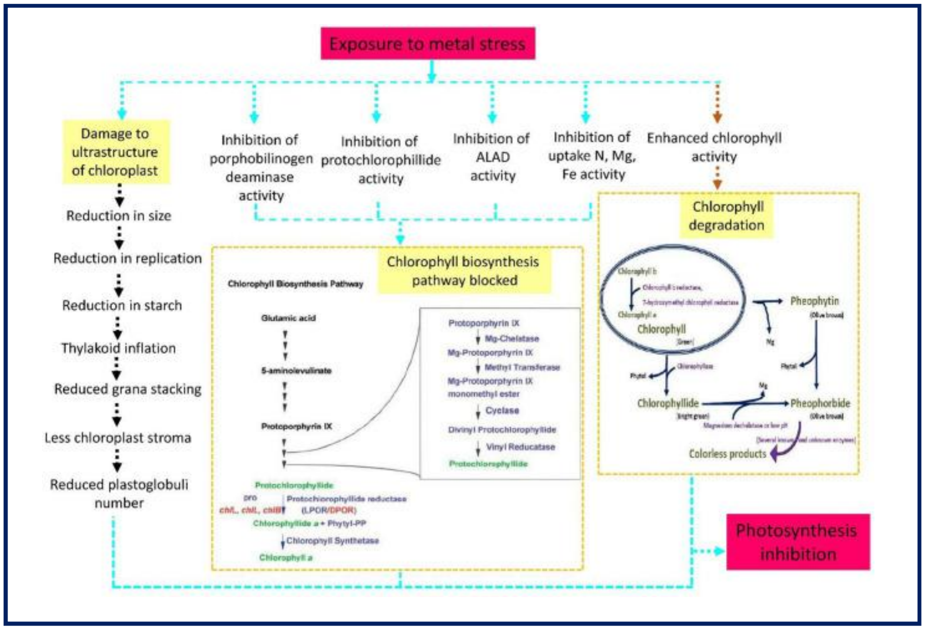

Fig. 27: Heavy metal stress damages the chloroplast structure and chlorophyll (Chl) biosynthesis and degradation processes during photosynthesis. Toxicity due to metal ions gradually affects enzymatic activity and inhibits Chl components and the uptake of essential elements, finally blocking the Chl biosynthesis pathway. The blue arrow depicts this process in a step-by-step manner. After Muhammad *et al.,* (2021)

Cadmium, a potent inhibitor of photosynthesis, alters the chloroplast shape, decreases chloroplast size, destroys Chl, reduces starch accumulation and expands the thylakoids Najeeb *et al.,* (2011); Parmar *et al.,* (2013); Kapoor *et al.,* (2019). Other metals such as Cr decrease the absorption of magnesium (Mg) and nitrogen (N), consequently, reducing the Chl content Singh *et al.,* (2013). Pb toxicity accelerates Chl degradation by increasing the activity of chlorophyllase Drazkiewicz, (1994). High levels of Ni affect the photosynthetic apparatus and inhibit the synthesis of pigments Soares, *et al.,* (2016a), (2019); Shahzad *et al.,* (2018 a,b). Additionally, Ni stress alters the composition of lipid membrane and disturb the activity of chlorophyll molecule and Rubisco (ribulose-1,5-bisphosphate carboxylase oxygenase) Kohli *et al.,* (2020). Early studies established that the photosynthetic apparatus, Chl and carotenoid concentrations and plant growth were greatly decreased under Ni and UV-B combination stress. It is possible that Ni, which destroys Chl and damages thylakoid membranes in cabbage leaves, replaces Mg in Chl and wheat shoots, respectively Molas, (2002); Gajewska *et al.,* (2006). Similarly, the combined effect of heavy metals and drought stress can cause deleterious effects on Chl content in red maple and affect the xylem structure and hydraulic conductivity De Silva, *et al.,* (2012). Transition metals (Cu, Zn, (Mn), and (Fe) play critical roles in physiological processes of all living organisms, such as Cu is essential for respiration, photosynthesis, cell wall integrity, ethylene perception, and ROS metabolism in plants Burkhead *et al.,* (2009). Excess amounts of transition metals lead of Chl degradation by Chl-degrading enzymes, thereby increasing the sensitivity of PSII to light Pätsikkä *et al.,* (2002). Cu, Hg, Ni, Zn, and aluminum (Al) metal ions interact with three extrinsic polypeptides, situated in the lumen of the thylakoid membrane, additionally, intrinsic proteins (inner antenna protein), are released from the PSII reaction center under Cu toxicity Sigfridsson *et al.,* (2004); Boisvert *et al.,* (2007). At optimum concentrations, Zn plays an important role in plant growth; however, excess Zn significantly reduces the synthesis of photosynthetic pigments and negatively affects photosynthesis Paunov *et al.,* (2018). Zn and Cd stresses exert a synergistic effect by increasing the oxidative stress and restoring the Chl content Cherif *et al.,* (2011). Therefore, we speculate that transition metals in combination may reduce or restore the damage caused to the photosynthetic machinery for a short period under specific conditions. Comparative analysis of Cd and Zn stresses in tobacco (*Nicotiana benthamiana*) leaves revealed that under Cd stress, key enzymes involved in Chl biosynthesis were significantly down-regulated, decreasing the Chl content, expression of PSII (donor, receptor and core side) proteins and photosynthesis Zhang *et al.,* (2020). Several studies have reported the harmful effects of Cd and Zn on photosynthesis, thylakoid membrane ultra-structure, photosynthetic pigments, Chl fluorescence, electron transport, light capture, dark respiration, stomatal conductance, and Calvin cycle enzymes Krupa (1999); Vassilev *et al.,* (2011); Paunov *et al.,* (2018). Furthermore, both metals considerably reduce the activity of PSII and to some extent that of PSI as well as the rate of photosynthetic electron transport Krupa, (1999); Vassilev *et al.,* (2004).

It is generally accepted that Cd ion replaces Mn^{2+} in PSⅡ, thereby inhibiting the reactions occurring there Li and Yu, (2018). The negative effects of Cd^{+2} can also be observed in dark reaction stage of photosynthesis. Two key of CO_2 fixation enzymes are affected by Cd: ribulose 1,5-bisphosphate carboxylase (RuBPC) and phosphoenol pyruvate carboxylase (PEPC) Chen, *et al.,* (2012). Cd reduces RuBPC activity and damages its structure by replacing Mg^{+2}. Furthermore, Cd causes irreversible dissociation of the large and small subunits of RuBPC, thus leading to total inhibition of the enzyme. Krantev *et al.,* (2008) showed that in maize seedlings, PEPC activity decreased significantly when treated with 5 mg.L^{-1} Cd, however, RuBPC activity showed that a strong decrease at all Cd concentrations (higher than mg.L^{-1} Cd) has been observed Somashekaraiah, *et al.,* (1992).

4.3. Impacts of cadmium on the antioxidant system of plants

Several researchers Guo, *et al.,* (2015), Mzoughi, *et al.,* (2019), have shown that when plants stressed by heavy metals, the associated excessive production of reactive oxygen species (ROS) causes serious damage. In order to abate the oxidative damage initiated by heavy metals, plants usually activate antioxidant defenses and alter cellular metabolism to maintain cellular redox homeostasis Gotoh, et al.(2018), Pang and Wang, (2011), Hengliang, *et al.,* (2019). Despite the plants' stress responses, when exposed to Cd the ROS content in plants will increase, thereby disrupting the normal metabolic balance. ROS bind to proteins, lipids, and DNA, causing reduced enzyme activity, enhanced membrane permeability, and mutations, respectively Han, *et al.,* (2018), Chen *et al.,* (2012). Cadmium -tolerant plants have powerful and effective antioxidant defense systems are activated in response to cadmium stress. Jithesh *et al.,* (2006), Tzang *et al.,* (2017), stated that antioxidant response system (ARS) in plants consists of an enzymatic and a non-enzymatic reaction system Fig. (28).

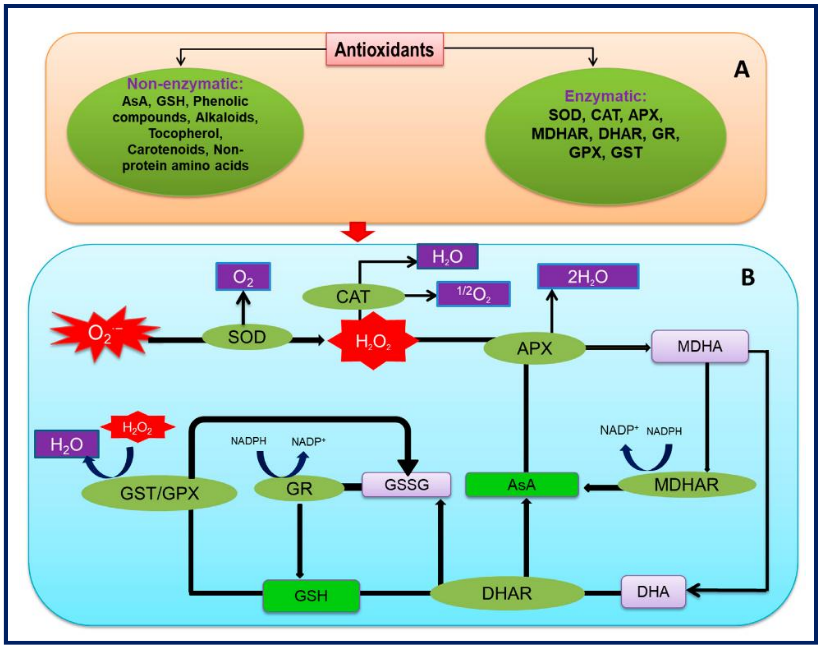

Fig. 28: Outline of antioxidant defense mechanisms in plants; (**A**) types of antioxidants and (**B**) mechanism of antioxidant enzymes and low molecular weight antioxidants to detoxify ROS. After Hasanuzzaman *et al.,* (2020)

Hasanuzzaman *et al.* (2020) stated that metals/metalloids toxicity interrupts not only morpho-physiological traits but also causes enhanced oxidative stress resulting from lack of balance between antioxidant defense system and ROS production Nahar *et al.,* (2016), Mahmud *et al.,* (2018). El-Amier, *et al.,* (2019) reported increased levels of LPO and H_2O_2 accumulation in Ni (100 µM) stressed *Pisum sativum* L. seedlings. Such increments of oxidative stress indicators were even higher in the same crop with the same concentration of cadmium as well. Meanwhile, cadmium stress raised the MDA and H_2O_2 production in different crops including *V. radiata* L. Nahar, et al.(2016), *B. napus* L. Hasanuzzaman *et al.,* (2017), B. juncea L. Mahmud *et al.,* (2018), *A. thaliana* Gupta, *et al.,* (2017), and *Cucumis sativus* Kabała *et al.,* (2019) under different levels of stress. Apart from MDA and H_2O_2, the rate of $O_2^{-\bullet}$ production was also higher in *V. radiata* L. Nahar *et al.,* (2016). Another study demonstrated the oxidative damages under Pb stress conditions in wheat plants Hasanuzzaman *et al.,* (2018). Nahar *et al.,* (2017) reported higher levels of H_2O_2 , $O_2^{-\bullet}$, and MDA contents, and LOX activity by 83, 110, 97 and 72%, respectively, in *V. radiata* L. cv. BARI Mung-2 when exposed to Al stress (0.5 µM) for 48 h. *B. juncea* seedlings exposed to Cr stress (0.15 and 0.3 µM, 5 d) exhibited higher TBARS and H_2O_2 contents as well as LOX than that of the control plants Mahmud, *et al.,* (2018). Thus, it is clear that metals/metalloids toxicity increased oxidative stress as depicted by oxidative stress markers such as MDA and H_2O_2. Huang *et al.,* (2004) reported that non-enzymatic system mainly consisted of glutathione, ascorbic acid, and flavonoids. However, key components of the enzymatic arm of the ARS include SOD, catalase (CAT), ascorbate peroxidase (APX), glutathione peroxidase (GPOX), and glutathione Transferase (GST) and monodeoxyascorbic acid reductase (MDAR). Among these antioxidant enzymes, SOD, CAT, and GPOX are involved in the detoxification of $O_2^{-\bullet}$ and H_2O_2 and inhibition of the formation of OH – radicals. Nevertheless, the enzymatic and non-enzymatic components of the ARS are not completely isolated; for example, APX, GR, glutathione, and ascorbic acid are important components of the ascorbate–glutathione cycle, which is responsible for removal of H_2O_2 in different cellular compartments. Malondialdehyde (MDA) content is often used to indicate the degree of oxidative damage Chaoui *et al.,* (1997), Meng *et al.,* (2015) since ROS can produce MDA. The MDA content of Cd-treated maize plants is higher than that of the control. Similar data have been reported for many plant species, including soybeans, Gallego *et al.,* (1996) pea, Pal *et al.,* (2005) *Helianthus annuus*, Cobbett, (2000) and maize Ogawa *et al.,* (2011). Under cadmium stress, SOD activity increased in maize at all cadmium concentrations tested, peaking at mg.L^{-1} Cd. In contrast to SOD, APX activity was suppressed by all cadmium concentrations tested. When maize plants were exposed to mg.L^{-1} Cd, APX activity decreased by more than 2-fold compared to the control Fig (29).

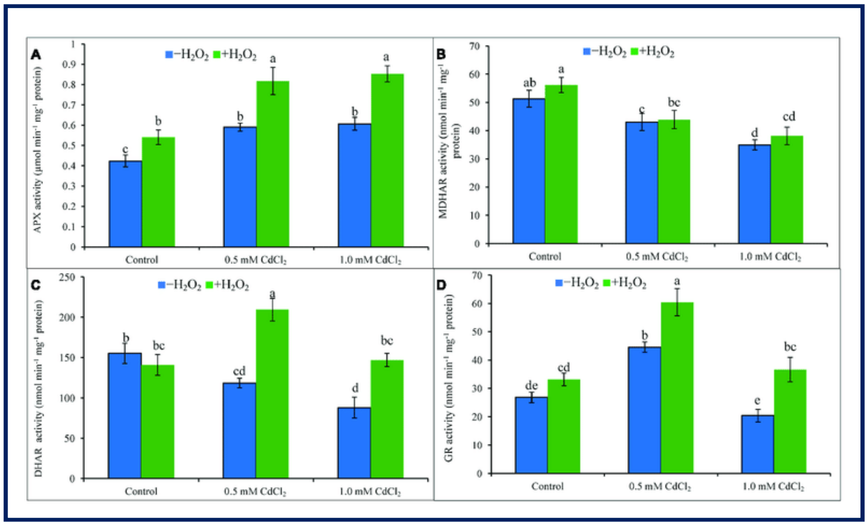

Fig. 29: Illustrates the activities of AsA-GSH cycle enzymes, APX (A), MDHAR (B), DHAR (C), and GR (D) in rapeseed leaves induced by exogenous H 2 O 2 under Cd stress. Mean (±SD) was calculated from three replicates for each treatment. Bars with different letters are significantly different at $P < 0.05$ applying Tukey's HSD test. After Hasanuzzaman *et al.,* (2017)

However, POD activity had no significant change in all the treatments when compared with SOD and APX Wang *et al.,* (2013). Results indicated that an effective and powerful antioxidant system in plants particularly, with cadmium stress and maintain metabolic balance.

Hasanuzzaman *et al.,* (2017) reported that cadmium (Cd) is considered as one of the most toxic metals for plant growth and development. In the present study, we investigated the role of externally applied hydrogen peroxide (H_2O_2) in regulating the antioxidant defense and glyoxalase systems in conferring Cd-induced oxidative stress tolerance in rapeseed (*Brassica napus* L.). Seedlings were pretreated with 50 μM H_2O_2 for 24 h. These pretreated seedlings as well as non-pretreated seedlings were grown for another 48 h at two concentrations of Cd Cl_2 (0.5 and 1.0 mM). Both the levels of Cd increased MDA and H_2O_2 levels and lipoxygenase activity while ascorbate (AsA) declined significantly. However, reduced glutathione (GSH) content showed an increase at 0.5 mM Cd Cl_2, but glutathione disulfide (GSSG) increased at any level of Cd with a decrease in GSH/GSSG ratio. The activities of ascorbate peroxidase (APX) and glutathione S-transferase (GST) upregulated due to Cd treatment in dose-dependent manners, while glutathione reductase (GR) and glutathione peroxidase (GPX) increased only at 0.5 mM Cd Cl_2 and decreased at higher dose. The activity of monodehydroascorbate reductase (MDHAR), dehydroascorbate reductase (DHAR), catalase (CAT), glyoxalase I (Gly I), and glyoxalase II (Gly II) decreased under Cd stress. On the other hand, H_2O_2 pretreated seedlings, when exposed to Cd, AsA and GSH contents and GSH/GSSG ratio increased noticeably. H_2O_2 pretreatment increased the activities of APX, MDHAR, DHAR, GR, GST, GPX, and CAT of Cd affected seedlings. Thus, enhancement of both the nonenzymatic and enzymatic antioxidants helped to decrease the oxidative damage as indicated by decreased levels of H_2O_2 and MDA. The seedlings that were pretreated with H_2O_2 also showed enhanced glyoxalase system. The activities of Gly I, and Gly II and the content of GSH increased significantly due to H_2O_2 pretreatment in Cd affected seedlings, compared to the Cd-stressed plants without H_2O_2 pretreatment that were vital for methylglyoxal detoxification. Therefore, the major roles of H_2O_2 were improvement of antioxidant defense system and glyoxalase system that protected plants from the damage effects of ROS and MG. The mechanism of H_2O_2 to induce antioxidant defense and glyoxalase system and improve physiology under stress conditions is not known clearly, which should be elucidated. The signaling roles of H_2O_2 and its interaction with other signaling molecules, phytohormones or other biomolecules and their roles in stress protection should be explored.

Generally, heavy metals cause oxidative damage to plants, either directly or indirectly through reactive oxygen species (ROS) formation. Certain heavy metals such as copper and iron can be toxic through their participation in redox cycles like Fenton and/or Haber-Weiss reactions. In contrast, Cd is a non-redox metal unable to perform single electron transfer reactions, and does not produce ROS such as the superoxide anion (O_2•–), singlet oxygen ($^1O_2$), hydrogen peroxide (H_2O_2), and hydroxyl radical (OH•), but generates oxidative stress by interfering with the antioxidant defense system Benavides, *et al.,* (2005); Cho and Seo, (2005); Gratao *et al.,* (2005). Cd inhibits the photo activation of photosystem 2(PS2) by inhibiting electron transfer. Thus, Cd could lead to the generation of ROS indirectly by production of a disturbance in the chloroplasts.

In addition, other reports suggested that Cd might stimulate the production of ROS in the mitochondrial electron transfer chain Heyno *et al.,* (2008). Treatment of pea and rice plants with Cd stimulates the plasma–membrane-bound NADPH oxidase in peroxisomes and thus generates ROS. The activation of ROS generation is fast. For example, in Scots pine (*Pinus sylvestris*) seedlings, treatment with 50 mM Cd led to an increase in ROS in 6 h. In *Medicago sativa,* exposure to Cd for 6–24 h caused a rapid accumulation of peroxides and depletion of glutathione (GSH) and homoglutathione (hGSH), and led to redox imbalance. Cadmium induced cell death in bright yellow-2 (BY-2) tobacco cells was preceded by NADPH-oxidase-dependent accumulation of H_2O_2 followed by cellular O_2 and fatty acid hydro peroxide accumulation Gill and Tuteja, (2010). The manifestations of ROS damages in plants involve lipid peroxidation, protein peroxidation, and DNA damage. Cd produced an enhancement of lipid peroxidation in *Phaseolus vulgaris* Chaoui *et al.,* (1997), *Helianthus annuus* Gallego *et al.,* (1996), and *Pisum sativum* Lozano-Rodriguez *et al.,* (1997). DNA damage caused by cadmium-involved destruction of nucleic acids, cell membrane, lipids, and proteins; reduction of protein synthesis; and damage of photosynthetic proteins, which affects growth and development of the whole organism. DNA damage has also been defined via determination of frequency of abnormalities such as fragments, precocious separation, laggards, single and double bridges, and stickiness Gill and Tuteja, (2010) ;

Kranner and Colville, (2011). A variety of proteins functions as scavengers of superoxide and hydrogen peroxide. These include, among others, superoxide dismutase (SOD), catalase (CAT), ascorbate peroxidase (APX), monodehydroascorbate reductase (MDHAR), Dehydroascorbate reductase (DHAR), peroxidases (POD), and glutathione reductase (GR), and non-enzymatic scavengers, including, but not limited to, glutathione (GSH), ascorbic acid (ASA), carotenoids, and tocopherols. SOD, GR, APX, POD, and CAT showed variations in their activities that depend on the Cd concentration and plant species used. Increased activity of SOD has been detected in many Cd-treated plants, such as pea Sandalio *et al.,* (2001), wheat Milone *et al.,* (2003) and bean Cardinaels, *et al.,* (1984). Decline in the enzymatic activity of CAT and SOD has been associated with Cd toxicity in *Phaseolus vulgaris* Chaoui *et al.,* (1997), *Phaseolus aureus* Shaw, (1995), *H. annuus* Gallego *et al.,* (1996), and *Pisum sativum* Sandalio *et al.,* (2001). Variable activity of CAT has been observed under cadmium stress.

