The role of phytohormones in reducing the arsenic-induced stress in plants

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Abstract

Arsenic (As) toxicity in crops is a major global concern, adversely affecting sustainable agricultural practices, and serving as a potential carcinogenic pollutant. As contamination in soil poses a significant threat to plant health and productivity, adversely impacting growth, photosynthesis, and the antioxidant system. To address this issue, plants endogenously regulate the levels of various phytohormones, and the exogenous application of phytohormones to mitigate As-induced stress has gained significant attention. Phytohormones act as secondary (2°) messengers, participating in diverse signaling cascades under As stress. As uptake in plants leads to the As-accumulation and generation of excessive reactive oxygen species (ROS) which can be alleviated by phytohormones. Numerous studies have highlighted the role of phytohormones, such as auxins, methyl jasmonates, salicylic acid, brassinosteroids, and Mel, in regulating pathways that enhance plant growth, biomass accumulation, ROS scavenging, antioxidative enzyme and photosynthesis under As stress. This review summarizes the detailed mechanism of As phytotoxicity, its detoxification mechanism, and the exogenous application of phytohormones to alleviate As stress. Additionally, we provide insights into recent findings on the possible roles of various genes, proteins, transgenic factors, and genome editing approaches in phytohormone-mediated As-stress tolerance.

Keywords: Phytohormones, As-stress, Oxidative stress, Antioxidants, Transcriptomic, Genome editing, Proteomics, Transgenic

1. Introduction

Water, air, and soil resource contamination with As, an extraneous metalloid exhibiting potentially mutagenic characteristics, is a global environmental issue (Ahammed and Yang, 2022; Nurchi et al., 2020). The ingress of As can occur from natural sources, such as weathering of As-rich minerals, volcanic eruptions, and artificial/anthropogenic sources (the excessive use of chemical fertilizers, herbicides, pesticides, mining, and smelting in the agricultural and industrial sectors) (I. Khan et al., 2021). In a recent article, Kumar et al. explained the As mobilization in groundwater and soil, and that would help understand how the various activities led to As toxicity in plants, as shown in Figure 1 (Kumar et al., 2023). Chronic As ingestion through food can cause various diseases in humans and animals, including skin, neurological, lung, and vascular diseases, as well as diabetes and multiple types of cancer (Bahrami et al., 2020; Ozturk et al., 2022).

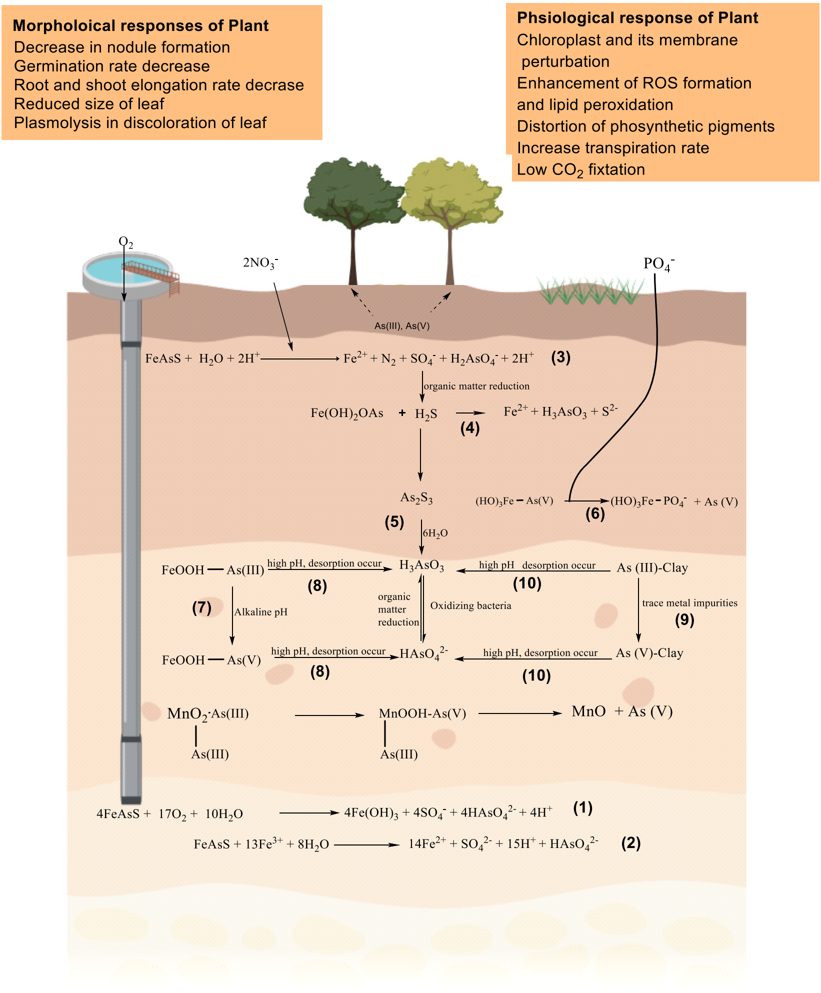
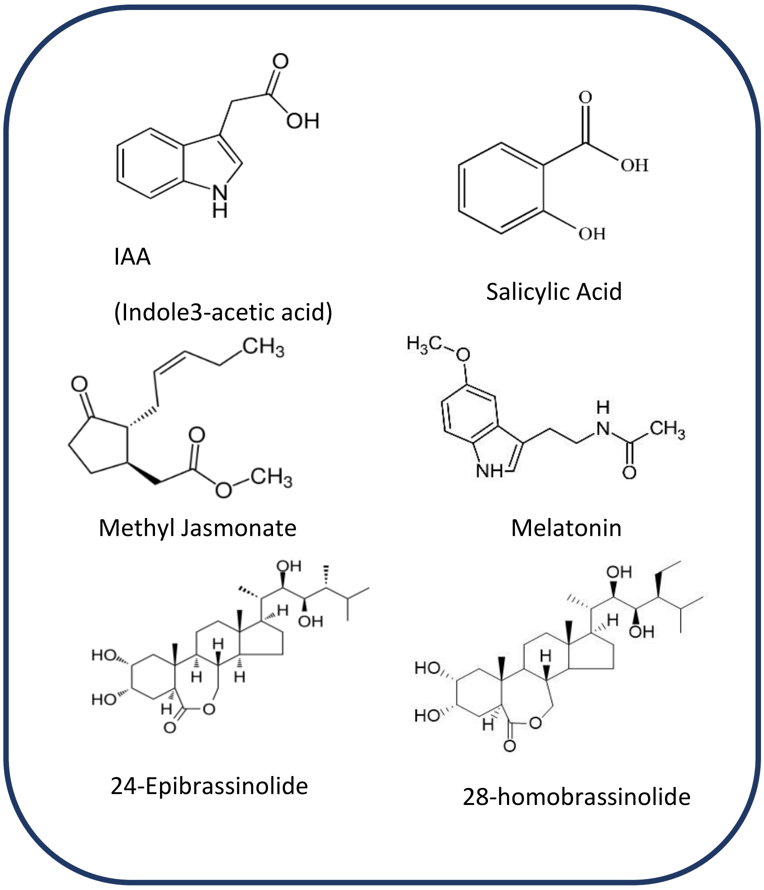


Figure 1. The various possible pathways for the chemical mobilization of As inside the soil and groundwater. Figure adapted from reference 4 with permission. (Kumar et al., 2023)

Furthermore, As adversely affects plant biochemical and morpho-physiological processes, leading to poor plant quality, growth, and development, and some commonly observed effects include wilting, reduced photosynthetic efficiency, biomass, chlorosis, and leaf necrosis (Abbas et al., 2018; Singh et al., 2013). At the physiological level, As increases the production of ROS, leading to oxidative stress ultimately damaging the plant's membrane proteins, lipids, and nucleic acids. Additionally, these oxidized species may interfere with other major metabolic pathways either directly or indirectly (Ahmad et al., 2020; Ghasemi-Omran et al., 2021; Mousavi et al., 2020a). To counter metal-induced oxidative stress, plants possess their own enzymatic [include enzymes such as, catalase (CAT), monodehydroascorbate reductase (MDHAR), dehydroascorbate reductase (DHAR), ascorbate peroxidase (APX), and superoxide dismutase (SOD)], and non-enzymatic [include molecules such as, ascorbic acid (AsA), α-tocopherols, glutathione (GSH), and phenolic compounds] antioxidant defense systems to maintain ROS homeostasis (Begum et al., 2016a; S. Samanta et al., 2021). Moreover, the role of the glyoxalase enzyme system (Gly I and Gly II) in defense mechanisms to enhance plant tolerance to As toxicity has been reported by Hasanuzzaman and Fujita (Hasanuzzaman and Fujita, 2013).

Figure 2. Structures of some common phytohormones used in alleviating As-stress



Plant scientists are continuously working to discover new ways to reduce the adverse effects of As-stress on crop plants. Therefore, they employed an array of methods, including the application of plant nutrients, phytohormones, signaling molecules, chelating agents, beneficial microbial inoculants, chemical elicitors, antioxidants, osmolytes, and soil amendments, to investigate their contribution to minimizing oxidative stress. However, here, we concentrate on phytohormones, including brassinolide, Mel, salicylic acid, methyl jasmonates, and indole 3-acetic acid, and their chemical structures are shown in Figure 2. It has been established that foliar application of salicylic acid (SA) and indole 3-acetic acid (IAA) enhanced tolerance to As-stress in rice and wheat plants by reducing oxidative stress and As accumulation (He et al., 2022a; Jung et al., 2019; Karam et al., 2016; Maghsoudi et al., 2020). Similarly, seed soaking with 24-epi-Brassinolide (in radish) and SA(in wheat) has been shown to increase endurance levels against As toxicity (Álvarez-Robles et al., 2022; Gautam et al., 2020; Raghu et al., 2014; Shah et al., 2022; Shukla and Singh, 2015). Several studies have illustrated that the exogenous application of these phytohormones improves seed germination, nutrient uptake, antioxidant defense systems, photosynthesis, plant metabolite regulation, transcript levels of PIN proteins and increases auxin transport in plants thereby enhancing overall plant growth (González-Moscoso et al., 2021; Nazarian and Ghanati, 2020; Praveen and Gupta, 2018). The amelioration of As-phytotoxicity has also been reported by applying phytohormones like MeJA and Mel in nutrient solutions during hydroponic culture in rice plants (S. Samanta et al., 2021; M. Singh et al., 2015; Verma et al., 2020a). Along with these approaches, genetic manipulation methods have been explored to study the differential gene expression associated with the phytohormone biosynthetic pathways and to understand hormone regulation and function in tolerating As-induced oxidative damage (Yanshan Chen et al., 2017; Hedden and Phillips, 2000; Krishna Kumar Rai and Rai, 2020). Transgenic approaches offer great potential for improving crop quality and productivity under As-stress, such as the introduction of OsPT genes in the As-stress defense system (Wang et al., 2017, 2016). By contemplating all the studies conducted so far, this review would appraise the mechanism of As-induced toxicity, the detoxification mechanisms involved, and the potential amelioration of these effects through an exogenous supply of phytohormones in crop plants.

2. As uptake, accumulation, and its Phytotoxicity

Plants depend on transporters to absorb nutrients from the soil. However, these mechanisms are not always able to differentiate between nonessential elements. For example, arsenate behaves like phosphate, which can disrupt the functioning of plants by affecting processes such as phosphorylation and ATP synthesis. When present in environments, both As(V) and P(V) take the form of oxyanions: arsenate (AsO_4^{3-}) and phosphate (PO_4^{3-}). These oxyanions have a coordination structure with four oxygen atoms surrounding them. Because of their chemical nature, phosphate and arsenate are considered analogs (Strawn, 2018), and their resemblance stems from their shared position on the table and comparable electron configurations. Additionally, As(III) binds to the sulfhydryl groups of proteins, impacting their integrity and ability to catalyze reactions (Tripathi et al., 2007; Zhao et al., 2010).

Generally, As present in two forms: arsenate $[As(V)]/AsO_4]^{3-}$ and arsenite $[As(III)]/AsO_3]^{3-}$ and the examples of the organic As compounds that are often encountered are monomethylarsinic acid (MMA; $CH_3AsO(OH)_2$) and dimethylarsinic acid (DMA; $(CH_3)_2AsOOH$). Microbes transform As(V)/As(III) into MMA and DMA through distinct pathways (Awasthi et al., 2017). Several phosphate transporters are implicated in As(V) uptake in various plants, such as *OsPHT1;1*, *OsPHT4*, and *OsPHT1;8* in rice (Wu et al., 2011; Ye et al., 2017) and *AtPHT1*;1, *AtPHT1;4*, *AtPHT1;5*, *AtPHT1;7*, *AtPHT1;8*, *AtPHT1;9* in *A. thaliana* (Catarecha et al., 2007; Fontenot et al., 2015; LeBlanc et al., 2013; Remy et al., 2012; Shin et al., 2004). In addition to that, the role of phosphate transporters such as *PHTF1* (phosphate transporter traffic facilitator 1) and PHR2 (phosphate starvation response 2) for the absorption and movement of As(V) were also explored and established (Wu et al., 2011).

