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REVIEW

Role of Nitric Oxide in Mitigating Cadmium Stress in Plants: Mechanisms and Perspectives

Mohammad Reza Boorboori[1,2] **and Haiyang Zhang**[1,2,*]

[1]College of Environment and Surveying and Mapping Engineering, Suzhou University, Suzhou, Anhui, China
[2]Key Laboratory of Environmental Processes and Pollution Control in Tuohe River Basin, Suzhou, Anhui, China
[*]Corresponding Author: Haiyang Zhang. Email: seazhang188@ahszu.edu.cn

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ABSTRACT: Cadmium (Cd) is a toxic heavy metal pollutant released from various human activities including industrial production and agricultural practices. This pollutant adversely affects plant physiology by damaging root systems, inhibiting photosynthesis, and inducing oxidative stress through the accumulation of reactive oxygen species (ROS). This review highlights the critical role of nitric oxide (NO) as a key signaling molecule that enhances plant tolerance to cadmium stress. The application of exogenous NO effectively alleviates Cd toxicity by stimulating the activity of antioxidant enzymes such as superoxide dismutase (SOD) and catalase (CAT), scavenging harmful ROS, and preventing membrane damage. Furthermore, NO improves nutrient absorption and photosynthetic efficiency under Cd stress. The review also explores the complex interactions between NO and other phytohormones, including auxin and brassinosteroids, especially in regulating root development under stressful conditions. Despite these protective effects, the review concludes that further investigations are needed to better understand the molecular mechanisms of NO signaling, its concentration-dependent responses, and its specific crosstalk with other plant signaling molecules.

KEYWORDS: Cadmium; nitric oxide; stress reduction; plants; mechanisms

1 Introduction

Cadmium (Cd) is one of the main heavy metals that adversely affects various physiobiochemical processes of plants, including metabolism, the photosynthetic apparatus, and the antioxidant defense system, leading to a decrease in crop yield and quality [1]. Plants initiate defense strategies at the physiological, cellular, and molecular levels by controlling the cellular level of toxic ions through various pathways, including vacuolar compartmentalization, chelation with thiol-peptides, immobilization, and elimination, or by transducing stress signals to activate defense responses [2]. In recent decades, several methods have been pursued to reduce Cd toxicity, such as the use of nutrients, hormones, and biological purification, which can significantly reduce the harmful effects of Cd stress on plant physiological processes [3]. However, one of the possible strategies to increase plant adaptation to Cd-contaminated environments is the use of signaling molecules such as nitric oxide (NO) [4].

NO is a gaseous signaling molecule that is synthesized through enzymatic and non-enzymatic pathways and is widely distributed in plants, playing a role in a wide range of physiological and biochemical processes such as seed germination, regulation of normal growth and development, hormonal regulation, closure of plant stomata, maturation and senescence, and programmed cell death [3,5]. Furthermore, NO plays a crucial role in increasing plant tolerance to abiotic stresses such as drought, ultraviolet-B radiation, cold, nutrient deficiencies, salt, and heavy metal toxicity [6,7]. Evidence suggests that the exogenous application of NO alleviates oxidative stress caused by Cd stress and improves plant resistance [8,9]. Previous studies have demonstrated that the balance between NO and reactive oxygen species (ROS) is essential for plant tolerance to Cd stress, and since ROS is highly reactive, it can damage the function and structure of cells in the absence of protective mechanisms [2,8]. Moreover, ROS and NO levels in cells may cause oxidative/nitrosative stress or act as signaling molecules [10]. However, excessive intracellular ROS is scavenged through the upregulation of antioxidant enzymes and non-enzymatic antioxidants, a process that can be mediated by NO [8,11].

Literature Search Strategy

Literature searches were conducted using the Web of Science, Scopus, PubMed, and Google Scholar. Combinations of the following keywords were used: “nitric oxide”, “NO”, “cadmium”, “Cd stress”, “heavy metal toxicity”, and “antioxidant enzymes”. The search was limited to peer-reviewed articles published in English between 2010 and 2025. Relevant papers were selected based on their focus on the role of nitric oxide in alleviating cadmium toxicity in plants.

Despite the growing number of studies on this topic, several critical aspects remain poorly understood. The molecular mechanisms by which NO alleviates Cd toxicity, especially its concentration-dependent effects and its contrasting role under short-term versus long-term Cd exposure, are not yet clearly elucidated. Furthermore, the complex crosstalk between NO and other phytohormones under Cd stress requires deeper investigation. The present review critically examines the current literature, identifies these key knowledge gaps, and highlights important directions for future research.

