Review

The Role of Salicylic Acid in Plants Exposed to Heavy Metals

Anket Sharma 1,*,†, Gagan Preet Singh Sidhu 2,†, Fabrizio Araniti 3,*,†, Aditi Shreeya Bali 4, Babar Shahzad 5, Durgesh Kumar Tripathi 6, Marian Brestic 7,*,†, Milan Skalicky 8,† and Marco Landi 9,10,11,*,†

1 State Key Laboratory of Subtropical Silviculture, Zhejiang A&F University, Hangzhou 311300, China
2 Department of Environment Education, Government College of Commerce and Business Administration, Chandigarh 160047, India; gagan1986sidhu@gmail.com
3 Dipartimento AGRARIA, Università Mediterranea di Reggio Calabria, Località Feo di Vito, SNC I-89124 Reggio Calabria, RC, Italy
4 Mehr Chand Mahajan D.A.V. College for Women, Chandigarh 160036, India; shreeyaditi02@gmail.com
5 School of Land and Food, University of Tasmania, Hobart, TAS 7005, Australia; babar.shahzad@utas.edu.au
6 Amity Institute of Organic Agriculture, Amity University Uttar Pradesh, Noida 201313, India; dktripathiau@gmail.com
7 Department of Plant Physiology, Faculty of Agrobiology and Food Resources, Slovak University of Agriculture, 94976 Nitra, Slovakia; marian.brestic@uniag.sk
8 Department of Botany and Plant Physiology, Faculty of Agrobiology, Food and Natural Resources, Czech University of Life Sciences, 16500 Prague, Czech Republic; skalicky@af.czu.cz
9 Department of Agriculture, Food and Environment, University of Pisa, I-56124 Pisa, Italy
10 CIRSEC, Centre for Climatic Change Impact, University of Pisa, Via del Borghetto 80, I-56124 Pisa, Italy
11 Interdepartmental Research Center Nutraceuticals and Food for Health, University of Pisa, I-56124 Pisa, Italy
* Correspondence: anketsharma@gmail.com (A.S.); fabrizio.araniti@unirc.it (F.A.); marco.landi@unipi.it (M.L.)
† Authors contributed equally.

Academic Editor: Francesca Giampieri
Received: 11 December 2019; Accepted: 25 January 2020; Published: 26 January 2020

Abstract: Salicylic acid (SA) is a very simple phenolic compound (a C 7 H 6 O 3 compound composed of an aromatic ring, one carboxylic and a hydroxyl group) and this simplicity contrasts with its high versatility and the involvement of SA in several plant processes either in optimal conditions or in plants facing environmental cues, including heavy metal (HM) stress. Nowadays, a huge body of evidence has unveiled that SA plays a pivotal role as plant growth regulator and influences intra- and inter-plant communication attributable to its methyl ester form, methyl salicylate, which is highly volatile. Under stress, including HM stress, SA interacts with other plant hormones (e.g., auxins, abscisic acid, gibberellin) and promotes the stimulation of antioxidant compounds and enzymes thereby alerting HM-treated plants and helping in counteracting HM stress. The present literature survey reviews recent literature concerning the roles of SA in plants suffering from HM stress with the aim of providing a comprehensive picture about SA and HM, in order to orientate the direction of future research on this topic.

Keywords: metal toxicity; ortho-hydroxybenzoic acid; plant hormone; metal pollution; polyphenols; signaling compound

1. Introduction

Salicylic acid (SA) (from Latin Salix, willow tree), also known as ortho-hydroxybenzoic acid, is a phenolic derivative widely distributed in the plant kingdom and is known as a regulator of several
physiological and biochemical processes such as thermogenesis, plant signaling or plant defense, and response to biotic and abiotic stress [1,2].

From a chemical point of view, SA belongs to a large group of plant phenolics, and SA can be isolated in plants in both free and conjugated form. In particular, the conjugated form proceeds from the methylation, hydroxylation, and/or glucosylation of the aromatic ring [3,4].

Salicin, one of the natural SA derivatives, was first isolated from the bark of the willow tree (Salix sp.) by Johan Büchner in 1828 [5,6]. Successively, it was discovered that almost all the willow trees including Salix alba, S. purpurea, S. fragilis, and S. daphnoides were particularly rich in this natural compound, in which the concentration in plants significantly fluctuates during the different seasons (highest content during spring and summer, lowest content during autumn and winter [7]) reaching values of 3 mg/g of fresh biomass in plants of S. laponum [8]. The first scientist who was able to identify this natural compound in species different from Salix sp. was the Italian chemist Raffaele Piria in the late 1838, who obtained SA in both flower and buds of the European species Spiraea ulmaria successively renamed as Filipendula ulmaria (L.) Maxim. The discovery that this molecule was not exclusive to the Salix genus has opened the door to the study of its biosynthesis, as well as its biochemical and physiological role in plants and in 1899 the Bayer Company formulated a new drug known today as aspirin [9].

Concerning the biosynthesis of SA, it is known to be produced through the shikimate pathway by two metabolic routes (Figure 1). In the first discovered route, also known as phenylalanine route, occurring in the cytoplasm of the cell, the enzyme phenylalanine ammonia lyase (PAL) converts phenylalanine (Phe) to trans-cinnamic acid (t-CA), which gets oxidized to benzoic acid (BA). Subsequently, the enzyme benzoic-acid-2-hydroxylase (BA2H) catalyzes the hydroxylation of BA aromatic ring and leads to SA formation. The enzymatic conversion of BA into SA by BA2H requires the presence of hydrogen peroxide (H$_2$O$_2$) [10–12].

The first evidences for the first route were given by Ellis and Amrchein [13], who observed that feeding Gaultheria procumbens plants with labeled 14C-benzoic acid or 14C-cinnamic acid resulted in the production of labeled SA. Successively, Yalpani et al. [14] and Silverman et al. [15], working on rice and tobacco, proposed that the side chain of trans-cinnamic acid is decarboxylated to generate BA. Then, BA is hydroxylated at the C2 position forming SA. Anyway, recent results indicated that benzoyl glucose, a conjugated form of BA, is more likely to be the direct precursor of SA [12,14].

The second route is called isochorismate (IC) pathway and occurs in the chloroplast [16–18]. In plants, chorismate is transformed to isochorismate and then to SA, a reaction which is catalyzed by two enzymes isochorismate synthase (ICS) and isochorismate pyruvate lyase (IPL). Recent studies carried on Arabidopsis thaliana demonstrated that the ~90% of defense-related SA is produced from isochorismate generated by the plastid-localized isochorismate synthase1, whereas ~10% is derived from the cytosolic PAL pathway [1,17].

From the physiological point of view, it is known that SA plays a pivotal role in the regulation of plant growth, development, in defense from biotic and abiotic stress, and in plant immune responses [4,19–23].

For several years, SA was believed to be just one of the several phenolic compounds synthetized by plants with relatively low importance [5,16]. In 1974, after more than a hundred of years from its discovery, it was provided the first evidence that SA could play a role as plant hormone, when Clealand and Ajami [24] observed that SA was a mobile signaling molecule localized in the phloem inducing flowering in different plant species.

However, the final evidence that SA was a plant hormone was only provided several years later by Raskin et al. [25], who described its role during the thermogenesis in Saurodactum guttatum.

From that moment, an exponential increase of manuscripts focused on SA (acting alone or in concert with other plant hormones) as a plant growth regulator, signaling molecule, as well as plant elicitor protecting plants from biotic and abiotic stress, was observed [22,23,26–31].
Recently, it has also been demonstrated that SA could play a pivotal role in protecting plants from environmental stress, including heavy metals (HM). In fact, several recent manuscripts reported that SA can alleviate HM toxicity influencing both their uptake and/or accumulation in plant organs [32–38], as well as scavenging of reactive oxygen species (ROS) and/or decreasing their accumulation and/or enhancing the antioxidant defense system [39–42], protecting membrane stability and integrity [43], interacting with plant hormones [44], upregulating heme oxygenase [45], and improving the performance of the photosynthetic machinery [42,46,47].

Focusing on these aspects, the present review provides a comprehensive assemblage concerning SA roles in plant defense from HM stress, with the aim to provide a clear view of SA and HM to orientate the direction of future research on this topic.

Figure 1. Metabolic pathways involved in the biosynthesis of salicylic acid (SA). Plants use two pathways for SA production, the phenylalanine ammonia-lyase (PAL) (which is divided into two sub-pathways, benzoic acid, and o-coumaric acid) and the isochorismate. In both routes, shikimate serves as a precursor.
2. HM Stress and Its Impacts on Plants

Metals and metalloids with atomic density more than 6 g cm$^{-3}$ are defined as (HM). Both, essential elements, micronutrients that are required in low concentration (e.g., Cu, Cr, Co, and Zn), and nonessential metals such as Pb, Cd, Hg, are incorporated in this group [48,49]. Increased concentration of both essential and nonessential elements is phytotoxic to flora and fauna [50,51]. Heavy metal contamination has become a serious environmental problem worldwide. The increased industrialization, injudicious population growth, and urbanization releases HM that compromise soil and water and pose harms to living biota due to their biomagnification through the food chain [52]. Natural activities such as eruption of volcano and erosion of rocks have contribute in increasing the release of toxic elements to the environment; however, increased human activities such as mining, painting, and refining have enhanced their concentration in the biosphere [53–55].

Soil pollution by HM poses serious concerns to the biotic and abiotic components of the ecosystem [56]. The increased amount of HM in soil leads to greater uptake by plants that can reduce plant growth, biomass, photosynthesis, crop yield, and quality in plant [57]. From a biological point of view, the top soil is the most active zone of soil that accumulates a large amount of toxic metals that poses serious concern to the environment [49,58,59].

The increased level of HM accumulation in plant organs negatively affects the cell metabolism in plants [60]. The different physiological activities in plants such as protein metabolism, photosynthesis, respiration, and morphogenesis are naturally affected by a high concentration of toxic compounds, such as HM [53,54,61,62]. For instance, Rascio et al. [63] documented a decreased root growth and altered morphogenesis in rice seedlings upon treatment with Cd. Many plant species such as Brassica napus, Helianthus annuus, Thalaspi caerulescens, Vigna radiata showed inhibition in photosynthesis in response to Cd treatment [64–68]. Recently, Tandon and Srivastava [69] investigated the Pb effect on the morphology and metabolism of Sesamum indicum and found that the increasing concentration of metal affected the growth of the plant. Further, the plant showed severe symptoms of chlorosis, necrosis and reduced chlorophyll, and protein content at higher doses of Pb [69].

The major outcome of metal toxicity is the peaked production of ROS due to impairment of photosynthetic process by HM [70]. ROS such as hydroxyl, superoxide, and hydrogen peroxide are produced as by-product during electron transport in photosynthesis and respiration pathways [71]. Under physiological conditions, ROS play a multitude of signaling roles in plants, as well as in other organisms and they take part in a finely-tuned and well-orchestrated regulatory network [72,73]. ROS are indeed integrated into a complex regulatory system in plants which encompasses ROS, plant hormones (e.g., ethylene (ET) and abscisic acid (ABA)), signaling molecules (e.g., salicylic acid (SA) and jasmonic acid (JA)), and secondary messengers (e.g., Ca$^{2+}$) [74,75]. However, when ROS production exceeds the physiological levels, their accumulation can lead to oxidative stress in the cells, that cause lipids peroxidation, macromolecular degradation, membrane disruption, DNA breakage, and ion leakage in plants [70,74,75]. For instance, Kaur et al. [76] explored Pb-induced ultrastructural changes in roots of wheat and concluded that Pb inhibited root growth, caused ROS generation, and disrupted mitochondrial and nuclear integrity in the tested plant.