The role of aquaglyceroporins (especially the nodulin 26-like intrinsic protein (NIP) class of aquaporin channels) in transporting the undissociated As(III) and methylated As species w also discovered (Mosa et al., 2012; Zhao et al., 2010) (Figure 3). In *A. thaliana*, various transporters such as *AtNIP1;1*, *AtNIP1;2*, *AtNIP5;1* (Kamiya and Fujiwara, 2009), *AtNIP3;1* (Xu et al., 2008), *AtNIP6;1* (Bienert et al., 2008), and *AtNIP7;1* (Isayenkov and Maathuis, 2008) were discovered for assisting in the uptake of As(III). In rice plants, transporters like *OsNIP1;1*, *OsNIP2;2* (*OsLsi6*), *OsNIP3;1* (Ma et al., 2008), *OsNIP3;2* (Bienert et al., 2008), and *OsNIP3;3* (Katsuhara et al., 2014) participated in the As uptake process. Recent studies have emphasized the role played by *OsNIP3;2* in absorbing As(III) through roots in rice plants (Yi Chen et al., 2017), and this specific gene is primarily found in the central region of roots. When there are mutations in *OsNIP3;2*, the concentrations of As(III) decrease in the roots but not in the shoots.

Moreover, the role of *OsLsi2* (member of NIPs) in As(III) efflux and transporting into the xylem in rice was shown by Ma et al. (Ma et al., 2008). Mosa et al. (2012) have reported that aquaporins belonging to the PIP class, such as *OsPIP2;4*, *OsPIP2;6*, and *OsPIP2;7*, were involved in taking up and moving As(III) (Mosa et al., 2012). Additionally, other transporters, like *NRAMP1* (Natural Resistance Associated Macrophage Protein 1), have been suggested to participate in taking up and transporting As(III) (Tiwari et al., 2014). Generally, As accumulates in the roots and is then transported to the plant's parts, such as shoots and grains. Researchers have identified the xylem as a tissue for moving As within the root-shoot system. Nahar et al. (2022) explained the role of the xylem in promoting the accumulation of pentavalent As(V) more than trivalent arsenic As(III) in plants (Nahar et al., 2022).

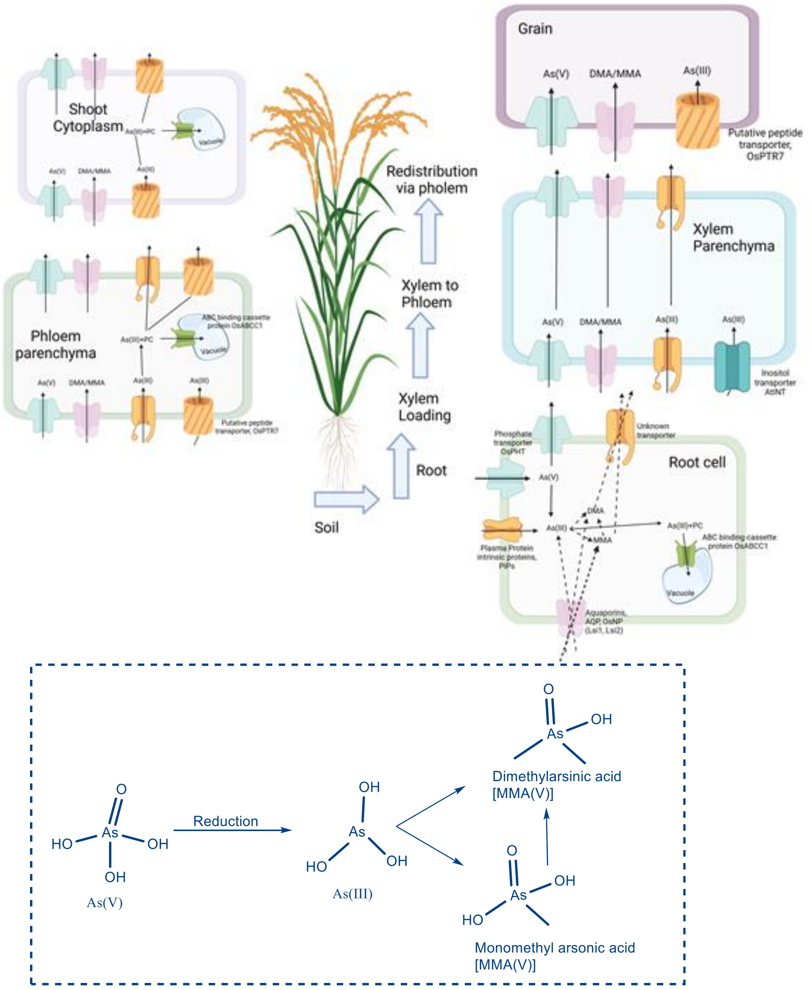


Figure 3. As uptake and accumulation mechanism

After absorption As(III) was transported to vacuoles in two ways: either through *PvACR3* (As Compounds Resistance) in *Pteris vittata*, as observed by Indriolo et al. (2010), or by forming complexes with phytochelatins (Indriolo et al., 2010). These complexes with phytochelatins, called PC-As(III) complexes, are then transported through members of the ATP Binding Cassette (ABC) transporter family, *ABCC1* and *ABCC2*, found in *Arabidopsis* and rice (Song et al., 2014b, 2010), as shown in Figure 3. Although there is still much to discover about the transporters involved in moving from xylem to phloem and into seeds, recent advancements have shed light on this matter. Specifically, researchers identified the significance of inositol transporters (INTs), known for their role in phloems uptake of inositol among *Arabidopsis* plants. It has been found that these INTs played a role in loading As(III) into the phloem. By disrupting *INT2* and *INT4* transporters within *Arabidopsis* plants, Duan et al. noticed a decrease in As levels within the phloem, silique, and seeds compared to wild-type plants (Duan et al., 2015).

While several AR genes have been identified in plants, their role in As(V) reduction remains uncertain, but the role of the enzyme arsenate reductase in regulating the conversion of As(V) to As(III) in plants was well established (Chao et al., 2014; Zhao et al., 2010). Recent research in *Arabidopsis* has identified two AR genes, *ATQ1* (arsenate tolerance QTL1) and *HAC1* (High As Content1) (Chao et al., 2014; Sánchez-Bermejo et al., 2014) and their participation in As reduction. Notably, *HAC1* has been found to actively reduce As(V) to As(III) in the outer cell layer of the root and facilitate the efflux of As(III) from the roots into the soil. In rice, Shi et al. found two genes called *OsHAC1*;*1* and *OsHAC1;2* that functioned as effective As(V) reductases (Shi et al., 2016). These genes are similar to *HAC1*. They are mainly expressed in the roots with *OsHAC1;1* being particularly abundant in the epidermis root hairs and pericycle.

On the other hand, *OsHAC1;2* is found primarily in the epidermis, cortex layers, and endodermis. It's worth noting that *OsHAC1;1* is also expressed significantly in stems and nodes. Another important As(V) reductase called *HAC4* was found in the root elongation and maturation zone within the epidermis and exodermis but was not detected in leaves (Xu et al., 2017). Interestingly, mutations in *OsHAC1;1*, *OsHAC1;2*, and *OsHAC4* led to a decrease in As(V) reduction ability in roots, resulting in As(III) efflux and increased accumulation of As in shoots (Shi et al., 2016; Xu et al., 2017).

In plants, the mobilization of As in its inorganic form is limited, for instance, in rice, only about 10% of As(III) reached the shoots, and a mere 3.3% made its way to the grain within 2-4 days (Zhao et al., 2012). Conversely, organic As species exhibit greater mobility due to processes like phytochelatin (PC)-mediated complexation (Moore et al., 2014; Raab et al., 2007). Plant nodes served as connections, influencing how As moved throughout the plant, as in the rice plant by Moor et al.. These nodes controlled the storage and distribution of As and act as filters for As(III) containing concentrations compared to internodes and leaves (Moore et al., 2014;

Yamaji and Ma, 2014). It's also worth mentioning transporters like *OsABCC1* located on the tonoplast of phloem cells in nodes that help transport PC As(III) into vacuoles and effectively store them. The presence of *OsABCC1* in the phloem companion cells of nodes further strengthens its function in preventing As movement into grains by transporting PC-As complexes to vacuoles (Moore et al., 2014). However, in mutants that lack *OsABCC1*, this storage mechanism is disrupted (Song et al., 2014b).

3. As detoxification mechanisms

Plants employed different strategies to minimize the effects of As-toxicity, including the production of proteins that bind to metals, allowing for compartmentalization and removal through transporters (Begum et al., 2016b; Dixit et al., 2016). Additionally, plants activated antioxidant systems, both non-enzymatic, to counteract oxygen species formation caused by metal toxicity (Armendariz et al., 2016; Saidi et al., 2017; Silveira et al., 2015). Osmolytes like proline, glycine betaine, and sugars also supported in detoxifying As by aiding in cellular partitioning (Garg and Singla, 2011).

The reduction of As(v) into As(III) and its transportation to the vacuole for disposal by binding with phytochelatins (PCs) (Abbas et al., 2018) is one of the crucial detoxification pathways for plants (Li et al., 2021; Fig 5). Rice plants were recognized for accumulating levels of As and producing PCs that help sequester As complexes in the vacuole, thus reducing toxicity (Batista et al., 2014). Several transporters in the vacuole have been discovered to transport As complexes into it (Song et al., 2014a, 2010). In *Arabidopsis*, ABC (ATP binding cassette) transporter family members, *ABCC1* and *ABCC2* transfer As(III) PC complexes to the vacuole, thereby enhancing *Arabidopsis*'s ability to tolerate As-stress (Song et al., 2014a). Li et al. showed that knocking ABC transporter genes in rice species led to the accumulation of As and cell death when exposed to growth media containing As (Li et al., 2016). Conversely, plants that overexpress genes for ABC transporters exhibited capabilities for detoxifying As by promoting its efflux into the environment, thus enhancing their tolerance towards As (Abbas et al., 2018; Chen et al., 2013).

Different breeding techniques have been employed across plant species to reduce the uptake and toxicity of As, ultimately improving their tolerance. Interestingly, previous studies had shown that when specific transporters, like *OsNRAMP1*, *OsPIP2;4*, *OsPIP2;6*, and *OsPIP2;7*, were taken from rice were overexpressed in *Arabidopsis thaliana*, there was a decrease in the uptake of As—this reduction in As uptake was linked to tolerance and increased biomass (Mawia et al., 2021). Furthermore, researchers have found that enhancing the expression of genes associated with the γ-amino butyric acid (GABA) shunt can effectively reduce the entry and uptake of As in rice seedlings (Kumar et al., 2017).

The uptake of As resulted in the increase of ROS, causing oxidative stress in plants. Therefore, the detoxification of ROS is regulated by antioxidant enzyme activities such as peroxidase (POD), superoxide dismutase (SOD), ascorbate peroxidase (APX), glutathione reductase (GR), and enzymes involved in the ascorbate-glutathione cycle (Shukla and Singh, 2015). Souri et al. reported that the activity of antioxidant enzymes reduced ROS and malondialdehyde MDA content, reducing membrane lipid peroxidation and improving plant growth under As stress (Souri et al., 2020). Alongside antioxidant enzymes, As exposure also enhanced the presence of non-enzymatic antioxidants in plants. For example, glutathione directly participates in the detoxification of ROS through the glutathione-S-transferase (GST) pathway, preventing cell damage from As stress. Similarly, Hasanuzzaman et al. discovered that ascorbate played a role in As-detoxification and provided tolerance to plants against oxidative stress through the ascorbate-glutathione (AsA-GST) pathway (Hasanuzzaman et al., 2019). Recent studies have shown that plants also increased the production of phenolic compounds under As exposure, accompanied by increased antioxidant enzyme activities (Kumar et al., 2022).

Recently, the role of the ubiquitin-proteasome pathway in regulating As (As) uptake and tolerance in plants has been studied (Hwang et al., 2016; Kim et al., 2021; Navarro et al., 2021). Sung et al. cloned and characterized the *ARS5*, a gene that translates the proteasome alpha subunit F1 protein (PAF1) of the 26S proteasome complex that has a vital role in protein degradation after ubiquitination. Through in-depth study, they demonstrated the function of PAF1 in the negative regulation of thiol biosynthesis and As tolerance in *Arabidopsis* (Sung et al., 2009).