Yilmaz and Parlak, (2011) reported that the observed high tolerance of *Groenlandia densa* to Cd stress was partially due to high activity of CAT. Its activity increased in rice, mustard, wheat, chickpea, and black bean (*Vigna unguiculata* subsp. *cylindrica*) roots and declined in soybean, *Phragmites australis*, *Capsicum annuum*, and *Arabidopsis* under cadmium stress Gill and Tuteja, (2010). APX and GPX are scavengers of H_2O_2 in ROS detoxification. An increase in leaf APX activity under cadmium stress has been reported in *Ceratophyllum demersum*, mustard, wheat, and black bean. An increase in GPX activity in cadmium -exposed plants was reported in wheat, *Arabidopsis*, and *Ceratophyllum demersum*. It was found that an initial increase in GPX activity in spruce needles subjected to cadmium stress and subsequent cadmium treatments caused a decline in the activity Gill and Tuteja, (2010). A decrease in POD activity caused by cadmium was reported in mustard (*Brassica juncea*) Markovska *et al.,* (2009). An increase in GR activity was found in cotton, *Arabidopsis*, black gram, wheat, and mustard upon Cd treatment Markovska *et al.,* (2009); Gill and Tuteja, (2010). The activities of MDHAR and DHAR were found to increase in mustard plants exposed to 10 μM Cd Markovska *et al.,* (2009). An increase of glutathione-S-transferases (GST) activity was found in rice shoots, while in roots the activity of the enzyme was inhibited by Cd treatments. Compared with shoots, rice roots had higher GST activity, indicating that the ability of Cd detoxification was much higher in roots than in shoots Zhang and Ge, (2008). Dixit *et al.,* (2011) reported the cloning of a *GST* gene from *Trichoderma virens*, a biocontrol fungus, and trated with tobacco plants by *Agrobacterium*-mediated gene transfer, showed that the transgenic plants expressing the *TvGST* gene, under exposure to different cadmium concentrations, were more tolerant in comparison with wild-type plants. The levels of GST showed enhanced values in transgenic plants expressing *TvGST* compared to control plants, when exposed to cadmium, although cadmium accumulation in the plant biomass in transgenic plants was similar or lower than that in wild-type plants. Cadmium stress increases the activity of POD in radish (*Raphanus sativus* L.) El-Beltagi *et al.,* (2010) and causes no significant change in the leaves of pea plants. An increase in ASH content during Cd exposure was found in barley. In contrast, a decrease in ASH in the roots and nodules of soybean under cadmium stress was also observed. Cadmium also decreased the ASH content in cucumber chloroplasts and in the leaves of *Arabidopsis* and pea, whereas it remained unaffected in *Populus canescens* roots Gill and Tuteja, (2010). An increase in GSH levels, which resulted in enhanced antioxidant activity against Cd toxicity, has been found in the leaves and chloroplasts of *Phragmites australis* Trin. (Cav.) ex Steudel. Increased concentration of GSH has been observed with increasing cadmium concentration in pea, *Sedum alfredii*, and black bean. A decrease in GSH, which could weaken the antioxidative response and defensive strength against cadmium stress in the more sensitive genotypes, was also found in pea Metwally *et al.,* (2005). Accumulation of large amounts of osmolytes (proline) is an adaptive response in plants exposed to a stressful environment. Proline accumulation appeared to be a suitable indicator of heavy metal stress. The role of proline as an antioxidant was reported in tobacco (*Nicotiana tabacum* L.) cells exposed to Cd stress. Islam *et al.,* (2009) reported that tobacco cells exposed to cadmium treatment accumulated high levels of proline furthermore alleviate the inhibitory effect of Cd on cell growth.

5. Cadmium and their adaptation mechanism

5.1. Chelation

Plant-chelating peptides are a type of heavy metal chelating peptide with rich sulfhydryl content playing an important role in the detoxification of and defense against heavy metals as reported by Blum *et al.,* (2007). As heavy metal, ions enter plants, the content of the Phytochelatins (PC) synthesis precursor glutathione (GSH) increases, which increases the synthesis of PCs Guo *et al.,* (2009). Heavy metal ions can be chelated with PCs, resulting in nontoxic chelates, which are then transferred to plant vacuoles for storage Clemens *et al.,* (2002), Sun *et al.,* (1995). The Phytochelatins (PC) synthesis process not only requires sufficient substrate (GSH), but also requires plant chelating peptide synthase (PCS) to catalyze it. Clemens *et al.,* (2006) stated that the activity of PCS is crucial for plant tolerance to cadmium. PCs may be combined with cadmium (Cd) in various forms and distributed in plant tissues, cadmium in *Brassica juncea* always occurred as Cys-Cd4, GSH-Cd, PC2-Cd, and PC3-Cd, reducing the toxicity effects Fig.(30). Yamaguchi, (2020) reported that sulfur (S) assimilation, which is initiated by sulfate uptake, generates cysteine, the substrate for glutathione (GSH) and phytochelatin (PC) synthesis. GSH and PC contribute to cadmium (Cd) detoxification by capturing it for sequestration. Although Cd exposure is known to induce the expression of S-assimilating enzyme genes, including sulfate transporters (SULTRs), mechanisms of their transcriptional regulation are not well understood. Transcription factor SLIM1 controls transcriptional changes during S deficiency (−S) in Arabidopsis thaliana. We examined the potential involvement of SLIM1 in inducing the S assimilation pathway and PC accumulation. Cd treatment reduced the shoot fresh weight in the sulfur limitation1 (slim1) mutant but not in the parental line (1;2 PGN). Cd-induced increases of sulfate uptake and SULTR1;2 expressions were diminished in the slim1 mutant, suggesting that SLIM1 is involved in inducing sulfate uptake during Cd exposure. The GSH and PC levels were lower in slim1 than in the parental line, indicating that SLIM1 was required for increasing PC during Cd treatment. Hence, SLIM1 indirectly contributes to Cd tolerance of plants by inducing −S responses in the cell caused by depleting the GSH pool, which is consumed by enhanced PC synthesis and sequestration to the vacuole.

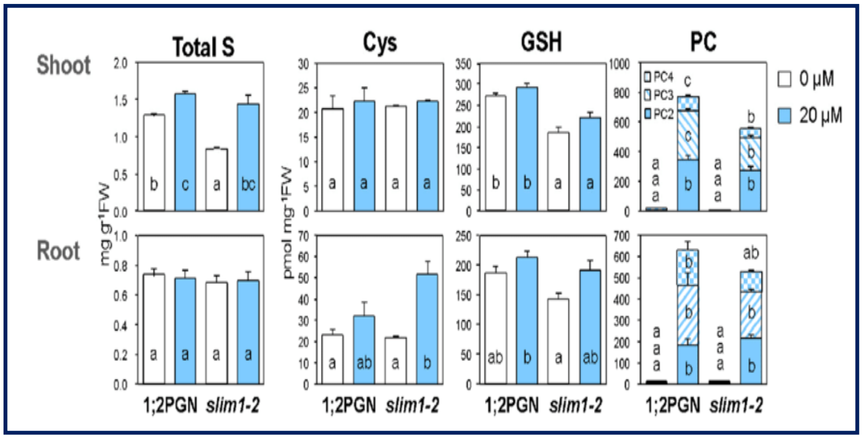

Fig. 30: Illustrated the effects of Cd treatment on the total content of S, Cys, GSH, and PC in 1;2 PGN and slim1-2. 1;2 PGN and slim1-2 were grown for 10 days on MGRL agar medium containing 0 (white bars) or 20 (light blue bars) µM CdCl2. Shoot and root tissues of 1;2PGN and slim1-2 were used as samples. ICP-MS. Contents of Cys, GSH, analyzed total S content and PCs were analyzed using a HPLCfluorescence detection system after labeling the thiol bases with monobromobimane. Cys: Cysteine, GSH: Glutathione, PC: Phytochelatin. The average values are indicated with error bars denoting SEM (n = 3-4). Different letters indicate significant differences among experimental groups (Tukey-Kramer test; $p < 0.05$). After Yamaguchi, (2020)

Cadmium is highly toxic but non-essential for living organisms Nawrot *et al.,* (2006), Clemens, *et al.,* (2013). It is released from natural and anthropogenic sources into the environment where it accumulates in the soil. Plants growing in contaminated soil particularly cadmium typically absorb the heavy metal via cation transporters located on the root surface and facilitate its transport to aerial tissues Thomine *et al.,* (2000), Choppala *et al.,* (2014). Phytotoxic effects of cadmium include growth inhibition, leaf chlorosis, and nutrient deficiencies Clemens *et al.,* (2013), Choppala *et al.,* (2014), and Clemens *et al.,* (2006). However, plants have evolved multiple mechanisms to tolerate cadmium exposure Clemens *et al.,* (2006), Cobbett, (2000). It has been demonstrated that cadmium is chelated by low-molecular, sulfur (S)-containing compounds, such as glutathione (GSH) or phytochelatin (PC), and sequestrated into the vacuole as GSH-Cd or PC-Cd complexes, respectively Clemens *et al.,* (2016), Clemens *et al.,* (2006), Cobbett *et al.,* (2002), and Salt *et al.,* (1995). Thus, plants can diminish the toxicity of cadmium by lowering its cytosolic concentration Verbruggen *et al.,* (2009), Cobbett *et al.,* (2002), Seth *et al.,* (2012), Lu (2013). GSH is a tri-peptide thiol synthesized from cysteine (Cys), glutamate (Glu), and glycine (Gly) by γ-glutamylcysteine synthetase (GSH1) and glutathione synthetase (GSH2) Fig. (31).

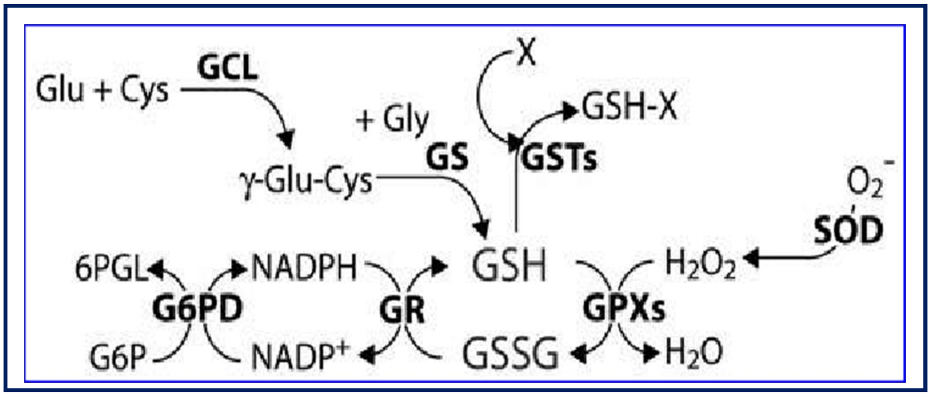

Fig. 31: Illustrates outline of GSH metabolism. GSH is synthesized from glutamate (glu), cysteine (cys), and glycine (gly) by the sequential actions of glutamate cysteine ligase (GCL) and glutathione synthetase (GS). GSH is used to eliminate reactive oxygen species such as hydrogen peroxide (H_2O_2) in a reaction catalyzed by the glutathione peroxidases (GPX). H_2O_2 is produced from superoxide (O_2^-) by superoxide dismutase (SOD). The glutathione disulfide (GSSG) produced in this reaction can be converted back to GSH through the action of glutathione disulfide reductase (GR). GR requires NADPH for its activity which is mainly supplied from the conversion of glucose 6-phosphate (G6P) to 6-phosphogluconod-lactone (6PGL) by glucose-6-phosphate dehydrogenase (G6PD), the first enzyme of the pentose phosphate shunt. GSH can also be used to detoxify. After Jan Lewerenz and Pamela Maher, (2011)

It contributes to cadmium detoxification both as a scavenger of reactive oxygen species (ROS) and as a substrate of PC synthesis Chmielowska-Bąk *et al.,* (2014), Cobbett *et al.,* (2002). Phytochelatin synthase (PCS) synthesizes PC by sequentially adding γ-glutamylcysteine to GSH to generate PC oligomers of variable lengths with the general structure (γ-Glu-Cys)n Gly (n = 2–11) Vatamaniuk *et al.,* (2000). PC levels and PCS activity are highly enhanced upon Cd exposure, whereas the transcript levels of PCS genes, PCS1 and PCS2 in Arabidopsis, remain relatively constant Herbette *et al.,* (2006), Zenk, (1996). PCS is activated by binding to heavy metals, resulting in the quick initiation of PC synthesis upon heavy metal exposure Vestergaard *et al.,* (2008), Howden *et al.,* (1995). The importance of GSH and PC for Cd tolerance is also indicated by the observation that certain mutations in either the PCS1 or GSH1 gene are associated with the Cd-sensitive phenotypes of the corresponding cad1 or cad2 mutants Cobbett *et al.,* (1995), Ha *et al.,* (1999). Cd exposure-induced synthesis of GSH and PC stimulates S assimilation by Cys, a major substrate for GSH synthesis Saito, (2004), Davidian and Kopriva, (2010). Recent studies reported the close relation between sulfur availability and increased plant tolerance to Cd stress Lu *et al.,* (2019), Zaid *et al.,* (2019). Sulfur S assimilation in plants starts with the uptake of sulfate by the rhizosphere via sulfate transporters (SULTR) Long *et al.,* (2015), Davidian and Kopriva, (2010), Takahashi *et al.,* (2000). Sulfate is absorbed by the root cells and translocated to the plastids, where it is reduced to sulfide by several enzymatic reactions, and assimilated into Cys Saito, (2004), Davidian and Kopriva, (2010). The SULTR family in Arabidopsis contains 12 members, which divided into four distinct functional groups Long *et al.,* (2015), Davidian and Kopriva, (2010), Takahashi *et al.,* (2000). Two high-affinity group 1 SULTR proteins, SULTR1;1 and SULTR1;2, facilitate the uptake of sulfate into roots Takahashi *et al.,* (2011), Long, *et al.,* (2015), Zaid, *et al.,* (2019), Takahashi *et al.,* (2000). Group 2 SULTR proteins are low-affinity sulfate transporters that contribute to the sulfate transport through vascular tissues Long *et al.,* (2015), Davidian and

Kopriva, (2010), Takahashi *et al.,* (2000), Maruyama-Nakashita *et al.,* (2015). Group 3 SULTR proteins reside in the plastid membrane to ensure the sulfate influx into the plastids Cao, *et al.,* (2013), Maruyama-Nakashita and Ohkama-Ohtsu, (2017). Group 4 SULTR proteins are responsible for the efflux of sulfate from vacuoles Kataoka, *et al.,* (2004). Transcript levels of the genes involved in S assimilation and GSH synthesis, including SULTR, GSH1, and GSH2, are increased in response to cadmium stress, resulting in the upregulation of enzymatic activities Zenk, (1996), Xiang and Oliver, (1998), Rouached *et al.,* (2008). Indeed, Cd-induced sulfate uptake mainly depends on the elevated expression of SULTR1;2 Shibagaki, *et al.,* (2002) Yamaguchi *et al.,* (2016). Cadmium exposure causes increased sulfate distribution to the shoots, along with an increased sulfate concentration in xylem sap and the upregulated expression of the SULTR genes involved in root-to-shoot sulfate transport, such as SULTR2;1 and SULTR3;5 Kataoka *et al.,* (2004), Cao *et al.,* (2013), Yamaguchi *et al.,* (2016). There are many similarities between plant responses to cadmium exposure and S deficiency (−S); both stimulate sulfate uptake, sulfate translocation to shoots, and sulfate reduction, along with its assimilation into Cys Zenk, (1996) Maruyama-Nakashita, *et al.,* (2004),

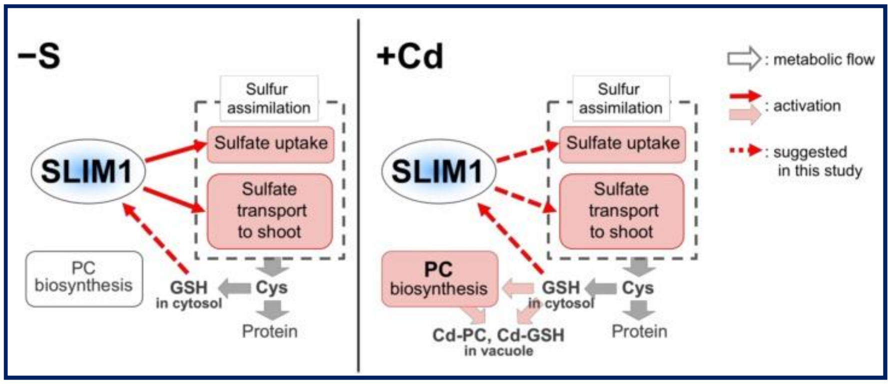

Fig. 32: Represents the role of SLIM1 in the regulation of S assimilation under −S and Cd treatment. Left panel: Plants increase sulfate uptake and its translocation to shoots in response to −S. SLIM1 stimulates the expression of genes involved in S assimilation, including SULTR1;2. Right panel: Cd treatment increases sulfate uptake, distribution to shoots, and PC accumulation. Shortage of cytosolic GSH can occur because of either sulfate deficiency (left panel) or the enhanced PC synthesis and the compartmentalization of Cd-PC or Cd-GSH to the vacuole (right panel). As a result, SLIM1 is activated in either scenario. Open arrow: metabolic flow; red or pink arrow: activation; dotted arrow: suggested in this study. After Yamaguchi *et al.,* (2020)

Maruyama-Nakashita *et al.,* (2006). In −S responses, Sulfur LIMitation1 (SLIM1), an ethylene insensitive 3-like (EIL) family transcription factor, plays a central role in inducing the transcriptional responses Maruyama-Nakashita *et al.,* (2006). SLIM1 activates sulfate acquisition for S assimilation by upregulating SULTR1;1, SULTR1;2, SULTR4;1, and SULTR4;2 in response to –S conditions Maruyama-Nakashita, *et al.,* (2006) Fig. (32).

Lu *et al.,* (2019) reported that exogenous sulfur protects tartary buckwheat from Cd toxicity. Tartary buckwheat seedlings formed shorter roots and shoots, and a lower biomass under the cadmium exposure condition. However, supplementation with S significantly increased biomass, shoot, and root heights, compared with the Cd treatment alone Fig. (33) Treating tartary buckwheat with cadmium promoted the production of O_2^- and H_2O_2, while net photosynthesis decreased compared to the control. However, adding 100 mM SO_4^{-2} to plants under Cd stress increased net photosynthesis by 81.60% and decreased H_2O_2 and O_2^- contents in leaves by 43.25% and 45.90%, respectively relative to the cadmium treatment. Application of sulfate SO_4^{-2} to plant roots particularly, under Cd stress gradually decreased H_2O_2, and O_2^- contents by about 53.48% and 51.88%, respectively as compared to cadmium treatment alone. Results also indicated that exogenous- S mitigated adverse effects on tartary buckwheat plants

They also stated that supplying exogenous sulfur-rich compounds gradually increases the content of glutathione (GSH) and phytochelatins (PCs) in plant tissues, enabling plants to enhance their cellular defense capacity and/or compartmentalize Cadmium into vacuoles. However, the mechanism by which surplus S modulates tolerance to cadmium stress in different tissues sulfur significantly mitigated cadmium -induced oxidative stress with the aids of antioxidant enzymes and agents in both leaves and roots, including peroxidase (POD), ascorbate peroxidase (APX), glutathione peroxidase (GPX), glutathione S-transferase (GST), ascorbic acid (AsA), and GSH, but not superoxide dismutase (SOD) and catalase (CAT). Results provided the fundamental information for the application of exogenous S in reversal of heavy metal stress.