2 Cadmium as a Hazardous Element

Cadmium (Cd) is one of the most toxic heavy metals and a widespread environmental pollutant. It causes detrimental effects on humans, animals, and plants [8,12,13]. Cd concentration in soil is increasing alarmingly, and research shows that approximately 5.6–38 thousand tons of Cd enter the soil globally each year, thus making it a serious environmental problem [14,15]. A rising level of Cd contamination is observed in many agricultural regions in Asia, North America, and Europe [14,16]. Cd is highly bioavailable and persistent in the environment, with a biological half-life of more than 20 years in humans. Due to its high solubility and mobility, it readily accumulates in living tissues and enters the food chain [16,17]. The World Health Organization (WHO) has listed cadmium as one of the ten chemicals of major public health concern [18]. The WHO has suggested an average monthly Cd tolerance of 25 mg/kg body weight, and Codex Alimentarius Commission (CAC) has narrowed the maximum permissible Cd level in cereal grains to 0.1 mg/g [14]. Cd is a highly carcinogenic substance that causes diseases including Itai-itai, kidney damage, cardiovascular problems, and immune disorders [9,19]. Geological processes (weathering of rocks, and volcanic activity), and human processes (application of phosphate fertilizers, cement production, fossil fuels, electroplating, metal smelting, mining, sewage sludge, municipal waste, wastewater irrigation, and leather tanning) increase Cd levels in various ecosystems [1,20,21].

In soil, Cd primarily exists as Cd^{2+}. Elevated Cd levels disrupt the balance of macro- and micronutrients and adversely affect beneficial soil microorganisms, including nitrogen-fixing bacteri [2,22–24]. The low levels of Cd in the soil are also absorbed by the plant roots and then, after being loaded into the xylem, rapidly transported to the aerial organs and then to the phloem and seeds [25]. Cd enters root cells through essential nutrient transporters including *ZIP*, *IRT*, and *Nramp*, along with aquaporins, natural resistance-associated macrophage protein (*NRAMP1*), and heavy metal ATPase 3 (*HMA3*) [26–28]. Cd accumulation in plants causes disruption in the morphological, physiological, metabolic, molecular, and biochemical processes in plants [29]. Cd reduces water and nutrient absorption, cell elongation, transpiration, root growth, seed germination, respiration, and yield in plants [30,31]. In addition, Cd disrupts sugar metabolism, enzyme activity, and stomatal function [32] (Fig. 1).

Cd disrupts photosynthesis efficiency through chlorosis and necrosis of leaves, damage to the thylakoid membrane in chloroplasts, reduction of photosynthetic pigments, and changes in the configuration and structural stability of pigment-protein complexes [33–35]. Cd also inhibits chlorophyll biosynthesis through upregulation of chlorophyllase and replacement of Mg^{2+} with Cd^{2+} ions [36]. Furthermore, Cd can replace Ca^{2+} in the photosystem II (PSII) reaction center, inhibiting PSII light response activity, and decreasing photosynthetic efficiency [37]. Moreover, cadmium can reduce NADPH production in cells and disrupt the electron transport chain (ETC) from PSII to photosystem I (PSI) in chloroplasts, and from complex I to IV in mitochondria [38,39]. Cd stress in plants increases NADPH oxidase activity, which produces reactive oxygen species (ROS) such as hydrogen peroxide (H_2O_2), superoxide radicals ($O^{2\bullet -}$), and hydroxyl radicals (•OH) [40,41]. Oxidative stress in plants causes disruption of cellular redox homeostasis, cell membrane leakage, phospholipid degradation, enzyme inactivation, and an increase in malondialdehyde (MDA) content [4,42,43]. Plants naturally use various strategies to combat Cd toxicity, including Cd removal, limiting Cd influx, and chelation (by organic molecules such as metallothioneins, phytochelatins, and histidines) [7]. Furthermore, the root cell wall, as the main binding site for Cd in plants, plays a crucial role in Cd deposition, and reducing its toxicity in plants [44,45]. Plants can also complex Cd through various metal ligands or sequester Cd into vesicles to mitigate its harmful effects [46]. Further, plants can eliminate the toxic effects of oxidative stress by increasing the synthesis of enzymatic and non-enzymatic antioxidants [ascorbate peroxidase (APX), superoxide dismutase (SOD), catalase (CAT), glutathione reductase (GR), glutathione (GSH), and ascorbate (AsA)], nutrient homeostasis, and the production of osmolytes such as proline [4,47,48] (Fig. 1).