The expression of the *Arabidopsis* phosphate transporter 1;1 (*PHT1;1*), which is crucial for the uptake of As(V), is controlled through a process called ubiquitination (Navarro et al., 2021). Chao et al. demonstrated that As(V) entered the cells using *PHT1;1* transporter and quickly converted them into As(III) with the help of *HAC1* (Chao et al., 2014). Navarro et al. displayed that As(III) activated SKP1-like proteins (ASK18) and interacted with PHR1 interactor F BOX (PHIF1), forming an SCF complex that led to the degradation of PHR1 (starvation response 1), which was responsible for activating *PHT1;1*. Consequently, the expression of *PHT1;1* is suppressed, alleviating the uptake of As(V) (Navarro et al., 2021).

In rice, Hwang et al. and Lim et al. discovered the activation of an *OsHIR1* gene by As triggering that was responsible for encoding a protein known as RING E3 ubiquitin ligase (Hwang et al., 2016; Lim et al., 2014). It was found that RING E3 ligase interacted with another protein called *OsTIP4;1* 1 (tonoplast intrinsic protein 4;1), which was believed to be involved in transporting As(III) into vacuoles.

Due to RING E2 ligase, *OsTIP4;1* was degraded through the ubiquitin-proteasome pathway. These findings suggested that the higher expression of *OsHIR1* caused by As exposure could enhance As tolerance by degrading an As transporter located on membranes, thus limiting As accumulation in roots. However, further research is required to confirm whether sequestering As in vacuoles through *OsTIP4;1* negatively regulates the mobilization of As within rice roots and if treatment with As indeed leads to degradation of *OsTIP4;1*(Hwang et al., 2016; Lim et al., 2014).

Sequestering As within vacuoles could impede the removal or efflux of As(III) from roots into the surrounding rhizosphere. Nevertheless, reducing sequestration or storage through ubiquitination could potentially facilitate the removal or efflux of As from cytosol using transporters near the surfaces of plant roots. Given that, Nguyen et al. found plasma membrane proteins (PIPs) in the roots of rice plants are responsible for transporting As into and out of the root plasma membrane (Nguyen et al., 2013). In *Arabidopsis* and rice, Mosa et al. revealed that overexpression of PIPs could enhance tolerance to As(III) by limiting its accumulation (Mosa et al., 2012). Ubiquitination data holded the potential to provide insights into the molecular processes that drove plant responses to As exposure. To gain more insights into the role of proteins contributing to As tolerance in plants, conducting an extensive analysis using the K63 polyubiquitination sensor combined with remnant profiling of protein samples from plants grown under different As conditions is necessary.The role of phytohormones in coordinating plant development and combating various environmental stresses was well discussed elsewhere

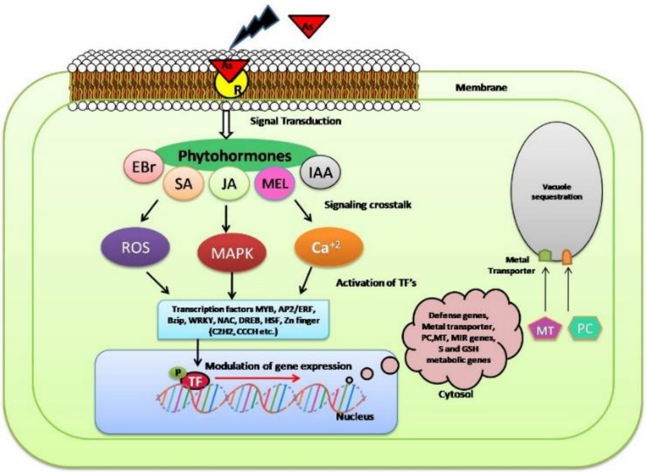


Figure 4. Schematic representation of the possible mechanism of phytohormone-mediated As stress tolerance in plants. As-stress facilitates its entry into the cell through an unknown receptor present on the cell membrane. Phytohormones such as (Epi-brassinolide (EB), SA, JA, Mel, and IAA induce signal transduction mechanisms and activate the transcription factors (TF's) such as MYB, AP2/ERF, Bzip. These TF's then modulate gene expression in the nucleus, enhancing the expression of defense-related genes and metal transporters in the cytosol. These metal transporters facilitate the transport of As into the vacuole.

(Zhao et al., 2021). Past research also demonstrated that applying phytohormones like methyl jasmonate, melatonin (Mel), salicylic acid, indole-3-acetic acid (IAA), and brassinosteroids (BR) externally could enhance tolerance to As in plants (Bano et al., 2022b; Chaudhary et al., 2023; He et al., 2022b; Li et al., 2021a; Mousavi et al., 2020a). As exposure to plants increased H_2O_2 levels in wild-type plants, but after treatment with phytohormones, the level of H_2O_2 decreased (Z. H. Dai et al., 2023). Under As-stress, a receptor on the cell membrane facilitates their entry into the cells. Phytohormones such as Epi-brassinolide (EB) SA Jasmonic acid (JA) Mel and Indole 3 acetic acid activated signal transduction mechanisms that involved transcription factors like MYB, AP2/ERF, and Bzip, as shown in Figure 4. These transcription factors then regulate gene expression within the nucleus by enhancing the expression of defense-related genes and metal transporters within the cytosol. These studies suggested the positive role of phytohormones in improving plant tolerance to As-stress through ROS-mediated signaling (Mitra et al., 2023; Singh et al., 2019).

4. Impact of exogenous supply of phytohormones on plants under As stress

4.1 Reduces As Accumulation

As accumulated in plants primarily as arsenate (As(V)) and arsenite (As(III)), utilizing phosphate and aquaporin transporters . Soil conditions, redox potential, microbial activity, plant genetics, and nutrient interactions influenced As uptake (Li et al., 2016). The study on Brassica juncea plants also highlighted age-dependent responses to As (V) exposure. In 30-day-old plants, significant As accumulation occurred, peaking at 0.3 mM As treatment, while 60-day-old plants showed reduced efficiency with increasing concentrations (Kanwar et al., 2015).

The phytohormones influence physiological and molecular processes, contributing to As detoxification and reducing its adverse effects on plant growth. Studies have shown that the application of IAA could substantially reduced As concentrations in rice grain by influencing the distribution of As within different plant parts, emphasizing its potential role in targeted As management. He et al. revealed that IAA application led to a substantial reduction in grain As concentrations in both Mo Wang Gu Nei (MWGN, *indica*) and Dong Ting Wan Xian (DTWX, *indica*) *Oryza sativa* cv., with decreases of 16% and 31%, respectively as compared to control (He et al., 2022c).

Additionally, IAA significantly altered the As concentrations in husks and rachis in response to IAA As concentration decreased n by 63.2% in MWGN, but in DTWX, it increasedby almost 55.3%. Further insights from the study emphasized the variations in As concentrations in leaves and internodes, notably in the upper second and third leaves. Interestingly, the effects of IAA varied, on the fourth leaves and internodes in DTWX, showcasing that IAA differentially distributed the As. However, more research is needed to understand the mechanisms behind these responses and improve the use of IAA to manage As in rice cultivation. It has been observed that there was a genotype-dependent response to As toxicity. This phenomenon might be attributed to inherent genetic differences among rice varieties, influencing their ability to absorb, translocate, and detoxify As.

Numerous research studies have examined externally applied SA's role in coping with As stress. Here, we have discussed the effectiveness of SA in reducing As accumulation in *Glycine max*, *Zea mays,* and *Brassica napus* plants. The investigation into *Glycine max* L. exposed to different concentrations of As (10 µM and 100 µM) revealed a consistent rise in As levels over a 5-day exposure period. However, the addition of exogenous SA demonstrated a 7-27% reduction in As accumulation, suggesting a stress-alleviating response of SA in this specific species (Chandrakar et al., 2016). Similarly, findings from studies on *Zea mays* exposed to As (0.1 mM) showed a significant increase in As levels in both leaves (18 µg As g $^{-1}$ DW) and roots (69 µg As g $^{-1}$ DW). However, treatments with SA, sodium nitroprusside (SNP), and their combination (SA+SNP) exhibited pronounced efficacy in reducing As content to 9, 14, and 7 µg As g^{-1} DW in leaves and 39, 42, and 20 µg As g^{-1} DW in roots, respectively (Kaya et al., 2020a). In *Brassica napus,* it was observed that the exposure of 200 mg of As per kg of soil led to varied accumulation of As in different parts of the plant. Specifically, the roots accumulated higher As levels (195.11 µg g^{-1} DW) than the leaves (131.41, µg g^{-1} DW). SA treatments at 250 mM and 500 mM concentrations demonstrated significant reductions of As content in roots (by 51.2% (250 mM) and 63.6% (500 mM)) and leaves (by 54.4% (250 mM) and 65.7% (500 mM)), demonstrating the potential of SA in alleviating As-stress (Bano et al., 2022c).

Moreover, exogenously applied methyl jasmonates (MeJA) on As-exposed plants revealed substantial reductions in As accumulation in various plants. It has been discovered that the application of MeJA showed efficacy in limiting As uptake and translocation, resulting in noteworthy decreases in As content in both leaves and roots. For instance, Farooq et al. investigated the use of MeJA in As-stressed varieties of *Brassica napus* (Zheda 622 and ZS 758). With the increase of As concentration (0, 50, and 200 μM) in the nutrient solution, the higher As concentration was found in Zheda 622 (1.15 mg/kg DW) than ZS 758 (0.95 mg/kg DW), with roots being significantly higher than leaves [(Zheda 622 (0.32 mg/kg DW); ZS 758 (0.24 mg/kg DW)] (Farooq et al., 2016). However when MeJA was applied externally (1 μM MeJA) it significantly reduced the concentration of As in the leaves [Zheda 622; leaves (0.12 mg kg^{-1} DW) and ZS 758; leaves (0.026 mg kg^{-1} DW)] as in the roots for both *B. Napus varieties* [Zheda 622; roots (1.04 mg/kg DW) and ZS758; roots (0.89 mg/kg DW)] under conditions of As-stress. In a study by Mousavi et al. corroborated that As treatment increased the As accumulation in roots and leaves. It was due to the increase in the expression *of the Lsi1, Lsi2, and Lsi6 genes*. On the other hand, when a same plant was treated with methyl jasmonates (MeJA), a reduction in As accumulation was observed due to the downregulation of these genes. Methyl jasmonates (MeJA) also led to an increase in iron (Fe) accumulation in leaves by upregulating the expression of transporters FRDL1 and YSL2 (Mousavi et al., 2020b). This iron (Fe) translocation counteracted the impact of As toxicity. Likewise, As(III)-treated rice seedlings exhibited elevated As accumulation in roots and shoots. The co-application of As(III) + Me-JA significantly decreased As accumulation, indicating that MeJA portrayed a crucial role in mitigating As-induced stress and promoting plant growth in rice. Specifically, As(III)-treated seedlings accumulated 18,209 and 16,957 μg g^{-1} DW of As in roots on the 10th and 15th day, respectively. However, the co-application of As(III) + Me-JA resulted in a significant decrease in As accumulation, recording 13,637 and 13,940 μg g^{-1} DW of As in roots on the 10th and 15th day, respectively (Verma et al., 2020b).

In the context of mitigating As accumulation in plants, the role of BR is also noteworthy. Studies have explored the impact of various treatments, including silicon (Si), SA, and their combinations with BR, on reducing As concentration in wheat plants. For instance, in 100 μM As supplementation, the co-application of 0.75 μM BR and 12 mM Si demonstrated a substantial reduction in root As concentration by 42.21%, surpassing the effects of Si, SA, and BR applied individually or in other combinations. Similarly, leaves and grains also exhibited marked reductions in As concentration under Si and BRs, highlighting the potential of these treatments in alleviating As stress in wheat (Maghsoudi et al., 2020). Yu and his coworkers studied the impact of exogenous application of brassinosteroids (Br24 and Br28) on As accretion in As-exposed rice plants (Yu et al., 2021). The results revealed intriguing dynamics in various plant tissues and highlighted the interplay between BR, iron addition, and their combined effects on As accumulation. Br24, Br28L, Fe, and Fe + Br24/Br28 significantly decreased As content in rice grains, with reductions of 18%, 24%, 73%, and 72%, respectively. Br24 and Br28, particularly when combined with Fe, demonstrated a substantial reduction in As concentrations in rice grains, with alleviations of 66%, highlighting their potential to enhance food safety. It may be attributed to enhanced iron plaque formation, modulation of As transporters, antioxidant defense, interference with uptake pathways, and synergistic effects with iron, collectively preventing As uptake and translocation in rice plants.