However, it is still unclear how much the –S induced changes in the transcriptome contribute to the cadmium -induced responses and the cadmium tolerance in plants. In this study, we investigated the involvement of SLIM1 in plant responses to cadmium exposure and its significance in cadmium tolerance by comparing the cadmium responsive

Fig. 33: Illustrates the effect of surplus - S on seedling growth in the leaf and root of tartary buckwheat. Photo was taken at 10 days after treatment. CK: control plants without Cd or surplus Sulfur treatment; Cd: plants treated with cadmium; Cd+S: plants treated with cadmium and surplus sulfur. After Lu *et al.,* (2019)

Phenotypes of the slim1 mutant with those of the parental line PSULTR1;2-GFP (1;2PGN). The analysis demonstrated the significant contribution of SLIM1 to the Cd-responsive induction of Sulfate uptake, sulfate distribution to shoots, and PC accumulation.

5.2. Compartmentalization

Cadmium, tolerant plants may reduce cadmium transport from root-to shoot (regionalization) or minimize cadmium content in the cytoplasm (compartmentalization) particularly under cadmium stress. Regionalization may play an important role articularly in plant tolerance to cadmium stress and their detoxification. Guo, *et al.,* (2009) reported that under cadmium stressed for *Solanum nigrum* seedlings, the content of cadmium was significantly higher in roots as compared to shoots as reported by Salt and Rauser, (1995). Kneer and Zenk, (1992) stated that similar trend was noticed in *Brassica Chinensis*. Accumulation of cadmium in roots can reduce damage to shoots and photosynthetic organs. In addition, cadmium in the cytoplasm is transported to the vacuole, creating a reduction of cadmium-induced damage to proteins in the cytoplasm Fig. (34).

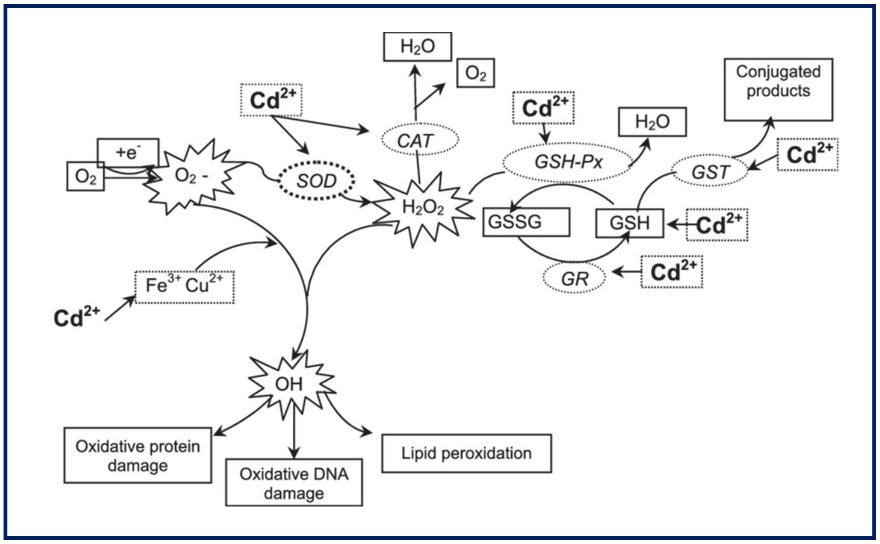

Fig. 34: The up-regulated expression of *TaHMA3* and *TaVP1*, which encode proteins related to Cd, was associated with increased Cd tolerance in wheat and decreased Cd translocation to aboveground parts. After Zhang *et al.,* (2022)

Salt *et al.,* (1995) & Krotz *et al.,* (1989) stated that the concentration of the accumulated cadmium in the vacuole is approximately 38 times that in the cytoplasm. Furthermore, large amount of sulfur S^{-2} on the tonoplast, that can bind to cadmium and facilitate its transport into the vacuole Ogawa, *et al.,* (2011). Moreover, Krotz *et al.,* (1989) reported that several organic and amino acids inside the vacuole that can react with cadmium to form polymer complexes, and reducing their toxicity and restricting its flow Fig. (35).

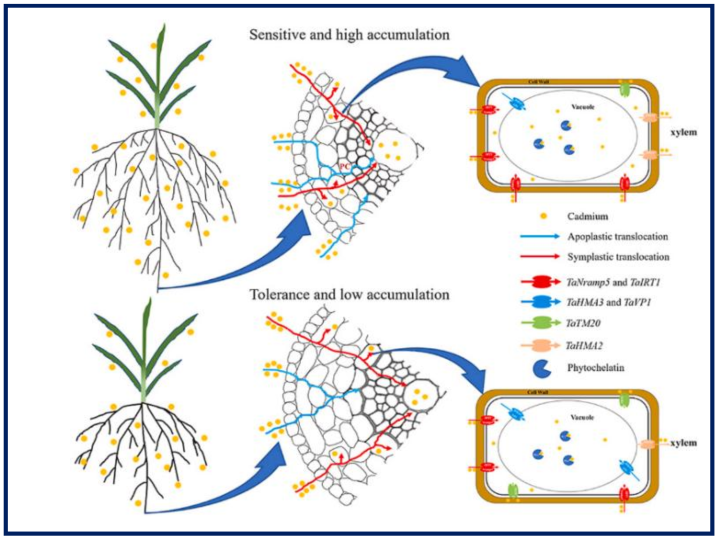

Fig. 35: Scheme of cadmium stress and detoxification. Pathways of Cd-induced generation of reactive oxygen species. Cadmium impairs enzyme activity of antioxidative defence system (superoxide dismutase, SOD; catalase, CAT; glutathione peroxidase, GSH-Px; glutathione-S-transferase, GST; gluathione reductase, GR) and of the non-enzymatic component glutathione, GSSG and GSH. Cadmium also elevates the levels of Fenton metals (Fe^{3+}, Cu^{2+}), which can break down hydrogen peroxide, H_2O_2 to a reactive hydroxyl radical, OH

6. Effect of Cd on mineral nutrition

Nutrient elements play an important role in plant tolerance to cadmium toxicity and furthermore, minimize the content of cadmium in plants. Sarwar *et al.,* (2010), Suzuki (2005), revealed that N, P, S, Ca, Fe, Zn gradually increase cadmium tolerance of plants. It was noticed that Ca alleviates Cd ion toxicity since both Ca and Cd compete for the same Ca channels in plants Fig. (36). Choi *et al.,* (2001) showed that plant cadmium tolerance in tobacco plants was gradually increased by Ca ion application due to formation of Cd – Ca containing crystals, and removal of these crystals through the head cells of trichomes.

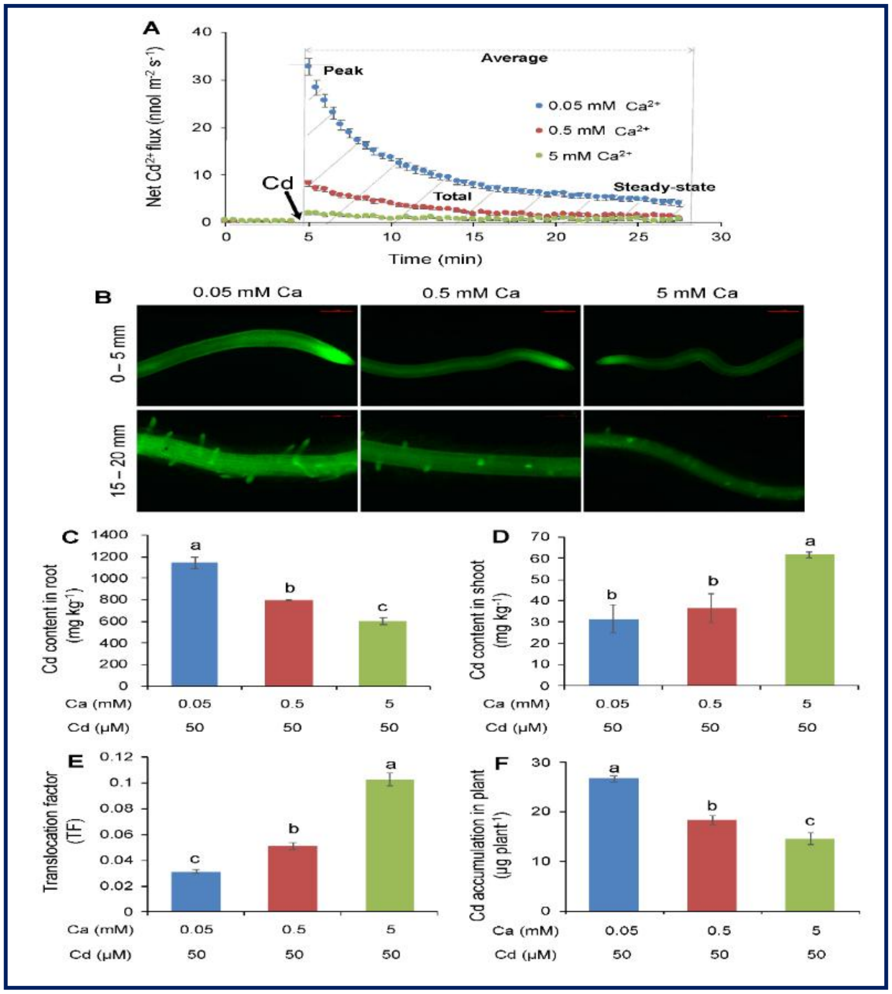

Fig. 36: Effects of external Ca concentrations on Cd uptake, distribution, and accumulation in rice. (**A**) Transient Cd2+ flux in rice root epidermis under deferent Ca conditions; Cd treatment was applied at time as indicated by arrows. Peak flux, steady-state flux, average flux, and total flux are shown. (**B**) Visualization of Cd2+ in the segments of 0–5 mm and 15–20 mm from root tip under different Ca conditions by fluorescent imaging using Leadmium Green AM dye. (**C**) Cd content in rice roots. (**D**) Cd content in rice shoots. (**E**) Translocation factor (TF) of Cd from roots to shoots. (**F**) Cd accumulation in rice plant. Cd exposure: 50 _M; Ca concentrations: 0.05, 0.5, and 5 mM. Data are means ± standard error (SE) (n = 6–8). Deferent letters represent a significant deference between treatments at $p < 0.05$. After Zhang *et al.,* (2020)

Zhang *et al.,* (2020) reported that cadmium contaminated soils poses great risks to both agricultural production and human health. Calcium is an essential element playing a significant role in protecting plants against cadmium toxicity. However, how Ca affects Cd uptake and translocation in rice is still not fully elucidated. In this study, the regulatory role of Ca in Cd uptake and upward translocation was investigated in rice at different growth stages. Results showed that the supplement of 5 mM Ca significantly reduced Cd uptake by rice roots, because of their competition for Ca-permeable channels as an absorption site and Ca-induced down regulation of OsNRAMP1 and OsNRAMP5. However, application of calcium facilitated the upward translocation of Cd by both upregulating OsHMA2 to induce xylem loading of Cd and down regulating OsHMA3 to reduce vacuolar sequestration of cadmium, suggesting a double-edged role of Ca in regulating root Cd uptake and root-to-shoot Cd translocation in rice. Although it increased Cd content in the aboveground vegetative tissues during the whole growth period, the addition of 5 mM Ca eventually decreased Cd content in rice grains at the ripening stage. All these results suggested that Ca-based amendments possess great potential for the production of low-Cd rice grains. They also used microelectrode ion flux estimation (MIFE) technique for measuring the net Cd ion flux from the rice roots Fig. (36-A). Prior to adding cadmium treatments, Cd ion fluxes under different Ca concentrations were all kept at $\sim 0\ \text{nmol}\cdot\text{m}^{-2}\cdot\text{s}^{-1}$, indicating that no Cd uptake occurred under the pretreated conditions. Addition of 50 μM Cd to the bath solution resulted in an instantaneous Cd ion influx, with a peak value ranging from (2 to 33) $\text{nmol}\cdot\text{m}^{-2}\cdot\text{s}^{-1}$ in the mature zone under different external Ca concentrations. The influxes were then gradually reduced in all rice roots. With the external Ca concentration increasing from 0.05 mM to 5 mM, net Cd ion influx was significantly decreased ($p < 0.05$), resulting in 4–40-fold lower peak, steady-state, average, and total values in the roots pretreated with 0.5 and 5 mM Ca than those in the roots pretreated with 0.05 mM Ca . We next looked at the effect of Ca on Cd distribution along rice root in the segments of 0–5 mm (including meristem and elongation zones) and 15–20 mm (including mature zone) from the root cap Fig.(36 - B). Consistent with MIFE data, the higher external Ca concentration in the basal solution resulted in the significantly weaker intensity of Cd green fluorescence in both root segments, suggesting the inhibitory effect of Ca on Cd uptake by rice roots. The effect of Ca on Cd uptake was further investigated in terms of Cd content in rice tissues. As shown in Fig. (36 - C), the increase in the external Ca concentration considerably reduced Cd content in rice roots, with about a 50% reduction in root Cd content under 5 mM Ca relative to that under 0.05 mM Ca. Unexpectedly, Cd contents in rice shoots were significantly enhanced with the increase in Ca concentration in the nutrient solution, with roots treated with 5 mM Ca showing twofold higher Cd content than those grown with 0.05 mM Ca Fig. (36 - D). As a result, a considerable increase in the translocation factor of Cd was observed when plants were exposed to higher external Ca concentration Fig. (36 - E). However, the accumulation of Cd in rice plant was significantly decreased with increasing Ca concentrations Fig. (36 - F), due to the reduction in Cd uptake by rice roots Fig. (36 A–C). All these results indicated that Ca decreases root Cd uptake but facilitates root-to-shoot Cd translocation in rice.

Uptake, transport, and subsequent distribution of nutrient elements by the plants affected by the presence of Cd ions. In general, Cd has been shown to interfere with the uptake, transport, and use of several elements (Ca, Mg, P, and K) and water by plants Das *et al.,* (1997). In sugar beet, Chang *et al.,* (2003), observed deficiency of Fe in roots induced by Cd. In pea plants, the uptake of P, K, S, Ca, Zn, Mn, and B was inhibited strongly after Cd exposure Metwally *et al.,* (2005) Fig. (37). Treatment of barley plants with 1.0 μM Cd decreased the concentrations of P, K, Ca, Mg, Cu, Fe, Mn, Zn, Mo, and B in roots, whereas the concentrations of these elements in shoots were not decreased in comparison with the control Guo *et al.,* (2007). Rizwan *et al.,* (2019) stated that increasing cadmium pollution in agricultural soils has raised serious concerns worldwide. Several exogenous substances can be used to mitigate the toxic effects of Cd in plants. Zinc is one of the essential plant micronutrients and is involved in several physiological functions in plants. Zinc may alleviate Cd toxicity in plants owing to the chemical similarity of Zn with Cd. Several researchers demonstrated that Zn could alleviate toxic effects of Cd in plants by increasing plant growth, regulating Cd uptake, increasing photosynthesis, and reducing oxidative stress. The role of Zn on Cd accumulation by plants is very controversial and depends upon several factors including concentrations of Cd and Zn in the medium, exposure duration, plant species and genotypes, and growth conditions. The role of Zn in reducing Cd toxicity in plants and provides new insight that proper level of Zn in plants may enhance plant resistance to excess cadmium.

The uptake and translocation of essential elements in plants were restricted under cadmium stress Hussain *et al.,* (2019), Kukier and Chaney, (2002); Rizwan *et al.,* (2016a); Murtaza *et al.,* (2017). Excess of cadmium gradually decreased zinc contents in numerous plant species which may cause Zn deficiency in plants Mohammad and Moheman, (2010); Murtaza *et al.,* (2017). However, external Zn supply gradually increased zinc concentrations in plants under cadmium stress depending upon plant species and exposure conditions Qaswar *et al.,* (2017); Rizwan, *et al.,* (2017b); Wang *et al.,* (2018). Studies reported that zinc might be the dominant factor in affecting plant growth at higher Zn treatments despite lower Cd concentrations in plants. Exogenous supply of Zn might enhance Cd tolerance in plants through the increased uptake of essential elements by plants under cadmium stress. Soil application of Zn + Cd application gradually increased the essential elements of Fe, Mn, Cu, Ca, Mg in cabbage and lettuce than cadmium treatment alone He *et al.,* (2004). Zinc application decreased Fe and Cu concentrations in wheat shoots more than Zn-deficient plants while Cd + Zn treatments increased Zn and did not significantly affect Fe and Cu concentrations in shoots Köleli *et al.,* (2004) Sarwar *et al.,* (2015). Application of Zn + Cd unaltered the essential elements uptake under hydroponic conditions in bean Chaoui *et al.,* (1997) and barley Wu and Zhang, (2002). Thus, Zn application could enhance Cd tolerance in plants by increasing the essential mineral elements uptake by plants that may positively affect plant growth under cadmium stress.

Decreasing uptake of Ca and K by Cd has been found in a Cd-hyperaccumulator, *Atriplex halimus subsp. schweinfurthii* Nedjimi and Daoud, (2009). Cadmium also reduced the absorption of nitrate and its transport from roots to shoots, by inhibiting nitrate reductase activity in the shoots Hernandez *et al.,* (1996). Appreciable inhibition of the nitrate reductase activity was also found in plants of *Silene cucubalus* Mathys, (1975). Nitrogen fixation and primary ammonia assimilation decreased in nodules of soybean plants during Cd treatments Karina *et al.,* (2003).

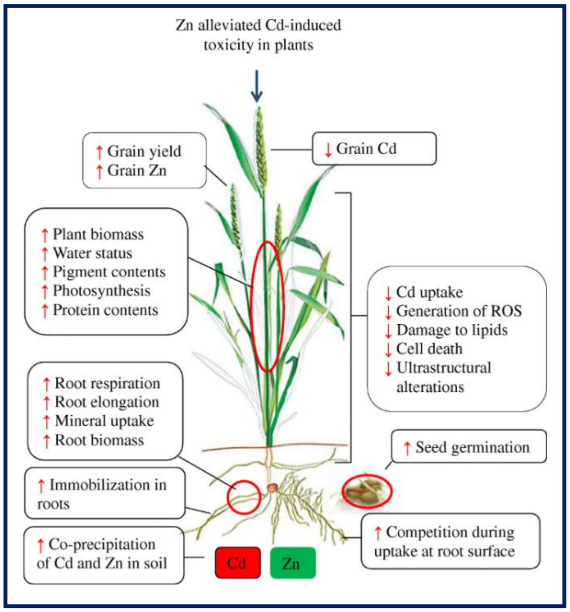

Fig. 37: Possible mechanisms of Zn-mediated alleviation of Cd toxicity in plants. In the figure, upward and downward arrows represent increase and decrease of the parameters, respectively. After Rizwan *et al.,* (2019)

Application of cadmium in soybean seedlings showed that there was an increase in laccase activity (laccases are responsible for lignin biosynthesis), during the early stage of cadmium treatment, and inducing the lignin synthesis particularly, in early stage of root growth causing inhibition of root elongation Yang *et al.,* (2007). In maize, cadmium treatment induced an inhibition of H^+- ATPase in root cells. Many studies revealed that H^+- ATPase is an integral protein associated with the plasma membrane and is located preferentially at the epidermal and cortical cell layers of roots. H^+- ATPase functions as an ion transporter across the plasmalemma and this is dependent on the electrochemical gradient generated by the plasma membrane H^+- ATPase. Thus, cadmium, which causes a decrease in activity of H^+- ATPase, might inhibit absorption of some essential elements Astolfi *et al.,* (2005). In addition, application of cadmium in poplar (*Populus jaquemontiana* var. glauca) could inhibit mineral nutrition by competition between this metal and other metal ions Solti *et al.,* (2011). The authors have suggested two mechanisms. In the first type (type 1), the mechanism was like the influence of cadmium on Fe. It is known that Cd might inhibit the chelating process of Fe and the loading of Fe into the xylem. Thus, cadmium as type 1 influenced the metals that are transported in the xylem, as occurred with Fe Fig. (38).