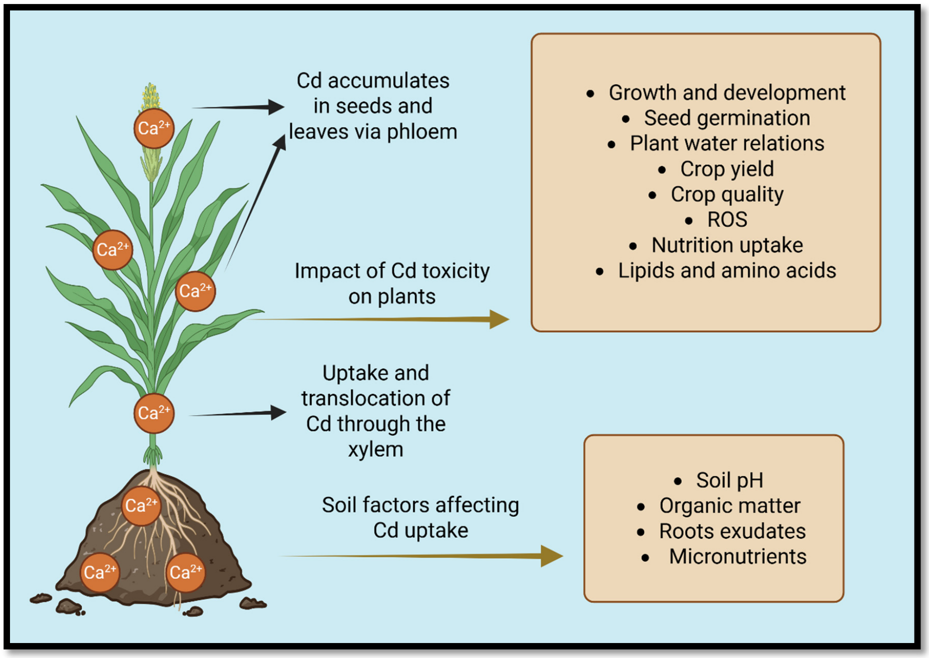

Figure 1: Cadmium uptake, transport, accumulation, and toxicity in plants. Cadmium is taken up by roots from the soil, where its absorption is influenced by soil factors such as pH, organic matter, root exudates, and micronutrients.

Once absorbed, Cd is translocated upward through the xylem to the shoots and leaves, and further distributed to seeds via the phloem. The figure highlights the negative impacts of Cd toxicity on plant growth and development, seed germination, water relations, crop yield and quality, reactive oxygen species (ROS) production, nutrient uptake, lipids, and amino acids.

3 Nitric Oxide (NO) in Plants

NO is a small gaseous molecule with a short half-life that plays a crucial role in plant signaling [2,49]. NO, which is part of the nitrogen cycle in plants, plays a widespread function in increasing growth and in the activity of defense mechanisms under abiotic stress conditions (heavy metals, ozone, salinity, and ultraviolet radiation) [32,50,51]. NO, which is soluble in water and fat, can diffuse intracellularly and modulate its capacity directly through post-translational modifications (PTMs) of proteins or interaction with other signaling molecules [5,52,53]. NO is produced as an intracellular and intercellular signaling molecule through various pathways, including non-enzymatic, reductive, and oxidative reactions [54,55]. Nitrate reductase (NR) is one of the key enzymes for NO synthesis/accumulation in various organelles such as the cytoplasm, cytosol, peroxisomes, chloroplasts, and mitochondria [56–58]. NR uses NADH/NADPH as an electron donor to catalyze nitrate and nitrite reduction into NO, and is considered the main source of NO [56]. Additionally, in higher plants, NR activity is dependent on PTMs of proteins, such as redox and phosphorylation, which affect NO production [44,59]. Other enzymes are also involved in NO production, including copper amine oxidase (CuAO), polyamine oxidase (PAO), pyrroline-5-carboxylate reductase (POR), cytochrome P450 (CYP), xanthine dehydrogenase (XDH), and xanthine oxidoreductase (XOR) [5]. Furthermore, under low oxygen conditions, several molybdoenzymes can oxidize nitrite to NO, including sulfite oxidase (SO), aldehyde oxidases (AOs), and xanthine oxidase (XO) [60] (Fig. 2).