The enhanced generation of ROS in the plant cell is controlled by a complex network of antioxidant machinery that maintains ROS homeostasis in the cell [77]. Plants have a finely-tuned and well-orchestrated defense system that includes enzymatic antioxidants such as catalase (CAT), superoxide dismutase (SOD), ascorbate peroxidase (APX), glutathione peroxidase (GPX) and glutathione reductase (GR), and nonenzymatic antioxidants such as ascorbic acid, glutathione, alkaloids, phenol compounds, and α-tocopherol for scavenging excessive ROS [49,61]. Moreover, phytohormones such as auxins, gibberellins, cytokinins, abscisic acid, ethylene, brassinosteroids, jasmonic acid, and SA take part in the defensive mechanism of plants against HM stress.
3. Physiological Roles of SA in Plants Under HM Stress

Concerning the physiological role in plants, SA is known to play a pivotal role in regulating plant morphology, development, flowering, and stomatal closure [78,79]. SA also affects seedling germination, cell growth, and nodulation in legumes [80]. Khan et al. [81] reported increased leaf area and dry weight production in corn and soybean in response to SA. Furthermore, Hussein et al. [82] reported pot studies that documented improved growth, leaf number, dry biomass, and stem diameter in wheat plants when leaves were sprayed with SA. The rate of transpiration and stomatal index of plants increased in response to supplementation of SA [81]. The pigment concentration in wheat seeds significantly enhanced upon exposure to a low concentration (10^{-5} M) of SA. However, foliar application of SA reduced transpiration rate in test plants, *Phaseolus vulgaris* and *Commelina communis* which might be due to the SA-evoked stomatal closure [83–87]. Moreover, SA has been reported to increase the shelf life of cut flowers of rose and defer senescence by controlling water level in rose plants [86].

Plant growth regulators or phytohormones especially, gibberellins, auxin, cytokinins, ethylene, brassinosteroids, and also SA play a key role in providing HM tolerance in plants [83]. SA, a phenolic plant hormone, regulates photosynthesis, respiration, and antioxidant defense mechanism in plants under different abiotic stress such as high temperature, salinity, and HM [78,88,89]. SA pretreatment provides protection from various metals such as Pb, Hg, Cd, in different plants [90–92].

Supplementation of SA in combination with plant growth promoting bacteria reduces Cr-induced oxidative damage in maize by enhancing activities of antioxidant and nonantioxidant enzymes [93,94]. Earlier, Song et al. [95] reported SA mediated enhancement in the activities of CAT and SOD enzymes in barley leaves under Zn, Cu, and Mn stress. Further, carbohydrate metabolism in Cr-treated maize plants improved upon exposure to SA [94]. Alleviation of Cd toxicity was reported in mustard plants in response to exogenous treatment of SA [93]. Recently, SA treatment mitigated Cd stress in *Brassica juncea* plants and enhanced growth and photosynthesis in plants. Moreover, supplementation of SA reduced reactive oxygen species levels by strengthening the antioxidant defense system in plants and provides stability to the plant membrane [96]. The exogenous application of SA upregulates the antioxidant system, improves growth and yield, and results in lowering of oxidative damage under Pb stress in *B. campestris* [97].

A schematization of the protective role exerted by SA in HM-stressed plants is reported in Figure 2, whereas a literature survey on the effect of different HM on plant metabolism is reported in Table 1.

![Figure 2. Schematization of the protective role exerted by SA in HM-stressed plants. HM: Heavy metals; ROS: Reactive oxygen species; SA: Salicylic acid.](image-url)
Table 1. Salicylic acid (SA) effect on different heavy metals (HM) stressed plants.

| HM   | Species                      | Effects of SA in plant metabolism                                                                 | References |
|------|------------------------------|--------------------------------------------------------------------------------------------------|------------|
| Cd   | *Lemna minor* L.             | Induced a reduction of Cd uptake, the maintenance of ionic homeostasis, improvement of PAL activity, activation of ROS scavenger and of the heat shock proteins. | [98]       |
|      | *Oryza sativa* L.           | SA in association with NO reduced Cd uptake and accumulation, as well as ROS accumulation and malondialdehyde production through the maintenance of ascorbate and glutathione levels, and redox status. Improved the activities of antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), glutathione S-transferase, and mono dehydroascorbate reductase. | [41]       |
|      | *Brassica juncea* Czern     | Stimulating the stomatal activity and pore size, alleviated the inhibitory effect of Cd on photosynthesis. The Cd-generated oxidative burst was reduced via enhanced antioxidant activity (CAT and SOD) promoted by SA. | [96]       |
|      | *Nymphaea tetragona*        | SA pretreatment decreased Cd concentration and increased the contents of glutathione, nonprotein thiol and phytochelatins. | [99]       |
|      | *Solanum tuberosum*         | Cd stress increased endogenous SA level, relative water content, chlorophyll, and proline. Reduced lipid peroxidation, H$_2$O$_2$ and O$_2$·. SA stimulated enzymatic antioxidants. | [100]      |
|      | *Triticum aestivum* L.      | Induced a transient upregulation of protein kinases (SIPK). | [101]      |
|      | *Mentha piperita*           | Improved photosynthesis by enhancing activity of RuBisCo and carbonic anhydrase. Reduced the oxidative stress by mitigating the production of free radicals by the maintenance of reduced glutathione pool and free radical scavenging enzymes. Furthermore, restored essential oils production previously affected by Cd. | [102]      |
| Pb   | *Brassica juncea* Czern     | Co-application of 24-epibrassinolide and SA mitigates the negative effects of Pb, by lowering Pb metal uptake and enhancing the heavy metal tolerance index, antioxidative capacities, organic acid levels, phenolic content, water content, and relative water content. | [37]       |
|      | *Zea mays* L.               | Improved nitrate reductase activity, glutathione content, and regulated the amino acids metabolism. | [103]      |
|      | *Triticum aestivum* L.      | Suppressed chlorophyll degradation, electrolyte leakage, and malondialdehyde accumulation. Furthermore, enhanced the production of total soluble carbohydrates, proline, and the activities of SOD, CAT, and peroxidases. | [104]      |
|      | *Brassica campestris* L.    | Improved plant growth and yield upregulating, in the antioxidant defense system, both enzymatic and nonenzymatic components. | [93]       |
|      | *Zea mays* L.               | In combination with sodium hydrosulfide reduced arginine, proline, and methionine accumulation and increased nitric oxide and glycine betaine content. Moreover, it regulated the expression of ZmSAMD and ZmAACS6 genes (genes involved in methionine metabolism). | [105]      |
Table 1. Cont.

| HM  | Species                              | Effects of SA in plant metabolism                                                                 | References |
|-----|--------------------------------------|---------------------------------------------------------------------------------------------------|------------|
| As  | *Trigonella foenum-graecum* L.       | Enhanced root growth and increased protein content, free amino acids, and soluble sugars in both   | [106]      |
|     |                                       | cotyledons and radicles. Moreover, it enhanced the activity of hydrolytic enzymes (α- and β-amylase). |            |
|     | *Artemisia annua* L.                 | Increased endogenous SA level, reduced H$_2$O$_2$ and O$_2$•$^-$ generation, as well as lipid      | [107]      |
|     |                                       | peroxidation. Reverted biomass and chlorophyll content. Increased artemisinin, and dihydroartemisinic |            |
|     |                                       | acid level. Upregulated the expression of four key artemisinin biosynthetic pathway genes (CYP71AV1, |            |
|     |                                       | ALDH1, ADS, and DBR2).                                                                             | [107]      |
|     | *Artemisia annua* L.                 | Upregulated proteins related to energy metabolism, photosynthesis, secondary metabolism,           | [108]      |
|     |                                       | transcriptional regulators, transport proteins, and proteins related to lipid metabolism.           |            |
|     | *Helianthus annuus* L.               | Alleviated the negative effect of As on growth and decreased oxidative injuries through the        | [109]      |
|     |                                       | increasing of the enzymatic activity of ROS scavengers such as CAT, ascorbate peroxidase (APX),     |            |
|     |                                       | and glutathione peroxidase, whereas the activity of SOD and guaiacol peroxidase activities was     |            |
|     |                                       | reduced.                                                                                           | [109]      |
|     | *Oryza sativa* L.                    | As enhanced endogenous level of SA and NO level through the enhancement of nitrate reductase       | [110]      |
|     |                                       | activity.                                                                                          |            |
| Cr  | *Sorghum bicolor* L.                 | Increased both APX and hydrogen peroxide content and decreased the peroxidase activity and ascorbic | [111]      |
|     |                                       | acid content.                                                                                      |            |
|     | *Brassica napus* L.                  | Increased dry biomass, enhanced plant growth, and strengthened the reactive oxygen scavenging       | [112]      |
|     |                                       | system by improving the activity in Cr-damaged organelles.                                          |            |
|     | *Oryza sativa* L.                    | Reduced the concentration and translocation of Cr in shoots but not in roots, suggesting a         | [113]      |
|     |                                       | detoxification strategy based on Cr sequestration in roots. Increased growth parameters, membrane   |            |
|     |                                       | stability, and protein content.                                                                     |            |
| Ni  | *Brassica juncea* L. Czern. & Coss.   | Restored growth and photosynthesis increasing the activities of enzymes associated with antioxidant | [114]      |
|     |                                       | systems, especially the glyoxalase system and the ascorbate–glutathione cycle (AsA–GSH) cycle.     |            |
|     |                                       | It had an additive effect on the activities of the ascorbate and glutathione pools, and the AsA–GSH |            |
|     |                                       | enzymes and restored the content of mineral nutrient.                                              |            |
|     | *Eleusine coracana* L.               | Inhibited Ni transport from roots to shoots, increased chlorophyll content, and the photosynthetic  | [115]      |
|     |                                       | rate, increased the uptake of mineral content, reduced H$_2$O$_2$ and proline content, and          |            |
|     |                                       | enhanced the activity of antioxidant enzymes (SOD, CAT, APX).                                      |            |
|     | *Melissa officinalis* L.             | Decreased Ni transport to the shoots, increased carotenoid content, induced a significant decrease  | [116]      |
|     |                                       | in electrolyte leakage in stressed plants.                                                        |            |
|     | *Alyssum inflatum* Náyvr.             | Mitigated Ni oxidative effects by reducing H$_2$O$_2$ concentration. Reversed the detrimental effects | [117]      |
|     |                                       | of Ni on carotenoid content and reduced the proline content.                                       |            |
**Table 1.** Cont.

| HM | Species                  | Effects of SA in plant metabolism                                                                 | References |
|----|--------------------------|----------------------------------------------------------------------------------------------------|------------|
| Co | *Triticum aestivum* L.   | Decreased the accumulation of H$_2$O$_2$ and MDA and improved the activity of antioxidant enzymes. | [40]       |
| Cu | *Gossypium barbadense* L.| Limited Cu translocation and improved the activities of antioxidant enzymes.                        | [118]      |
|    | *Zea mays* L.            | Lowered Cu and H$_2$O$_2$ accumulation in roots. Induced a reduction of MnSODII activity accompanied by a decrease in H$_2$O$_2$ concentration. | [119]      |
|    | *Zea mays* L.            | Increased the biomass, root and shoot length, number and leaves area.                               | [119]      |
3.1. Effect of SA to Photosynthesis in Plants Subjected to HM Stress

The different stressful conditions encountered by plants affect multiple physiological and biochemical mechanisms in plants. Among these, photosynthesis is usually one of the most affected mechanisms by HM (see a schematization of the effect of HM on chloroplast in Figure 2). HM accumulated in various organs of plants and affect the synthesis of photosynthetic pigments, including carotenoids and chlorophylls [53,54]. HM also alter the chloroplast membrane structure and affect electron transport, thus impairing light-dependent reactions of photosynthesis [120]. Moreover, it was found that the negative effect of HM on PSI and PSII depends on exposure time and concentrations [121,122]. Experiments performed by Khan et al. [123] indicated that PSII is more sensitive to HM stress compared to PSI, however, at high concentrations the activity of PSI resulted inhibited as well. Photosynthesis inhibition caused by HM is also attributable to the impairment of stomatal conductance and transpiration rate [124].