Exogenous application of Mel also demonstrates a substantial reduction in As accumulation in plants' root and shoot systems. Exogenous supplementation of Mel significantly reduced the endogenous bioaccumulation of As by about 1.5-fold and 1.3-fold in stressed seedlings of Khitish and Muktashri, respectively, compared to non-stressed seedlings (Santanu Samanta et al., 2021). The preferential reduction of As in roots suggests that Mel may influence As uptake and translocation processes within the plant, offering a targeted approach to limit As in edible parts. Under As stress, both Khitish and Muktashri exhibited a substantial increase in total As content in both roots and shoots, with roots accumulating significantly higher levels than shoots. The roots of Khitish and Muktashri accumulated 4961% and 1594% higher total As, respectively, compared to the control. Mel treatment resulted in a considerable reduction in As bioaccumulation in roots, lowering it by about 59% and 15% in Khitish and Muktashri, respectively, compared to As-treated sets. In shoots, a notable increase in As content (2114% and 3561%) was observed in Khitish and Muktashri under As stress. Mel supplementation reduced As bioaccumulation by about 12% in Muktashri shoots compared to As-alone treated shoots, with negligible reduction in Khitish (Samanta et al., 2022). Additional research could delve into the interactions between plant physiology and phytohormones like IAA and MeJa Mel, BR, and SA to understand how they influence the uptake and distribution of As. This deeper understanding would improve the effectiveness of these methods, leading to precise and sustainable solutions for mitigating As contamination in crops.

4.2 Enhances root growth

Roots are responsible for absorbing water and nutrients from the soil, so they need to be adaptable and flexible for plant survival (Ogura et al., 2019). As stress causes root growth retardation by decreasing auxin concentration within plant tissue (Tu et al., 2021). In *Arabidopsis thaliana*, optimal levels of auxin in root cells were found to be responsible for the cell division near the root tip to promote both elongation and differentiation of the roots (Petersson et al., 2009). Notably, studies have demonstrated that applying 200 nM of auxin stimulated mitotic activity and led to the expansion of the meristematic zone in plants (Růžička et al., 2009).

In As stressed plants, the activity of genes that produce auxin in leaves and further transport to the roots decreases, leading to reduced auxin levels in the roots (Tu et al., 2021). For example, when *Brassica juncea* plants were exposed to stress-specific genes involved in auxin movements, such as *BjPIN5* and *BjPIN3,* change occurred in both leaves and roots. This alteration impacts the growth of the roots meristem, hindering its development (Praveen et al., 2019). A study by Krishnamurthy and Rathinasabapathi (2019) emphasized that applying auxin externally in *Arabidopsis thaliana* enhanced the plant's tolerance to As. In the case of *Arabidopsis thaliana,* when auxin (IAA) was externally applied, it significantly increased tolerance levels in an auxin mutant known as aux1. This result suggested that the exogenous application of auxin could be a directed approach to enhance As stress tolerance by regulating processes related to auxin transportation and signaling pathways (Krishnamurthy and Rathinasabapathi, 2013). However, exploring the exact molecular mechanisms and pathways involved could give a clearer and more detailed understanding. Alamri and colleagues discovered that As accumulation, inhibition of phosphorus uptake, and induction of oxidative stress were all negative impacts of As-stress on brinjal root growth (Alamri et al., 2021). However, root growth was significantly enhanced when IAA was applied alongside As (V). This improvement was attributed to the reduction in As accumulation, mitigation of stress markers, sequestration of As into vacuoles, and enhancement of the status of glutathione (an antioxidant) (Alamri et al., 2021).

Similarly, the interplay of jasmonates and auxins was found to be pivotal in governing the development of adventitious roots in thin cell layers (TCLs) of tobacco (Fattorini et al., 2009). Applying methyl jasmonate (MeJA) to plants like *Brassica napus* (canola) and rice has shown promising results in promoting better root growth, increased biomass, and stronger antioxidant activities. This study suggested that MeJA could play a role in protecting roots from damage caused by As (Farooq et al., 2016; Muhammad A. Farooq et al., 2018; Muhammad Ahsan Farooq et al., 2018a; Mousavi et al., 2020a). In a study by Farooq and colleagues (2017), it was found that the exposure of oilseed rape (*Brassica napus* L.) roots to As hampered its growth

(Muhammad A. Farooq et al., 2018). However, methyl jasmonate (MeJA) demonstrated its potential to mitigate this hindrance. Plants treated with different doses of MeJA (0, 0.1, and 1 μM) showed more root growth than those solely subjected to As stress. Methyl jasmonate's protective effect on root development was linked to its ability to reduce damage from ROS and enhance antioxidant activities within the roots. Similarly, in rice varieties like T. Hashemi and Fajr, external application of methyl jasmonate (MeJA) has demonstrated positive effects in enhancing the ability of rice roots to tolerate As (Mousavi et al., 2020a). Methyl jasmonate treatment effectively reduced the effects of As by boosting the activity of antioxidant enzymes and regulating the ASA-GSH cycle in the roots. They propounded that controlling the expression of (As) transporters like *Lsi1*, *Lsi2*, and *Lsi6* MeJA might help reduce As accumulation in the roots. This targeted action of MeJA on the roots contributes to growth, resilience, and overall tolerance to As stress in rice varieties. A study on rice plants conducted by Ronzan and colleagues discovered that the application of methyl jasmonate boosted the density of lateral roots in normal and wild-type plants, even in the presence of As (Ronzan et al., 2019). This report suggested that MeJA could potentially reduce the harmful effects of As on forming lateral roots. Moreover, Betti et al. displayed that MeJA influenced the levels of auxin hormone in the roots by affecting the activity of specific genes, such as *OsASA2* and *OsYUCCA2*, related to auxin production. They concluded that exogenous methyl jasmonate application counteracted the As-induced reduction in lateral root density and modulated auxin biosynthesis, potentially enhancing the plant's ability to tolerate As stress (Betti et al., 2021).

Brassinosteroid (BR) hormone plays a crucial role in governing root growth by regulating cell division and elongation (Vukašinović et al., 2021). BR also exerted pivotal regulatory functions in modulating root growth and exhibit promising efficacy in enhancing As stress tolerance (Chandrakar et al., 2017; Maghsoudi et al., 2020; Raghu et al., 2014; Siddiqui et al., 2018a). The application of a brassinosteroid called 24 epibrassinolide (24 eBL) has been found to strengthen the resilience of rice root systems against As exposure regardless of whether it was in the form of arsenite (As(III)) or arsenate (As(V)). At 10^{-7} M concentration, 24 epibrassinolide (24 eBL) boosted root growth by up to 50% under As stressed conditions. It also helped mitigate the effects of As on cell structure and histology, such as thickened cell walls and lignin deposition on adventitious roots. It's worth noting that the exogenous application of BR also would play a role in restoring nitric oxide (NO) levels that were disrupted due to exposure to As, as reported by Piacentini et al. (Piacentini et al., 2023). The restorative impact highlighted in this case emphasizes the role of BR in regulating the synthesis and distribution of nitric oxide (NO). This regulation process was shown to be facilitated through the upregulation of *OsNOS1* expression, as discovered by Piacentini et al. 2023.

Mel, known for its role as a plant growth regulator, is derived from the same precursor, tryptophan, as the plant hormone auxin indole-3-acetic acid (IAA). While the relationship between Mel and IAA has been a subject of debate, recent findings in *Arabidopsis* indicated that Mel supported primary root growth influenced by IAA (Yang et al., 2021). Mel application demonstrated efficacy in combating As-induced stress, as observed in spinach studies (Asif et al., 2023). When Mel and *Bacillus licheniformis* were applied to Spinacia oleracea L. plants under As-stress, significant improvements were observed in root-related characteristics, including increased root length and biomass attributed to improved antioxidant activities. Furthermore, Mel showed a promising effect in mitigating the impact of As on rice roots. In hydroponic experiments with rice seedlings, Mel effectively reduced As levels in roots by 26.4% (Li et al., 2023).

SA actively participates in a plant's reaction to diverse abiotic stresses such as chilling, drought, salinity, and heavy metals. Furthermore, recent studies have shown that SA significantly influenced the development of plant roots (Bagautdinova et al., 2022). For instance, SA promoted root growth in rice plants exposed to As stress (A. P. Singh et al., 2015). SA prevented As from reaching the rice roots, showing its crucial role in controlling As accumulation. Furthermore, SA modulated antioxidant enzyme activities in the roots, thereby alleviating As(V)-induced oxidative stress specifically in the root system (Kanwar et al., 2013; A. P. Singh et al., 2015). Further, the combination treatment involving SA (0.5 mM) and SNP (0.1 mM) demonstrated greater effectiveness in enhancing maize plant root growth and this was accomplished by alleviating oxidative stress, lowering As content, and fortifying antioxidant defense mechanisms (Kaya et al., 2020a). Based on the preceding discussion, it could be asserted that phytohormones played a essential role in managing As stress by modulating gene expression, facilitating antioxidant production, and engaging in various regulatory processes.

4.3 Enhances Plant growth and Biomass

As adversely affects plant growth, impeding seed germination, stunting overall development, and disrupting root growth and nutrient uptake. It also causes chlorosis, leaf abnormalities, and oxidative stress, eventually leading to lower biomass accumulation. Scientists have studied using plant hormones, like auxins, salicylic acid, jasmonic acid, BR, and ethylene, to help plants cope with heavy metal stresses (Z.-H. Dai et al., 2023). By encouraging root growth, boosting stress resilience, and regulating growth processes, plant hormones helped alleviate As's impact on plant development, overall growth, and biomass. For example, He et al. investigated the effect of As on rice seedlings. They explored the efficacy of indole-3-acetic acid (IAA), SA, and gibberellins (GA) in mitigating As-induced inhibition (He et al., 2022c). Applying IAA, SA, and GA resulted in positive changes in plant morphology, including enhanced root and shoot elongation, biomass, total root length, surface area, volume, and tip number by counteracting the inhibitory effects of As on rice seedlings.. Under soil culture conditions, adding 20 mg L^{-1} IAA enhanced the growth of rice grains and the weight of each grain by 1000 times, thereby improving the plant's overall growth. Additionally, the application of brassinosteroid (Br24) significantly enhanced the biomass of rice’s shoots and roots, when exposed to As stress (Xu et al., 2020).

SA also activates stress responses and reduces damage by stabilizing cell membranes and maintaining redox balance. Moreover, these factors contributed to strengthening plant resilience and promoting growth when facing challenges caused by As exposure. A study by Kumari and her colleagues (Kumari et al., 2018) identified that exposure to As in Artemisia annua L. reduced plant growth factors (Table 1). The application of exogenous SA demonstrated a mitigating effect on the toxic consequences of As exposure. However, a subsequent exploration by Kumari and Shashi Pandey Rai in 2018 delved deeper into the mitigating effects of externally applied SA (100 µM) in As (100 µM) stressed *Artemisia annua* L. plants and showed applying SA proved effective in lessening As's impact by stabilizing cell membranes, balancing hormones, deactivating ions, and promoting antioxidant activity and thereby enhancing the plant growth (Kumari and Pandey-Rai, 2018). In the *Brassica napus* cultivar, the inhibited growth caused by As-stress was associated with the formation of ROS, inhibition of photosynthesis, and disruption of metabolic enzymes. It has been discovered that applying SA exogenously mitigated these harmful effects and improved plant growth and biomass in *Brassica napus* cultivar under As stress (Bano et al., 2022a). Kaya et al. demonstrated that SA supplementation effectively reversed oxidative stress-related parameters and reduced As content in both leaves and roots, improving plant growth (Kaya et al., 2020a) (Table 1). Singh et al. explored the protective functions of nitric oxide (NO) and SA against arsenite (As(III)) toxicity in rice plants. The research observed a decline in endogenous NO and SA levels under As(III) stress, which inhibited plant growth (Singh et al., 2017). However, the application of NO and SA exhibited a protective effect, ultimately enhancing plant growth in the presence of As(III) toxicity.

Methyl jasmonate acts as a signaling molecule in plants, triggering defense responses and impacting vital growth aspects, such as root development, flowering, and biomass accumulation. Numerous scientists have documented its ability to regulate stress responses and improve plant resilience in the presence of stress. For instance, Verma et al. investigated the impact of MeJA (0.25 µM) on As-stressed (25 µM As(III)) rice seedlings (Verma et al., 2020b). The co-application of MeJA with arsenite (AsIII) resulted in increased biomass, chlorophyll content, and enhanced antioxidant enzyme activities compared to As (III) treatment alone and suggested that MeJA had the potential to alleviate the detrimental effects of As on plant growth and development. Similarly, Siddique et al. examined the supplementation of calcium ions (Ca^{2+}; 40 mM) and JA (100 µM) in As-stressed tomato seedlings (Siddiqui et al., 2022). They found that the addition of Ca^{2+} and JA led to increased shoot length and biomass compared to As-stressed seedlings. Applying methyl jasmonate (MeJA) to As-stressed plants significantly improved the dry weight of rice cultivars, ZS 758 and Zheda 622. The enhancement was substantial, with a 31% increase in shoot dry weight for ZS 758 and a 27% increase for Zheda 622 rice cultivars. The root dry weight exhibited gains of 18% for ZS 758 and 23% for Zheda 622 rice cultivars compared to plants solely exposed to As stress (Table 1) (Farooq et al., 2016). While the studies provided valuable insights into the positive impacts on plant growth and stress resilience, it would be even more beneficial to delve deeper into the specific gene signaling cascades and biochemical processes involved. This deeper understanding would help us better apply and target these interventions in environments contaminated with As.