NO, along with S-nitrosoglutathione (GSNO), dinitrogen trioxide (N_2O_3), and peroxynitrite (NO_3^-), are known as reactive nitrogen species (RNS) in plants, and are produced in large quantities when plants are exposed to adverse stresses [62,63]. It has been shown that different types of RNS affect each other, for example, NO_3^- synthesis causes a decrease in cellular NO levels [64]. Evidence suggests that low levels of RNS are not toxic to plant cells, however excessive nitrosylation caused by RNS can damage carbohydrates, proteins, membrane lipids, and DNA, affecting cellular function [65,66]. The researchers stated that NO readily interacts with a wide range of biological molecules such as lipids, proteins, and nucleic acids in plant cells and modulates their activity [2,67]. In addition, NO can limit ROS toxicity and levels by regulating plant antioxidant defenses [68]. Studies have also shown that there is a signalling topology between H_2O_2 and NO [69]. NO mitigates oxidative stress by modulating the activity of antioxidant enzymes such as catalase (CAT), ascorbate peroxidase (APX), and superoxide dismutase (SOD), thereby regulating H_2O_2 levels. Additionally, NO can directly react with superoxide radicals ($O_2^{\bullet-}$) to form peroxynitrite ($ONOO^-$), which influences cellular redox signaling [70,71]. Furthermore, NO has direct chemical interactions with $O_2^{\bullet-}$ in one of the fastest reactions in biological systems, ultimately forming NO_3^- [2,72]. NO prevents ROS carbonylation of thiol proteins, as well as improving membrane peroxidation and reducing ion leakage [73,74]. NO has a significant effect on many metabolic and physio-biochemical processes in plants, including photosynthesis, seed germination, flowering, growth of pollen tubes, stomatal closure, regulation of auxin transport, root formation, and regulating element absorption (iron and sulfur) [4,32,48,75,76]. NO also plays a role in fruit development and fruit quality characteristics including texture, color, flavor, and nutritional content [50,77].

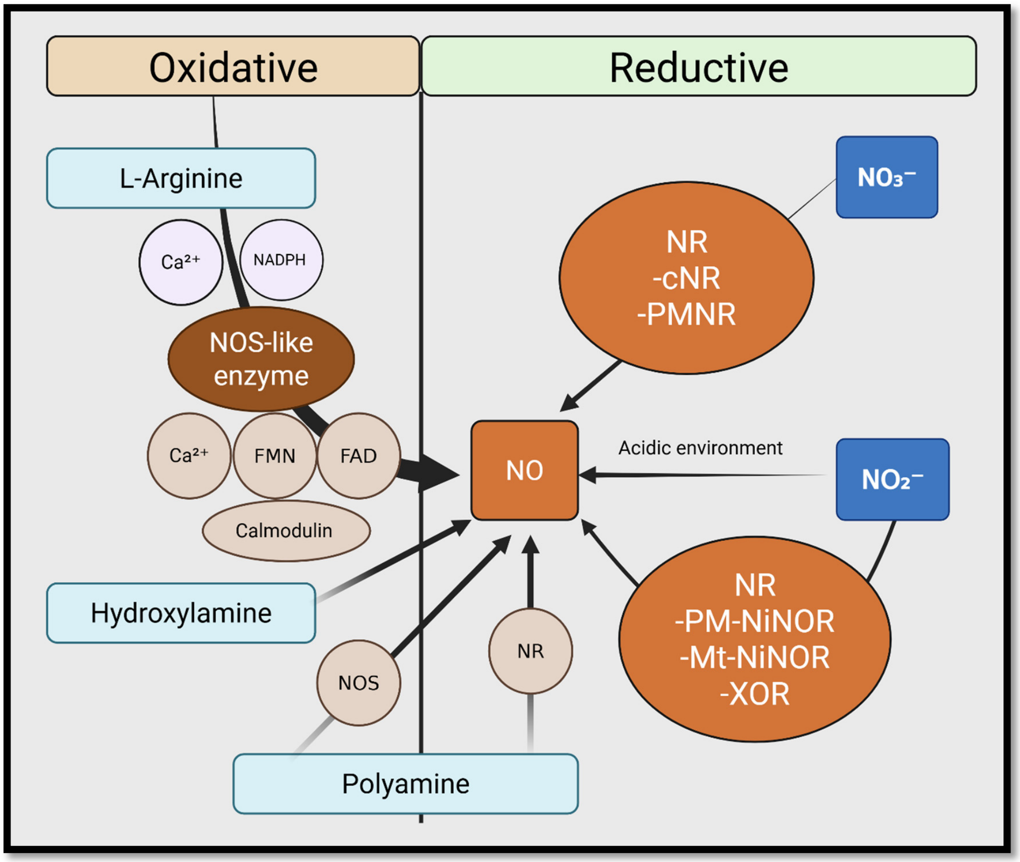

Figure 2: A diagram shows the major routes for the synthesis of nitric oxide (NO). Nomenclature is as proposed by Lau, et al. [61]. In the oxidative pathway (left), NO is synthesized from L-arginine by a NOS-like enzyme in the presence of Ca^{2+}, calmodulin, NADPH, FMN, and FAD. Additional contributions come from polyamine and hydroxylamine oxidation. In the reductive pathway (right), NO is produced from nitrate (NO_3^-) and nitrite (NO_2^-) through the activity of nitrate reductase (NR) and several nitrite: NO reductases, including cytosolic NR, PM-NiNOR, Mt-NiNOR, and xanthine oxidoreductase (XOR), particularly under acidic and hypoxic conditions. This diagram highlights the dual enzymatic routes that maintain NO levels in plant cells.