Plants are equipped with multiple mechanisms to preserve the photosynthetic machinery from HM-promoted damages. SA is a major photosynthesis regulator which influences chlorophyll content, stomatal conductivity, and photosynthesis-related enzyme activities in plants [125]. It enhances photosynthetic efficiency and improves photosynthetic apparatus under HM stress [34]. Exogenous application of SA (500 µM) enhanced chlorophyll concentration, CO\(_2\) fixation, and activities of phosphoenolpyruvate carboxylase and RuBISCO in *Triticum aestivum* under Cd toxicity [126]. Further, gas exchange parameters and carbonic anhydrase improved in *B. juncea* under Ni [120] and Mn [127] stress after the exposure to 10 µM SA. SA treatment enhanced Chla, Chlb, and carotenoid content in barley plants under Pb stress by increasing antioxidant activity in the plants which might be due to blockage of Ca channels that help in translocation of Pb in roots [60]. Recently, Guo et al. [38] studied the role of SA in Cd alleviation and accumulation in tomato plants. The exogenous exposure of SA also increased pigment content and photosynthetic performance in tomato plants [38]. The consistently observed protective role of SA to the photosynthetic apparatus might be due to increased detoxification of ROS species exerted by SA or by the activation of antioxidant apparatus promoted by SA [125].

3.2. Regulation Mechanism of ROS and Enzymatic Antioxidants Promoted by SA Acid under HM Stress

The generation of ROS is one the first response in plants under HM stress. ROS production is either directly due to Haber-Weiss reaction or it is indirectly because of interference in the antioxidant defense system or electron transport chain [128]. ROS (H\(_2\)O\(_2\); hydrogen peroxide, OH\(^-\); hydroxyl radical, and O\(_2\)\(^-\); superoxide radical) are very harmful to plants since they lead to oxidative degeneration of cell membranes and large macromolecules [129]. Plants possess a powerful antioxidant apparatus to counteract oxidative stress, which includes different enzymes (SOD, CAT, APX, GR) and nonenzymatic antioxidants (e.g., glutathione, ascorbic acid, phenolics, carotenoids) that scavenge and detoxify ROS over-production in plants [130].

Lipid peroxidation is the first oxidative injury in plants due to HM stress and SA have been shown to provide stability against HM-induced oxidative damage by increasing antioxidant machinery in plants [125]. Parashar et al. [127] and Zhang et al. [131] observed the reduction in lipid peroxidation, electrolyte leakage, and superoxide ion in Mn- and Cd-treated *B. juncea* and *Cucumis melo* upon addition of SA. Few experiments suggest that SA can promote free radical scavenging of HM-promoted ROS by regulating antioxidant enzymes and expression of some proteins and molecules such as OsWRKY45 as reported in rice by Chao et al. [132] that lowers H\(_2\)O\(_2\) accumulation in plants. This helps in maintaining the balance between ROS generation and membrane integrity, thereby preventing membrane disruption [133]. Recently, Lu et al. [98] and Gu et al. [99] documented activation of antioxidant enzymes including SOD, APX, and other peroxidases in *Lemna minor* and *Nymphaea tetragona* upon supplementation of SA in plants subjected to Cd stress, which were helpful in conferring Cd tolerance in plants.
3.3. Regulation of Osmolytes and Polyphenols by SA under HM Stress

Plants have evolved various mechanisms to counteract HM-triggered ROS production. Different antioxidant metabolites such as proline, glycine betaine, polyamines, sugars, and polyphenols are all involved in maintaining the ROS balance in plants under stressful conditions, including excess of HM. Below, the intimal connections between SA and other antioxidant compounds are described with the attempt to provide a clear and exhaustive picture about the SA-promoted regulation of antioxidant molecules in plants exposed to HM.

3.3.1. Proline

Proline acts as a free radical scavenger, osmo-protectant, and stabilizer of cellular structures [130,134]. The synthesis of proline occurs from glutamate, which is converted to glutamate-semialdehyde, and then spontaneously to pyrroline-5-carboxylate (P5C) with the help of P5C synthase enzyme. Later, the enzyme P5C reductase aids in the reduction of P5C to proline. The stimulation of proline levels under HM stress was observed, for example, in *Olea europaea* [135] and *Phoenix dactylifera* [136]. However, this is not clear whether the accumulation was attributable to enhanced production of enzymes responsible for proline synthesis, the decrease in enzymes related to its oxidation or both. SA is involved in enhancing proline level under HM toxicity [96]. Parashar et al. [127] reported that SA ameliorated the Mn stress through enhanced accumulation of proline in *Brassica juncea* which might be due to the increased activity of enzymes responsible for proline synthesis [137]. Enhanced proline content also maintains water balance in plants to contrast stressful conditions leading to osmotic stress [138] a condition which can occur when plants reduce the stomatal conductance in order to reduce HM uptake. Further, Chen and Dickman [139] proposed that proline is a powerful ROS scavenger and a pivotal component of protein pathway in plants, besides serving as an osmoprotectant [140]. Zanganeh et al. [141] observed however that SA pre-treatment decreased proline accumulation in *Zea mays* under Pb stress that was supported by the findings of Mostafa et al. [142] in rice plants. Therefore, the pattern of proline (activation/decrement) can be species- or metal-specific and also dependent on the dose of HM experienced by the plant species.

3.3.2. Glycine Betaine

Glycine betaine (GB) is a quaternary level ammonium compound found in higher plants under stress conditions and it acts as osmoprotectant or compatible solutes in plants [143], in which it accumulates at cytosolic level. GB is involved in providing protection against drought, salinity [93], drought [143], and HM stress, as well [144]. Exogenous application of GB is very effective in providing tolerance from HM stress [94,145]. The role of SA in regulating the accumulation of GB in plants under metal stress is still unknown. However, few studies reported that exogenous treatment of GB together with SA can help in alleviating HM toxicity [145]. Recently, Aldesuquy et al. [146] opined that GB and SA regulates osmotic pressure and concentration of osmolytes in plants that maintain osmotic balance and helps in ameliorating the adverse effect of drought stress in wheat, thereby suggesting a possible cooperation. It was also reported that the SA induced the rise in GB level which helped the growth of *Rauwolfia serpentina* plants grown under Na excess [147].

3.3.3. Sugars

The term sugars, collectively used for disaccharides (sucrose, trehalose) and fructans, are water-soluble carbohydrates involved in plant stress tolerance. Sucrose, an important product of photosynthesis, is required for growth, development, storage, and signaling in plants [148,149]. Carbohydrates are building blocks of plants that provide energy and act as a signaling molecule during transcriptional, post-transcriptional processes [150]. Accumulation of soluble sugars has been observed in plants under stressful conditions which indicate their role as osmoprotectant and in maintaining cellular balance in plants [151,152]. The exogenous addition of SA enhanced the amount of
polysaccharides and sugars in plants and helped in improving their growth [153]. El-tayeb et al. [154] observed that SA provided Cu tolerance in *Helianthus annuus*. The authors reported an increasing level of soluble sugars in plants treated with SA that protects the photosynthetic pigments from Cu toxicity [154]. Similarly, 0.01 M SA enhanced growth and sugar accumulation in tomato plants and provided stress avoidance and tolerance against Na toxicity [155].

### 3.3.4. Polyamines

Polyamines (PAs) are water-soluble molecules that play an important role in regulating morphological, developmental, and stress responses in plants [156]. PA have the potential to scavenge HM-triggered ROS [157] and regulate plant defense response to HM toxicity [156,158]. Under stressful conditions, PA operate as signaling compounds and control ion homeostasis and ion transportation in plants, thus actively participating in stress tolerance [159,160]. Many reports suggest that SA treatment influence PA content in plants [131,161]. Recently, Tajti et al. [162] studied the role of putrescine and spermidine on wheat under Cd stress and also reported increased levels of SA in those plants; however, the exact mechanism involved in SA-mediated HM stress tolerance and the relationship between PA and SA in plants are still unknown.

### 3.3.5. Polyphenols

Phenolics are one of the largest groups of secondary metabolites which include a plethora of compounds with simple aromatic rings to very complex molecules, such as tannins and lignans. They originate from phenylalanine by the activity of PAL. Many reports have demonstrated that enhanced production of phenolic compounds under HM stress can protect from oxidative damage [163,164]. The accumulation of phenolics is principally driven by increased expression of enzymes responsible for phenylpropanoid biosynthesis such as phenylalanine ammonia-lyase, chalcone synthase, shikimate dehydrogenase, cinnamyl alcohol dehydrogenase, and polyphenol oxidase [165,166]. Many studies have documented the role of phytohormones in enhancing the level of some classes of polyphenols, such as anthocyanins [167,168]. Dong et al. [169] reported increased concentrations of phenolics, such as caffeic acid due to exogenous treatment by SA. Similarly, peaked activity of PAL was observed in *Matricaria chamomilla* plants under Ni and Cd stress with the application of SA [170].

### 3.4. Regulation of Cell Signaling by SA under HM Stress

The HM stress tolerance induced by SA is supportive for its role in stress signaling. The mechanism of tolerance not only depends on the concentration and mode of application of SA but also on the overall status of plants [171]. Abiotic stress not only affects growth and development of plants, but also regulates DNA replication machinery. SA application upregulates the topoisomerase gene and chloroplast elongation factor that help in plant adaptation under stressful conditions [172,173]. Moreover, SA is known to induce expression of *TLC1*, a long terminal repeated retrotransposon family in vivo [171]. This family is transcriptionally activated during stressful conditions and its expression by SA suggests their role in SA-mediated signaling pathways [171]. Another mechanism adopted by SA in regulating HM stress plant response is the increased activity of enzymes involved in AsA-GSH pathway [174]. Both AsA and GSH are active redox compounds that maintain cellular redox balance in plants [175]. SA supplementation also increased SOD and POD level in *Cannabis sativa* and improved Cd-tolerance [34] which might be related to increased concentration of Ca$^{2+}$ (a second messenger) and H$_2$O$_2$, that eventually promote the activity of antioxidant enzymes which reduce cellular ROS level in plants [176,177].

### 3.5. Crosstalk of SA with Other Plant Growth Regulators

SA regulates different plant responses both under optimal and stressful conditions through the crosstalk with other plant growth regulators or plant hormones [81,178]. The interaction of SA with
other hormones such as auxin [179], cytokinin [180], gibberellins [181], abscisic acid [182], ethylene [178], and brassinosteroids [87] has been studied under optimum and stressful environments. The possible outcome of interaction of SA with hormones can be either synergistic or antagonistic under stressful conditions. Recently, Tamás et al. [44] studied the SA regulated alleviation of Cd-stress by restriction of Cd-induced auxin-mediated ROS production in barley roots. The authors suggest that SA treatment reversed indole-3-acetic acid (IAA)-induced stress responses in plants suggesting a role of SA in IAA signaling pathway. Similarly, Agtuca et al. [183] reported an opposite role of IAA and SA in roots of maize. The exogenous application of IAA enhanced lateral growth by depriving primary root growth, while SA increased total root biomass [183].

Exposure to various environmental stresses, such as HM, can enhance ethylene production and induce oxidative stress in plants [175]. The increased ethylene production is due to peaked expression of ethylene-related biosynthetic genes or expression of ethylene-responsive genes [184]. Exogenous SA was reported to mitigate Cd stress in wheat [174] by increasing GSH content that resulted in metal detoxification and scavenging ROS induced by HM-triggered ethylene production. SA supplementation promoted increased ABA level in wheat seedlings under Cd stress that was attributed to a de novo ABA biosynthesis [185]. Further, endogenous ABA controlled SA-mediated alteration of the concentration of dehydrin proteins under HM stress that demonstrate protective mechanism of SA in wheat plants [185].