4.4 Reduced Oxidative damage

Plant hormones demonstrated their potential in reducing oxidative damage induced by As. Coelho et al. observed a 36% reduction in superoxide ($O_2^{\bullet -}$) levels in As stressed *Lemna valdiviana* with 100 µM JA, indicating JA's role in modulating ROS (Coelho et al., 2020). Verma et al. (2020) reported that MeJA significantly reduced malondialdehyde (MDA) content in rice seedlings under As(III) stress. In *Brassica napus*, Farooq et al. (2016, 2018) also found that exogenous MeJA alleviated As-induced oxidative stress by reducing MDA formation, hydrogen peroxide (H_2O_2), and OH^- contents in leaves. Ghorbani et al. further highlighted the effectiveness of MeJA and SA in reducing hydrogen peroxide, methylglyoxal, and malondialdehyde levels in As-stressed rice plants (Ghorbani et al., 2023). Siddiqui et al. (2023)

explored the synergistic effect of Ca^{2+} and JA in mitigating As-induced oxidative stress in tomato seedlings.

SA has been extensively studied for its role in mitigating oxidative stress under As exposure. Kumari (2018) demonstrated SA's effectiveness in reducing H_2O_2 content in *Artemisia annua* under different As concentrations. However, Bano et al. (2022) showed a significant reduction in H_2O_2, $O_2^{\bullet-}$, MDA, and electrolyte leakage levels in SA-treated *Brassica napus* plants under As stress (Bano et al., 2022c). Kaya et al. (2020) revealed a substantial reduction in H_2O_2, MDA, and electrolyte leakage when SA and SNP were jointly applied. Singh et al. (2015) observed decreased MDA and H_2O_2 levels in rice plants with SA pre-treatment and co-application of SA and As. In *Helianthus annuus,* Saidi et al. (2017) demonstrated SA's role in reducing membrane lipid peroxidation and H_2O_2 levels under As exposure (Fig 5). In a sequential exploration of plant responses to As stress, Sadeghipour and Monem (2021) explored the effect of SA on membrane lipid peroxidation in mungbean plants, revealing significant mitigation of oxidative damage under As stress (Sadeghipour and Monem, 2021). Naeem et al. (2020) extended the investigation to *Artemisia annua* L., uncovering that SA application reduced lipid peroxidation and H_2O_2 production (Naeem et al., 2020).

Mel emerged as a crucial player in alleviating As-induced oxidative stress across diverse plant species. Building upon the insights provided by Farouk and Al-Amri(Farouk and Al-Amri, 2019), who demonstrated a reduction in H_2O_2, MDA, and protein carbonyl group (PCG) levels in rosemary herbs upon exogenous Mel application, Jan et al. (2023) further highlighted Mel's pivotal role in mitigating membrane damage and oxidative stress in rice plants (Jan et al., 2023). The marked decrease in MDA levels observed in both studies underscores Mel's consistent and beneficial impact in reducing plant oxidative damage. Li et al. corroborated these findings in tea plants, illustrating Mel's ability to reduce H_2O_2 and $O_2^{\bullet-}$ accumulation (Li et al., 2021b). In As-stressed rice cultivars Khitish and Muktashri, Samanta et al. observed a reduction in MDA and lipoxygenase (LOX) activity with improved reducing power (Samanta et al., 2020). Lately, Zulfiqar et al. (2023) demonstrated that Mel, especially in tandem with SA, significantly curtailed MDA, H_2O_2, and electrolyte leakage in As-stressed plants (Zulfiqar et al., 2023).

BR also emerged as a promising candidate in alleviating As-induced oxidative stress. Maghsoudi et al. (2020) demonstrated that BR, particularly in combination with silicon, effectively reduced H_2O_2 and MDA levels in wheat leaves, showcasing their role in enhancing plant resilience to As stress. These studies collectively highlighted the intricate regulatory mechanisms of JA, SA, BR, and Mel in modulating ROS levels, mitigating lipid peroxidation, and preserving membrane integrity under As stress. These synergistic effects emphasized the complexity of the signaling networks involved in plant responses to As.

4.5 Improved Antioxidant Mechanism

Plants not only face the harmful effects of As but also deal with a rise in the generation of ROS, causing oxidative stress (Figure 4), and the plant's antioxidant system could mitigate this stress. In plants, essential antioxidants enzymes like superoxide dismutase (SOD), catalase (CAT), ascorbate peroxidase (APX), glutathione reductase (GR), and glutathione peroxidase (GPX) play a crucial role in this process. SOD helps to convert radicals O_2 into H_2O_2, while CAT and APX convert H_2O_2 into water molecules. GR helps convert oxidized glutathione (GSSG) to its reduced form, GSH, and GPX aids in converting H_2O_2 into water using GSH as a reductant. Non-enzymatic antioxidants like GSH and ascorbate also contribute to managing stress. GSH regulates the potential for acids and proteins to counter oxidative damage, while water-soluble ascorbate acts as a substrate for ascorbate peroxidase by donating electrons to ROS (Hu et al., 2020).

During As stress, phytohormones boost the activity of antioxidant enzymes. For example, the application of indole acetic acid (IAA) improved the plant’s tolerance against As toxicity. Krishnamurthy and Rathinasabapathi's research demonstrated that applying IAA to *Arabidopsis thaliana* during As-stress effectively hampered the levels of H_2O_2 and the excessive production of ROS (Krishnamurthy et al., 2019) (Table 1).

Recent studies showed that BRs protected plants from various challenges like heavy metals, drought, salt, extreme temperatures, and pathogens (Yaqoob et al., 2022). The application of BRs made plants more resilient by working together with other hormones like auxins, cytokinins, jasmonic acid, and salicylic acid, triggering defense mechanisms (Ahanger et al., 2018). In As stress, EBL demonstrated significant modulatory effects on the vital biochemical parameters in *A. thaliana*. Co-treatment with 100 µM As(V) and EBL resulted in a noteworthy increase in total SOD and CAT enzyme activities compared to individual exposure to 100 µM As(V). Moreover, the EBL application alone substantially augmented the total antioxidant content, showcasing its role in enhancing the plant's antioxidant defense mechanisms under As stress (Surgun-Acar and Zemheri-Navruz, 2019). The application of BR, such as brassinolide (BL) and 24-epibrassinolide (24 eBL), enhanced the antioxidative mechanisms in plants when they face As-stress. Research conducted by Siddiqui et al. and Farooq and their colleagues demonstrated that BR boosted the activity of antioxidant enzymes like CAT, POD, and SOD and reduced the levels of MDA and lipid peroxidation under As-stress conditions (Farooq et al., 2016; Muhammad A. Farooq et al., 2018; Muhammad Ahsan Farooq et al., 2018a; Manzer H. Siddiqui et al., 2020) (Table 1). BR (24-epi-brassinolide; 0, 0.5, and 0.75 μM) significantly enhanced both the growth and quality of wheat, concurrently reducing As accumulation, and activating antioxidant defense mechanisms in various plant parts under As stress (Fleta-Soriano et al., 2017). Piacentini and his coworkers in 2023 demonstrated that BRs regulated the ROS levels in rice roots under As stress. The application of 24-eBL (10^{-7} M) effectively mitigated oxidative stress induced by As(III) and As(V), contributing to maintaining cellular redox balance (Piacentini et al., 2023).

SA regulates numerous antioxidant enzyme activity and levels of non-enzymatic antioxidants (Koo et al., 2020). SA performed a dual function, acting as both a pro-oxidant (accumulating ROS) and an antioxidant (scavenging ROS) via the AsA-GSH cycle (Saleem et al., 2021)' and under stressed conditions, helping to interconnect the ROS and SA signaling upstream and downstream (Herrera-Vásquez et al., 2015). Singh et al. illustrated the ameliorative effect of SA against As stress in rice plants. They observed enhanced biomass, shoot, and root length growth and decreased levels of H_2O_2 and MDA in rice plants growing under As-stressed conditions (A. P. Singh et al., 2015). Furthermore, in soybean plants, the metabolic and physiological aspects of As stress tolerance were conferred by the exogenous application of salicylic acid. A study by Chandrakar et al. revealed that SA application stimulated antioxidant enzyme (APX, CAT, SOD) activity while decreasing As levels by inhibiting the formation of ROS in *Glycine max* (JS335 variety) (Chandrakar et al., 2016). In the presence of As, SA effectively enhanced the activities of SOD and peroxidase (POD) by 46.33-48.5%, counteracting the oxidative impact of As in *Helianthus annuus*. Conversely, SA mitigated the As-induced decline in CAT, APX, and GPX activities by approximately 24.3%, 31%, and 22%, respectively (Saidi et al., 2017).

Recently, Kaya et al. confirmed the positive role of SAin stimulating antioxidant enzyme activity (MDHAR, POD, CAT, SOD) and non-enzymatic antioxidants levels (AsA and GSH), thus inhibiting the overproduction of ROS to provide As tolerance in maize plants (Kaya et al., 2020b). Additionally, the combined role of SA and nitric oxide in the aforementioned physiological processes was higher than when applied individually. Additional research ca investigate how SA interacts with molecules or compounds to determine if they have a combined effect in improving plant tolerance to As stress. Exploring the connections between signaling molecules may offer possibilities for enhancing stress resilience.

Farooq and colleagues studied the effect of methyl jasmonate in boosting the activity of antioxidant enzymes and revealed that it could trigger antioxidant responses in plants. These responses include increasing the levels of GSH, enhancing the activities of antioxidant enzymes, like CAT and SOD, and influencing the expression of genes involved in ROS (oxygen species) metabolism [(Farooq et al., 2021, 2016; Muhammad A. Farooq et al., 2018; Muhammad Ahsan Farooq et al., 2018b); Table 1; Fig 5] and propounded that all these effects might work together to reduce stress caused by As toxicity. However, more research is needed to understand how MeJA interacts with molecular pathways and modulates the natural antioxidative defenses.

Several studies, especially those conducted by Farouk and Al-Amri. (2019), Jan et al. (2023), Li et al. (2021), and Zulfiqar et al. (2023) collectively emphasized the crucial role of Mel in enhancing antioxidative defense mechanisms under As (As) toxicity in rosemary herb, rice, tea and sword lily plants. These study revealed that melatonin application led to increased activity of essential enzymes like SOD, APX, CAT, GPX, and GR, contributing to the effective detoxification of ROS under As stress (Fig 5) [(Bano et al., 2022a; Samanta et al., 2022b; Santanu Samanta et al., 2021b)); (Table 1)].

4.6 Effect on the gene expression

In *Brassica napus*, Farooq et al. (2016, 2018) demonstrated that MeJA application significantly alleviated As-induced oxidative stress by up-regulating key enzymes involved in the glutathione cycle. The expression of γECS (gamma-glutamylcysteine; an intermediate compound in the glutathione biosynthetic pathway), a vital enzyme for glutathione biosynthesis, increased after As treatment, and MeJA further enhanced this response, leading to elevated GSH levels. The study also highlighted the positive impact of MeJA on the expression of the glutathione reductase (GR) gene and its enzymatic activity, reinforcing its role in mitigating As-induced damage. Additionally, the research emphasized the genotype-specific responses, with ZS 758 and Zheda 622 cultivars showing distinct variations in gene expression and enzyme activities. Ghorbani et al. extended the scope to As-stressed rice plants and demonstrated that MeJA particularly in combination with SNP, significantly upregulated GSH1 and PCS gene expressions in rice roots under As stress. Conversely, MeJA + SA treatment downregulated GSH1 expression. ABCC1 expression increased in both roots and leaves under As stress, with MeJA, MeJA + SNP, and MeJA + SA + SNP treatments further enhancing expression, while MeJA + SA treatment led to downregulation in leaves (Ghorbani et al., 2023).