4 NO and Cd Stress

The results of findings indicate that Cd increases endogenous NO levels [78,79]. In a study conducted on peas and mustard treated with 100 M Cd for one day, endogenous NO production in the roots increased significantly [80]. Although the role of NO in the response and protection of plants against Cd stress has been elucidated, nevertheless, the metabolic and molecular mechanisms of NO-induced Cd stress reduction and the precise mechanisms of NO signaling remain to be clarified [2,81,82]. However, changes in endogenous NO levels in plants under Cd stress are influenced by various factors such as plant genotype and species, plant size, Cd concentration, and treatment time [5]. On the other hand, some studies also indicate that Cd stress inhibits endogenous NO production in plants [78]. As an example, a study on alfalfa showed that treating seedlings with 50 M Cd for two days significantly reduced NO levels in roots, as well as in peas treated with Cd for 14 days, NO levels in roots and leaves were decreased [83]. Several authors have reported that although short-term stress may increase NO production levels, long-term stress decreases NO levels [84]. Some studies have suggested that the reduction of NO in plants may be due to calcium (Ca) deficiency caused by Cd stress in the leaves, which leads to a reduction in enzyme activity, such as nitric oxide synthase (NOS) [85]. During recent decades, numerous studies have reported the role of exogenous NO application as an efficient method of increasing plant resistance to Cd stress [9,86]. One of the most widely used methods to improve plant resistance in Cd-contaminated environments is the foliar application of sodium nitroprusside (SNP), which is a NO donor [87,88]. The effect of SNP application on increasing various plants' resistance to Cd stress has been reported, such as perennial ryegrass, peanuts, wheat, *Medicago truncatula*, and rice [32].

4.1 NO's Role in Cd Toxicity, Absorption, and Transport in Plants

Various studies have shown that exogenous NO affects Cd uptake by plants but also its stabilization within cell walls, thereby improving plants' resistance to Cd stress [5,22,89]. When applied exogenously, NO acts as a cell membrane regulator and protector of plant cells under Cd stress [22]. Furthermore, NO, due to its significant role in the lignification of plant cell walls, regulates Cd uptake by plants and increases their resistance to stress [90,91]. Additionally, exogenous NO, by affecting the composition of root cell wall components, in addition to inducing Cd fixation and removal in the roots, regulates Cd distribution in plants and prevents its transfer to aerial organs [12,45]. Pectin, cellulose, and hemicellulose are the main components of the cell wall, and research has also shown that adding NO increases the content of these cell wall components, leading to increased Cd deposition in root cell walls [92,93]. In a study conducted on *Panax notoginseng* under Cd stress, it was shown that the use of Sodium Nitroprusside (SNP) as a NO donor caused a significant increase (about 2.9-fold) in Cd accumulation in root cell walls by increasing the synthesis of pectin and hemicellulose 1, and pectin methylesterase activity [45]. NO, as a gaseous signaling molecule, can regulate the expression of Cd-related genes, by enhancing the signaling cascade, thereby increasing plant resistance to Cd stress [94]. It is well documented that NO can increase cytoplasmic Ca^{2+} concentration by regulating transporter proteins, Ca^{2+} channels, and some protein kinases, as well as activate some other secondary signaling factors such as cyclic adenosine diphosphate ribose (cADPR) and cyclic guanosine monophosphate (cGMP), thereby enhancing the signaling cascade [95]. Research has also shown that exogenous NO elevates metallothioneins (MTs), which are cysteine-rich metal-binding proteins [96]. MTs bind to Cd through sulfhydryl groups and prevent Cd toxicity to plant cells by forming less toxic or non-toxic complexes [5,97] (Table 1).