Under abiotic stress conditions, crosstalk between SA and jasmonates play a crucial role in regulation of plant growth [186]. Generally, SA and jasmonic acid (JA) signaling pathways work in an antagonistic manner [187]. The Mitogen-activated protein kinase (MAPK) signaling pathway mediates the antagonistic action between SA and JA cell signaling [188]. However, nonantagionistic interaction between SA and JA are also reported, but an exact mechanism is still unclear and it needs further studies [186]. For example, in maize plants Cu stress induced the biosynthesis of SA, which further induced JA priming and JA induced volatile organic compounds [189,190].

4. Conclusions

Heavy metal stress has been accepted as one of the major threats for plants growing in contaminated areas. In order to deal with the harmful effects of heavy metals, plants have developed several molecular, metabolic, and physiological processes which allow them to avoid stressful factors or cope with them. Several researches highlighted that SA, when used at low doses, plays a pivotal role in both alleviating and reducing heavy metal stress in plants. An increase in the endogenous level, as well as exogenous application of this plant hormone has been demonstrated to be helpful for plants either in optimal or in stress conditions. In fact, this ubiquitous plant hormone is involved in the regulation of several metabolic processes in plants, regulating the ex novo biosynthesis of secondary metabolites and osmoprotectants involved in the protection from oxidative stress, thereby increasing the activity of ROS scavenger enzymes and/or acting as antioxidants. However, at high concentrations SA can also act as a negative plant growth regulator [171,191,192].

The scientific literature cited in the present review highlights the important role played by SA in protecting plants from heavy metal stress. However, most of the researches available on this topic are mainly focused on the role played by this molecule after an exogenous application, while very few researches, because of the complexity of the cascade effects generated, have unveiled the defense mechanisms triggered by its endogenous stimulation in response to heavy metals. Therefore, there are still several questions which need further investigation. For example, it would be extremely interesting to disentangle the complexity of SA signaling in response to heavy metals, as well as to unveil if exogenous application of SA might directly or indirectly enhance endogenous SA levels. In the meantime, more genomic, transcriptomic, proteomic, and metabolomics studies are necessary to detect SA responsive genes, proteins, and metabolites altered by heavy metal stress. In addition, it is necessary that a molecular dissection deeply understands the crosstalk between SA with other
phytohormones and/or metabolites and the feedback processes involved in controlling the endogenous levels of SA in response to heavy metal stress.

**Author Contributions:** All authors contributed in writing part of the original draft and also reviewed and edited the whole manuscript. All authors have read and agreed to the published version of the manuscript.

**Funding:** This research received no external funding.

**Conflicts of Interest:** The authors declare no conflict of interest.

**References**

1. Chen, Z.; Zheng, Z.; Huang, J.; Lai, Z.; Fan, B. Biosynthesis of salicylic acid in plants. *Plant Sign. Behav.* **2009**, *4*, 493–496. [CrossRef] [PubMed]
2. Wani, A.B.; Chadar, H.; Wani, A.H.; Singh, S.; Upadhyay, N. Salicylic acid to decrease plant stress. *Environ. Chem. Lett.* **2017**, *15*, 101–123. [CrossRef]
3. Lovelock, D.A.; Šola, I.; Marschollek, S.; Donald, C.E.; Rusak, G.; van Pee, K.H.; Ludwig-Müller, J.; Cahill, D.M. Analysis of salicylic acid-dependent pathways in *Arabidopsis thaliana* following infection with *Plasmodiophora brassicae* and the influence of salicylic acid on disease. *Mol. Plant Pathol.* **2016**, *17*, 1237–1251. [CrossRef]
4. Maruri-López, I.; Aviles-Baltazar, N.Y.; Buchala, A.; Serrano, M. Intra and extracellular journey of the phytohormone salicylic acid. *Front. Plant Sci.* **2019**, *10*, 423. [CrossRef] [PubMed]
5. Raskin, I. Role of salicylic acid in plants. *Annu. Rev. Plant Biol.* **1992**, *43*, 439–463. [CrossRef]
6. Muthulakshmi, S.; Lingakumar, K. Role of salicylic acid (SA) in plants—A review. *Int. J. Appl. Res.* **2017**, *3*, 33–37.
7. Foster, S. *Tyler’s Honest Herbal: A Sensible Guide to the Use of Herbs and Related Remedies*; Routledge: New York, NY, USA, 1999.
8. Petrek, J.; Havel, L.; Petrylova, J.; Adam, V.; Potesil, D.; Babula, P.; Kizek, R. Analysis of salicylic acid in willow barks and branches by an electrochemical method. *Russ. J. Plant Physiol.* **2007**, *54*, 553–558. [CrossRef]
9. Arif, H.; Aggarwal, S. *Salicylic Acid (Aspirin)*; StatPearls Publishing LLC.: Tampa, FL, USA; St. Petersburg, Russia, 2019.
10. Shine, M.; Yang, J.W.; El-Habbak, M.; Nagyabhyru, P.; Fu, D.Q.; Navarre, D.; Ghabrial, S.; Kachroo, P.; Kachroo, A. Cooperative functioning between phenylalanine ammonia-lyase and isochorismate synthase activities contributes to salicylic acid biosynthesis in soybean. *New Phytol.* **2016**, *212*, 627–636. [CrossRef]
11. Zhang, Y.; Fu, X.; Hao, X.; Zhang, L.; Wang, L.; Qian, H.; Zhao, J. Molecular cloning and promoter analysis of the specific salicylic acid biosynthetic pathway gene phenylalanine ammonia-lyase (*AaPAL1*) from *Artemisia annua*. *Biotech. Appl. Biochem.* **2016**, *63*, 514–524. [CrossRef]
12. Chong, J.; Pierrel, M.-A.; Atanassova, R.; Werck-Reichhart, D.; Fritig, B.; Saindrenan, P. Free and conjugated benzoic acid in tobacco plants and cell cultures. Induced accumulation upon elicitation of defense responses and role as salicylic acid precursors. *Plant Physiol.* **2001**, *125*, 318–328. [CrossRef]
13. Hayat, S.; Ali, B.; Ahmad, A. Salicylic acid: Biosynthesis, metabolism and physiological role in plants. In *Salicylic Acid: A Plant Hormone*; Springer: Dordrecht, The Netherlands, 2007; pp. 1–14.
14. Yalpani, N.; León, J.; Lawton, M.A.; Raskin, I. Pathway of salicylic acid biosynthesis in healthy and virus-infected tobacco. *Plant Physiol.* **1993**, *103*, 315–321. [CrossRef] [PubMed]
15. Silverman, P.; Seskar, M.; Kanter, D.; Schweizer, P.; Metraux, J.-P.; Raskin, I. Salicylic acid in rice (biosynthesis, conjugation, and possible role). *Plant Physiol.* **1995**, *108*, 633–639. [CrossRef] [PubMed]
16. Metraux, J.-P. Recent breakthroughs in the study of salicylic acid biosynthesis. *Trends Plant Sci.* **2002**, *7*, 332–334. [CrossRef]
17. Garcia, C.; Lohmann, A.; Lamodière, E.; Catinot, J.; Buchala, A.; Doermann, P.; Metraux, J.-P. Characterization and biological function of the Isochorismate Synthase2 gene of *Arabidopsis*. *Plant Physiol.* **2008**, *147*, 1279–1287. [CrossRef] [PubMed]
18. Rekhter, D.; Lüdeke, D.; Ding, Y.; Feussner, K.; Zienkiewicz, K.; Lipka, V.; Wiermer, M.; Zhang, Y.; Feussner, I. Isochorismate-derived biosynthesis of the plant stress hormone salicylic acid. *Science* **2019**, *365*, 498–502. [CrossRef] [PubMed]
19. Wei, Y.; Liu, G.; Chang, Y.; He, C.; Shi, H. Heat shock transcription factor 3 regulates plant immune response through modulation of salicylic acid accumulation and signalling in cassava. *Mol. Plant Pathol.* 2018, 19, 2209–2220. [CrossRef]

20. Hartmann, M.; Zeier, J. N-Hydroxypyepicolic acid and salicylic acid: A metabolic duo for systemic acquired resistance. *Curr. Opin. Plant Biol.* 2019, 50, 44–57. [CrossRef]

21. El-Shazoly, R.M.; Metwally, A.A.; Hamada, A.M. Salicylic acid or thiamin increases tolerance to boron toxicity stress in wheat. *J. Plant Nutr.* 2019, 42, 702–722. [CrossRef]

22. Luo, J.; Xia, W.; Cao, P.; Xiao, Z.A.; Zhang, Y.; Liu, M.; Zhan, C.; Wang, N. Integrated transcriptome analysis reveals plant hormones jasmonic acid and salicylic acid coordinate growth and defense responses upon fungal infection in poplar. *Biomolecules* 2019, 9, 12. [CrossRef]

23. Pasternak, T.; Groot, E.P.; Kazantsev, F.V.; Teale, W.; Omelyanchuk, N.; Kovrizhnykh, V.; Palme, K.; Mironova, V.V. Salicylic acid affects root meristem patterning via auxin distribution in a concentration-dependent manner. *Plant Physiol.* 2019, 180, 1725–1739. [CrossRef]

24. Cleland, C.F.; Ajami, A. Identification of the flower-inducing factor isolated from aphid honeydew as being salicylic acid. *Plant Physiol.* 1974, 54, 904–906. [CrossRef] [PubMed]

25. Raskin, I.; Skubatz, H.; Tang, W.; Meueuse, B.J. Salicylic acid levels in thermogenic and non-thermogenic plants. *Ann. Bot.* 1990, 66, 369–373. [CrossRef]

26. Dempsey, D.M.A.; Klessig, D.F. How does the multifaceted plant hormone salicylic acid combat disease in plants and are similar mechanisms utilized in humans? *BMC Biol.* 2017, 15, 23. [CrossRef]

27. Klessig, D.F.; Choi, H.W.; Dempsey, D.M.A. Systemic acquired resistance and salicylic acid: Past, present, and future. *Mol. Plant-Microbe Interact.* 2018, 31, 871–888. [CrossRef] [PubMed]

28. Subban, K.; Subramani, R.; Srinivasan, V.P.M.; Johnpaul, M.; Chelliah, J. Salicylic acid as an effective elicitor for improved taxol production in endophytic fungus *Pestalotopsis microspora*. *PLoS ONE* 2019, 14, e0212736. [CrossRef]

29. Tripathi, D.; Raikhy, G.; Kumar, D. Chemical elicitors of systemic acquired resistance—Salicylic acid and its functional analogs. *Curr. Plant Biol.* 2019, 17, 48–59. [CrossRef]

30. Nadeem, M.; Ahmad, W.; Zahir, A.; Hano, C.; Abbasi, B.H. Salicylic acid-enhanced biosynthesis of pharmacologically important lignans and neo lignans in cell suspension culture of *Linum ussitatsimum*. *Eng. Life Sci.* 2019, 19, 168–174. [CrossRef]

31. Li, N.; Han, X.; Feng, D.; Yuan, D.; Huang, L.-J. Signaling crosstalk between salicylic acid and ethylene/jasmonate in plant defense: Do we understand what they are whispering? *Int. J. Mol. Sci.* 2019, 20, 671. [CrossRef]

32. Safari, F.; Akramian, M.; Salehi-Arjmand, H.; Khadivi, A. Physiological and molecular mechanisms underlying salicylic acid-mitigated mercury toxicity in lemon balm (*Melissa officinalis L.*). *Ecotoxic Environ. Safety* 2019, 183, 109542. [CrossRef]

33. Dalvi, A.A.; Bhalerao, S.A. Response of plants towards heavy metal toxicity: An overview of avoidance, tolerance and uptake mechanism. *Ann. Plant. Sci.* 2013, 2, 362–368.