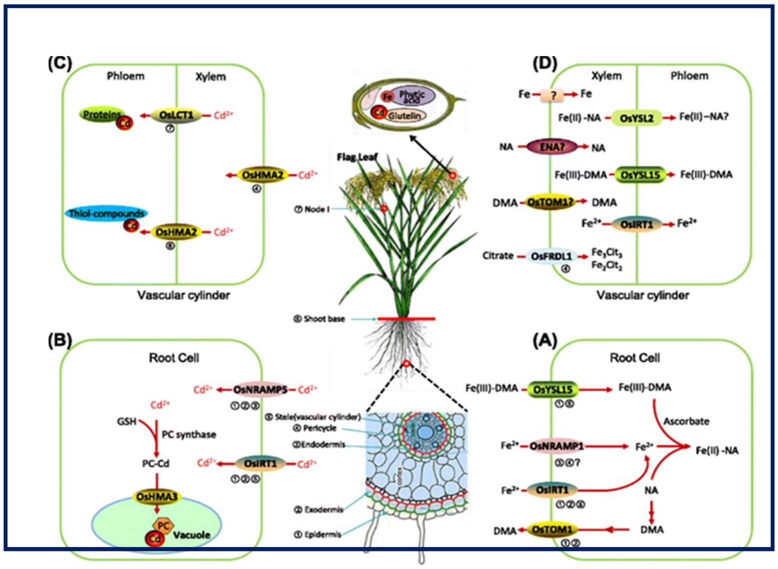

Fig. 38: Illustrates the mechanisms of Fe/Cd uptake and translocation in rice. a Fe uptake from rhizosphere into root cells by specific root transporters. DMA is synthesized in cells and secreted into the rhizosphere by OsTOM1. DMA chelates rhizospheric Fe (III), forming Fe (III)-DMA complexes. OsYLS15 then takes up complexes into root cells. Roots also take up Fe (II) directly by metal transporters (OsIRT1/OsNRAMP1). b Cd is absorbed from rhizosphere into root cells mediated by OsIRT1 and OsNRAMP5. OsHMA3 plays a critical role in Cd compartmentalization into vacuoles in root cells. c Cd xylem loading in roots for translocation to shoots by OsHMA2, and Cd phloem loading for storage to grain sink. OsLCT1 and OsHMA2 mediate xylem-to-phloem transfer at nodes. d Fe xylem loading in roots for translocation to shoots and the remobilization of Fe through phloem from leaves for storage to grain sink. OsFRDL1, which is a citrate transporter, localized at the root pericycle cells. OsFRDL1 loads citrate into the xylem and combines with Fe. ENA may be involved in efflux of NA into xylem. OsYSL2 then mediate Fe (II)-NA for phloem loading. OsTOM1 potentially participates in DMA transport, followed by mediating Fe (III)-DMA through OsYSL15. Furthermore, OsIRT1 directly transports Fe (II) in phloem companion cells of shoots. The encircled numerals represent the main localization of specific transporters. Right parts of the figure are adapted partially, from Kobayashi *et al.,* (2014) and Yoneyama *et al.,* (2015). After Gao *et al.,* (2016)

Gao *et al.,* (2016) stated that iron is essential nutrient for rice growth and humans rice as their staple food, whereas Cd is nonessential and toxic. Rice grains contain both Fe and Cd. The latter may cause damage to human bodies if accumulating at high levels. Basic transport processes are as follows: During the vegetative stage, Fe and Cd are absorbed by specific root transporters and then transport to xylem, delivering to aerial parts via xylem-to phloem transfer system. Compared with cadmium of which such transfer system mainly at nodes, Fe is preferentially allocated to leaves through xylem. At grain filling, grain Fe and Cd are derived from phloem. Particularly, grain Fe is largely acquired from leaves by remobilization. Due to limited source of Fe in soil and Cd toxicity, rice has evolved mechanisms against Fe deficiency and cadmium stress. Rice can secrete DMA to chelate insoluble Fe^{3+} by strategy II. In response to cadmium toxicity, compartmentalization of Cd into vacuole is thought to be effective tolerance mechanism for reducing Cd translocation to grains. However, relying on rice self-mechanisms are not enough to tackle issues of Fe deficiency and Cd toxicity. Besides traditional soil remediation and fertilizers management, breeding high Fe but low Cd cultivars through genetic methods are considered as promising approaches based on understanding of Fe/Cd transport and accumulation processes at cellular level. QTL analysis, regulation and manipulation of genes involved in Fe/Cd accumulation are generally utilized to produce novel cultivars. Despite these advances in enhancing Fe in grains, limited Fe in edible parts due to combining with phytic acid and inevitable loss during polishing process restricts Fe nutritional assimilation for human bodies. In addition, some low-Cd cultivars are reported to enhance other toxic metals, such as Arsenic, though reduce Cd content to some extent. Thus, further investigation into these issues will be conducive to develop Fe-fortified cultivars with increased assimilation and low-Cd cultivars without other toxic metals accumulation.

In the second type (type 2), the mechanism was like the influence of cadmium on Ca in competition for Ca transporters. The alkaline earth metals (except Mg) belong to type 2. It should be mentioned that several plant nutrients have many direct as well as indirect effects on Cd availability and toxicity. Direct effects include decreased Cd solubility in soil by precipitation and adsorption Matusik *et al.,* (2008) Fig.(39), competition between cadmium and plant nutrients for the same membrane transporters Zhao, *et al.,* (2005), and cadmium sequestration in the vegetative parts to avoid its accumulation in the grain/edible parts Hall, (2002). Indirect effects include dilution of cadmium concentration by increasing plant biomass and alleviation of physiological stress.

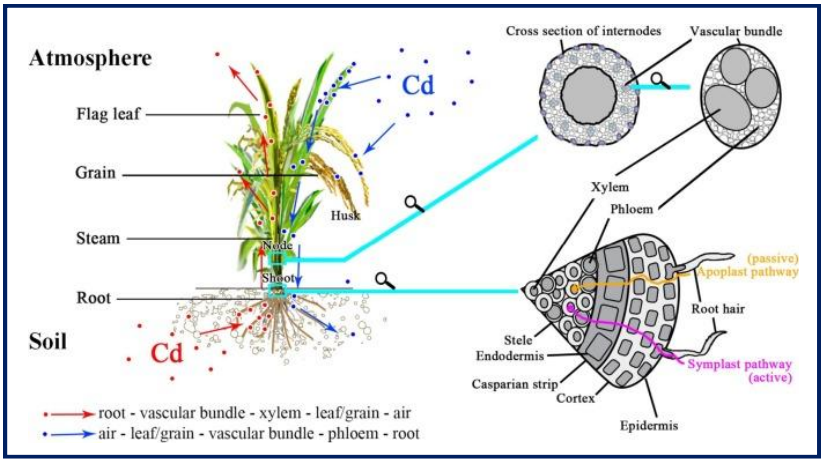

Fig. 39: Migration of Cd in the soil-rice system via two channels with opposite direction (Root-to-Air and Air-to-Root). After, Li *et al.,* (2021)

7. Toxicity of cadmium in plants

Tudoreanu and Phillips, (2004) reported that cadmium has no physiological importance in plants. Asgher *et al.,* (2015) stated that cadmium occurs in the form of Cd ions in soil and enters the root cells with the help of zinc-regulated transporters/iron-regulated transporters. The epidermal layer of the root is the first site for the contact of free Cd ions in soil Sidhu *et al.,* (2019a). The root hairs provide large surface area and aid in absorption of Cd ions from the soil through diffusion Seregin and Ivanov, (1997). Plant roots also secrete certain organic compounds such as chelates that complex with Cd ions to form ligands, allowing entry into root epidermis Sidhu *et al.,* (2019a). Certain protein transporters such as natural resistance-associated macrophage proteins (NRAMPs) impart a critical role in cadmium transport across the cell membrane Song *et al.,* (2014). In general, after Cd- uptake by plant roots, maximum portion of cadmium is fractionized into the root cells and only a small portion is fractionized to the upper aerial plant parts and grains Song *et al.,* (2014). In the process of cadmium transport in plants, commonly intracellular transport occurs in plant vacuole. Cd-chelating components such as metallothioneins, phytochelatins and organic acids are crucial for the transport. Sulfhydryl and carboxylic groups in these chelating compounds form with Cd and bind it before its transport to the vacuole. Vacuolar transporter proteins such as natural resistance-associated macrophage proteins, ATP binding cassette transporters (ABC transporters) and P-type ATPase are involved in Cd–chelate complex into the vacuole. The intracellular cadmium transport facilitates cadmium detoxification in the roots and hence promotes cadmium tolerance in plants against cadmium toxicity Fig. (40). Cadmium transport process in plants may be a short or long-distance transport. From the soil, the plant roots and then the short-distance transportation of water occurs through both apoplastic and symplastic pathways. Parrotta *et al.,* (2015) documented that the apoplastic pathway facilitates cadmium binding in the cell wall, while the carboxyl group present in the cell wall binds and immobilizes Cd. In apoplastic movement, the plasticity of cell wall imparts a decisive role in Cd movement. During Cd transport through apoplastic route, suberin layer acts as a barrier for Cd transport Tao *et al.,* (2017). The symplastic route enables Cd transport from epidermis to water-conducting elements.

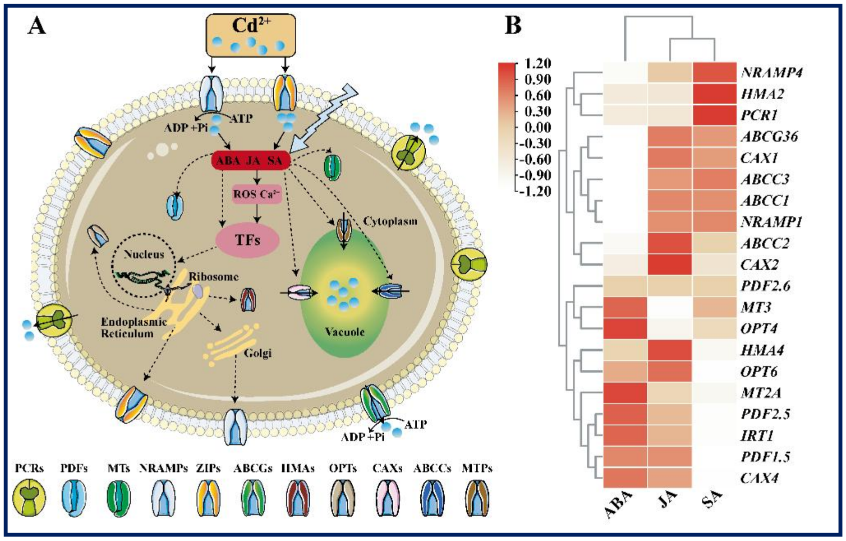

Fig. 40: Plant hormone signaling regulation and related gene expression analysis under Cd stress. A: The regulatory pathway of plant hormones under Cd stress. Plant hormones such as ABA, JA, and SA enhance the detoxification ability of plants against cadmium stress by regulating the expression of downstream proteins. TFs stands for transcription factors. The arrows with solid lines indicate that the regulation methods have been reported so far, and the arrows with dotted lines indicate that the regulation methods are not yet clear. Polyline arrows indicate exogenous additions. B: Effects of ABA, JA and SA on the expression of genes involved in Cd transport and detoxification (taking Arabidopsis as an example). A red box means more correlation, a white box means less correlation. Plant hormones like ABA, JA, and SA are closely related to the expression of these genes. After Li *et al.,* (2022)

Ueno *et al.,* (2010) revealed that certain transporter proteins such as *Oryza sativa* heavy metal P-type ATPase 3 (OsHMA3*)* play a consequential role in decreasing Cd transport to the shoots Fig. (41). *Oryza sativa* heavy metal P-type ATPase 3 transporter protein enhanced Cd sequestration in the vacuole of root cells and decreased Cd transport to upper aerial parts.

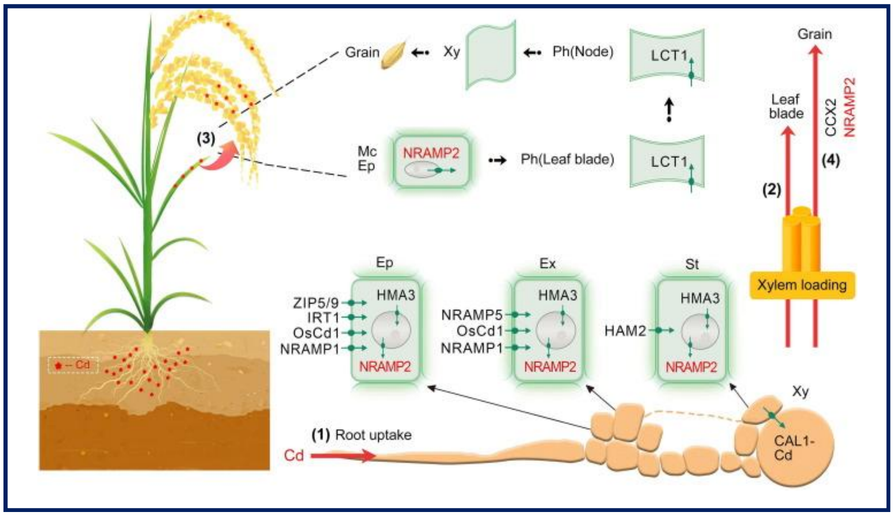

Fig. 41: Illustrates a molecular model of Cd transport processes from soil to grain in rice. Transport of Cd from soil to grain can be divided into four steps: (1) uptake by roots; (2) xylem loading and root-to-shoot translocation; (3) Cd remobilization from leaves to grain via phloem; (4) newly absorbed Cd transport to grain via xylem. The OsNRAMP2 identified in this study is highlighted in red. cadmium transporters that have been reported are shown. Details of each transporter can be found in the main text. Xy, xylem; Ph, phloem; St, stele; Ep, epidermis; Ex, exodermis; MC, mesophyll cell. After Wang *et al.,* (2022)

Wang *et al.,* (2022) reported that cadmium accumulation in rice grains is of health concern. Identifying genes involved in grain Cd accumulation and performing molecular breeding may reduce it. In this study, knockout of OsNRAMP2, a member of the NRAMP family, reduced grain Cd concentrations by more than 38%, and overexpressing OsNRAMP2 increased grain Cd concentrations by more than 50%. Physiological experiments showed that OsNRAMP2 facilitated Cd translocation from root to shoot by positively regulating Cd efflux from the vacuoles. At filling stage, OsNRAMP2 was highly expressed in all tissues except for husk, suggesting its role in Cd remobilization. Changes in OsNRAMP2 expression affected the concentrations of Fe, Mn, Zn, and Cu in grain and affected rice growth. Phylogenetic analysis showed that the distribution of OsNRAMP2 haplotypes between japonica and indica was different. Among the four haplotypes of OsNRAMP2, Hap 1, with a 6-bp nucleotide insertion in exon 1, had grain Cd concentration at least 45.3% lower than any of the other three haplotypes. Almost all (99.3%) japonica accessions but rare indica accessions (4.44%) from the 3K sequenced rice genomes carry Hap 1 of OsNRAMP2. Our study sheds light on the molecular mechanism of grain Cd accumulation and provides a promising target for low-Cd rice breeding.

Another metal transporter protein from low-affinity cation transporter 1 (LCT1) family was found to remobilize Cd via phloem by forming association with metal complexes Uraguchi *et al.,* (2011). Low-affinity cation transporter 1 protein exists in the nodes and leaf blades and functions as a Cd transporter Uraguchi *et al.,* (2011) Fig. (42). Nevertheless, previous studies have revealed the active participation of P1BATPase and zinc/iron permease (ZIP) family transporter proteins in Cd transport across the plasmalemma into the shoots by utilizing energy obtained from ATP hydrolysis to transport Cd against the concentration gradient Hanikenne *et al.,* (2008); Wong and Cobbett, (2009). In phloem, certain Cd-binding agents such as glutathione and phytochelatins are predominantly present. After prolonged Cd exposure, the concentration of amino acid cysteine increased in the phloem and influenced long-distance Cd transport in the plants Jozefczak *et al.,* (2012).

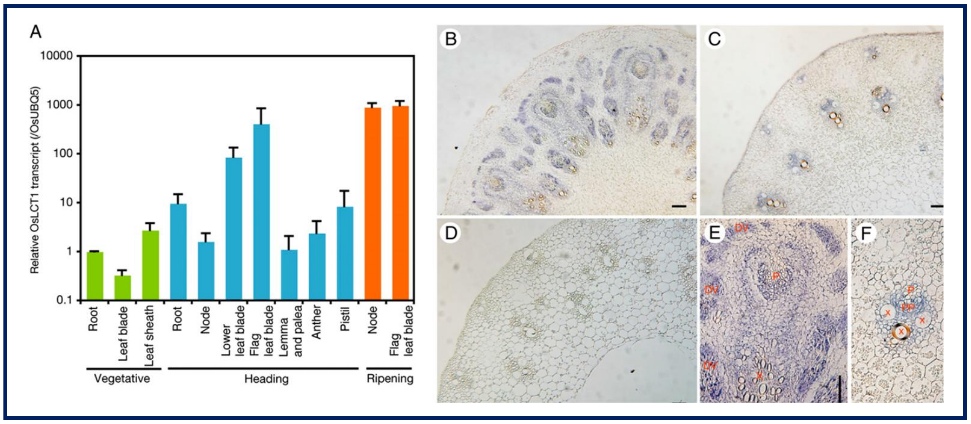

Fig. 42: Illustrates the expression profiles of OsLCT1 in rice. (A) Real-time PCR analysis. cDNAs were synthesized from total RNA extracted from various tissues of rice grown in a greenhouse, and the mRNA levels were quantified by real-time PCR. The data were normalized to OsUBQ5 and are shown relative to the vegetative root sample. The data are presented as means ± SD (n = 3). (B–F) In situ hybridization of OsLCT1 in node I. (B–D) Cross-sections of the middle of node I (B), the border region of node I and internodeII (C), and internode II (D). (E and F) Enlarged images of vascular bundles in the middle of node I (E) and in the border region of node I and internode II (F). (Scale bars = 10 μm.) DV, diffuse vascular bundles; P, phloem regions of large vascular bundles; PP; phloem parenchyma cells; X, xylem regions of large vascular bundles. After Uraguchi *et al.,* (2011).

Uraguchi *et al.,* (2011) reported that accumulation of cadmium (Cd) in rice (Oryza sativa L.) grains poses a potential health problem, especially in Asia. Most Cd in rice grains accumulates through phloem transport, but the molecular mechanism of this transport has not been revealed. In this study, we identified a rice Cd transporter, OsLCT1, involved in Cd transport to the grains. OsLCT1-GFP was localized at the plasma membrane in plant cells, and OsLCT1 showed Cd efflux activity in yeast. In rice plants, strong OsLCT1 expression was observed in leaf blades and nodes during the reproductive stage. In the uppermost node, OsLCT1 transcripts were detected around large vascular bundles and in diffuse vascular bundles. RNAi-mediated knockdown of OsLCT1 did not affect xylem-mediated Cd transport but reduced phloem-mediated Cd transport. The knockdown plants of OsLCT1 accumulated approximately half as much Cd in the grains as did the control plants. The content of other metals in rice grains and plant growth were not negatively affected by OsLCT1 suppression. These results suggested that OsLCT1 functions at the nodes in Cd transport into grains and that in a standard japonica cultivar, the regulation of OsLCT1 enables the generation of “low-Cd rice” without negative effects on agronomical traits. These findings identify a transporter gene for phloem Cd transport in plants Fig. (43).