On the other hand, studies have shown that endogenous NO accumulation caused by Cd stress can increase Cd toxicity to plants through the following factors [5]. Excessive production of endogenous NO stimulates genes related to iron absorption (*FRO2*, *IRT1*, and *FIT*) and leads to enhanced uptake and accumulation of Cd by plants [7,98]. In addition, Cd-induced endogenous NO through s-nitrosylation can bind to phytochelatins (PCs) (which chelate and sequester Cd within vesicles), thereby reducing their detoxifying effect on Cd [87,99,100]. Excess endogenous NO also binds to metal ions, tyrosine residues, and proteins containing cysteine residues (sulfhydryl groups) via *S*-nitrosylation, weakening their detoxifying effect on cadmium [5,101]. Furthermore, NO contributes to Cd toxicity to plants by increasing the activities of apoptosis-related enzymes such as caspase-3 [102,103]. In a study on Arabidopsis, it was shown that the application of gibberellin (GA) also reduces Cd toxicity and absorption through the expression of the *IRT1* gene and mediating NO accumulation [104] (Table 1).

4.2 Involvement of NO in Cd-Stressed Plant Growth

Recent findings indicate that NO improves the carotenoids and chlorophyll content in plants under Cd stress [22]. Furthermore, NO spraying under Cd stress conditions, besides preserving the chloroplast structure, maintains the function and integrity of stomatal components and enhances gas exchange [4,105].

NO can also accept electrons from the electron transport chain in addition to reducing Cd toxicity by improving the function of PSII [106,107]. Therefore, NO improves plant growth by increasing photosynthesis indices in plants under Cd toxicity [22,108]. Moreover, numerous studies have shown that exogenous NO application can improve plant growth and biomass by increasing physiological functions, antioxidant enzyme activity, nutrient absorption, and cell expansion, as well as reducing Cd accumulation in various plant organs and membrane ion leakage [3,109,110] (Table 1).

Cd stress, in addition to reducing NO levels in lateral roots (LRs) and adventitious roots (ARs), suppresses auxin transport and biosynthesis, reduces primary roots (PRs) length, and inhibits the quiescent center's (QC) function, ultimately leading to abnormal cell proliferation and root morphological abnormalities [2,78,111]. Additionally, Evidence suggests that NO modulates auxin (IAA, and IBA) levels under normal and Cd stress conditions by increasing the expression of the *AUXIN-RESISTANT 1* (*AUX1*) gene, as well as affecting signaling, distribution, conjugation, degradation, and biosynthesis [97,112]. Thus, exogenous NO application reduces Cd effects on the root system and promotes AR, LR, and PR growth and development [78,113]. On the other hand, some studies show that NO accumulation caused by Cd stress in roots suppresses auxin levels and transport, inhibiting root growth [114,115]. The results of the research showed that high levels of NO have an adverse effect on auxin accumulation and root length, while low levels of NO lead to increased root length under Cd stress conditions [113]. It has been shown that brassinosteroids (BRs) play a positive role in exopetal auxin transport, interaction with auxin signaling, and control of QC cell identity [116,117]. Research has also shown that exogenous BR application induces endogenous NO production whilst enhancing AR formation [118]. Furthermore, BRs do not cause any changes in NO signaling in the presence of Cd exposure, suggesting that synergy between exogenous BR and NO does not occur in the presence of Cd [78]. However, using lower levels of BRs neutralized the negative effects of cadmium on the apical structure and greatly increased the formation of AR and LR, confirming the significant protective role of BRs in the root system [78] (Table 1).

4.3 NO Improves Antioxidant Activity in Plants under Cd Stress

Plant cells produce ROS during their normal growth to participate in various physiological and metabolic activities such as respiration and photosynthesis [119]. However, environmental stresses such as Cd stress cause excess ROS production in plant cells, leading to oxidative stresses such as protein denaturation, DNA damage, hydrogen peroxide (H_2O_2) accumulation, and membrane lipid peroxidation [86,120]. NO enhances plant tolerance to Cd stress by alleviating oxidative damage through several mechanisms: (1) increasing antioxidant defense capacity, (2) regulation of peroxisomal proteins, (3) preservation of ultrastructural configuration and chloroplast membranes, (4) direct reaction with superoxide anion ($O_2^{-\bullet}$) to form peroxynitrite, and (5) formation of peroxynitrite, which is less toxic than ROS [4,121,122] (Table 1; Fig. 3).

Table 1: Effect of exogenous nitric oxide on alleviation of cadmium toxicity in different plant species.