34. Shi, G.; Cai, Q.; Liu, Q.; Wu, L. Salicylic acid-mediated alleviation of cadmium toxicity in hemp plants in relation to cadmium uptake, photosynthesis, and antioxidant enzymes. *Acta Physiol. Plant.* 2009, 31, 969–977. [CrossRef]

35. Wang, C.; Zhang, S.; Wang, P.; Hou, J.; Qian, J.; Ao, Y.; Lu, J.; Li, L. Salicylic acid involved in the regulation of nutrient elements uptake and oxidative stress in *Vallisneria natans* (Lour.) Hara under Pb stress. *Chemosphere* 2011, 84, 136–142. [CrossRef] [PubMed]

36. Wei, T.; Lv, X.; Jia, H.; Hua, L.; Xu, H.; Zhou, R.; Zhao, J.; Ren, X.; Guo, J. Effects of salicylic acid, Fe (II) and plant growth-promoting bacteria on Cd accumulation and toxicity alleviation of Cd tolerant and sensitive tomato genotypes. *J. Environ. Manag.* 2018, 214, 164–171. [CrossRef] [PubMed]

37. Kohli, S.K.; Handa, N.; Sharma, A.; Gautam, V.; Arora, S.; Bhardwaj, R.; Ayliemeni, M.N.; Wijaya, L.; Ahmad, P. Combined effect of 24-epibrassinolide and salicylic acid mitigates lead (Pb) toxicity by modulating various metabolites in *Brassica juncea* L. seedlings. *Protoplasma* 2018, 255, 11–24. [CrossRef] [PubMed]

38. Guo, J.; Zhou, R.; Ren, X.; Jia, H.; Hua, L.; Xu, H.; Lv, X.; Zhao, J.; Wei, T. Effects of salicylic acid, Epi-brassinolide and calcium on stress alleviation and Cd accumulation in tomato plants. *Ecotoxic. Environ. Saf.* 2018, 157, 491–496. [CrossRef]
39. Malik, Z.A.; Lal, E.P.; Mir, Z.A.; Lone, A.H. Effect of salicylic acid and indole acetic acid on tomato crop under induced salinity and cadmium stressed environment: A Review. *Int. J. Plant Soil Sci.* 2018, 26, 1–6. [CrossRef]

40. Mohamed, H.E.; Hassan, A.M. Role of salicylic acid in alleviating cobalt toxicity in wheat (*Triticum aestivum* L.) seedlings. *J. Agric. Sci.* 2019, 11. [CrossRef]

41. Mostofa, M.G.; Rahman, M.; Ansary, M.; Uddin, M.; Fujita, M.; Tran, L.-S.P. Interactive effects of salicylic acid and nitric oxide in enhancing rice tolerance to cadmium stress. *Int. J. Mol. Sci.* 2019, 20, 5798. [CrossRef]

42. Wang, Y.-Y.; Wang, Y.; Li, G.-Z.; Hao, L. Salicylic acid-altering Arabidopsis plant response to cadmium exposure: Underlying mechanisms affecting antioxidation and photosynthesis-related processes. *Ecotoxicol. Environ. Safety* 2019, 169, 645–653. [CrossRef]

43. Belkadhi, A.; De Haro, A.; Obregon, S.; Chaibi, W.; Djebali, W. Positive effects of salicylic acid pretreatment on the composition of flax plastidial membrane lipids under cadmium stress. *Environ. Sci. Poll. Res.* 2015, 22, 1457–1467. [CrossRef]

44. Tamás, L.; Mistrík, I.; Alemayehu, A.; Zelinová, V.; Bočová, B.; Huttová, J. Salicylic acid alleviates cadmium-induced stress responses through the inhibition of Cd-induced auxin-mediated reactive oxygen species production in barley root tips. *J. Plant Physiol.* 2015, 173, 1–8. [CrossRef] [PubMed]

45. Cui, W.; Li, L.; Gao, Z.; Wu, H.; Xie, Y.; Shen, W. Haem oxygenase-1 is involved in salicylic acid-induced alleviation of oxidative stress due to cadmium stress in *Medicago sativa*. *J. Exp. Bot.* 2012, 63, 5521–5534. [CrossRef] [PubMed]

46. Tahjib-Ul-Arif, M.; Siddiqui, M.N.; Sohag, A.A.M.; Sakil, M.A.; Rahman, M.M.; Polash, M.A.S.; Mostofa, M.G.; Tran, L.-S.P. Salicylic acid-mediated enhancement of photosynthesis attributes and antioxidation capacity contributes to yield improvement of maize plants under salt stress. *J. Plant Grow. Regul.* 2018, 37, 1318–1330. [CrossRef]

47. Yin, Q.-S.; Yuan, X.; Jiang, Y.-G.; Huang, L.-L.; Li, G.-Z.; Hao, L. Salicylic acid-mediated alleviation in NO2 phytotoxicity correlated to increased expression levels of the genes related to photosynthesis and carbon metabolism in Arabidopsis. *Environ. Exp. Bot.* 2018, 156, 141–150. [CrossRef]

48. Adrees, M.; Ali, S.; Rizwan, M.; Ibrahim, M.; Abbas, F.; Farid, M.; Zia-ur-Rehman, M.; Irshad, M.K.; Bharwana, S.A. The effect of excess copper on growth and physiology of important food crops: A review. *Environ. Sci. Poll. Res.* 2015, 22, 8148–8162. [CrossRef]

49. Pinto, A.; De Varennes, A.; Fonseca, R.; Teixeira, D.M. Phytoremediation of soils contaminated with heavy metals: Techniques and strategies. In *Phytoremediation*; Springer: Dordrecht, The Netherlands, 2015; pp. 133–155.

50. Kumar, A.; Usmani, Z.; Ahirwal, J.; Rani, P. Phytomanagement of chromium contaminated brown fields. In *Phytomanagement of Polluted Sites*; Elsevier: Amsterdam, The Netherlands, 2019; pp. 447–469.

51. Park, J.H.; Lamb, D.; Paneerselvam, P.; Choppala, G.; Bolan, N.; Chung, J.-W. Role of organic amendments on enhanced bioremediation of heavy metal (loid) contaminated soils. *J. Haz. Mat.* 2011, 185, 549–574. [CrossRef]

52. Kumar, V.; Sharma, A.; Kaur, P.; Sidhu, G.P.S.; Bali, A.S.; Bhardwaj, R.; Thukral, A.K.; Cerda, A. Pollution assessment of heavy metals in soils of India and ecological risk assessment: A state-of-the-art. *Chemosphere* 2019, 216, 449–462. [CrossRef]

53. Sidhu, G.P.S.; Singh, H.P.; Batish, D.R.; Kohli, R.K. Effect of lead on oxidative status, antioxidative response and metal accumulation in *Coronopus didymus*. *Plant Physiol. Biochem.* 2016, 105, 290–296. [CrossRef]

54. Sidhu, G.P.S.; Singh, H.P.; Batish, D.R.; Kohli, R.K. Tolerance and hyperaccumulation of cadmium by a wild, unpalatable herb *Coronopus didymus* (L.) Sm. (*Brassicaceae*). *Ecotox. Environ. Safety* 2017, 135, 209–215. [CrossRef]

55. Sidhu, G.P.S.; Singh, H.P.; Batish, D.R.; Kohli, R.K. Appraising the role of environment friendly chelants in alleviating lead by *Coronopus didymus* from Pb-contaminated soils. *Chemosphere* 2017, 182, 129–136. [CrossRef]

56. Keesstra, S.; Mol, G.; de Leeuw, J.; Okx, J.; de Cleen, M.; Visser, S. Soil-related sustainable development goals: Four concepts to make land degradation neutrality and restoration work. *Land* 2018, 7, 133. [CrossRef]

57. Ramzani, P.M.A.; Iqbal, M.; Kausal, S.; Ali, S.; Rizwan, M.; Virk, Z.A. Effect of different amendments on rice (*Oryza sativa* L.) growth, yield, nutrient uptake and grain quality in Ni-contaminated soil. *Environ. Sci. Poll. Res.* 2016, 23, 18588–18595. [CrossRef] [PubMed]
58. Ihedioha, J.; Ukoha, P.; Ekere, N. Ecological and human health risk assessment of heavy metal contamination in soil of a municipal solid waste dump in Uyo, Nigeria. *Environ. Geochim. Health* 2017, 39, 497–515. [CrossRef] [PubMed]

59. Van Nevel, L.; Mertens, J.; Staelens, J.; de Schrijver, A.; Tack, F.M.; de Neve, S.; Meers, E.; Verheyen, K. Elevated Cd and Zn uptake by aspen limits the phytostabilization potential compared to five other tree species. *Ecol. Eng.* 2011, 37, 1072–1080. [CrossRef]

60. Arshad, T.; Maqbool, N.; Javed, F.; Wahid, A.; Arshad, M.U. Enhancing the defensive mechanism of lead affected barley (*Hordeum vulgare L.*) genotypes by exogenously applied salicylic acid. *J. Agric. Sci.* 2017, 9, 139–146. [CrossRef]

61. Foyer, C.H.; Noctor, G. Redox homeostasis and antioxidant signaling: A metabolic interface between stress perception and physiological responses. *Plant Cell* 2005, 17, 1866–1875. [CrossRef]

62. Guerra, F.; Gainza, F.; Pérez, R.; Zamudio, F. Phytoremediation of heavy metals using poplars (*Populus spp.): A glimpse of the plant responses to copper, cadmium and zinc stress. In *Handbook of Phytoremediation*; Nova Science: New York, NY, USA, 2011; pp. 387–413.

63. Rascio, N.; Dalla Vecchia, F.; La Rocca, N.; Barbato, R.; Pagliano, C.; Raviolo, M.; Gonnelli, C.; Gabbielli, R. Metal accumulation and damage in rice (cv. Vialone nano) seedlings exposed to cadmium. *Environ. Exp. Bot.* 2008, 62, 267–278. [CrossRef]

64. Baryla, A.; Carrier, P.; Franck, F.; Coulomb, C.; Sahut, C.; Havaux, M. Leaf chlorosis in oilseed rape plants (*Brassica napus*) grown on cadmium-polluted soil: Causes and consequences for photosynthesis and growth. *Planta* 2001, 212, 696–709. [CrossRef]

65. Di Cagno, R.; Guidi, L.; De Gara, L.; Soldatini, G. Combined cadmium and ozone treatments affect photosynthesis and ascorbate-dependent defences in sunflower. *New Phytol.* 2001, 151, 627–636. [CrossRef]

66. Küpper, H.; Parameswaran, A.; Leitenmaier, B.; Trt, E.; Vernieri, P.; et al. Losing the warning signal: Drought compromises the cross-talk of signaling molecules in *Quercus ilex* exposed to ozone. *Front. Plant Sci.* 2017, 8, 1020. [CrossRef] [PubMed]

67. CAD, T.A.; Popova, L.P. Functions and toxicity of cadmium in plants: Recent advances and future prospects. *Turkish J. Bot.* 2013, 37, 1–13.

68. Wahid, A.; Ghani, A.; Javed, F. Effect of cadmium on photosynthesis, nutrition and growth of mungbean. *Agr. Sustain. Develop.* 2008, 28, 273–280. [CrossRef]

69. Tandon, P.K.; Srivastava, P. Growth and metabolism of sesame (*Sesamum indicum*) plants in relation to lead toxicity. *Agric. Sci.* 2014, 6, 91–92.

70. Rascio, N.; Navari-Izzo, F. Heavy metal hyperaccumulating plants: How and why do they do it? And what makes them so interesting? *Plant Sci.* 2011, 180, 169–181. [CrossRef] [PubMed]

71. Kadukova, J.; Kavuličova, J. *Phytoremediation of heavy metal contaminated soils—Plant stress assessment.* In *Handbook of Phytoremediation*; Nova Science: New York, NY, USA, 2011; pp. 185–222.