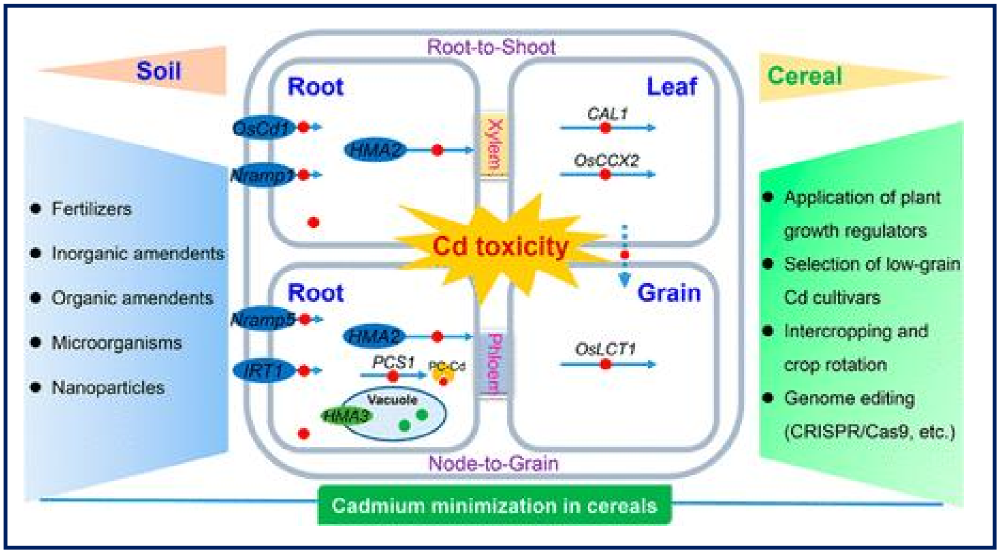

Fig. 43: Illustrates cadmium uptake, translocation, and accumulation mechanisms in cereal crops and reduce Cd uptake as well as potential remediation strategies, including the applications of plant growth regulators, microbes, nanoparticles, and cropping systems and developing low-Cd grain cultivars by CRISPR/Cas9. After Hu *et al.,* (2022)

Hu *et al.,* (2022) stated that cadmium contamination in soils and accumulation in cereal grains has posed food security risks and serious health concerns worldwide. Understanding the Cd transport process and its management for minimizing Cd accumulation in cereals may help to improve crop growth and grain quality. In this review, we summarize Cd uptake, translocation, and accumulation mechanisms in cereal crops and discuss efficient measures to reduce Cd uptake as well as potential remediation strategies, including the applications of plant growth regulators, microbes, nanoparticles, and cropping systems and developing low-Cd grain cultivars by CRISPR/Cas9. In addition, miRNAs modulate Cd translocation, and accumulation in crops through the regulation of their target genes was revealed. Combined use of multiple remediation methods may successfully decrease Cd concentrations in cereals. The findings in this review provide some insights into innovative and applicable approaches for reducing Cd accumulation in cereal grains and sustainable management of Cd-contaminated paddy fields.

Cadmium adversely disrupts the plant metabolic functions by affecting photosynthesis, respiration, opening and closing of stomata, hinders nutrient and water uptake and cell division and impedes nitrogen metabolism and protein expression Gallego *et al.,* (2012) , He, *et al.,* (2015). Cadmium excess inhibits the plant growth and production by posing toxic effects on the enzymes involved in Calvin cycle and carbohydrate metabolism Shi *et al.,* (2010); Javed *et al.,* (2017). Elevated Cd level impedes plant growth, promotes chlorosis by restricting chlorophyll biosynthesis and alters uptake of vital micronutrients Sidhu *et al.,* (2017). In leaves, Cd alters the photosynthetic machinery by interfering with enzymes of Calvin cycle, retarding photosystem I (PS I) and photosystem II (PS II) activity or by causing dissociation of ribulose-1, 5-bisphosphate carboxylase oxygenase enzyme (RuBisCO) Zoghlami *et al.,* (2011) Fig. (44).

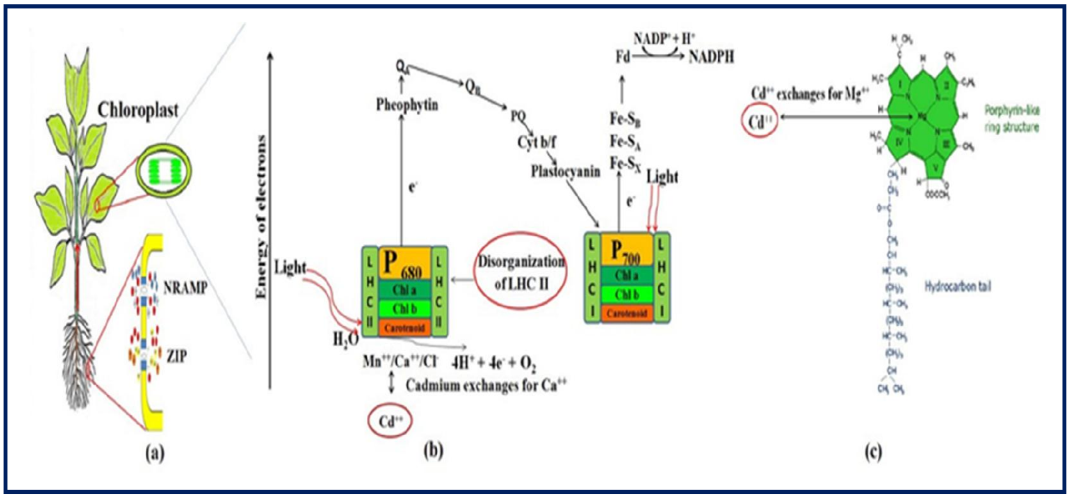

Fig. 44: Illustrates effects of Cd exposure to plants at different levels in photosynthetic machinery. (**a**) Cd uptake in cells through plasma membrane transporters. (**b**) Alteration in organization of oxygen evolving and light harvesting complexes, Cd also binds with QB pocket thus slows down electron flow from QA to QB. (**c**) Incorporation of Cd in chlorophyll molecule. After Parmar *et al.,* (2013)

Parmar *et al.,* (2013) stated that cadmium is a potentially toxic heavy metal that hampers plant productivity by interfering with their photochemistry. Cadmium causes disturbances in a range of physiological processes of plants such as photosynthesis, water relations, ion metabolism and mineral uptake. Cadmium pronouncedly affects photosynthesis by alteration of its vital machinery in all aspects. Photosynthesis is a well-organized and sequential process fundamental to all green plants and microorganisms that involves various components, including photosynthetic pigments and photosystems, the electron transport system and CO_2 reduction pathways. Any damage at any level caused by cadmium, critically affects overall photosynthetic capacity. Present review focuses on key effects of cadmium on photosynthetic apparatus including chloroplast structure, photosynthetic pigments, Chl-protein complexes and photosystems resulting in overall decrease in efficiency of carbon assimilation pathway. They also reported that photosynthetic machinery under cadmium stress Chloroplast structure Cadmium convincingly resulted in marked distortion of chloroplast ultrastructure leading to disturbed shape and inflated thylakoids Najeeb *et al.,* (2011). Chloroplast structure disturbance has been partly manifested by a notable decrease in chloroplast number and size, grana stacking, starch grain content and accumulation of plastoglobuli observed in various plants such as *Picris divarticata* (75 µM, 14 days after treatment (DAT)), *Hordeum vulgare* (5 µM, 15 DAT) and *Brassica* Ying *et al.,* (2010); Wang *et al.,* (2011); Elhiti *et al.,* (2012). Further, plants show differential aggregation of grana in young and older leaves. For instance in willow, older leaves showed swollen but organized thylakoids whereas young leaves appear to be more dense structured accompanied by tannin precipitation. Reed plant chloroplasts displayed a disturbed shape, wavy appearance of grana and stroma thylakoids and swollen intra thylakoidal space owing to lipid peroxidation, a consequence of increased lipid accumulation in thylakoids Hakmaouia *et al.,* (2007). Disruption in chloroplast structure also ensued due to increased peroxidation of membrane fatty acid and lipid contents resulting from enhanced lipooxygenase (LOX) activity Remans (2010). LOX mediates polyunsaturated fatty acid oxidation including chloroplast membrane lipids such as monogalactosyldiacyl-glycerol (MGDG), digalactosyldiacyl-glycerol (DGDG) and phosphatidyl glycerol (PG) hence, resulting in production of free radicals. LOX activity has been positively correlated with increased lipid peroxidation in plants such as Arabidopsis, Barley, Lupine and Phaseolus under Cadmium stress Maksymiec and Krupa, (2006), Tamas *et al.,* (2009). A significant decrease has also been reported in the content of polaracyl lipids especially MGDG, DGDG and PG in tomato chloroplasts membranes Djebali *et al.,* (2005) which is considered indispensable for maintenance of membrane integrity. Grana disorganization can be attributed to reduced MGDG level, as well as the decrease in 16:1 trans fatty acid content in MGDG and PG. In Brassica napus (50 µM, 15 DAT) leaves, remarkable decrease up to 80–84 % was observed in DGDG and MGDG respectively Nouairi *et al.,* (2005), which may possibly be a reason for disintegrated grana.

Inside the plant cell, cadmium accumulation hinders the activities of various mitochondrial enzymes such as isocitrate dehydrogenase, succinate dehydrogenase and malate dehydrogenase Bansal, *et al.,* (2002) Fig. (45). Cadmium distress in plants stimulates the formation of reactive oxygen species (ROS) that causes protein oxidation by rupturing peptide bonds, induces damage to lipid and nucleic acids and alters carbohydrate metabolism Sobrino- Plata, *et al.,* (2014) Fig. (45). Additionally, excess of cadmium imparts oxidative stress, alters the gene expression and cell cycle and instigates apoptosis in plants Kapoor *et al.,* (2014); Sidhu *et al.,* (2017).

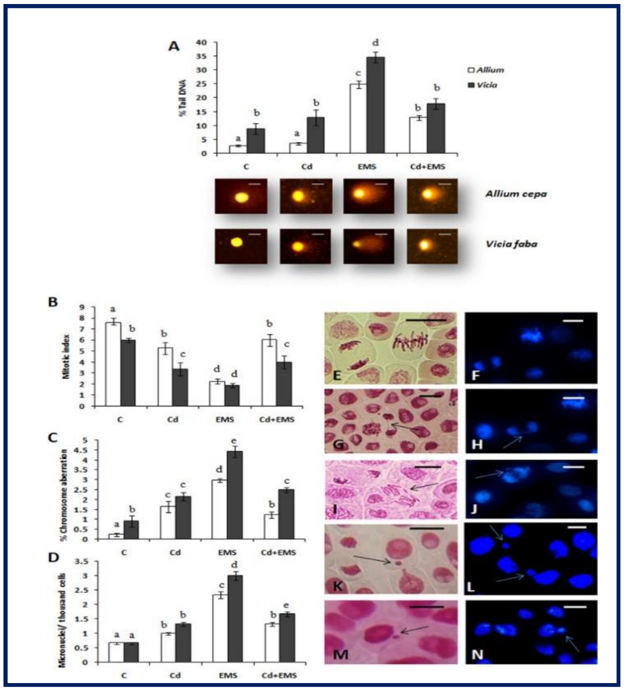

Fig. 45: Assessment of Genotoxicity (A) DNA damage estimated by comet assay in root nuclei of *Allium cepa* and *Vicia faba.* Representative images are of % tail DNA in *A. cepa* and *V. faba*. (B) Mitotic index (MI), (C) Chromosome aberrations (CA), (D) Micronuclei (MN) frequency. (E) Normal metaphase plate in *A. cepa*, (F) Normal metaphase plate in *V. faba*, (G) Anaphase bridge in *V. faba*, (H) Anaphase bridge in *A. cepa*, (I) Chromosome fragmentation in *A. cepa*, (J) Chromosome fragmentation in *V. faba*, (K-L) Micronucleus in *A. cepa*, (M-N) Micronucleus in *V. faba.* Scale bar: 50 µm. Error bars are mean ± SEM values of three independent experiments, different alphabets represent significant differences ($P < 0.05$) by Holm–Sidak multiple comparison test. After Chakrabarti Manoswini and Anita Mukherjee, (2021).

Cadmium toxicity causes inhibition and abnormalities of general growth in many plant species. After long-term exposure to cadmium, roots are mucilaginous, browning, and decomposing; reduction of shoots and root elongation, rolling of leaves, and chlorosis can occur. Cadmium was found to inhibit lateral root formation while the main root became brown, rigid, and twisted Krantev, *et al.,* (2008); Yadav, (2010); Rascio and Navari-Izzo, (2011). The main reason indicated is disordered division and abnormal enlargement of epiderma and cortical cell layers in the apical region. The changes in the leaf included alterations in chloroplast ultrastructure, low contents of chlorophylls, which caused chlorosis, and restricted activity of photosynthesis He *et al.,* (2008); Rascio *et al.,* (2008); Lee *et al.,* (2010); Liu, *et al.,* (2010); Miyadate *et al.,* (2011). Rascio *et al.,* (2008) reported that treatment of rice seedlings with cadmium led to inhibition of root growth and alterations in their morphogenesis. In pea plants, the Cd stress also caused disorders in root elongation and the mitotic process and caused chromosomal aberrations of root tips. The observation showed that in these abnormalities as ligands, bridges, stickiness, precocious separation, and fragments were most common Siddiqui *et al.,* (2009). High Cadmium concentration (250 µM), the disorder of mitosis of roots in pea happens rapidly, even after 24 h of treatment. An unusual number of nucleus populations in the differentiated roots were found Fusconi *et al.,* (2006), (2007). In *Allium cepa*, the inhibition of mitotic index, induction of chromosome aberration, mitotic aberrations, and micronucleus formation were observed after 24 h of treatment with Cd. In addition, damage to the DNA in root-cap cells has been found Seth *et al.,* (2008) Fig. (45).

Chakrabarti Manoswini and Anita Mukherjee, (2021) reported that Plants as sessile organisms have developed some unique strategies to withstand environmental stress and adaptive response (AR) is one of them. In the present study Cadmium induced AR was evaluated to ameliorate the genotoxicity of a known chemical mutagen ethyl methanesulphonate (EMS) based on cytotoxicity, genotoxicity and oxidative stress in two model plant systems *Allium cepa* L. and *Vicia faba* L. Priming the plants with cadmium chloride (CdCl2, 25 and 50 µM) reduced the genotoxicity of EMS (0.25 mM). Cd-induced adaptive response (AR) was evident by the magnitude of adaptive response (MAR) values calculated for cytotoxicity, genotoxicity and biochemical parameters. In addition, the involvement of some major metabolic pathways and epigenetic modifications in AR was investigated. Metabolic blockers of protein kinase cascades, DNA repair, oxidative stress and *de novo* translation interfered with the adaptive response implying their role in AR whereas, inhibitors involved in post-replication repair and autophagy were ineffective implicating that they probably have no role in the AR studied. Moreover, to find the role of DNA methylation in AR, methylation-sensitive comet assay was carried out. Simultaneously 5-methyl- 2'-deoxycytidine (5mdC) levels were quantified by HPLC (high performance liquid chromatography). AR was eliminated in cells treated with a demethylating agent, 5-aza-2'deoxycytidine (AZA). Results implied a contribution of DNA hyper methylation. To the best of our knowledge, this is a first report correlating DNA methylation to Cd-induced adaptive response in plants undergoing genotoxic stress Fig. (46).

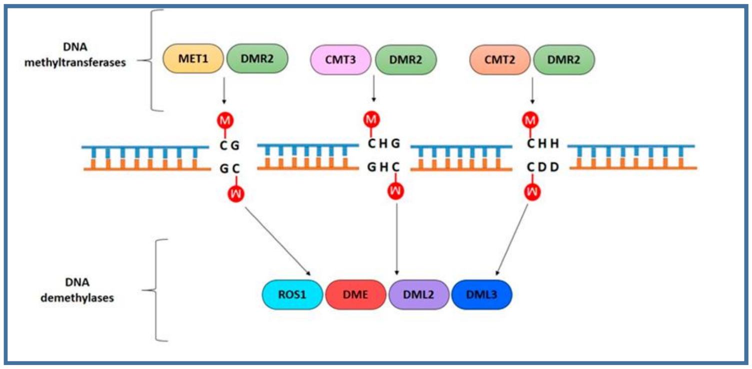

Fig. 46: Specific DNA methyltransferases and demethylases mediate cytosine methylation (red circle) in different sequence contexts. CG, CHG, and CHH methylation are carried out by MET1, CMT3, and CMT2, respectively. DRM2, involved in the RdDM pathway, regulates all sequence context methylation. ROS1, DME, DML2, and DML3 act as demethylases. After Lucibelli *et al.,* (2022)

Lucibelli *et al.,* (2022) reported that DNA methylation is an epigenetic modification of the genome involved in the regulation of gene expression and modulation of chromatin structure. Plant genomes are widely methylated, and the methylation generally occurs on the cytosine bases through the activity of specific enzymes called DNA methyltransferases. On the other hand, methylated DNA can also undergo demethylation through the action of demethylases. The methylation landscape is finely tuned and assumes a pivotal role in plant development and evolution. Different molecular aspects of DNA methylation and some plant physiological processes are influenced by this epigenetic modification in model species, crops, and ornamental plants such as orchids. In addition, the relationship between the changes in plant DNA methylation levels and the response to biotic and abiotic stress.

8. Effect of Cd on stress proteins

Extreme changes in environment could cause changes in gene expression, whereby leading to changes in the diversity of proteins in the cell. Therefore, changes in protein abundances under stressful conditions can be molecular markers for the manifestations of the responses to stress in organisms. In plants, the proteomics approach is developed as an important method for research on stress tolerance Nanjo *et al.,* (2011). In recent years, much evident revealed that the response to stress in terms of proteomics occurred rather rapidly in plants after the exposure began. Heat-shock proteins (HSPs) are presently known as proteins that have functions to resist stress in eukaryotes Fig. (47).

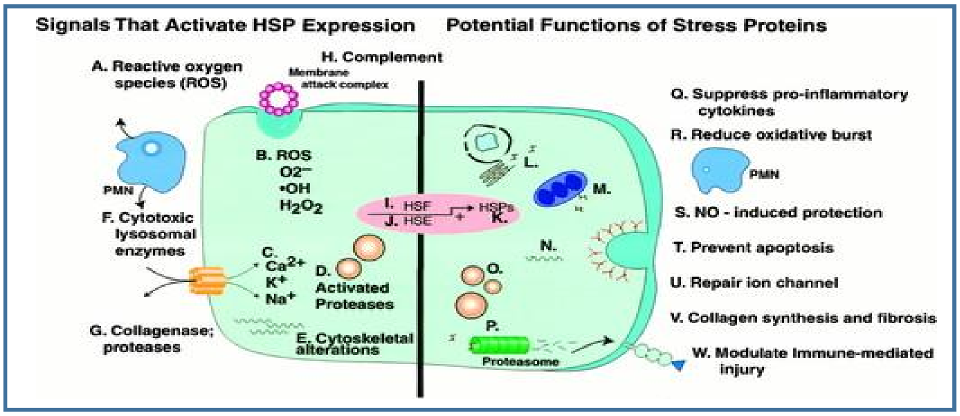

Fig. 47: Illustrates summary of the major pathophysiological signals that activate HSP synthesis (left of vertical solid line) and the potential functions of HSPs (right of vertical solid line). Cellular injury is manifested by increased generation of ROS, availability of redox-active iron, peroxidation of membrane lipids, and protein damage, among others. The extracellular sources of ROS (A) could be endothelial cells, VSMCs, and even myocytes in the surrounding tissue; mitochondrial electron transport of molecular oxygen (B) may be the main intracellular source for ROS generation. Intracellular free calcium (C), which increases 10-fold within 10 minutes of reperfusion, has been implicated in the activation of proteases (D), which, in turn, are thought to contribute to intracellular myocardial injury. Damage to the cytoskeleton (E) is an early event of ischemic injury, which causes ventricular dysfunction or "myocardial stunning" when the injury is reversible.87 Myocardial injury could also occur from recruitment of polymorphonuclear leukocytes (PMNs) by multiple mechanisms into the ischemic territory and by the release of oxygen-derived free radicals (A), cytotoxic lysosomal enzymes (F), extracellular proteases (G), and complement activation (H) Diverse physiological signals are thought to activate the stress-inducible HSF1 (I), which binds to the sequence-specific heat shock element (HSE) (J), contained in the promoters of all HSPs (K). Although the precise mechanism of Hsp70-mediated ischemic protection is poorly understood, it is widely attributed to the biological property of "molecular chaperones," which are proposed to assist in the assembly or repair of newly synthesized or damaged proteins. In physiological terms, potential functions for molecular chaperones in the ischemic heart include the following: protein folding of newly synthesized polypeptides essential for maintaining oxidative metabolism after myocytes damage (L), protection of mitochondria from ROS and cytokines such as TNFa and translocation of newly synthesized proteins during organelle repair (M), repair of critical structural proteins after ischemia-induced cytoskeletal alterations (N), recycling of membrane vesicles (Hsc70) (O), transport of potential toxic byproducts for degradation by the proteasome (P), suppression of proinflammatory cytokines such as pro– interleukin-1b (Q), suppression of NADPH oxidase and the oxidative burst by the heat shock response (R), protection by NO production from inducible synthesis of HSP expression (S), prevention of apoptosis either through the mitochondrial chaperone Hsp60 binding of cytochrome c and/or Hsp70 binding of cytosolic targets (T), repair of ion channel (U), collagen synthesis by Hsp chaperone for reparative fibrosis (V), and modulation of the immune-mediated ischemic injury (W). After Benjamin McMillan, (2010).