	Plant Type	NO Dose	Cd Dose	Experiment Results and Observations	References
1	*Arundinaria pygmaea*	200 µM	200 µM	Increased antioxidant activity Increased protein content Increased photosynthetic properties Increased plant growth and plant biomass Limiting Cd movement from roots to shoots	[22]
2	*Oryza sativa* L.	50 and 100 µM	100 µM	Reducing root system changes caused by Cd Reduced Cd absorption Reducing ROS levels	[2]
3	*Festuca arundinacea Schreb*	100 and 200 µM	50 mg/L	Increased antioxidant capacity Accumulation of secondary metabolites related to Cd chelation and sequestration Activity of ABC transporters Increased nitrogen metabolism Expression of genes encoding *CAT*, *GLT1*, *GSTs* and *ADH1* Reduced isotrifolin and acastin content	[81]
4	*Arachis hypogaea* L.	250 µM	5 and 200 µM	Improve plant growth Improve chlorophyll content Regulation of the antioxidant system Reducing the rate of superoxide radical production Reducing malondialdehyde content	[32]
5	rice	50 µM	50 µM	Suppression of Cd absorption Increases antioxidant levels Reduce oxidative stress Improving growth	[8]
6	*Satureja Hortensis* L.	0, 75, 100 and 150 µM	0, 50, 100 and 200 µM	Improve plant growth Increased proline Increased chlorophyll (a, b and carotenoids) Increased carbohydrates Increased peroxidase activity Reducing Cd accumulation in shoots and roots	[3]
7	Aromatic Rice	50 or 100 µM	0 and 50 mg·kg^{-1} of soil	Reduce oxidative stress Improving the photosynthetic apparatus Reducing Cd concentration in leaves and seeds Increase grain yield Improving 2-Acetyl-1-pyrroline (2AP) content	[4]

Interpretation: Table 1 shows that exogenous nitric oxide (NO) consistently alleviates cadmium (Cd) toxicity across diverse plant species. In most cases, appropriate NO concentrations improved plant growth, chlorophyll content, and biomass production. Additionally, NO enhanced the antioxidant defense system, reduced reactive oxygen species (ROS) levels, and lowered lipid peroxidation. Several studies have also reported that NO effectively restricted Cd uptake and translocation from roots to shoots, thereby reducing Cd accumulation in edible tissues. These protective effects highlight NO as a potent signaling molecule capable of activating multiple defense mechanisms under Cd stress. However, the effective NO dose varied considerably among all species, indicating that optimal concentrations are highly species-specific.

Existing studies have shown that Cd stress causes a decrease in endogenous NO content in plants, which can be enhanced through the exogenous application of NO compounds such as SNP [123]. Several Current literature shows that SNP application increases the antioxidant capacity (GST, APX, GR, POD, CAT, and SOD) in yellow lupine, clover, lobelia, and sunflower under Cd stress and leads to the removal of ROS compounds in various plant organs [5,85,89,124,125]. On the other hand, exogenous NO increases the activity of the AsA-GSH cycle and consequently reduces the levels of EL, MDA, and H_2O_2 in plants under Cd stress [4,126,127]. Since GSH is a precursor of phytochelatins (PCs), and NO can enhance the expression of glycosyl hydrolases (GHs) and gamma-glutamylcysteine synthetase (γ-ECS) genes, it can be assumed that NO may increase PC synthesis [5]. NO can also react with GSH to produce GSNO, which serves as the main internal stored form of NO and mediates protein nitrosylation modification [128]. Furthermore, NO can scavenge Cd-induced ROS directly without crossing through the antioxidant system and reduce oxidative damage [5]. SNP also increases nitrate reductase activity and proline content (by regulating *P5CS1*, which encodes 1-pyrroline 5-carboxylate synthetase) in plants under Cd stress [129,130]. In general, it is well documented that exogenous NO application significantly reduces Cd-induced MDA and H_2O_2 accumulation and limits lipid peroxidation, possibly due to improved antioxidant activities, reduced ROS production, and increased membrane stability [3,4,131] (Table 1; Fig. 3).

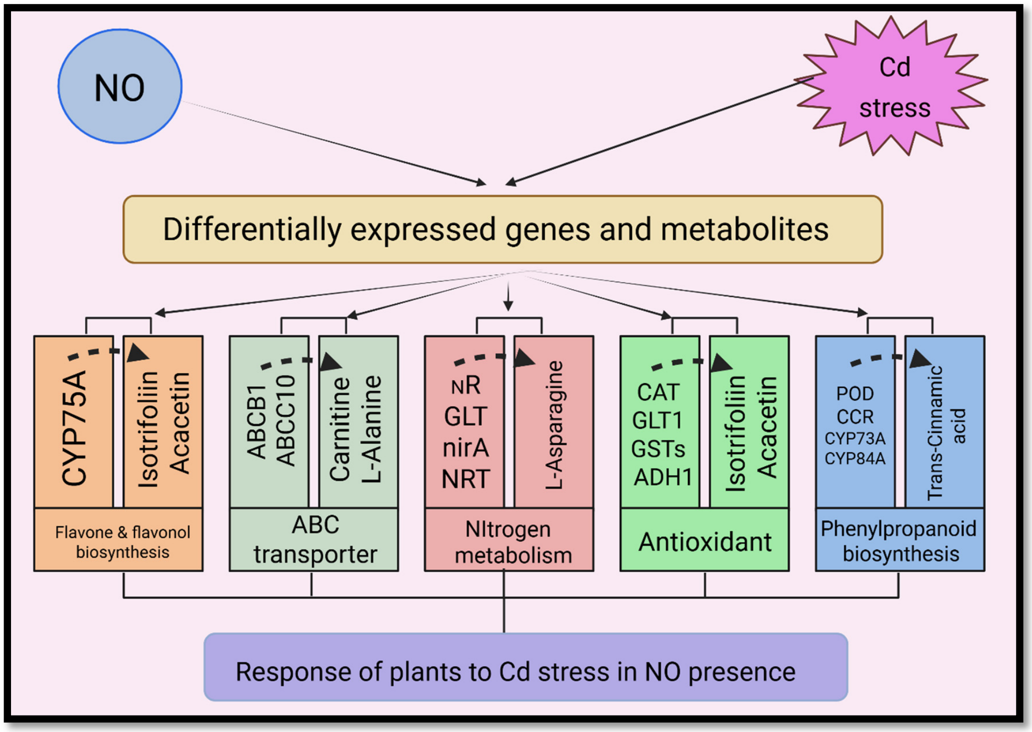

Figure 3: In plants, nitric oxide (NO)-regulates the response to cadmium stress. Nomenclature is as proposed by Zhu, Ai, Hu, Du, Sun, Chen and Chen [81]. Under Cd stress, NO regulates the expression of various genes and accumulation of metabolites involved in different defense pathways. These include genes and metabolites associated with flavonoid and flavonol biosynthesis (CYP75A, isorifolin, acacetin), ABC transporters (ABCB1, ABCC10), nitrogen metabolism (nR, GLT, nirA, NRT, L-asparagine), antioxidant defense (CAT, GLT1, GSTs, ADH1), and phenylpropanoid biosynthesis (POD, CCR, CYP73A, CYP84A, trans-cinnamic acid). This diagram summarizes the key molecular mechanisms by which NO alleviates Cd toxicity in plants.

4.4 Molecular Mechanisms of NO-Mediated Cd Tolerance

Nitric oxide mediates cadmium tolerance primarily through *S*-nitrosylation, a reversible post-translational modification that directly alters the function of target proteins [132]. This modification regulates key antioxidant enzymes such as SOD, CAT, and APX, enhancing their activity and improving ROS scavenging capacity [133]. Additionally, *S*-nitrosylation modulates metal transporters including *IRT1* and *HMA3*, thereby reducing cadmium uptake and root-to-shoot translocation [133]. NO also upregulates the expression of genes involved in glutathione and phytochelatin biosynthesis (*GSH1*, *GSH2*, and *PCS1*), which increases the plant's capacity for Cd chelation and vacuolar sequestration [134,135]. Furthermore, NO interacts with calcium signaling pathways by activating Ca^{2+}-dependent protein kinases (*CDPKs*) and cyclic GMP (*cGMP*), forming a complex signaling cascade that coordinates stress responses [136]. These molecular events collectively enable NO to maintain cellular redox homeostasis, protect photosynthetic apparatus, and promote root system remodeling under Cd stress [137]. Despite these advances, the specific *S*-nitrosylated target proteins and the complete downstream signaling networks vary among plant species and remain to be fully characterized through proteomic and transcriptomic studies [138].

5 Conclusion

This review indicates that nitric oxide (NO) plays a vital role as a signalling molecule in mitigating Cd-induced toxicity in plants. Exogenous NO application can effectively reduce Cd uptake and translocation, enhance antioxidant defense systems, improve photosynthetic efficiency, and promote plant growth under Cd stress. Most studies report NO's beneficial effects without sufficiently addressing its concentration-dependent responses or the differences between short-term and long-term Cd stress. While low NO concentrations enhance plant tolerance, high concentrations may disrupt auxin signaling or exacerbate stress. Additionally, endogenous NO levels tend to increase during acute exposure but decline under prolonged Cd stress, suggesting a complex temporal regulation that remains poorly understood.

Future research should prioritize systematic dose-response experiments across a wide range of NO concentrations and conduct time-course studies comparing short-term versus chronic cadmium exposure. A deeper understanding of the molecular mechanisms underlying NO signaling and its crosstalk with other phytohormones under varying stress durations is also essential.

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