The role of exogenously applied Mel in regulating the antioxidative machinery and gene expression in response to As stress in rice varieties was also discovered. In Khitish seedlings, the As stress induced a significant increase in SOD and CAT activities, while Mel supplementation mitigated CAT activity and exhibited variable effects on SOD activity. These findings are consistent with previous studies on As-induced SOD activity in different plant species (Singh et al., 2017). Mel did not detectably influence SOD activity in either variety but reduced CAT activity in Khitish but increased it in Muktashri variety during As stress. Even Li et al. observed similar trends in Khitish and Muktashri (Li et al., 2019). In As stress, glutathione peroxidase (GPOX) activity increased in Khitish but decreased in Muktashri, and Mel further increased GPOX activity in Khitish and Muktashri (Khan et al., 2021). Tripathi et al. discovered that mMel alleviated As-induced suppression of GST and GPX activities in Khitish, while in Muktashri, only GPX activity was stimulated by Mel (Tripathi et al., 2012). The AsA-GSH cycle enzymes, APX, MDHAR, and DHAR, were regulated by Mel in a variety-specific manner. Mel reduced APX activity in Muktashri and influenced MDHAR and DHAR activities differently in both varieties. Differential gene expression between rice varieties (Khitish and Muktashri) under As stress and Mel supplementation was attributed to genetic diversity, stress tolerance levels, evolutionary adaptations, physiological characteristics, variances in metabolic pathways, and Mel sensitivity. These factors collectively contributed to unique molecular responses, highlighting the complexity of plant stress adaptation. Moreover, Mel influenced osmolyte accumulation, gene expression related to osmolyte biosynthesis, and anthocyanin levels, supporting its role in enhancing stress tolerance (Fig 5). These studies provided comprehensive insights into the gene regulatory mechanisms of Mel in mitigating As-induced stress in rice varieties, presenting a promising avenue for further research and applications in stress management in crops (Samanta et al., 2020; Samanta et al., 2021).

The effect of exogenously applied 24-epibrassinolide (EBL) on gene regulation in *Arabidopsis thaliana* under As (V) stress was investigated using quantitative real-time PCR. EBL treatment demonstrated a significant impact on the expression of genes associated with antioxidative responses, including SOD, CAT, proline synthase (P5CS), and heat shock proteins (HSP). This study revealed intricate regulatory patterns, suggesting the potential of BR in fine-tuning gene expression to enhance plant tolerance to As stress (Surgun-Acar and Zemheri-Navruz, 2019).

4.7 Effect on various metabolites

In response to As stress, the modulation of plant secondary metabolites by exogenously applied phytohormones has been extensively investigated. Furthermore, Mel, when exogenously applied, played a crucial role in regulating the expression of genes related to osmolyte biosynthesis, altered carbohydrate metabolism, and exhibited antioxidant properties (Li et al. 2019), (Samanta et al., 2020); Jan et al., 2023). For instance, the application of exogenous Mel resulted in a notable upregulation of proline content and the activities of proline biosynthetic enzymes, including P5CS and GK (Nazir et al., 2023). Mel supplementation counteracted the As stress-induced reduction in carbohydrate levels and significantly increased glucose, sucrose, total soluble sugars, and starch. This study demonstrated Mel's role in enhancing carbohydrate reserves, contributing to the plant's resilience under As- stress (Bano et al., 2022). Mel also displayed some influence on the activity of enzymes associated with sugar metabolism, such as invertase (INV) and sucrose synthase (SPS), further contributing to the antioxidant defense system (Jan et al., 2023; Samanta et al., 2020). These studies revealed a complex network of interactions between phytohormones (MeJA, EBL, and Mel) and the regulation of various metabolites under As stress. While MeJA demonstrated its potential in glutathione cycle modulation, EBL fine-tunes antioxidative responses, and Mel played a crucial role in diverse aspects of plant adaptation against As stress.

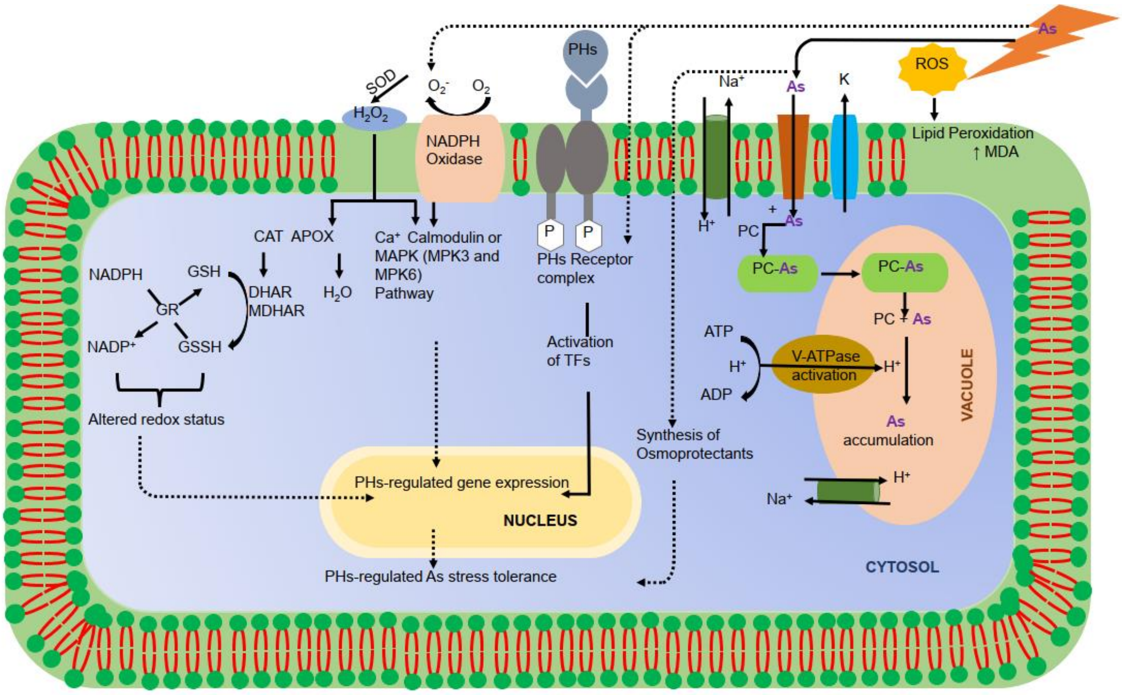


Figure 5. Diagrammatic representation of the regulation of antioxidant defense machinery by phytohormones in plant cells, including sequestration inside vacuoles, to counteract the adverse effects of redox imbalance induced by As stress. PHs- Phytohormones, As- As, TFs- Transcription Factors

4.8 Improved Photosynthesis Process

As stress exerts detrimental effects on the photosynthetic processes of plants, manifesting through the inhibition of key enzymes, disruption of chlorophyll synthesis, and impairment of the electron transport chain. These disruptions contribute to a reduction in photosynthetic efficiency, consequently hampering plant growth and biomass accumulation. The intricate interference with photosynthesis under As stress extends to oxidative stress induction, exacerbating damage to the photosynthetic machinery. The role of plant hormones in coordinating photosynthetic processes in response to As stress was also very well demonstrated (Muhammad et al., 2021).

For instance, BR increased chlorophyll levels by enhancing enzyme production and protected the repair protein photosystem II protein D1 from damage caused by ROS during water splitting (Siddiqui et al., 2018b). Additionally, BRs facilitated stomatal opening, enabling CO_2 absorption and promoting the formation of the enzyme ribulose bisphosphate carboxylase/oxygenase in the Calvin cycle. This phytohormone also aided in sugar synthesis, thereby improving photosynthetic efficiency. Conversely, abscisic acid regulated the stomatal closure, affecting CO_2 diffusion (Ghorbel and Brini, 2023), while cytokinins, auxin, and ethylene stimulated stomatal opening. Notably, methyl jasmonate exhibited concentration-dependent effects on photosynthesis. Lower concentrations enhanced photosynthesis, while higher concentrations inhibited photosynthetic activity. This intricate regulation by plant hormones highlighted their diverse roles in modulating key processes essential for plant growth (Müller and Munné-Bosch, 2021).

In a greenhouse study, the addition of EBL to wheat, along with SA and silicon (Si), played a crucial role in alleviating As toxicity, particularly in enhancing photosynthesis (Table 1; (Maghsoudi et al., 2020)). Similarly, in the *Brassica napus* cultivar Neelam, As-induced toxicity negatively impacted photosynthetic attributes and carbon assimilation, reducing growth. However, foliar salicylic acid spray (500 mM) effectively alleviated these negative impacts. SA application enhanced the activity of a key photosynthetic enzyme such as ribulose 1,5-bisphosphate carboxylase (Rubisco), thereby improving photosynthetic efficiency under As-stress conditions (Table 1; (Bano et al., 2022c)). To understand how SA enhances tolerance to stress, it would be advantageous to explore the effects of SA on downstream targets involved in detoxifying As. Additionally, investigating how these targets influence the expression of genes related to photosynthesis would provide insights.

Furthermore, research on *Artemisia annua* under As stress revealed that the exogenous application of SA has a multi-faceted impact on photosynthesis. When subjected to a combined treatment of SA (100 μM) and As (100 μM), a significant increase in total chlorophyll content was observed compared to As treatment alone, indicating a beneficial influence on the photosynthetic apparatus. These findings offered insights into the potential roles of SA in alleviating the adverse effects of As stress on photosynthesis in *A. annua* (Kumari and Pandey-Rai, 2018). When rice plants are exposed to As, plants undergo increased As absorption, higher levels of oxidative stress, and a decline in photosynthesis and growth. However, the SA's application positively impacts photosynthesis and plant growth by interacting with ethylene and nitric oxide (NO), enhancing the plant's defense mechanisms. The positive impact of SA on improving photosynthesis under As stress is associated with its influence on the rice plants' ascorbate-glutathione cycle/glyoxalase system (M. I. R. Khan et al., 2021). However, there is a potential research gap in understanding the precise signaling pathways and molecular mechanisms through which SA interacts with other signaling molecules, such as ethylene and nitric oxide, to enhance photosynthesis.

Siddiqui et al. demonstrated that Mel also stimulated photosynthesis by upregulating the expression of related genes and inhibiting chlorophyll (Chl) degradation (Manzer H Siddiqui et al., 2020). They demonstrated that the combined application of Mel and calcium ions (Ca^{2+}) to *Vicia faba* (cv. Tara) effectively alleviated the detrimental effects of As toxicity. This synergistic approach efficiently improved gas exchange parameters and increased the activity of enzymes associated with photosynthesis (carbonic anhydrase and RuBisco) and chlorophyll biosynthesis such (δ-aminolevulinic acid dehydratase) in *Vicia faba* plants. Simultaneously, it decreased the activity of the chlorophyll-degrading enzyme (chlorophyllase) under As toxicity. However, conducting an experiment on the interplay between Mel and calcium signaling pathways is crucial. Acquiring knowledge about the genes and proteins involved in this process and investigating the regulatory networks upstream and downstream would considerably enhance our understanding of how Mel and calcium work together to enhance photosynthesis and mitigate the effects of As stress.

5. Phytohormone and Transcriptome under As-stress

The term "transcriptome" encompasses all RNAs produced by a particular cell or tissue during a specific functional state, while transcriptomics studies the transcriptome (structure, function, and regulation). After the development of next-generation sequencing (NGS) technologies platforms (Illumina, Ion Torrent, PacBio, and Nanopore sequencing), the whole transcriptome study was used to decipher the complex gene expression and regulatory networks under different stresses at the entire genome level in various plants. Like other stresses, in response to the As-stress, phytohormones altered gene expression and enzyme activities of various cellular pathways to plants to mitigate the harmful effects. Understanding the transcriptome behavior during the As-stress and phytohormone treatment will help design future resistant crops. Multiple studies have been performed using NGS to understand this relationship in plants to understand the genome-wide transcriptome behavior in plants under As-stress (Di et al., 2021; Fu et al., 2020; Huang et al., 2019; Liu et al., 2023; Shukla et al., 2018; Wang et al., 2017). However, no published report is available to explore the whole transcriptome for the phytohormones-mediated tolerance in As-stressed plants. Considering the importance of NGS for a deeper understanding of the role of phytohormones in the resilience of As-stress, it require more work to be done.

6. Phytohormones and proteome under As toxicity

Genomics and transcriptomics limit the information because these analyses may provide rough calculations of available amounts of expressed proteins because of the fast degradation of transcribed mRNA. Therefore, proteome analysis is more reliable for decoding the mechanism of a molecular process as it is stable and a vital component of metabolic activities (Yadav et al., 2023).

The first proteomic study under the As exposer was conducted on *Z. maize*, suggesting that this toxicity induced oxidative stress in plants (Requejo and Tena, 2006, 2005). In response to As exposer, maize roots and leaves up- and down-regulated various proteins involved in the redox process and As detoxification like SODs, GPXs, cytochrome P450s, translation elongation factor IF- 5A, ATP synthase, malate dehydrogenase, and protein kinase C inhibitor, etc. Later, proteomic analysis in *O. sativa* was also performed to identify mechanisms involved in As-stress detoxification (Ahsan et al., 2010, 2008).