In Cd-treated maize plants Reddy and Prasad, (1993) reported a synthesis of 70 kDa phosphoproteins (HSP). In *Lycopersicon peruvianum* L., pre-treatment with a short heat stress before Cd exposure induced a protective effect by preventing membrane damage. HSP17 (molecular weight 17 kDa) and HSP70 proteins were found in the cytosol of heat-shocked cells Neumann *et al.,* (1994). In Cd-treated pea plants, pathogen-related proteins PrP4A and HSP71 were found, and they probably serve to protect cells against damages induced by Cd Rodriguez- Serrano *et al.,* (2009). In wheat seedlings treated with 50 µM CdCl2 for 48 h, a 51-kDa soluble protein was found. This protein was designated as a Cd stress-associated protein. It was generated mainly in the root tissue of treated and control seedlings and located below the plasma membrane and outer periphery of the tonoplast Mittra *et al.,* (2008).

In poplar (*Populus tremula* L.) exposed to Cd for a short term (14 days) or a longer term (56 days) treatment, it was found that stress-related proteins, like HSPs, proteinases, and pathogenesis-related proteins, increased in abundance in leaves. The abundance of many typical stress-related proteins like HSPs or glutathione-S-transferases was increased, whereas most of the proteins from the primary metabolism (glycolysis, tricarboxylic acid cycle, nitrogen metabolism, and sulphur metabolism) were severely decreased in abundance Kieffer *et al.,* (2009) Fig. (48).

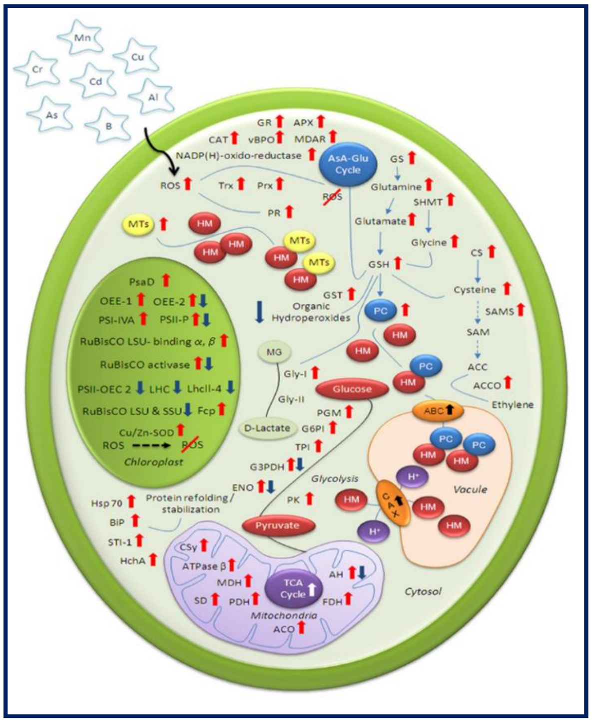

Fig. 48: Schematic illustration of various cellular mechanisms for mitigating heavy metal (HM) stress. Information about highlighted proteins gathered from published proteomic articles related to plant HM-toxicity. Up and down arrows indicate HM-induced increase and decrease protein abundance respectively. ATPase β, ATP synthase subunit beta; AH, aconitate hydratase; AsA-Glu, ascorbate glutathione; APX, ascorbate peroxidase; ACC, 1-aminocyclopropane-1-carboxylic acid; ACO, aconitase; CAT, catalase; CAX, cation/proton exchanger; CS, cysteine synthase; CSy, citrate synthase; ENO, enolase; FDH, formate dehydrogenase; G3PDH, glyceraldehyde-3-phosphate dehydrogenase; GR, glutathione reductase; Gly-I, glyoxalase I; GS, glutamine synthetase; GSH, reduced glutathione; LHC, light harvesting complex; LhcII-4, light-harvesting chlorophyll-a/b binding protein; LSU, large subunit; MTs, metallothioneins; MG, methylglyoxal; MDAR, monodehydroascorbate reductase; MDH, malate dehydrogenase; OEE, oxygen-evolving enhancer protein; PC, Phytochelatin; Prx, peroxidoxin; PR, pathogenesis-related; PDH, pyruvate dehydrogenase; PSII-OEC 2, photosystem II oxygen-evolving complex protein 2; PS, photosystem; ROS, reactive oxygen species; RuBisCO, ribulose-1,5-bisphosphate carboxylase oxygenase; SD, succinate dehydrogenase; SAM, S-adenosylmethionine; SSU, small subunit; Trx, thioredoxin; TPI, triosephosphate isomerases; TCA, tricarboxylic acid. After Hossain and Komatsu, (2013)

Hossain and Komatsu, (2013) reported that modulation of plant proteome composition is an inevitable process to cope with the environmental challenges including heavy metal (HM) stress. Soil and water contaminated with hazardous metals not only cause permanent and irreversible health problems, but also result substantial reduction in crop yields. In course of time, plants have evolved complex mechanisms to regulate the uptake, mobilization, and intracellular concentration of metal ions to alleviate the stress. Since, the functional translated portion of the genome plays an essential role in plant stress response, proteomic studies provide us a finer picture of protein networks and metabolic pathways primarily involved in cellular detoxification and tolerance mechanism. Role of metal stress-related proteins involved in antioxidant defense system and primary metabolism is critically reviewed to get a bird's-eye view on the different strategies of plants to detoxify HMs.

Lee *et al.,* (2010) reported that Cd affected the synthesis of 36 proteins in rice. In roots, the synthesis of 16 proteins was increased, while the synthesis of 1 protein was reduced. In leaves, the synthesis of 16 proteins was up regulated, while the synthesis of 3 proteins was down-regulated. Treatment of tomato plants with a low Cd concentration (10 μM) induced changes in 36 polypeptides, while higher cadmium concentration (100 μM) induced changes in 41 polypeptides Rodriguez-Celma *et al.,* (2010). In 3-week-old *Arabidopsis thaliana* seedlings exposed to 10 μM Cd, it was found that among 730 determined proteins 21 were up regulated in response to cadmium. These proteins can be classed into 5 groups in accordance with their functions: 8 proteins are involved in group **(a)** that involve ROS detoxification, 6 proteins belong to group **(b)** that involves carbon metabolism and photosynthesis, 4 proteins belong to group **(c)** that involve protein metabolism, and 5 proteins are classed in group **(d)** and group **(e)** that involve gene expression and with various or unknown function Semane, *et al.,* (2010). Studying barley tolerance to boron, Atik *et al.,* (2011) determined 7 proteins that were up-regulated in response to boron treatment. Some of the proteins were related to photosynthesis and others were located in the vacuole.

9. Cadmium impacts and remediation strategies

9.1. Defense mechanisms of cadmium toxicity in plants

The mechanisms leading to cadmium toxicity in plants can be distinguished into two strategies, i.e., tolerance and avoidance Tran and Popova, (2013). The avoidance strategy includes limiting the uptake of cadmium into the plant Liu *et al.,* (2015). The tolerance mechanism in plants includes storing and accumulating of Cd by binding it to peptides, amino acids, and proteins P′al *et al.,* (2006); Abbas, *et al.,* (2017) Fig.(49).

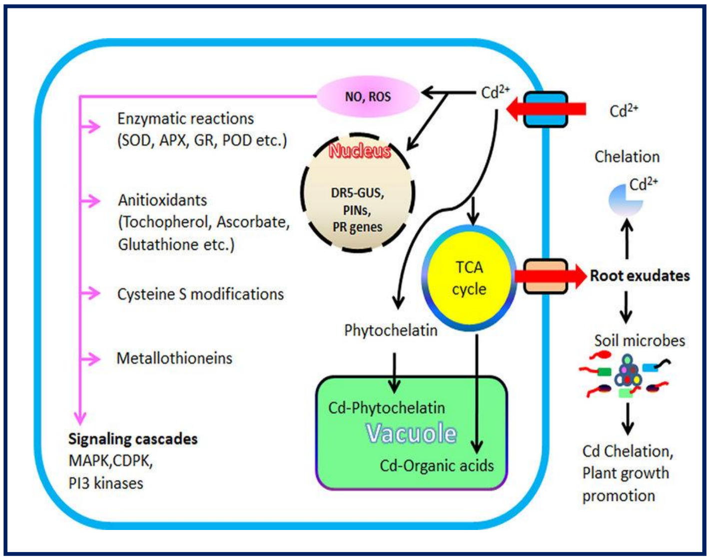

Fig. 49: Scheme of cadmium stress and detoxification. Tricarboxylic acid cycle (TCA) intermediates utilized for the synthesis of metal chelators (e.g., siderophores, organic acids) during Cd exposure. Cadmium traverses the cell walls via Zn, Fe, Cu, and Ca ions transporters. Entrance of Cd leads to the overproduction of reactive oxygen species (ROS) (e.g., H_2O_2, O_2 , and OH)

and nitric oxide (NO) resulting upregulation of antioxidant enzymes activity (e.g., ascorbate peroxidase (APX), guaiacol peroxidase (POD), superoxide dismutase (SOD), glutathione reductase (GR)), and synthesis of antioxidants. Excess Cd causes protein S-nitrosylation and metallothioneins production. The key signaling pathways involved in Cd stress are mitogen-activated protein kinase (MAPK), calcium-dependent protein kinase (CDPK), and phosphoinositide 3-kinases (PI3 kinases), respectively. Cadmium stress also activates auxin-responsive promoter (DR5-GUS), auxin efflux carriers (PINs), and pathogen related genes (PR genes). Phytochelatins synthesized in response to Cd stress act as a plant defense system against Cd via vacuolar sequestration of Cd. After El Rasafi, *et al.,* (2020)

Certain pathways formed by plants to cope with cadmium exposure are linked to some stress-signaling molecules, i.e., jasmonic acid, methyl jasmonate, humic acid, salicylic acid, ethylene, and nitric oxide Shahid, *et al.,* (2014). Stress-signaling compounds caused by treatment with Cadmium are involved in cell reaction to minimize the toxicity of Cadmium Popova, *et al.,* (2012). Most plants, even at high concentrations of cadmium, thrive, and produce grain and fruit in Cd-contaminated soils Garnier, *et al.,* (2006). Some plants damaged by cadmium toxicity possess a hyper-tolerant ability of their organelles and tissues Lehotai *et al.,* (2011); Shahid *et al.,* (2014). Strategies to deal with the toxicity of Cd involve the distribution and uptake of cadmium and are known as hyperaccumulation Younis, *et al.,* (2016). Similarly, other plants improved antioxidant activity against ROS to protect tissues and cells from cadmium destruction Zhao, *et al.,* (2012). Hyperaccumulating plants do not display phytotoxicity effects Lata *et al.,* (2019). Approximately 450 species of angiosperm were classified as hyperaccumulators of metals until 2011, and new plants having potential for hyperaccumulation continue to be found Rascio and Navari-Izzo, (2011); Tran and Popova, (2013). For hyperaccumulating plants under the control of detoxification processes, the toxic effect of metals at extreme concentration is minimized Altin¨ozlüm, *et al.,* (2012). Such types of mechanisms are based on sub-cellular compartmentalization and chelation Yadav, (2010); Lata *et al.,* (2019). Cadmium uptake in plants tends to occur mainly through transporters, i.e., Zn^{2+}, Mn^{2+}, Fe^{2+}, and Ca^{2+} Rascio and Navari-Izzo, (2011). The uptake of cadmium in non-hyperaccumulating plants is non-specific Lu, *et al.,* (2009). In maize, the adsorption of Cd on root apoplast may serve as the major driving force for plant uptake of this metal from the soil, but the effect in rice was contrary Redjala, *et al.,* (2009); Lu, *et al.,* (2009). Root-to-shoot transport of metals including Cd in hyperaccumulating plants is diverse from that in non-accumulating plants Yeh, *et al.,* (2007). This type of approach retains the majority of metal ions that are taken from the soil into the root cells, detoxifies them in the cytoplasm by storing or chelating them in the vacuoles, and quickly translocates these toxic substances to plant shoots with the help of xylem Liu, *et al.,* (2018). Also involved are various features in the tonoplast of root cells, which help metals ions to effluent quickly from the vacuoles Garnier, *et al.,* (2006); Popova, *et al.,* (2012). Free amino acids i.e., histidine that forms stable compounds with divalent cations, seem to play a vital part in hyperaccumulation of trace metals Hassan and Aarts, (2011). Sequestration, detoxification, and storage of trace metal ions including Cd in plant shoots are significant approaches of hyperaccumulating plants Lata, *et al.,* (2019). Most of the detoxification and sequestration of metals takes place in cuticles, epidermis, and trichomes where the photosynthetic activity is least injured Hasan *et al.,* (2009); Shahid *et al.,* (2014) Fig.(50).

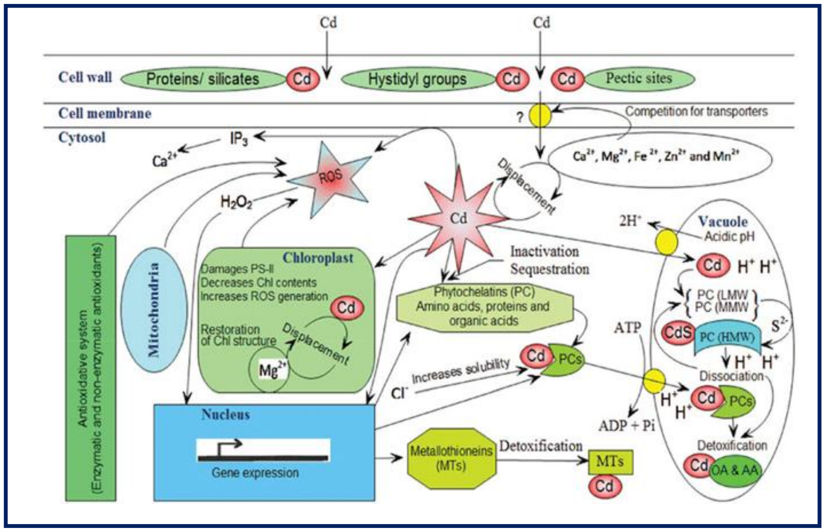

Fig. 50: Illustrates schematic diagram of different cellular processes involved in Cd sequestration in plants. After Choppala, *et al.,* (2014).

Sohail *et al.,* (2019) reported that metals are excluded from guard cells and subordinate cells of stomata. Furthermore, protecting the functionary stomatal cells from the phytotoxic effects of Cd ions Fig. (51). A significant plant technique for detoxifying trace metals ion is the production of unique low molecular weight chelators to prevent attaching to physiologically relevant proteins and promoting their transport into cell vacuoles Ahmad *et al.,* (2015).

Song *et al.,* (2019) reported that photosynthesis plays an essential role in plant growth and crop yield, and the mechanisms of the effects of cadmium on photosynthetic performance require more attention. The acute toxicity of cadmium in soil to the photosynthetic capacity of Hybrid Pennisetum was evaluated using gas exchange parameters, A/Ci curves, light response curves, and chlorophyll a fluorescence transients after exposure to elevated Cadmium concentrations (0, 10, 20, 50, 70, and 100 mg. kg^{-1}) for a 3-month period. The results indicated that leaf cadmium concentration in Hybrid Pennisetum increased with the strength of soil Cd stress and ranged from 4.9 to 15.8 µg .g^{-1} DW. The accumulation of leaf Cd severely restricted photosynthesis and its non-stomatal limitation in regulating the photosynthetic performance of Hybrid Pennisetum. The leaf chloroplasts at 10 and 20 mg. kg^{-1} Cd concentrations showed no noticeable change, but the chlorophyll content significantly decreased by 9.0–20.4% at 50–100 mg kg^{-1} Cd concentrations. The Cd treatments also decreased plant ribulose-1,5-bisphosphate (RuBP) activity (Vcmax) and regeneration capacity (Jmax), triose phosphate utilization (TPU), light-saturated photosynthesis (Amax), apparent quantum yield (AQY), light saturation point (LSP), and dark respiration (Rday), but Cadmium treatment increased the light compensation point (LCP). The shape of chlorophyll a fluorescence transients in leaves was altered under different Cd treatments. The increased OJ phase and the decreased IP phase in fluorescence induction curves suggested that Cd toxicity inhibited both light use efficiency and photo damage avoidance ability. These results suggested that the decrease in photosynthesis through exposure to Cadmium might be a result of the decrease in leaf chlorophyll content, Rubisco activity, and RuBP regeneration, inhibition of triose phosphate utilization, reduction of the ability to use light and provide energy, and restrictions on electron transport in PSII.

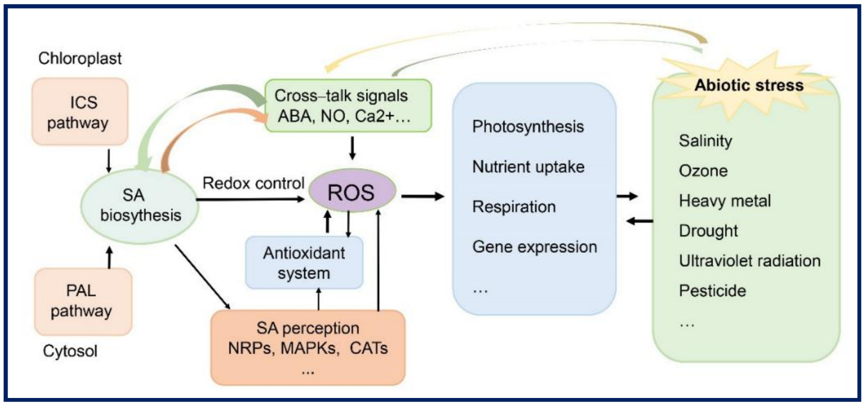

Fig. 51: Schematic representation of the non-stomatal limitation in regulating the photosynthetic performance of Hybrid Pennisetum under Cd stress conditions. The figure shows that the decrease in leaf chlorophyll content, reduction of the ability to use light, and restrictions on carbon assimilation caused by high Cd content in leaves limit the capacity of Hybrid Pennisetum in carbon fixation. After Song, *et al.,* (2019).

9.2. Mitigating cadmium toxicity in plants by phytohormones

Salicylic acid (SA) response against heavy metal stress is a new study subject in the field of crop physiology Fig. (52).