72. Baxter, A.; Mittler, R.; Suzuki, N. RO8 as key players in plant stress signalling. *J. Exp. Bot.* 2014, 65, 1229–1240. [CrossRef] [PubMed]

73. Mittler, R. ROS are good. *Trends Plant Sci.* 2017, 22, 11–19. [CrossRef] [PubMed]

74. Cotrozzi, L.; Pellegrini, E.; Guidi, L.; Landi, M.; Lorenzini, G.; Massai, R.; Remorini, D.; Tonelli, M.; Trivellini, A.; Vernieri, P.; et al. Losing the warning signal: Drought compromises the cross-talk of signalling molecules in *Quercus ilex* exposed to ozone. *Front. Plant Sci.* 2017, 8, 1020. [CrossRef] [PubMed]

75. Landi, M.; Cotrozzi, L.; Pellegrini, E.; Remorini, D.; Tonelli, M.; Trivellini, A.; Nali, C.; Guidi, L.; Massai, R.; Vernieri, P.; et al. When “thirsty” means “less able to activate the signalling wave triggered by a pulse of ozone”: A case of study in two Mediterranean deciduous oak species with different drought sensitivity. *Sci. Total Environ.* 2019, 657, 379–390. [CrossRef] [PubMed]

76. Kaur, G.; Singh, H.P.; Batish, D.R.; Kohli, R.K. Lead (Pb)-induced biochemical and ultrastructural changes in wheat (*Triticum aestivum*) roots. *Protoplasma* 2013, 250, 53–62. [CrossRef] [PubMed]

77. Das, K.; Roychoudhury, A. Reactive oxygen species (ROS) and response of antioxidants as ROS-scavengers during environmental stress in plants. *Front. Environ. Sci.* 2014, 2, 53. [CrossRef]

78. Miura, K.; Tada, Y. Regulation of water, salinity, and cold stress responses by salicylic acid. *Front. Plant Sci.* 2014, 5, 4. [CrossRef] [PubMed]

79. Mohsenzadeh, S.; Shahrtash, M.; Mohabatkar, H. Interactive effects of salicylic acid and silicon on some physiological responses of cadmium-stressed maize seedlings. *Iranian J. Sci. Tech. (Sciences)* 2011, 35, 57–60.
80. Vlot, A.C.; Dempsey, D.M.A.; Klessig, D.F. Salicylic acid, a multifaceted hormone to combat disease. *Ann. Rev. Phytopathol.* 2009, 47, 177–206. [CrossRef]
81. Khan, M.I.R.; Iqbal, N.; Masood, A.; Per, T.S.; Khan, N.A. Salicylic acid alleviates adverse effects of heat stress on photosynthesis through changes in proline production and ethylene formation. *Plant Sign. Behav.* 2013, 8, e26374. [CrossRef] [PubMed]
82. Hussein, M.; Balbaa, L.; Gaballah, M. Salicylic acid and salinity effects on growth of maize plants. *Res. J. Agricul. Biol. Sci.* 2007, 3, 321–328.
83. Khokon, M.A.R.; Okuma, E.; Hossain, M.A.; Munemasa, S.; Uraji, M.; Nakamura, Y.; Mori, I.C.; Murata, Y. Involvement of extracellular oxidative burst in salicylic acid-induced stomatal closure in Arabidopsis. *Plant Cell Environ.* 2011, 34, 434–443. [CrossRef]
84. Larque-Saavedra, A. Stomatal closure in response to acetalysalicylic acid treatment. *Zeitschrift für Pflanzenphysiologie* 1979, 93, 371–375. [CrossRef]
85. Larque-Saavedra, A. The antitranspirant effect of acetylsalicylic acid on *Phaseolus vulgaris*. *Physiol. Plant.* 1978, 43, 126–128. [CrossRef]
86. Alaey, M.; Babalar, M.; Naderi, R.; Kafi, M. Effect of pre-and postharvest salicylic acid treatment on physio-chemical attributes in relation to vase-life of rose cut flowers. *Postharvest Biol. Technol.* 2011, 61, 91–94. [CrossRef]
87. Divi, U.K.; Rahman, T.; Krishna, P. Brassinosteroid-mediated stress tolerance in Arabidopsis shows interactions with abscisic acid, ethylene and salicylic acid pathways. *BMC Plant Biol.* 2010, 10, 151. [CrossRef]
88. Wang, Y.; Hu, J.; Qin, G.; Cui, H.; Wang, Q. Salicylic acid analogues with biological activity may induce chilling tolerance of maize (*Zea mays*). *Botany* 2012, 90, 845–855. [CrossRef]
89. Zengin, F. Effects of exogenous salicylic acid on growth characteristics and biochemical content of wheat seedlings under arsenic stress. *J. Environ. Biol.* 2015, 36, 249.
90. Ghani, A.; Khan, I.; Ahmed, I.; Mustafa, I.; Abd-Ur, R.; Muhammad, N. Amelioration of lead toxicity in *Brassica juncea* (L.) by foliar application of salicylic acid. *J. Environ. Anal. Toxicol.* 2015, 5, 10–4172.
91. Gondor, O.K.; Pál, M.; Darkó, É.; Janda, T.; Szalai, G. Salicylic acid and sodium salicylate alleviate cadmium toxicity to different extents in maize (*Zea mays*). *PLoS ONE* 2016, 11, e0160157. [CrossRef] [PubMed]
92. Zhou, Z.S.; Guo, K.; Elbaz, A.A.; Yang, Z.M. Salicylic acid alleviates mercury toxicity by preventing oxidative stress in roots of *Medicago sativa*. *Environ. Exp. Bot.* 2009, 65, 27–34. [CrossRef]
93. Ahmad, P.; Nabi, G.; Ashraf, M. Cadmium-induced oxidative damage in mustard (*Brassica juncea* (L.) Czern. & Coss.) plants can be alleviated by salicylic acid. *South Afr. J. Bot.* 2011, 77, 36–44.
94. Islam, F.; Yasmeen, T.; Arif, M.S.; Riaz, M.; Shahzad, S.M.; Imran, Q.; Ali, I. Combined ability of chromium (Cr) tolerant plant growth promoting bacteria (PGPB) and salicylic acid (SA) in attenuation of chromium stress in maize plants. *Plant Physiol. Biochem.* 2016, 108, 456–467. [CrossRef]
95. Song, W.Y.; Yang, H.C.; Shao, H.B.; Zheng, A.Z.; Brestic, M. The alleviative effects of salicylic acid on the activities of catalase and superoxide dismutase in malting barley (*Hordeum vulgare* L.) seedling leaves stressed by heavy metals. *CLEAN–Soil, Air, Water* 2014, 42, 88–97. [CrossRef]
96. Faraz, A.; Faizan, M.; Sami, F.; Siddiqui, H.; Hayat, S. Supplementation of salicylic acid and citric acid for alleviation of cadmium toxicity to *Brassica juncea*. *J. Plant Growth Regul.* 2019, 1–15. [CrossRef]
97. Hasanuzzaman, M.; Matin, M.A.; Fardus, J.; Hasanuzzaman, M.; Hossain, M.S.; Parvin, K. Foliar application of salicylic acid improves growth and yield attributes by upregulating the antioxidant defense system in *Brassica campestris* plants grown in lead-amended soils. *Acta Agrobot.* 2019, 72. [CrossRef]
98. Lu, Q.; Zhang, T.; Zhang, W.; Su, C.; Yang, Y.; Hu, D.; Xu, Q. Alleviation of cadmium toxicity in *Lemna minor* by exogenous salicylic acid. *Ecotox. Environ. Saf.* 2018, 147, 500–508. [CrossRef] [PubMed]
99. Gu, C.-S.; Yang, Y.-H.; Shao, Y.-F.; Wu, K.-W.; Liu, Z.-L. The effects of exogenous salicylic acid on alleviating cadmium toxicity in *Nymphaea tetragona* Georgi. *S. Afr. J. Bot.* 2018, 114, 267–271. [CrossRef]
100. Li, Q.; Wang, G.; Wang, Y.; Yang, D.; Guan, C.; Ji, J. Foliar application of salicylic acid alleviate the cadmium toxicity by modulation the reactive oxygen species in potato. *Ecotox. Environ. Saf.* 2019, 172, 317–325. [CrossRef] [PubMed]
101. Tajti, J.; Németh, E.; Glatz, G.; Janda, T.; Pál, M. Pattern of changes in salicylic acid-induced protein kinase (SIPK) gene expression and salicylic acid accumulation in wheat under cadmium exposure. *Plant Biol.* 2019, 21, 1176–1180. [CrossRef]
102. Ahmad, B.; Jaleel, H.; Sadiq, Y.; Khan, M.M.A.; Shabbir, A. Response of exogenous salicylic acid on cadmium induced photosynthetic damage, antioxidant metabolism and essential oil production in peppermint. *Plant Growth Regul.* 2018, 86, 273–286. [CrossRef]

103. Zanganeh, R.; Jamei, R.; Rahmani, F. Role of salicylic acid and hydrogen sulfide in promoting lead stress tolerance and regulating free amino acid composition in Zea mays L. *Acta Physiol. Plant.* 2019, 41, 94. [CrossRef]

104. Alamri, S.A.D.; Siddiqui, M.H.; Al-Khaishany, M.Y.; Ali, H.M.; Al-Amri, A.; AlRubah, H.K. Exogenous application of salicylic acid improves tolerance of wheat plants to lead stress. *Adv. Agric. Sci.* 2018, 6, 25–35.

105. Zanganeh, R.; Jamei, R.; Rahmani, F. Impacts of seed priming with salicylic acid and sodium hydrosulfide on possible metabolic pathway of two amino acids in maize plant under lead stress. *Mol. Biol. Res. Commun.* 2018, 7, 83.

106. Mabrouk, B.; Kaab, S.; Rezgui, M.; Majdoub, N.; da Silva, J.T.; Kaab, L. Salicylic acid alleviates arsenic and zinc toxicity in the process of reserve mobilization in germinating fenugreek (*Trigonella foenum-graecum* L.) seeds. *S. Afr. J. Bot.* 2019, 124, 235–243. [CrossRef]

107. Kumari, A.; Pandey, N.; Pandey-Rai, S. Exogenous salicylic acid-mediated modulation of arsenic stress tolerance with enhanced accumulation of secondary metabolites and improved size of glandular trichomes in *Artemisia annua* L. *Protoplasma* 2018, 255, 139–152. [CrossRef]

108. Kumari, A.; Pandey-Rai, S. Enhanced arsenic tolerance and secondary metabolism by modulation of gene expression and proteome profile in *Artemisia annua* L. after application of exogenous salicylic acid. *Plant Physiol. Biochem.* 2018, 132, 590–602. [CrossRef]

109. Saidi, I.; Youssi, N.; Borgi, M.A. Salicylic acid improves the antioxidant ability against arsenic-induced oxidative stress in sunflower (*Helianthus annuus*) seedling. *J. Plant Nutr.* 2017, 40, 2326–2335. [CrossRef]

110. Singh, A.P.; Dixit, G.; Kumar, A.; Mishra, S.; Kumar, N.; Dixit, S.; Singh, P.K.; Dwivedi, S.; Trivedi, P.K.; Pandey, V. A protective role for nitric oxide and salicylic acid for arsenite phytotoxicity in rice (*Oryza sativa* L.). *Plant Physiol. Biochem.* 2017, 115, 163–173. [CrossRef] [PubMed]

111. Sihag, S.; Brar, B.; Joshi, U. Salicylic acid induces amelioration of chromium toxicity and affects antioxidant enzyme activity in *Sorghum bicolor* L. *Int. J. Phytochem.* 2019, 21, 293–304. [CrossRef]