While extensive research has delved into the physiological, biochemical, and transcriptional responses to As-stress across diverse plant species, there remains a scarcity of information concerning the context of proteomic studies. We found only two published reports on the proteome analysis associated with phytohormones mediated As tolerance in *B. napus* (cultivar ZS758 and ZD622) (Muhammad Ahsan Farooq et al., 2018b). This study investigated leaf proteome in MeJA-induced As tolerance to identify molecular mechanisms. There were 177 and 200 differentially expressed proteins in cultivars ZS758 and ZD622 under the treatment of As alone and As along with MeJA, respectively. Further, the authors identified 61 and 49 MeJA-regulated proteins under As-stress in cultivars ZS758 and ZD622, respectively. These proteins were divided into five groups, i.e., stress and defense, secondary metabolites, photosynthesis, protein metabolism, carbohydrates, and energy production. Another study by Farooq et al. (2021) on the same plant varieties (without phytohormones treatment) revealed that the proteomic profile associated with the oxidative defense system in plants exhibiting varying capacities to tolerate As-stress (Farooq et al., 2021). The As-tolerant cultivar of *B. napus* demonstrated elevated expression of antioxidant-related proteins compared to the sensitive counterpart.

Based on previous reports, we could say proteomic analysis could provide more reliable information to decipher the molecular mechanism of As tolerance and detoxification under the treatment of phytohormones and hence needed more work in this area.

7. Transgenic approach

Transgenic approaches offer significant potential for crop improvement, including enhancing quality, productivity, and abiotic stress tolerance (Wang et al., 2017, 2016). By manipulating the expression levels of various genes, such as *OsPT* genes involved in the stress defense system, transgenic technology provided a practical means to develop plants capable of withstanding As stress. The differential expression of these genes associated with phytohormone biosynthesis pathways enabled the study of hormone regulation and function. Additionally, these genes can introduce agriculturally beneficial traits into crops through genetic engineering, thereby increasing tolerance to As-induced oxidative damage, improving crop productivity, and developing superior genotypes (Yanshan Chen et al., 2017; Hedden and Phillips, 2000; Krishna Kumar Rai and Rai, 2020).

The similarity in chemical characteristics of As with phosphorous (Sharma et al., 2021; Zvobgo et al., 2018) led to its uptake in plants through phosphate transporters such as PHT-1. Overexpression of *OsPT8* in rice plants resulted in increased influx and translocation of As (V) from roots to shoots (Wu et al., 2011). In plant species such as *Pteris vittata*, rice, and *Arabidopsis*, As (20µM) is transported as As (V) and As (III) into root cells via the phosphate transporters family (Cao et al., 2017). Among these transporters, Pht1;1, Pht1;4, and Pht1;8 were expressed during As stress in rice and *Arabidopsis* plants, respectively (Shin et al., 2004; Wu et al., 2011). In 2017, Xu and his colleagues noticed that a rhodanase-like protein encoded by OsHAC4, an As reductase gene, when upregulated, provided tolerance to metal stress and reduced As accumulation by detoxification and effluxing As from rice plants (Xu et al., 2017). The lambda class of Glutathione S-transferases (OsGSTL2), a type of GST enzyme, plays a significant role in detoxification mechanisms. In this context, the expression of *OsGSTL2* was studied in rice genotypes growing under As-stress-induced conditions, and it was seen that OsGSTL2 imparts As tolerance (Kumar et al., 2013). Similarly, a group of transcription factors called WRKY, including WRKY28, WRKY6, and WRKY45, were involved in the regulation of Pht1;1 and facilitated the uptake of As (V) in *Arabidopsis* (Castrillo et al., 2013; Wang et al., 2018, 2014). Deng and co-workers observed two vacuolar sequestering genes, i.e., ScYCF1 and OsABCC1, working under the RCc3 promoter. On upregulating their expression in transgenic rice plants, they lessened the As translocation from root to shoot and internode to shoot (Deng et al., 2018). Further studies conducted in tobacco, rice, and *Pteris* plants have demonstrated that As (V) was reduced to As (III) by the enzyme As reductase (ACR) in different plants (Yanshan Chen et al., 2017; Duan et al., 2007; Nahar et al., 2017). Transgenic tobacco plants overexpressing the *Arabidopsis ACR2* gene exhibited increased tolerance to high As stress levels. Overexpression of *OsACR2.2*, *OsACR2.1*, and *PvACR3* in rice, tobacco, and *Pteris* plants decreased in As (III) stress and its assimilation in the shoots. Furthermore, *OsHAC1;1, OsHAC4, and OsHAC1;2* have been employed to limit As accumulation in rice grains and shoots (Shi et al., 2016). Another As reductase gene, High As Concentration 1 (HAC1) from *Arabidopsis thaliana,* was tested to convert As(V) to As(III), thereby improving efflux As(III) from roots and hindering As(V) translocation as well as reducing its accumulation in plant shoot (Fischer et al., 2021). Verma and his coworkers in 2016 found that upregulation of Glutaredoxins family members (OsGrx_C7 and OsGrx_C2.1) in *Arabidopsis thaliana* transgenic plants improved the As-stress tolerance(Verma et al., 2016). The increased activity of *OsGrx_C7* and *OsGrx_C2.1* decreased the As accumulation in shoots and seeds, improving seed germination and plant growth.

Class III peroxidases belong to a multigene family and are used in several physiological and developmental processes. An investigation done by Kidwai and his coworkers in 2019 recognized the Class III peroxidases (OsPRX38) in rice plants, and their activity improved under the As-stress. They also found that the overexpression of OsPRX38 increased total biomass and yield production in *Agrobacterium*-mediated transformed *Arabidopsis thaliana* transgenic plants compared to wild-type plants. This effect was observed due to lignin biosynthesis by OsPRX38 that restricted As entry inside root cells, thereby reducing As accumulation (Kidwai et al., 2019). One more protein, the MsHSP23, a heat shock protein from alfalfa, when inserted into a tobacco plant, provided tolerance to As stress by improving the rate of germination (Lee et al., 2012). Furthermore, transgenic *Arabidopsis thaliana* (L.) Heynh produced by introducing NADPH oxidase C (AtrbohC) showed reduced uptake and transport of various elements such as sulfur, phosphorus, iron, zinc, and copper. It was also observed that AtrbohC regulates the antioxidant enzymatic activity (Gupta et al., 2013). Recently, scientists discovered the role of SNAC3-overexpressing (SNAC3-OX) belonging to NAC transcription factors in improving grain productivity and As-stress tolerance in transgenic rice plants. Moreover, SNAC3-OX provided protection from oxidative stress by enhancing antioxidant enzymatic activity (CAT, SOD, POD, and APX) and the expression of stress tolerance genes (OsCATA, OsAPX2, OsCATB, OsSOD-Cu/Zn, OsDREB2B, OsDREB2A, OsLEA3, OsSNAC2, and OsSNAC1) (Pooam et al., 2023).

Recently, transgenic approaches have proven valuable in regulating internal hormone levels and their signaling pathways in crops, leading to a revolution in agriculture (Gupta et al., 2017). Transgenic plants exhibited high levels of osmolytes such as proline, glycine betaine, late embryogenesis abundant (LEA) proteins, and molecular chaperones. Additionally, they showed enhanced expression of defense-related genes in various crop plants, including rice and wheat (Anumalla et al., 2016; Großkinsky et al., 2016). Despite advancements in genetic engineering, transgenic plants only showed a moderate increase in resistance to abiotic stresses compared to non-transgenic alternatives, primarily through the accumulation of osmolytes such as glycine betaine, proline, and mannitol (Banerjee and Roychoudhury, 2016).

Several genes involved in the regulation and biosynthesis of phytohormones, such as gibberellins, auxins, jasmonic acid, and BR, have been employed to increase grain yield in rice and reduce As uptake (Gupta et al., 2017). For instance, overexpression of the exogenous *5-Enolpyruvylshikimate-3-Phosphate Synthase* (*EPSPS*) gene in transgenic *Arabidopsis* plants enhanced auxin content (Fang et al., 2018). Similarly, the overexpression of various genes, such as *AtMYC2*, *AtMYC3*, and *AtMYC4*, synergistically enhanced JA responses for different JA-regulated processes, including cotyledon greening rate and inhibition of root growth in *Arabidopsis* and maize plants (Fernández-Calvo et al., 2011; Fu et al., 2020; Liu et al., 2019). Furthermore, the *Brassica rapa* expansin-like B1 gene (*BrEXLB1*) might contribute to plant growth, leaf development, and germination in *Arabidopsis* plants depending on the availability of phytohormones such as JA and IAA (Krishnamurthy et al., 2019). While we have discussed individual contributions of transgenic approaches in enhancing As tolerance and improving phytohormone levels, there is insufficient information on the combined effects of transgenic approaches on phytohormones for conferring As tolerance in different plants.

8. Genome editing

Genome-editing methods have seen noteworthy progress, agreeing specific gene editing down to a single nucleotide level. The recently developed genome editing tools and advancements, such as clustered regularly interspaced short palindromic repeats (CRISPR)-CRISPR-associated protein-9 (Cas9), transcription activator-like effector nucleases (TALENs) and zinc-finger nucleases (ZFNs), are used to alter the genomic structure of plants to improve growth and yield in plants (Gaj et al., 2016); (Rao et al., 2022; Zafar et al., 2020). Moreover, these can also enhance crop tolerance towards abiotic stresses, including metal stress.

Among these tools, the CRISPR-Cas-mediated genome editing approach is widely used as it is easier to design. The upregulation of CRISPR relating to metal ligands allows improved metallothioneins and phytochelatins production, metal transport proteins, etc., which are targets for imparting heavy metal stress tolerance (Zulfiqar and Ashraf, 2022). However, we found no published reports on using genome editing to modify phytohormone concentrations to combat As stress.

Nevertheless, several groups have focused on editing phosphate transporters. In 2016, Shi and her coworkers recognized two different genes, i.e., OsHAC1;1 and OsHAC1;2, that played a role in arsenate reductase and As accretion. The investigators observed that knocking out these genes would decrease As accumulation in leaves and roots, thereby providing As tolerance in rice plants (Shi et al., 2016). Ye and colleagues (Ye et al., 2017) compared different rice plant lines, including *OsPT4* overexpression line (OsPT4-ov), *OsPT4* RNA interference line (OsPT4-Ri), *OsPT2* overexpression line (OsPT2-ov), and OsPT4 CRISPR line (OsPT4-cr), with wild type Nipponbare. Their findings suggested that the expression of OsPT4-cr plants, generated using a DNA spacer in NEB cutter1, showed decreased As accumulation of up to 17-30% compared to Nipponbare. Similarly, another study on the same plant produced the transgenic plants by knocking out OsPT4 (OsPht1;4) using two distinct T-DNA insertion mutants of OsPT4 (M1 and M2). The resultant transgenics developed by this genome editing method provided greater As resistance than wild-type plants (Cao et al., 2017). Recently, a mutated rice plant with As tolerance 1 (astol1) was produced using CRISPR gene editing technology. This mutated plant reduced As uptake in rice grains, facilitating the absorption of elements such as sulfur and selenium, leading to the synthesis of PCs, GSH, and cysteines (Sun et al., 2021). The genome editing system has also been used to modulate Gibberellic acid (GA) synthesis by targeting the *SIDELLA* gene, which codes for a negative GA phytohormone, resulting in different phenotypic expressions in tomato plants (Kashojiya et al., 2022).

There were limited reports on genome editing that enhances As tolerance. However, these reports demonstrated the potential of this powerful technology in developing plant's resistance to oxidative stress induced by As, similar to what has been attained for other metallic elements. Thus, intensive research is needed in genome editing that increases plant hormones to tolerate As stress conditions. Moreover, investigation must be conducted to fully harness the benefits of this compelling and innovative technology, which is widely employed globally to enhance a wide range of qualitative and quantitative characteristics in potential crop varieties.