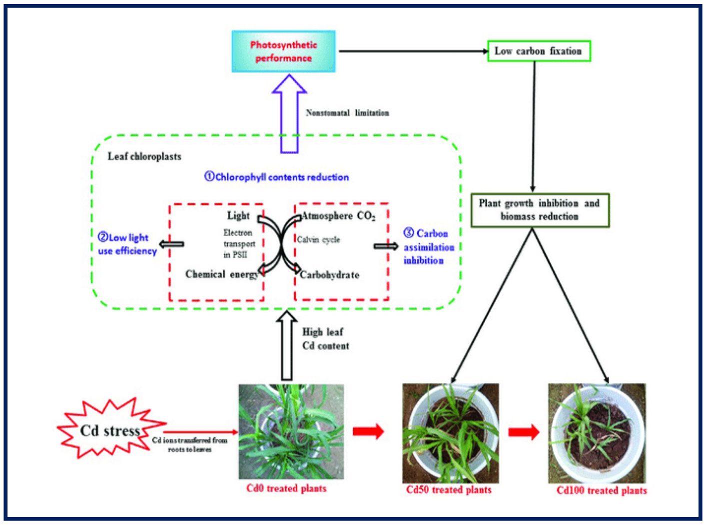

Fig. 52: Modulation of SA signalling in plant tolerance under abiotic stress. After Liu *et al.,* (2022)

Liu, *et al.,* (2022) stated that in recent decades, many new and exciting findings have paved the way to the better understanding of plant responses in various environmental changes. Some major areas are focused on role of phytohormones during abiotic stresses. Salicylic acid (SA) is one such plant hormone that has been implicated in processes not limited to plant growth, development, and responses to environmental stress. Summarizing the various roles and functions of SA in mitigating abiotic stresses to plants, including heating, chilling, salinity, metal toxicity, drought, ultraviolet radiation, etc. Consistent with its critical roles in plant abiotic tolerance, and identifies the gaps in the literature with regard to the complex network between SA and reactive oxygen species, ABA, Ca^{2+}, and nitric oxide. Furthermore, the molecular mechanisms underlying networks that control development, stress responses in plants.

Results indicated that seed imbibition with SA affected physiological processes related to growth and development and photosynthesis in maize plants. The beneficial effect of SA during the earlier growth period may help plants to avoid cumulative damage upon exposure to Cd Research over the past 20 years has strongly indicated that SA is a very promising molecule for the reduction of Cd toxicity in plants. Here, we reviewed reports describing the promoting role of SA in Cd resistance under various treatment methods, including pre-soaking, hydroponic exposure, and spraying. Fig. (53) Proposed the possible roles of SA in alleviating Cd toxicity to plants. However, there remains a contradiction between the effects of SA at low and high doses.

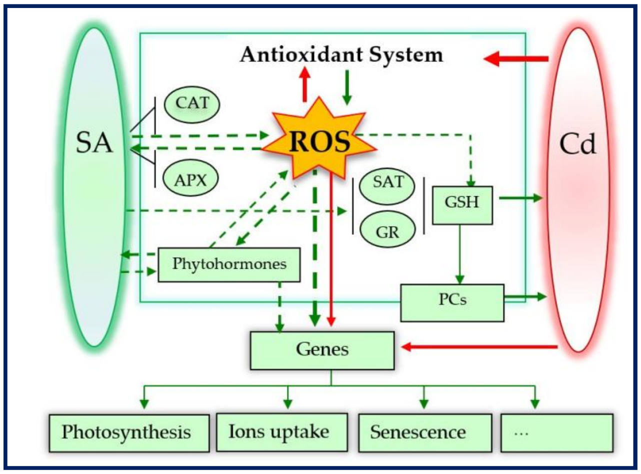

Fig. 53: Possible roles of SA in alleviating Cd toxicity to plants. The dotted arrows mean possible signalling pathways. Red and green arrows indicate damage and positive effects, respectively. After Guo *et al.,* (2019)

Guo *et al.,* (2019) stated that salicylic acid (SA), as an enigmatic molecule in plants, has been intensively studied to elucidate its role in defense against biotic and abiotic stresses. The role of the SA pathway in regulating cadmium tolerance in plants under various SA exposure methods, including pre-soaking, hydroponic exposure, and spraying. Pretreatment with appropriate levels of SA showed a mitigating effect on cadmium damage, whereas an excessive dose of exogenous SA aggravated the toxic effects of Cd. Salicylic acid (SA) mechanisms are mainly associated with modification of reactive oxygen species (ROS) levels in plant tissues. Then, ROS, as second messengers, regulate a series of physiological and genetic adaptive responses, including cell wall construction, balancing the uptake of Cd and other ions, refining the antioxidant defense system, and regulating photosynthesis, glutathione synthesis and senescence. These findings together elucidate the expanding role of SA in phytotoxicology.

They also reported that roles of SA in Alleviating cadmium toxicity taking a comprehensive view of SA roles in response to cadmium toxicity, this review focuses on the recent advances in the physiological and molecular mechanisms of the following aspects: plant growth, cadmium immobilization and distribution, element assimilation, photosynthesis, ROS and the antioxidant defense system, glutathione, and senescence. Cadmium exposure inhibits plant growth Sanità di, *et al.,* (1999). It also causes morphological changes in leaves and roots, such as leaf chlorosis and lignification of cell walls in root tissues Souza *et al.,* (2011). Cadmium induced growth inhibition is mainly due to reduction of net photosynthetic rate Qian, *et al.,* (2010), inactivation of enzymes involved in CO_2 fixation Perfus-Barbeoch *et al.,* (2002), disturbance of element metabolism Boussama *et al.,* (1998), and induction of lipid peroxidation Iannone, *et al.,* (2010). As a multifaceted phytohormones, SA mediates physiological and biochemical processes during all plant developmental stages, including seed germination, vegetative growth, seed production, and senescence Vicente and Plasencia, (2011), Morris, *et al.,* (2000). Arabidopsis mutants with constitutively high levels of SA, such as cpr5 Bowling, *et al.,* (1997), acd6−1 Rate *et al.,* (1999), agd2 Rate, *et al.,* (2001), and pi4kIIIβ1β2 Šašek *et al.,* (2014) exhibit dwarf phenotype. In contrast, the SA-depleted Arabidopsis NahG transgenic plants have a longer vegetative stage and higher growth rate compared with wild-type plants Abreu and Munné-Bosch, (2009). The biochemical events involved in the regulation of cell division and growth by SA still need to be clarified Janda and Ruelland, (2015) which may be cross-linked with AUX, ROS, Ca^{2+} and mitogen-activated protein kinase (MAPK) pathways Vicente and Plasencia, (2011). In the presence of Cadmium, exogenous treatment with SA showed a positive effect on the growth of various plant species, such as flax Belkhadi, *et al.,* (2010), bluegrass Guo *et al.,* (2013), radish Raza and Shafiq, (2013), and rice Guo, *et al.,* (2009), Guo, *et al.,* (2007). Soybean seedlings treated with 6 mg kg^{-1} Cd for 72 h showed retarded growth symptoms in roots, stems and leaves Drazic and Mihailovic, (2005). SA applied simultaneously at the levels of 1 µM, 10 µM and 100 µM significantly reversed these inhibitory effects. In barley, Cd exposure reduced the dry weight of shoots and roots by approximately 35%, whereas pretreatment with SA resulted in significant recovery of all the growth parameters Metwally, *et al.,* (2003).

Exogenous treatment with SA has a dose-dependent effect on plant growth, as observed in the Arabidopsis mutants with unnecessary or deficient SA levels. Presoaking treatment with 10 to 500 µM SA increased the germination of *Kentucky bluegrass* seeds, while the germination sharply declined under 1000 to 5000 µM SA treatments Guo *et al.,* (2013).The cadmium induced inhibitory effects on ryegrass growth were significantly alleviated by low SA concentrations, but no effects were found for the high SA concentration Bai *et al.,* (2015). Some plants, such as hemp Shi *et al.,* (2009), are vulnerable to high levels of SA but still benefit from SA treatment when they suffer from Cadmium toxicity. In castor bean seedlings, SA treatment significantly worsened plant growth in both the presence and absence of Cd Liu *et al.,* (2011). Furthermore; inconsistent conclusions were drawn in experiments with Arabidopsis transgenic plants or mutants. The cadmium inhibited growth in Arabidopsis was aggravated by unnecessary SA in snc1 mutants and mitigated by the depletion of SA in nahG transgenic lines Tao *et al.,* (2013). It seems that endogenous SA negatively regulates Arabidopsis tolerance to Cd. However, the sid2 mutants with SA-deficient phenotype showed a cadmium sensitive phenotype that manifested as having accentuated cadmium induced growth inhibition Guo *et al.,* (2016). Therefore, it is hypothesized that pretreatment with SA may increase cadmium accumulation in the cell wall and prevent cadmium translocation into other cell organelles. Until now, only a few experiments with peanut and ryegrass have shown that SA treatment reduced Cd influx by rearrangement of the cell wall composition Xu *et al.,* (2015), Wang *et al.,* (2013), Bai *et al.,* (2015). It has been reported that either SA pretreatment or cadmium treatment alone strengthened the root cell wall in rice Guo *et al.,* (2007). However, it was also found that SA treatment with Cd application failed to synergistically affect the cell wall construction or the activity of enzymes related to lignin synthesis, such as polyphenol oxidase (PPO), peroxidase (POD) and PAL. This might be because the strong toxicity of cadmium maximized the process of lignification, which concealed the SA signalling role in cell wall construction. Alternatively, SA could be involved in the expression of specific proteins or defence-related enzymes. These results may provide a good background for strategies aimed at manipulating plants for decreased cadmium content in order to develop crops capable of tolerating environmental changes with as little damage as possible Krantev *et al.,* (2008); Popova *et al.,* (2008), (2009) and (2012). Several hypothetical explanations may account for the positive effect of SA on cadmium induced stress in plants. SA prevented cumulative damage development in response to cadmium. The suggestion was supported by the data of the lowered root level of cadmium in SA- pretreated maize plants Krantev *et al.,* (2008). Szalai *et al.,* (2005) reported similar data in maize and by Popova *et al.,* (2009) in pea plants. Obviously, the lowered root level of cadmium in SA-pretreated plants reduced the harmful effect of Cd and exerted a beneficial effect on growth and photosynthesis. SA alleviated the oxidative damage caused by cadmium. Pretreatment with SA exerted a protective effect on the membrane stability judging by the increased total lipids level and by changes in their fatty acid composition Popova *et al.,* (2008), (2012). Hsu and Kao, (2003) have suggested a protective effect of abscisic acid (ABA) against Cd toxicity Fig. (54).

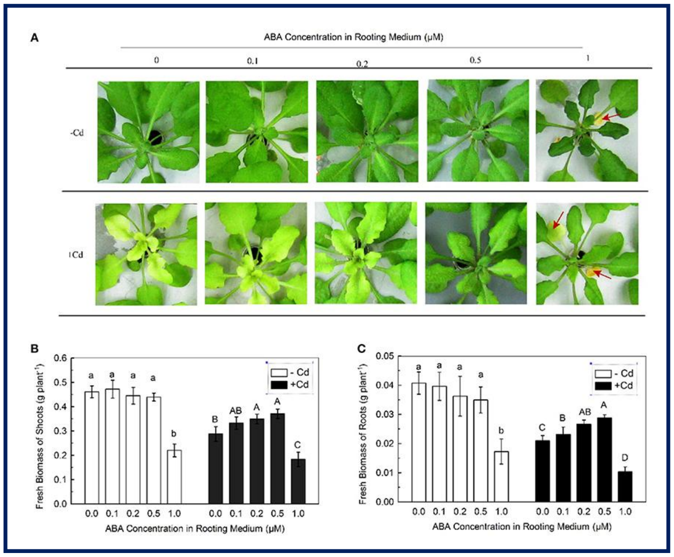

Fig. 54: Effects of varying doses of ABA on Cd tolerance of Col-0 plants. Plants were grown in Cd-free (−Cd) or 10µM Cd-added (+Cd) nutrient solution with varying concentrations of ABA added for 7 day. The Fe level in the nutrient solution was 25µM. (A) Leaf chlorosis. (B) Shoot biomass. (C) Root biomass. Red arrows indicate necrotic leaves. Data are means ± SD (n = 8). Different letters represent significantly different values at P < 0.05. After Fan, *et al.,* (2014)

Fan *et al.,* (2014) reported that cadmium under cadmium exposure condition, application with low doses of (0.1–0.5µM) abscisic acid (ABA) clearly inhibited Cd uptake by roots and decreased Cd level in *Arabidopsis* wild-type plants (Col-0). Expression of IRT1 in roots was also strongly inhibited by ABA treatment. Decrease in Cd uptake and the inhibition of IRT1 expression were clearly lesser pronounced in an ABA-insensitive double mutant snrk2.2/2.3 than in the Col-0 in response to ABA application. The ABA-decreased cadmium uptake was found to correlate with the ABA-inhibited IRT1 expression in the roots of Col-0 plants fed two different levels of iron. Furthermore, the cadmium uptake of irt1 mutants was barely affected by ABA application. These results indicated that inhibition of IRT1 expression is involved in the decrease of cadmium uptake in response to exogenous ABA application. Interestingly, ABA application increased the iron level in both Col-0 plants and irt1 mutants, suggesting that ABA-increased Fe acquisition does not depend on the IRT1 function, but on the contrary, the ABA-mediated inhibition of IRT1 expression may be due to the elevation of iron level in plants. From our results, we concluded that ABA application might increase iron acquisition, followed by the decrease in cadmium uptake by inhibition of IRT1 activity. Thus, for crop production in cadmium-contaminated soils, developing techniques based on ABA application potentially is a promising approach for reducing Cd accumulation in edible organs in plants

Exogenous application of ABA reduced the transpiration rate, decreased cadmium content, and enhanced cadmium tolerance of rice seedlings. There are data those other phytohormones, gibberellin, is also involved in plant adaptation to cadmium stress. Ghorbanli *et al.,* (2000) showed that the addition of 10 mg m^{-3} gibberellin reduced the negative effects of cadmium in shoot and root growth of soybean plants. The addition of gibberellin caused a partial elimination of the Cd effects on the roots and shoots and increased leaf area and length of stem. NO is a free radical that can react with O_2•− and, thus, regulate its accumulation in the tissue. NO is also a signal molecule involved in triggering the defense response of cells against different stress conditions. A protective role of NO has also been observed in sunflower Laspina *et al.,* (2005), soybean Kopyra *et al.,* (2006), pea Tran *et al.,* (2011), and wheat Singh *et al.,* (2008) under Cd toxicity Fig. (55).

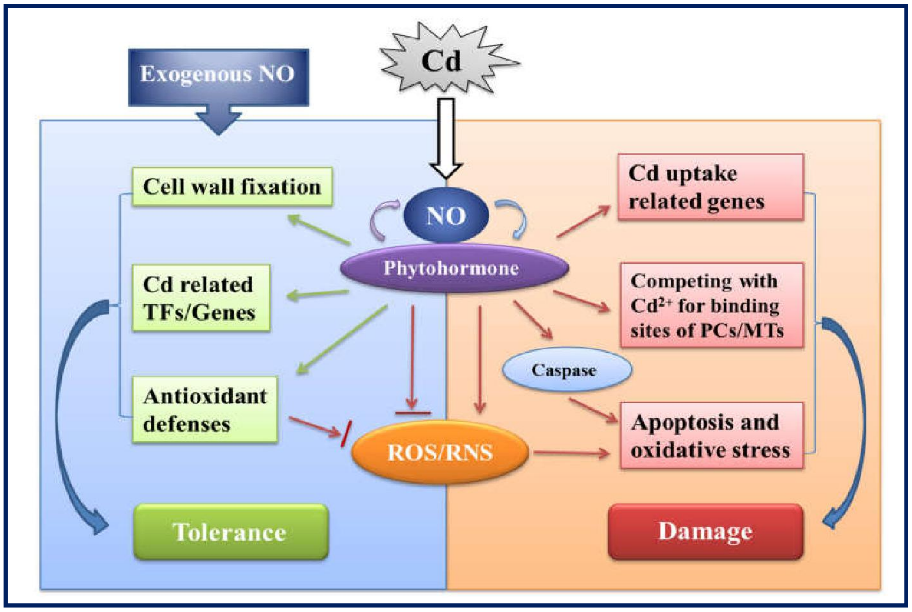

Fig. 55: Schematic representation of the role of nitric oxide in the response of plants to Cd stress. TFs (transcription factors), RNS (reactive nitrogen species), ROS (reactive oxygen species), PCs (phytochelatins), MTs (metallothioneins).After Meng *et al.,* (2022)

Meng *et al.,* (2022) stated that Nitric oxide (NO) is a widely distributed gaseous signaling molecule in plants that can be synthesized through enzymatic and non-enzymatic pathways and plays an important role in plant growth and development, signal transduction, and response to biotic and abiotic stresses. Cadmium is a heavy metal pollutant widely found in the environment, which not only inhibits plant growth but also enters humans through the food chain and endangers human health. To reduce or avoid the adverse effects of cadmium stress, plants have evolved a range of coping mechanisms. Many studies have shown that NO is also involved in the plant response to cadmium stress and plays an important role in regulating the resistance of plants to cadmium stress. However, until now, the mechanisms by which cadmium stress regulates the level of endogenous NO accumulation in plant cells remained unclear, and the role of exogenous NO in plant responses to Cd stress is controversial. This review describes the pathways of NO production in plants, the changes in endogenous NO levels in plants under Cd stress, and the effects of exogenous NO on regulating plant resistance to cadmium stress. They reported that the conflicting literature on the relationship between cadmium stress and NO indicates that NO production has many different sources and multiple functional properties, such as oxidative and antioxidant, harmful and beneficial, and inhibitory and inducing. We have drawn a diagram to explain these contradictions based on some of the current research findings Fig. (56). However, the complex network of regulatory mechanisms of NO in response to cadmium stress still needs to be further investigated. It is suggested that future research can strengthen the following aspects:

(a) To enhance the study of NO synthesis pathways in plants. Although some possible pathways have been proposed for NO synthesis in plants, the specific biochemical processes and molecular mechanisms of each pathway are still unclear, and the mechanisms of association between various pathways need to be explored.

(b) Strengthen the research on NO target molecules. As a signaling molecule, NO is bound to function by stimulating target molecules, and it is through the target molecules that NO regulates the resistance of plants to Cd stress, so it is meaningful to clarify the target molecules of NO.

(c) To strengthen the investigation of the mechanism of endogenous NO action. Under Cd stress, endogenous NO plays a more important role for plants to cope with Cd stress, and several studies have found that endogenous NO has a dual role in Cd stress, so the specific function of endogenous NO in Cd stress resistance needs to be studied.

(d) Strengthen the study of the interaction between NO and other substances such as signaling molecules, plant chelating proteins, phytohormones, etc. There are many substances involved in regulating plant response to Cd stress, and NO is likely to interact with these substances to regulate plant Cd stress resistance, which is particularly important for elucidating the complex regulatory mechanism network of NO response to Cd stress.

(e) In addition, exogenous application of NO donors or NO inhibitors may not accurately reflect the spatial and temporal characteristics of changes in endogenous NO signaling in plants . and there are differences in detection methods and quantitative techniques for characterizing endogenous NO levels in plants. Therefore, it is recommended that better experimental systems should be developed to accurately monitor NO levels in plants, and at least two or more methods should be used to assay NO levels under the same experimental conditions to ensure the accuracy of NO measurements, which is also necessary to better understand the mechanisms involved in the regulation of endogenous NO in response to Cd stress.

9.3. Roots exudation and their effect of Cd stress

Plants exude secondary metabolites in the rhizosphere through both active and passive transport pathways. However, the chemical properties of the exuded compounds influence their secretion at plant–soil interface Vives-Peris *et al.,* (2019). Baetz and Martinoia, (2014) opined that passive transport system imparts a critical role in root exudation through varied pathways: **(a)** transport through vesicles, **(b)** diffusion from the root membrane and **(c)** formation of ionic gradient. Root exudates like carbohydrates and carboxylates (malate, citrate, and oxalate) are exuded by ionic channels and are transported across the membrane through various transporter proteins Fig. (56). Two anionic channels like slow anionic channels (SLACs), S-type (take time to be activated), and quick anionic channels (QUAC), R-type (activated in few milliseconds), are involved in exudate transport across the membrane Dreyer *et al.,* (2012). In association with these anionic channels, aluminium-activated malate transporters (ALMT) are involved in various plant physiological activities such as malate secretion in soil under Al stress. Sharma *et al.,* (2016) studied the activation of anionic channels under Al stress and concluded the research by revealing the role of these channels in inducing plant tolerance towards Al stress.

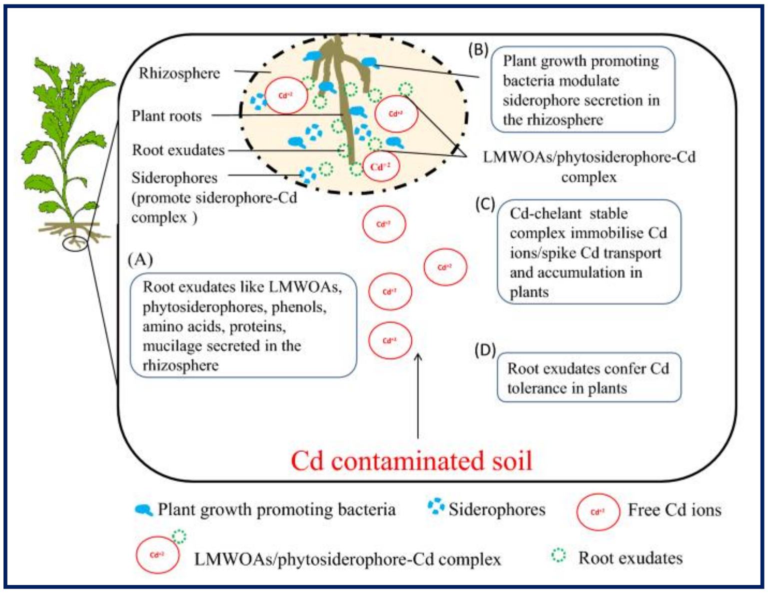

Fig. 56: Root exudates secreted in the rhizosphere influence Cd tolerance in plants. (A) Secretion of root exudates such as low-molecular-weight organic acids, phytosiderophores, phenols, amino acids, proteins, mucilage in the rhizosphere; (B) plant growth-promoting bacteria regulate siderophore secretion in the rhizosphere; (C) formation of Cd–chelate stable complex can immobilize Cd ions in the rhizosphere or can enhance the transport and accumulation of relatively less toxic Cd ions in the plant tissues; (D) secreted exudates induce Cd tolerance in plants. LMWOAs low-molecular-weight organic acids. After Bali *et al.,* (2020)

Bali *et al.,* (2020) stated that cadmium, as soil contaminant is a major problem for the human kind. Cadmium contamination of soil and food crops is a critical environmental concern as it deteriorates the soil quality and creates threat to the food safety and human health. High cadmium concentration in soils has negative effects on the plants at physiological, structural and molecular levels. Secretion of certain secondary metabolites in the rhizosphere is a survival mechanism adopted by plants to tolerate and encounter Cadmium toxicity. Under metal-stressed conditions, secretion of root exudates in soil increases the external strategies of the plants. The secreted phytochemicals are gaseous compounds, inorganic and especially organic in composition. In plants, the role of these metabolites to confront cadmium toxicity and induce tolerance under cadmium distress is underrated. The review paper focuses on cadmium sources, factors that affect its bioavailability, uptake and toxicity in the plants. Furthermore, it also highlights the contemporary progression in our understanding on the mechanisms of root exudation in plants and the effect of Cd toxicity on the root exudation. Finally, review provides important information on the role of different root exudates to subsist cadmium stress in plants naturally particularly, by reducing the dependence on synthetic amendments to enhance cadmium -tolerance and its acquisition in plants. Likewise, maximized auto transporter-mediated expression (MATE) family of transporter proteins induces citrate secretion in soil under metal stress Liu *et al.,* (2009). Recently, Maruyama *et al.,* (2019) opined that phosphorus deficiency in soil caused the activation of aluminium-activated malate transporter protein responsible to induce malate secretion in soil. The secretion of low molecular weight molecules such as carboxylic acids, sugars, amino acids and phenolics by the roots in the rhizosphere is mediated by diffusion. A concentration gradient is formed between the cytoplasm of the root cells and the rhizosphere that enable the release of exudates in the rhizosphere down the concentration gradient. However, polarity of the compounds, root membrane permeability and membrane integrity of the root cells effect the root exudation in the rhizosphere Badri and Vivanco, (2009). Proteins present on root plasma membrane are involved in the transport of exuded secondary metabolites from roots through passive transport mechanism Baetz and Martinoia, (2014). ATP-binding cassette transporters and maximized auto transporter-mediated expression are the two family transporter proteins involved in root secretions and transport Kang *et al.,* (2011). The primary transporter protein family includes ATP-binding cassette transporters as they use the energy from ATP hydrolysis to translocate variety of solutes Orelle *et al.,* (2018). The researchers have appraised the importance and the potential role of ATP-binding cassette transporters in root exudation. Five knockout mutants *Atmrp2*, *Atpgp4-1*, *Atpdr2*, *Atath6* and *Atpdr6* obtained from ATP-binding cassette transporters display their role as transporter protein that promotes root exudation in *Arabidopsis thaliana* plants, though a composition difference prevails between the mutants and those obtained from control plants Badri *et al.,* (2008). Rhizospheric microbiota of *Atabcg30* mutant showed variations in the secretion of phenolics and sugars in the rhizosphere. *Atabcg30* mutant exudes less concentration of sugars and more concentration of phenolics in the rhizosphere compared to the wild mutants Badri *et al.,* (2008). Maximized auto transporter-mediated expression family transporter proteins were first identified in *Arabidopsis thaliana* plants that act as secondary active transporters and allow the movement of various compounds across the plasma membrane by forming an electrochemical gradient Weston, *et al.,* (2012). The participation of maximized *auto transporter*-mediated expression transporter proteins in secretion of secondary metabolites has been observed in various genotypes having genes in barley (*HvAACT1*), *Arabidopsis* (*AtMATE1*) Yokosho *et al.,* (2011); Zhou, *et al.,* (2013) that modulate citrate secretion in rhizosphere under Al stress. Additionally, genotypes of rice such as *OsPEZ1* and *OsPEZ2* influence the secretion and transport of phenolics as secondary metabolites in rhizosphere Takanashi *et al.,* (2014). Presence of Cd ions in the growth medium increased the exudation of secondary metabolites in the rhizosphere of hyperaccumulator plant species. In a study conducted by Luo, *et al.,* (2014), Cd stress influences the secretion of root exudates in a hyperaccumulator plant *Sedum alfredii*.

Furthermore, sample analysis by GC–MS revealed the release of 20 compounds by *Sedum alfredii* in the rhizosphere on exposure to Cd stress. Certain secondary metabolites such as trehalose, erythritol, naphthalene and n-octacosane were found to be involved in Cd stabilization in the soil, while phosphoric acid, threonic acid, oxalic acid and glycine were probably related to Cd mobilization Luo *et al.,* (2014). Likewise, a study conducted by Pinto *et al.,* (2008) postulated the high secretion of malate from roots of sorghum and citrate from roots of maize plants when the plants were supplemented with 5.0 mg.L^{-1} Cd grown in hydroponic solution. The role of organic acids exuded from plant roots in decreasing Cd bioavailability by inducing Cd–organic acid complexation in the medium was observed which enhanced the stabilization of free Cd ions in the rhizosphere Pinto *et al.,* (2008). In a recent study, Lapie *et al.,* (2019) noticed the exudation of proteins, sugars, amino acids and about 40 molecules by maize plants in the rhizosphere when the plants were exposed for 6 weeks under 10, 20 and 40 µM Cd in nutrient solution.

Vives‑Peris *et al.,* (2020) reported that metabolites secreted to the rhizosphere by roots are involved in several processes. By modulating the composition of the root exudates, plants can modify soil properties to adapt and ensure their survival under adverse conditions. They use several strategies such as **(a)** changing soil pH to solubilize nutrients into assimilable forms, **(b)** chelating toxic compounds, **(c)** attracting beneficial microbiota, or **(d)** releasing toxic substances for pathogens. Plants have developed several mechanisms to secrete metabolites into the rhizosphere, including different types of passive and active transports. Traditionally, the secretion of root exudates has been considered a passive process, mediated through different pathways: the transport through the root membrane by diffusion, ionic channels, and vesicles transport Baetz and Martinoia, (2014). The chemical properties of the compounds to be exuded determine the secretion process that will take place in each case Fig. (57).

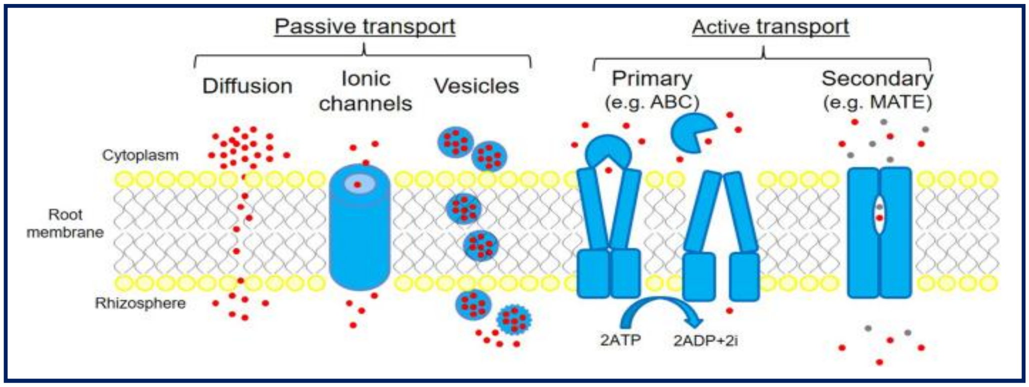

Fig. 57: Different mechanisms of root exudation. Red circles represent molecules released to the rhizosphere After Vives‑Peris *et al.,* (2020)

Diffusion is responsible of the release of low molecular weight molecules, including sugars, amino acids, carboxylic acids, and phenolics. This process is due to the gradient created by the different concentrations between the cytoplasm of root cells and the rhizosphere, affected by root membrane permeability, the integrity of root cells, and the polarity of the compounds to be exuded Badri and Vivanco, (2009). Ionic channels are responsible for the secretion of carbohydrates and specific carboxylates such as malate and oxalate (exuded in high quantities), which are transported across membranes not through diffusion, but through a transport mechanism mediated by proteins. Two different anionic channels have been described: SLow Anion Channels (SLACs), originally named S-type (Slow-type), which need several seconds to be activated; and QUick anion Channels (QUACs), originally named R-type (Rapid type), which can be activated in a few milliseconds Dreyer *et al.,* (2012). In this group, aluminium-activated-malate transporters (ALMT) have been widely studied. These ALMT transporters consist of several proteins involved in different physiological processes, such as the exudation of organic acids, mainly malate, in the presence of toxic Al^{3+} ions in the soil, the most studied. Since the secreted organic acids chelate and inactivate Al^{3+} toxic ions, these anion channels are responsible of conferring aluminium tolerance to the plants, being activated under aluminium stress conditions Sharma *et al.,* (2016) Fig (58).

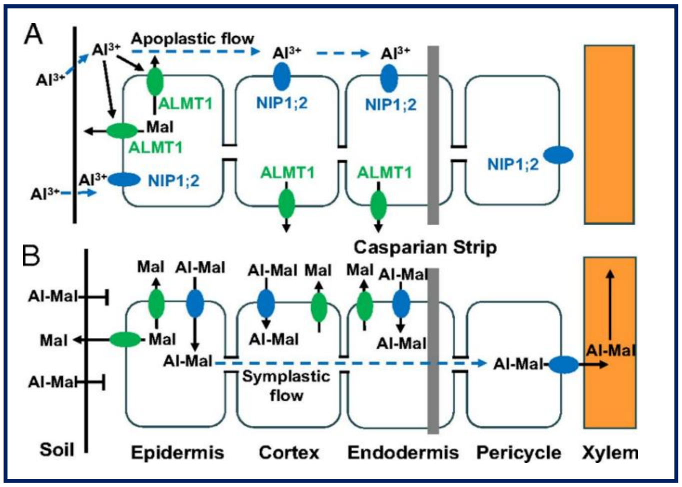

Fig. 58: Schematic diagrams of the coordinated functions of ALMT1 and NIP1;2 in Al tolerance in Arabidopsis. (A) Toxic Al3+ ions that enter the root cell wall activate ALMT1-mediated malate release from the root cells into the root apoplast and rhizosphere, where nontoxic Al-Mal complexes form. (B) Al-Mal in the rhizosphere is unable to enter the root apoplast, whereas the Al-Mal formed within the root cell wall is subjected to NIP1;2-mediated uptake into the root cytosol. Once inside the root cells, Al-Mal moves across the Casparian strip of endodermal cells through symplastic flow into xylem parenchyma cells, where NIP1;2 facilitates xylem loading of Al-Mal into the xylem vessels, followed by translocation of Al-Mal to the shoot. The vertical gray bar on the endodermis represents the Casparian strip. After Wang *et al.,* (2017)

The ALMT family of membrane transporters has been evolutionary classified into five different clades, and consists of 13 members in Arabidopsis thaliana, 12 in *Vitis vinifera* (grape vine), and 8 in *Oryza sativa* (rice) Sharma *et al.,* (2016). Although the ALMT transporters family is highly activated in the presence of aluminium and is the major contributor to aluminium tolerance, it is not the only protein family involved in plant responses against this stress, as the MATE family of active membrane transporters is also independently activated, and responsible for citrate exudation in this situation Liu *et al.,* (2009a). AtALMT3 is involved in malate secretion under phosphorus-deficient conditions Maruyama, *et al.,* (2019). Moreover, the malate secretion caused by the overexpression of AtALMT1 in the presence of aluminium, also mediates in the recruitment of beneficial rhizobacteria that induce plant immunity Kobayashi *et al.,* (2013). The last group of passive transport mechanisms is vesicle transport, which is involved in the secretion of metabolites with high molecular weight stored in vesicles Badri and Vivanco, (2009). This process is also known as exocytosis. The exuded metabolites proceed from the endoplasmic reticulum or Golgi apparatus and contribute to the protection against pathogens Weston *et al.,* (2012). On the other hand, proteins located in the root plasmatic membrane Baetz and Martinoia, (2014) mediate root secretion of metabolites through an active transport mechanism). In this context, there are two big families of membrane transporters, namely, ABC ("ATP-Binding Cassette") and MATE ("Multidrug and toxic compound extrusion") Kang *et al.,* (2011). Root exudation mediated by proteins can occur in three different situations depending on their specificity: transporters that secrete different metabolites; metabolites released to the rhizosphere through different membrane transporters; and compounds that are exuded by a unique transporter. ABC transporters family are considered primary transporters, since they utilize the energy from ATP (adenosine triphosphate) hydrolysis to translocate a wide variety of solutes Jones and George, (2002); Orelle *et al.,* (2018). This family of transporters is one of the most extended in living organisms, including mammals, and includes 130 members in A. thaliana, which have been classified into different families Kang *et al.,* (2011). The nomenclature of the genes that regulate these transporters has changed over time. However, a new unified classification has been developed depending on the organization of the domains TMD and NBD, grouping the different members into 9 families named with letters from A to I, although family H is not present in plants Verrier *et al.,* (2008). Some reports have the role of ABC transporters in root exudation and have determined their importance in this process. In *A. thaliana*, works analyzing root exudates obtained from ABC transporters knockout mutants Atpdr6, Atpdr2, Atmrp2, Atath6, and Atpgp4-1 have revealed that these transporters are involved in root exudation, since there were differences in root exudate composition in these mutants compared to those obtained from control plants Badri, *et al.,* (2008a). Moreover, analysis of the rhizosphere microbiota of Atabcg30 mutant has revealed that this transporter is also capable of modifying soil microbiota, since this mutant exudes more phenolic compounds and less sugar than wild genotype Badri *et al.,* (2009). Root exudates play an important role in the interaction with soil microorganisms Olanrewaju *et al.,* (2019). In plants, MATE transporters family was originally identified in *A. thaliana*, with 56 members named with the initials DTX (from detoxification) Li *et al.,* (2002), but over time, a total of 58 members have been identified, which are reported as secondary active transporters that use an electrochemical gradient to allow the movement of different compounds across membranes Weston *et al.,* (2012). The involvement of MATE transporters in root exudation has been tested in different genotypes, involving genes in sorghum (SbMATE1), rice (OsFRDL4), barley (HvAACT1), and arabidopsis (AtMATE1) Magalhaes, *et al.,* (2007); Liu *et al.,* (2009b); Yokosho *et al.,* (2011); Zhou *et al.,* (2013) which regulate citrate exudation in response to aluminium stress, chelating the Al^{3+} toxic ions Delhaize *et al.,* (2007). Moreover, other works in rice suggested that OsPEZ1 and OsPEZ2 are involved in the transport of phenolic compounds, taking part in the root exudation of these metabolites Takanashi *et al.,* (2014).

Furthermore, it was revealed that increased Cd levels reduced the content of total carbon, amino acids and sugars in the rhizodeposits of maize plants, while protein secretion was constant and the exudation of organic acids was increased. Lapie *et al.,* (2019) concluded the active participation of exuded secondary metabolites to combat cadmium toxicity and induce cadmium tolerance in maize plants.

10. Conclusion

Cadmium is not an essential element for plants and high cadmium content in the soil is harmful to plants. At the same time, edible plants, containing cadmium is harmful to human health. Therefore, for edible plants, measures must be taken to limit the absorption and transportation of cadmium in plants. Cadmium contaminated soil ecosystems pose serious threats on the morphological and physiological attributes of the plants. The exudation of secondary metabolites from roots an effective mechanism adopted by plants to react and modify their environment. Extraction of cadmium and acclimatization in plants depends upon the potential of a plant species and its rhizospheric environment that enables to restrict cadmium entry inside the roots through immobilization or promotes cadmium chelation with ionic species in rhizosphere that influence its solubilization and mobilization. OsHMA3 is a tonoplast-localized transporter for cadmium in the roots of rice (*Oryza sativa*) and limited cadmium in roots and thus cadmium accumulation in aerial parts is low. Overexpression of *OsHMA3* and other genes with similar functions that can decrease the cadmium content in aerial parts of edible plants and enhance edible plants cadmium tolerance. However, for some plants used to improve the soil and measures in order to facilitate the absorption and transportation of cadmium in plants. In addition, Arabidopsis *AtHMA2* and *AtHMA4* are mainly responsible for the transfer of cadmium from roots to shoots and overexpression of *AtHMA2* and *AtHMA4* and other genes with similar functions can increase the cadmium content in plants furthermore, reducing cadmium content of the soil and improve the contaminated soil particularly, under certain condition.

A better understanding of root exudation pattern of plants under cadmium stress can provide an effective approach to optimize various techniques in reducing cadmium acquisition and promote tolerance in plants and/or phytoremediation of cadmium contaminated soils that in turn prove beneficial for agriculture and environment development. However, the knowledge about the root exudates and their functional aspects to ameliorate cadmium tolerance in plants has not been completely developed yet. Therefore, future research should be focused on recognizing different genes or pathways that are modulated in the plants to secrete more secondary metabolites that aid them to confront cadmium toxicity when grown particularly, under contaminated soils. Besides, screening and identification of more crucial secondary metabolites having the potency to confer plant tolerance towards excess of cadmium should be emphasized. This would definitely assist in devising novel strategies for bettering plant performance and increasing their tolerance potential against cadmium excess.

Many strategies have been devised to minimize cadmium toxicity. Plant nutrition is a good strategy to alleviate the damaging effects of cadmium on plants and to avoid its entry into the food chain. Use of plant nutrients to alleviate cadmium toxicity in plants is a relatively inexpensive, time saving, and effective approach to avoid cadmium contamination of food. Applying fertilizers to obtain good crop yield, and so to alleviate cadmium toxicity the proper management of these plant nutrients is needed, keeping in mind the interactions between cadmium and plant nutrients. Crop rotation and using of other organic and inorganic amendments are some other approaches used to remediate the contaminated soils, but these approaches are time consuming and require extra resources. Selection and breeding of crop plants/cultivars that accumulate low cadmium in the grain and other edible plant parts is one of these approaches. Information communicated could illuminate the scientific community and flicker interest in future research on the employment of diverse root exudates in combating plant tolerance particularly, cadmium as well as and other heavy metal stress.

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