112. Gill, R.A.; Zhang, N.; Ali, B.; Farooq, M.A.; Xu, J.; Gill, M.B.; Mao, B.; Zhou, W. Role of exogenous salicylic acid in regulating physio-morphic and molecular changes under chromium toxicity in black-and yellow-seeded *Brassica napus* L. *Environ. Sci. Poll. Res.* 2016, 23, 20483–20496. [CrossRef]

113. Huda, A.N.; Swarz, A.; Reza, M.A.; Haque, M.A.; Kabir, A.H. Remediation of chromium toxicity through exogenous salicylic acid in rice (*Oryza sativa* L.). *Water Air Soil Poll.* 2016, 227, 278. [CrossRef]

114. Zaid, A.; Mohammad, F.; Wani, S.H.; Siddique, K.M. Salicylic acid enhances nickel stress tolerance by up-regulating antioxidant defense and glyoxalase systems in mustard plants. *Ecotoxicol. Environ. Saf.* 2019, 180, 575–587. [CrossRef]

115. Kotapati, K.V.; Palaka, B.K.; Ampasala, D.R. Alleviation of nickel toxicity in finger millet (*Eleusine coracana* L.) germinating seedlings by exogenous application of salicylic acid and nitric oxide. *Crop J.* 2017, 5, 240–250. [CrossRef]

116. Soltani Maivan, E.; Radjabian, T.; Abrishamchi, P.; Talei, D. Physiological and biochemical responses of *Melissa officinalis* L. to nickel stress and the protective role of salicylic acid. *Arch. Agron. Soil Sci.* 2017, 63, 330–343. [CrossRef]

117. Karimi, N.; Ghasempour, H.-R. Salicylic acid and jasmonic acid restrains nickel toxicity by ameliorating antioxidant defense system in shoots of metalloicous and non-metalloicous *Alyssum inflatum* Náyr. Populations. *Plant Physiol. Biochem.* 2019, 135, 450–459.

118. Mei, L.; Daud, M.; Ullah, N.; Ali, S.; Khan, M.; Malik, Z.; Zhu, S. Pretreatment with salicylic acid and ascorbic acid significantly mitigate oxidative stress induced by copper in cotton genotypes. *Environ. Sci. Poll. Res.* 2015, 22, 9922–9931. [CrossRef] [PubMed]

119. Moravcová, Š.; Tůma, J.; Dučaiová, Z.K.; Waligórski, P.; Kula, M.; Saja, D.; Słomka, A.; Bąba, W.; Libik-Konieczny, M. Influence of salicylic acid pretreatment on seeds germination and some defense mechanisms of *Zea mays* plants under copper stress. *Plant Physiol. Biochem.* 2018, 122, 19–30. [CrossRef] [PubMed]
120. Ventrella, A.; Catucci, L.; Piletska, E.; Piletsky, S.; Agostiano, A. Interactions between heavy metals and photosynthetic materials studied by optical techniques. *Bioelectrochemistry* 2009, 77, 19–25. [CrossRef] [PubMed]

121. Babu, N.G.; Sarma, P.A.; Attitalla, I.H.; Murthy, S. Effect of selected heavy metal ions on the photosynthetic electron transport and energy transfer in the thylakoid membrane of the cyanobacterium, *Spirulina platensis*. *Acad. J. Plant Sci.* 2010, 3, 46–49.

122. Chugh, L.K.; Sawhney, S.K. Photosynthetic activities of *Pisum sativum* seedlings grown in presence of cadmium. *Plant Physiol. Biochem.* 1999, 37, 297–303. [CrossRef]

123. Khan, N.; Samiullah Singh, S.; Nazar, R. Activities of antioxidative enzymes, sulphur assimilation, photosynthetic activity and growth of wheat (*Triticum aestivum*) cultivars differing in yield potential under cadmium stress. *J. Agron. Crop Sci.* 2007, 193, 435–444. [CrossRef]

124. Yusuf, M.; Fariduddin, Q.; Varshney, P.; Ahmad, A. Salicylic acid minimizes nickel and/or salinity-induced toxicity in Indian mustard (*Brassica juncea*) through an improved antioxidant system. *Environ. Sci. Poll. Res.* 2012, 19, 8–18. [CrossRef]

125. Parashar, A.; Yusuf, M.; Fariduddin, Q.; Ahmad, A. Salicylic acid enhances antioxidant system in Brassica juncea grown under different levels of manganese. *Int. J. Biol. Macromol.* 2014, 70, 551–558. [CrossRef]

126. Yadav, S. Heavy metals toxicity in plants: An overview on the role of glutathione and phytochelatins in heavy metal stress tolerance of plants. *S. Afr. J. Bot.* 2010, 76, 167–179. [CrossRef]

127. Gill, S.S.; Tuteja, N. Reactive oxygen species and antioxidant machinery in abiotic stress tolerance in crop plants. *Plant Physiol. Biochem.* 2010, 48, 909–930. [CrossRef] [PubMed]

128. Sharma, P.; Jha, A.B.; Dubey, R.S.; Pessarakli, M. Reactive oxygen species, oxidative damage, and antioxidative defense mechanism in plants under stressful conditions. *J. Bot.* 2012, 2012, 217037. [CrossRef]

129. Zhang, Y.; Xu, S.; Yang, S.; Chen, Y. Salicylic acid alleviates cadmium-induced inhibition of growth and photosynthesis through upregulating antioxidant defense system in two melon cultivars (*Cucumis melo* L.). *Protoplasma* 2015, 252, 911–924. [CrossRef]

130. Chao, Y.-Y.; Chen, C.-Y.; Huang, W.-D.; Kao, C.H. Salicylic acid-mediated hydrogen peroxide accumulation and protection against Cd toxicity in rice leaves. *Plant Soil* 2010, 329, 327–337. [CrossRef]

131. Liang, Y.; Chen, Q.; Liu, Q.; Zhang, W.; Ding, R. Exogenous silicon (Si) increases antioxidant enzyme activity and reduces lipid peroxidation in roots of salt-stressed barley (*Hordeum vulgare* L.). *J. Plant Physiol.* 2003, 160, 1157–1164. [CrossRef]

132. Verbruggen, N.; Hermans, C. Proline accumulation in plants: A review. *Amino Acids* 2008, 35, 753–759. [CrossRef]

133. Zouari, M.; Ahmed, C.B.; Elloumi, N.; Bellassoued, K.; Delmail, D.; Labrousse, P.; Abdallah, F.B.; Rouina, B.B. Impact of proline application on cadmium accumulation, mineral nutrition and enzymatic antioxidant defense system of *Olea europaea* L. cv Chemlali exposed to cadmium stress. *Ecotoxicol. Environ. Saf.* 2016, 128, 195–205. [CrossRef]

134. Zouari, M.; Ahmed, C.B.; Zorrig, W.; Elloumi, N.; Rabbi, M.; Delmail, D.; Rouina, B.B.; Labrousse, P.; Abdallah, F.B. Exogenous proline mediates alleviation of cadmium stress by promoting photosynthetic activity, water status and antioxidative enzymes activities of young date palm (*Phoenix dactylifera* L.). *Ecotoxicol. Environ. Saf.* 2016, 128, 100–108. [CrossRef]

135. Misra, N.; Saxena, P. Effect of salicylic acid on proline metabolism in lentil grown under salinity stress. *Plant Sci.* 2009, 177, 181–189. [CrossRef]

136. Zengin, F.K.; Munzuroglu, O. Effects of some heavy metals on content of chlorophyll, proline and some antioxidant chemicals in bean (*Phaseolus vulgaris* L.) seedlings. *Acta Biol. Cracov. Bot.* 2005, 47, 157–164.

137. Chen, C.; Dickman, M.B. Proline suppresses apoptosis in the fungal pathogen *Colletotrichum trifolii*. *Proc. Natl. Acad. Sci. USA* 2005, 102, 3459–3464. [CrossRef] [PubMed]

138. Szabados, L.; Savoure, A. Proline: A multifunctional amino acid. *Trends Plant Sci.* 2010, 15, 89–97. [CrossRef] [PubMed]
141. Zanganeh, R.; Jamei, R.; Rahmani, F. Modulation of growth and oxidative stress by seed priming with salicylic acid in Zea mays L. under lead stress. J. Plant Inter. 2019, 14, 369–375. [CrossRef]
142. Mostofa, M.G.; Fujita, M.; Tran, L.-S.P. Nitric oxide mediates hydrogen peroxide-and salicylic acid-induced salt tolerance in rice (Oryza sativa L.) seedlings. Plant Growth Regul. 2015, 77, 265–277. [CrossRef]
143. Raza, S.; Aown, M.; Saleem, M.F.; Jamil, M.; Khan, I.H. Impact of foliar applied glycinebetaine on growth and physiology of wheat (Triticum aestivum L.) under drought conditions. Pak. J. Agric. Sci. 2014, 51, 327–334.
144. Jabeen, N.; Abbas, Z.; Iqbal, M.; Rizwan, M.; Jabbar, A.; Farid, M.; Ali, S.; Ibrahim, M.; Abbas, F. Glycinebetaine mediates chromium tolerance in mung bean through lowering of Cr uptake and improved antioxidant system. Arch. Agron. Soil Sci. 2016, 62, 648–662. [CrossRef]
145. Cao, F.; Liu, L.; Ibrahim, W.; Cai, Y.; Wu, F. Alleviating effects of exogenous glutathione, glycinebetaine, brassinosteroids and salicylic acid on cadmium toxicity in rice seedlings (Oryza sativa). Agrotechnology 2013, 2, 107–112. [CrossRef]
146. Aldesuquy, H.S.; Abbas, M.A.; Abo-Hamed, S.A.; Elhakem, A.H. Does glycine betaine and salicylic acid ameliorate the negative effect of drought on wheat by regulating osmotic adjustment through solutes accumulation? J. Stress Physiol. Biochem. 2013, 9, 5–22.
147. Misra, N.; Misra, R. Salicylic acid changes plant growth parameters and proline metabolism in Rauwolfia serpentina leaves grown under salinity stress. Am-Eurasian J. Agric. Environ. Sci. 2012, 12, 1601–1609.
148. Keunen, E.; Peshev, D.; Vangronsveld, J.; Van Den Ende, W.; Cuypers, A. Plant sugars are crucial players in the oxidative challenge during abiotic stress: Extending the traditional concept. Plant Cell Environ. 2013, 36, 1242–1255. [CrossRef] [PubMed]
149. Salerno, G.L.; Curatti, L. Origin of sucrose metabolism in higher plants: When, how and why? Trends Plant Sci. 2003, 8, 63–69. [CrossRef]
150. Muller, B.; Pantin, F.; Génard, M.; Turc, O.; Freixes, S.; Piques, M.; Gibon, Y. Water deficits uncouple growth from photosynthesis, increase C content, and modify the relationships between C and growth in sink organs. J. Exp. Bot. 2011, 62, 1715–1729. [CrossRef] [PubMed]
151. Cheng, Y.-J.; Yang, S.-H.; Hsu, C.-S. Synthesis of conjugated polymers for organic solar cell applications. Chem. Rev. 2009, 109, 5868–5923. [CrossRef] [PubMed]
152. Van den Ende, W.; Peshev, D. Sugars as antioxidants in plants. In Crop Improvement under Adverse Conditions; Springer: Dordrecht, The Netherlands, 2013; pp. 285–307.
153. Luo, Y.; Su, Z.; Bi, T.; Cui, X.; Lan, Q. Salicylic acid improves chilling tolerance by affecting antioxidant enzymes and osmoregulators in sacha inchi (Plukenetia volubilis). Braz. J. Bot. 2014, 37, 357–363. [CrossRef]
154. El-Tayeb, M.; El-Enany, A.; Ahmed, N. Salicylic acid-induced adaptive response to copper stress in sunflower (Helianthus annuus L.). Plant Growth Regul. 2006, 50, 191–199. [CrossRef]
155. Wasti, S.; Mimouni, H.; Smiti, S.; Zid, E.; Ben Ahmed, H. Enhanced salt tolerance of tomatoes by exogenous salicylic acid applied through rooting medium. OMICS 2012, 16, 200–207. [CrossRef]
156. Nahar, K.; Hasanuzzaman, M.; Alam, M.M.; Rahman, A.; Suzuki, T.; Fujita, M. Polyamine and nitric oxide crosstalk: Antagonistic effects on cadmium toxicity in mung bean plants through upregulating the metal detoxification, antioxidant defense and methylglyoxal detoxification systems. Ecotoxicol. Environ. Saf. 2016, 126, 245–255. [CrossRef]
157. Benavides, M.P.; Groppa, M.D.; Recalde, L.; Verstraeten, S.V. Effects of polyamines on cadmium-and copper-mediated alterations in wheat (Triticum aestivum L.) and sunflower (Helianthus annuus L.) seedling membrane fluidity. Arch. Biochem. Biophys. 2018, 654, 27–39. [CrossRef]
158. Groppa, M.D.; Benavides, M.P.; Tomaro, M.L. Polyamine metabolism in sunflower and wheat leaf discs under cadmium or copper stress. Plant Sci. 2003, 164, 293–299. [CrossRef]
159. Hasanuzzaman, M.; Nahar, K.; Fujita, M. Regulatory role of polyamines in growth, development and abiotic stress tolerance in plants. In Plant Adaptation to Environmental Change: Significance of Amino Acids and Their Derivatives; MD University: Haryana, India, 2014; pp. 157–193.
160. Liu, J.-H.; Wang, W.; Wu, H.; Gong, X.; Moriguchi, T. Polyamines function in stress tolerance: From synthesis to regulation. Front. Plant Sci. 2015, 6, 827. [CrossRef] [PubMed]
161. Szepesi, Á. Interaction between salicylic acid and polyamines and their possible roles in tomato hardening processes. Acta Biol. Szeged. 2011, 55, 165–166.
162. Tajti, J.; Janda, T.; Majláth, I.; Szalai, G.; Pál, M. Comparative study on the effects of putrescine and spermidine pre-treatment on cadmium stress in wheat. Ecotoxicol. Environ. Saf. 2018, 148, 546–554. [CrossRef] [PubMed]
163. Kaur, R.; Yadav, P.; Sharma, A.; Thukral, A.K.; Kumar, V.; Kohli, S.K.; Bhardwaj, R. Castasterone and citric acid treatment restores photosynthetic attributes in *Brassica juncea* L. under Cd (II) toxicity. *Ecotoxicol. Environ. Saf.* 2017, 145, 466–475. [CrossRef] [PubMed]

164. Kohli, S.K.; Handa, N.; Sharma, A.; Gautam, V.; Arora, S.; Bhardwaj, R.; Wijaya, L.; Alyemeni, M.N.; Ahmad, P. Interaction of 24-epibrassinolide and salicylic acid regulates pigment contents, antioxidative defense responses, and gene expression in *Brassica juncea* L. seedlings under Pb stress. *Environ. Sci. Poll. Res.* 2018, 25, 15159–15173. [CrossRef]

165. Chen, S.; Wang, Q.; Lu, H.; Li, J.; Yang, D.; Liu, J.; Yan, C. Phenolic metabolism and related heavy metal tolerance mechanism in *Kandelia obovata* under Cd and Zn stress. *Ecotoxicol. Environ. Saf.* 2019, 169, 134–143. [CrossRef]

166. Zafari, S.; Shariﬁ, M.; Chashmi, N.A.; Mur, L.A. Modulation of Pb-induced stress in Prosopis shoots through an interconnected network of signaling molecules, phenolic compounds and amino acids. *Plant Physiol. Biochem.* 2016, 99, 11–20. [CrossRef]

167. Nakamura, M.; Takeuchi, Y.; Miyanaga, K.; Seki, M.; Furusaki, S. High anthocyanin accumulation in the dark by strawberry (*Fragaria ananassa*) callus. *Biotechnol. Lett.* 1999, 21, 695–699. [CrossRef]

168. Narayan, M.; Thimmaraju, R.; Bhagyalakshmi, N. Interplay of growth regulators during solid-state and liquid-state batch cultivation of anthocyanin producing cell line of *Daucus carota*. *Process Biochem.* 2005, 40, 351–358. [CrossRef]

169. Dong, J.; Wan, G.; Liang, Z. Accumulation of salicylic acid-induced phenolic compounds and raised activities of secondary metabolic and antioxidative enzymes in *Salvia miltiorrhiza* cell culture. *J. Biotechnol.* 2010, 148, 99–104. [CrossRef]

170. Kováčik, J.; Gruz, J.; Hedbavny, J.; Klejdus, B.I.; Strnad, M. Cadmium and nickel uptake are differentially modulated by salicylic acid in *Matricaria chamomilla* plants. *J. Agric. Food Chem.* 2009, 57, 9848–9855. [CrossRef] [PubMed]

171. Horváth, É.; Szalai, G.; Janda, T. Induction of abiotic stress tolerance by salicylic acid signaling. *J. Plant Growth Regul.* 2007, 26, 290–300. [CrossRef]

172. Hettiarachchi, G.H.; Reddy, M.K.; Sopory, S.K.; Chattopadhyay, S. Regulation of TOP2 by various abiotic stresses including cold and salinity in pea and transgenic tobacco plants. *Plant Cell Physiol.* 2015, 66, 1053–1067. [CrossRef] [PubMed]

173. Singh, B.; Mishra, R.; Agarwal, P.K.; Goswami, M.; Nair, S.; Sopory, S.; Reddy, M. A pea chloroplast translation elongation factor that is regulated by abiotic factors. *Biochem. Biophys. Res. Commun.* 2004, 320, 523–530. [CrossRef]

174. Kovács, V.; Gondor, O.K.; Szalai, G.; Darkó, É.; Majlóst, I.; Janda, T.; Pál, M. Synthesis and role of salicylic acid in wheat varieties with different levels of cadmium tolerance. *J. Hazard. Mater.* 2014, 280, 12–19. [CrossRef] [PubMed]

175. Khan, M.I.R.; Fatma, M.; Per, T.S.; Anjum, N.A.; Khan, N.A. Salicylic acid-induced abiotic stress tolerance and underlying mechanisms in plants. *Front. Plant. Sci.* 2015, 6, 462. [CrossRef]

176. Arfan, M. Exogenous application of salicylic acid through rooting medium modulates ionaccumulation and antioxidant activity in spring wheat under salt stress. *Int. J. Agric. Biol.* 2009, 11, 437–442.

177. Song, W.; Zheng, A.; Shao, H.B.; Chu, L.; Brestic, M.; Zhang, Z. The alleviative effect of salicylic acid on the physiological indices of the seedling leaves in six different wheat genotypes under lead stress. *Plant Omics J.* 2012, 5, 486–493.

178. Khan, M.I.R.; Asgher, M.; Khan, N.A. Alleviation of salt-induced photosynthesis and growth inhibition by salicylic acid involves glycinebetaine and ethylene in mungbean (*Vigna radiata* L.). *Plant Physiol. Biochem.* 2014, 80, 67–74. [CrossRef]

179. Iglesias, M.J.; Terrile, M.C.; Casalognué, C.A. Auxin and salicylic acid signalings counteract the regulation of adaptive responses to stress. *Plant Signal. Behav.* 2011, 6, 452–454. [CrossRef]

180. Jiang, C.-J.; Shimono, M.; Sugano, S.; Kojima, M.; Liu, X.; Iroue, H.; Sakakibara, H.; Takatsuji, H. Cytokinins act synergistically with salicylic acid to activate defense gene expression in rice. *Mol. Plant. Microbe. Interact.* 2013, 26, 287–296. [CrossRef] [PubMed]

181. Roghayyeh, S.; Saeede, R.; Omid, A.; Mohammad, S. The effect of salicylic acid and gibberellin on seed reserve utilization, germination and enzyme activity of sorghum (*Sorghum bicolor* L.) seeds under drought stress. *J. Stress Physiol. Biochem.* 2014, 10, 5–13.
182. Jiang, C.-J.; Shimono, M.; Sugano, S.; Kojima, M.; Yazawa, K.; Yoshida, R.; Inoue, H.; Hayashi, N.; Sakakibara, H.; Takatsuji, H. Abscisic acid interacts antagonistically with salicylic acid signaling pathway in rice–Magnaporthe grisea interaction. *Mol. Plant. Microbe. Interact.* 2010, 23, 791–798. [CrossRef] [PubMed]

183. Agtuca, B.; Rieger, E.; Hilger, K.; Song, L.; Robert, C.A.; Erb, M.; Karve, A.; Ferrieri, R.A. Carbon-11 reveals opposing roles of auxin and salicylic acid in regulating leaf physiology, leaf metabolism, and resource allocation patterns that impact root growth in *Zea mays*. *J. Plant Growth Regul.* 2014, 33, 328–339. [CrossRef]

184. Thao, N.P.; Khan, M.I.R.; Thu, N.B.A.; Hoang, X.L.T.; Asgher, M.; Khan, N.A.; Tran, L.-S.P. Role of ethylene and its cross talk with other signaling molecules in plant responses to heavy metal stress. *Plant Physiol.* 2015, 169, 73–84. [CrossRef]

185. Shakirova, F.; Allagulova, C.R.; Maslennikova, D.; Klyuchnikova, E.; Avalbaev, A.; Bezrukova, M. Salicylic acid-induced protection against cadmium toxicity in wheat plants. *Environ. Exp. Bot.* 2016, 122, 19–28. [CrossRef]

186. Per, T.S.; Khan, M.I.R.; Anjum, N.A.; Masood, A.; Hussain, S.J.; Khan, N.A. Jasmonates in plants under abiotic stresses: Crosstalk with other phytohormones matters. *Environ. Exp. Bot.* 2018, 145, 104–120. [CrossRef]

187. Khan, M.I.R.; Khan, N.A. Salicylic acid and jasmonates: Approaches in abiotic stress tolerance. *J. Plant Biochem. Physiol.* 2013, 1, e113. [CrossRef]

188. Petersen, M.; Brodersen, P.; Naested, H.; Andreasson, E.; Lindhart, U.; Johansen, B.; Nielsen, H.B.; Lacy, M.; Austin, M.J.; Parker, J.E.; et al. Arabidopsis MAP kinase 4 negatively regulates systemic acquired resistance. *Cell* 2000, 103, 1111–1120. [CrossRef]

189. Engelberth, J.; Viswanathan, S.; Engelberth, M.J. Low concentrations of salicylic acid stimulate insect elicitor responses in *Zea mays* seedlings. *J. Chem. Ecol.* 2011, 37, 263–266. [CrossRef]

190. Rostás, M.; Winter, T.R.; Borkowski, L.; Zeier, J. Copper and herbivory lead to priming and synergism in phytohormones and plant volatiles in the absence of salicylate-jasmonate antagonism. *Plant Signal. Behav.* 2013, 8, e24264. [CrossRef] [PubMed]

191. Kumar, B.; Ram, H.; Sarlach, R.S. Enhancing seed yield and quality of Egyptian clover (*Trifolium alexandrinum* L.) with foliar application of bio-regulators. *Field Crops Res.* 2013, 146, 25–30. [CrossRef]

192. Canakci, S. Effects of salicylic acid on growth, biochemical constituents in pepper (*Capsicum annuum* L.) seedlings. *Pak. J. Biol. Sci.* 2011, 14, 300. [CrossRef] [PubMed]

© 2020 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (http://creativecommons.org/licenses/by/4.0/).