9. Conclusions

To summarize the detailed investigation into how plants absorb, accumulate, and counteract the effects of As this review provided insights into the challenges posed by this harmful element and the sophisticated pathways plants employ to mitigate its negative impacts. Phosphate transporters, specifically aquaglyceroporins belonging to the nodulin 26 intrinsic protein (NIP) class, played a role in absorbing As(V). The ubiquitin-proteasome pathway has emerged as an As uptake and tolerance regulator, revealing molecular mechanisms. Plants employ detoxification mechanisms such as sequestering As in vacuoles and activating antioxidant systems to reduce the impact of As toxicity. The enzymatic function of reductase (AR) came out as one of the indispensable tools for transforming into less toxic As(III) with specific genes like *OsHAC1;1*, *OsHAC1;2*, and *HAC4*. Exploring plant hormones and signaling molecules like IAA, BR, Mel, SA, and MeJA highlights their potential to mitigate the effects caused by As stress and the plant’s resilence against induced stress. Researchers have made advancements in breeding techniques by increasing the expression of transporters. These approaches decreased the uptake and toxicity of As in plant species and provided a better understanding of how proteins interact within the ubiquitin-proteasome pathway for developing crops that could withstand exposure to As. Recent technological developments to understand molecular mechanisms like whole transcriptome analysis, gene transfer, genome analysis, and editing showed promising roles in As stress-tolerant plant production. Having an understanding of how to interact with plants not only expands our knowledge but also paves the way for strategies to minimize As contamination in food crops. Further, future research should focus on uncovering lasting impacts, specific pathways, and potential synergies among these compounds to develop solutions for managing As stress in different agricultural contexts.

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Table 1: Effect of different phytohormones on As-stressed plants

Plant	**Arsenic Stress**	**Method of exogenous application**	**Beneficial Phytohormone concentration**	**Experimental setup**	**Stress ameliorating effects**	**References**
Indole 3-acetic acid						
Arabidopsis thaliana (L.) Heynh.	12 and 25 µM (Sodium arsenite)	Foliar spray of IAA	0.01, 0.1, and 1 µM	Media plates	Promote cell division, stem and root growth, and absorption and accumulation of plant nutrients.	Krishnamurthy and Rathinasabapathi, 2013
Oryza sativa L.	10 µmol L^{-1} (Sodium Arsenate)	Foliar spray of IAA	20 mg L^{-1}	Pot culture	Promote cell division, stem and root growth, grain biomass, plant nutrient absorption and accumulation.	He et al., 2022
Salicylic Acid						
Triticum aestivum L.	50-400 µM (Arsenate)	Seed-priming with Salicylic acid	1 mM	Petri dishes	Enhance seed germination, root length, fresh and dry weight, chlorophyll and protein content, coleoptile length, and reduces oxidative damage.	Zengin, 2015
Glycine max L.	10 and 100 µM (Sodium arsenite)	Filter paper moistened with SA and As	500 µM	Petri dishes	Improves plant growth, limits As accumulation, reduces oxidative stress, stimulates activities of APX, SOD, CAT, and POD enzymes and promotes proline accumulation.	Chandrakar et al., 2016
Zea mays L.	0.1 mM (Sodium hydrogen arsenate heptahydrate)	Spraying of Salicylic acid and sodium	0.5 mM	Pot culture	Enhances growth parameters, chlorophyll content, increased leaf RWC, reduces As accumulation, improves photosynthetic traits,	Kaya et al., 2020

		Nitroprusside (donor of NO)			enhances antioxidant defense system, and regulates ascorbate-glutathione (AsA-GSH) cycle-related enzymes.	
Oryza sativa L.	25 and 50 µM (Sodium arsenate)	Salicylic acid added in nutrient medium	100 µM	Petri dishes	Decreases As translocation in shoots, enhances root and shoot growth and nitrate reductase activity, reduces translocation of iron in shoot, MDA and H_2O_2 content.	Singh et al., 2015
Brassica napus L.	200 mg kg^{-1} (Sodium arsenite)	Foliar spray of salicylic acid	250 and 500 mM	Pot culture	Improved carbohydrate metabolism, S-assimilatory pathway, cell viability, proline metabolism, antioxidant capacity, growth, and productivity and decreased As accumulation.	Bano et al., 2022
Artemisia annua L.	100 and 150 µM (Sodium arsenate)	Salicylic acid added in nutrient solution	100 µM	Hydroponic culture (Hoagland solution)	Improved chlorophyll content, biomass, SA level, artemisinin, and dihydroartemisinic acid, enzymatic and non-enzymatic antioxidant activity.	Kumari et al., 2017
Artemisia annua L.	100 µM (Sodium arsenate)	Salicylic acid added in nutrient solution	100 µM	Hydroponic culture (Hoagland solution)	Improved biomass, chlorophyll and flavonoids content, and metabolism-related proteins.	Kumari and Pandey-Rai, 2018
Triticum aestivum L.	50 and 100 µM (Sodium arsenate)	Seed priming with salicylic acid	0.5 and 1 mM	Pot culture	Improved RWC and gas exchange characteristics, growth, quality of plants and decreased As level.	Maghsoudi et al., 2019

Artemisia annua L.	45 mg kg^{-1} (Sodium hydrogen arsenate heptahydrate)	Foliar spray of salicylic acid	10^{-6} and 10^{-5} M	Pot culture	Enhanced antioxidant enzymatic activity and artemisinin content and yield.	Naeem et al., 2020
Vigna radiata (L.) Wilczek	50 mg kg^{-1} (Sodium arsenate)	Seed priming with salicylic acid	0.25, 0.5, and 1 mM	Pot culture	Increased RWC, chlorophyll content, plant length, biomass, leaf area, seed yield, antioxidant enzymes, and proline content.	Sadeghipour and Monem, 2021
Helianthus annus L.	10 µM (Sodium arsenate)	Salicylic acid added to nutrient solution	10, 50 and 100 µM	Hydroponic culture	Improved CAT, APX, and GPX activity and decreased SOD and POD activity.	Saidi et al., 2017
Oryza sativa L.	25 µM (Sodium arsenite)	Salicylic acid added in nutrient solution	40 µM	Hydroponic culture	Enhanced SA and NO level.	Singh et al., 2017
Methyl jasmonate						
Brassica napus L.	50 and 200 µM (Sodium arsenite)	Methyl Jasmonate added in solution	0.1 and 1 µM	Pot culture	Increases chlorophyll content, reduce MDA and As content in leaves and roots, improve ROS scavenging through enhanced antioxidant defense system and secondary metabolites.	Farooq et al., 2018; Farooq et al., 2018; Farooq et al., 2016
Oryza sativa L.	25 µM (Arsenite)	Me-JA added in Hewitt media solution (hydroponic culture)	0.25 µM	Hydroponic culture	Increased photosynthetic rate, chlorophyll and anthocyanin content, root and shoot length and biomass, decreased arsenic accumulation, MDA content and increased antioxidative enzyme activities.	Verma et al., 2020

Oryza sativa L.	25 and 50 µM (Sodium arsenite)	Me-JA in Hoagland solution	0.5 and 1 µM	Pot culture	Increases height, dry weight, chlorophyll, carotenoids, Fe and JA content, decreases As accumulation, MDA and H_2O_2 content. Regulates antioxidant enzymes and improves the ASA/DHA ratios.	Mousavi et al., 2020
Lemna valdiviana Phil.	4 mg L^{-1} (Sodium arsenate)	JAadded in nutrient solution	50, 100, 250, and 500 µM	Hydroponic culture	Improved antioxidant enzymatic activity and maintained ROS homeostasis.	Coelho et al., 2020
Solanum lycopersiucm L.	5 µM (Sodium arsenate)	Added in soil after seedling establishment	100 µM (Jasmonic acid) and 40 mM (Ca^{2+})	Pot culture	Enhanced biosynthesis of Chl, d-aminolevulinic acid dehydratase, Gly I and II activity and decreased ROS production	Siddiqui et al., 2022
Melatonin						
Oryza sativa L.	150 µM (Sodium arsenate)	Mel added in hydroponic culture	20 µM	Petri plates	Maintains pyruvic acid and citric acid levels, improves the activity of carbohydrate metabolic enzymes and enhances accumulation of reducing and non-reducing sugars.	Samanta et al., 2020
Oryza sativa L.	150 µM (Sodium arsenate)	Mel added in hydroponic culture	20 µM	Petri plates	Increases fresh and dry weight, Chl a and b content, root and shoot length, fresh and enhances antioxidant capacity.	Samanta et al., 2021
Oryza sativa L.	150 µM (Sodium arsenate)	Mel added in hydroponic culture	20 µM	Petri plates	Decreased electrolyte leakage, methylglyoxal content, protein carbonylation, MDA accumulation, LOX and protease activity and improved membrane stability,	Samanta et al., 2022

					nitrogen assimilation, accumulation of xanthophylls, anthocyanins, carotenes, and total phenolics.	
Oryza sativa L.	150 µM (Sodium arsenate)	Mel added in hydroponic culture	20 µM	Petri plates	Higher GSH/GSSG ratio, enhanced gibberellic acid content, phytochelatins (PCs), cysteine content, endogenous ABA and Mel level.	Samanta et al., 2021
Oryza sativa L.	25 µM (Sodium arsenite)	Mel added in nutrient solution	0.25 µM	Hydroponic culture	Reduced oxidative stress and increased the levels of TNPSH, GSH, and PCs which leading to detoxification of MDA content.	Nazarian and Ghanati, 2020
Vicia faba L.	5 µM (Sodium arsenate)	Mel and Calcium added into nutrient solution	50 µM	Sand culture in plastic pots	Reduced DNA damage and ROS level in plants. Enhanced photosynthesis, chl biosynthesis, and diminished activity of Chl degrading enzymes, upregulated expression of ATP synthase, Ca^{2+}-ATPase, and Hsp40 and increased plasma membrane H^{+}-ATPase activity and enzymes involved in antioxidant system.	Siddiqui et al., 2020
Spinach oleracea L.	25, 75, 12 and 5 ppm (Arsenic)	Mel added in Pot soil	100 µmol	Pot culture	Increased chlorophyll content, fresh and dry weight, and activities of antioxidant enzymes CAT, POD and SOD, while inhibiting lipid peroxidation.	Asif et al., 2020
Salvia Rosmarinus Spenn.	75 mg Kg^{-1} (Sodium arsenate)	Foliar spray of Mel	25 and 50 µM L^{-1}	Pot culture	Enhanced growth, ion concentration, photosynthetic pigment, organic	Farouk and Al-Amri, 2019

					osmolytes, yield, antioxidant enzymes and osmoregulation capacity.	
Oryza sativa L.	25 µM (Sodium arsenite)	Added in soil to 21 days old plants	100 µM	Pot culture	Induced anthocyanin biosynthesis genes, SA and ABA content and reduced PT-2 and PT-8 expression as well as As accumulation.	Jan et al., 2023
Camellia sinensis L.	25 µM (Sodium arsenate)	Foliar spray with Mel	100 µM	Pot culture	Improved anthocyanin content, CsCHS and CsANS gene expression and reduced As content.	Li et al., 2021
Oryza sativa L.	20 µM (Sodium arsenite)	Added in nutrient solution	50 µM	Hydroponic culture	Enhanced SOD, POD, and CAT activity and decreased As level in seedlings.	Li et al., 2023
Gladiolus grandifloras cv. Purple Flora	50 µM (Arsenic)	Foliar spray with Mel	100 µM Mel and 150 mg L^{-1} Salicylic acid	Pot culture	Decreased As induced oxidative stress.	Zulfiqar et al., 2023
Brassinosteroid						
Raphanus sativus L.	50 µM (Sodium arsenate)	Seed-priming with 24-epibrassinolide (EBL)/ 28-homobrassinolide (HBL)	0.5,1.0 and 2.0 µM	Petri plates	Increased levels of soluble proteins and proline, and activities of antioxidant enzyme such as CAT, SOD and POD and reduced membrane peroxidation.	Raghu et al., 2014
Glycine max L.	75 µM (Sodium arsenite)	Seeds germination over filter paper moistened with 24-epibrassinolide (EBL)	0.5 mM	Lab experiment	Increased fresh and dry mass, decreased As uptake, ROS and MDA levels, stabilized membrane, increased DNA content, antioxidant and P5CS enzyme activity, and endogenous proline levels.	Chandrakar et al., 2017

Oryza sativa L.	0.5 mg dm^{-3} (Sodium arsenite)	24-epibrassinolide (Br24) and iron plaque (IP) added along with nutrient solution	0.2 or 0.02 µM	Pot culture	Increased leaf and root biomass, and iron concentration in roots, but reduced As content.	Xu et al., 2018
Arabidopsis thaliana (L.) Heynh.	100 and 200 µM (Sodium arsenate)	24-Epibrassinolide (EBL) added in the medium	1 µM	Hydroponic culture	Enhanced total antioxidant and proline levels, the transcript level of Hsp70-4 and Hsp90-1, CSD1, CSD2, FSD1, FSD2, MSD1 and CAT2 genes and decrease MDA level, and elevated expression level of P5CS1 gene.	Surgun-Acar and Zemheri-Navruz 2019
Triticum aestivum L.	50 and 100 µM (Sodium arsenate)	Seed priming with Brassinolide	0.5, and 0.75 µM	Pot culture	Increased antioxidant enzyme activity and osmolyte level, relative leaf water content, photosynthetic rate and reduce H_2O_2 and MDA level as well as arsenic concentration.	Maghsoudi et al., 2019

Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: