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ROS and NO regulation by melatonin under abiotic stress in plants

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Abstract: Abiotic stress in plants is an increasingly common problem in agriculture, and thus, studies on plant treatments with specific certain compounds that may help to mitigate these effects have increased in recent years Melatonin (MET) application and its role in mitigating the negative effects of abiotic stress in plants have become important in the last few years. MET, a derivative of tryptophan, is an important plant-related response molecule involved in the growth, development, and reproduction of plants, and the induction of different stress factors. In addition, MET plays a protective role against different abiotic stresses such as salinity, high/low temperature, high light, waterlogging, nutrient deficiency and stress combination by regulating both the enzymatic and non-enzymatic antioxidant defense systems. Also, MET interacts with many signaling molecules, among these, reactive oxygen species (ROS) and nitric oxide (NO), and participates in a wide variety of physiological reactions. It is well known that NO produces S-nitrosylation and NO_2-Tyr of important antioxidant-related proteins, being this an important mechanism for maintaining the antioxidant capacity of the AsA/GSH cycle under nitro-oxidative conditions, being extensively reviewed here under different abiotic stress conditions. Lastly, in this review, we show the coordination between NO and MET as a long-range signaling molecule, regulating many responses in plants, including plant growth and abiotic stress tolerance. Despite all the knowledge acquired over the years, there is still more to know about how MET and NO act on tolerance to abiotic stresses.

Keywords: melatonin; ROS; NO; posttranslational modifications (PMTs), abiotic stress; drought; salinity; high temperature; high light; waterlogging; abiotic stress combination

1. Introduction

Abiotic or biotic stresses, such as drought, heat, cold, salinity, pathogen attack and high light, either occurring individually or combined, negatively affect plant growth, reproduction and survival, which will limit agricultural crop productivity and yield [1]. Climate change events are predicted to increase the negative impact of environmental stress factors on plant production in many regions of the world in the coming years [2], with the unavoidable question of how humanity will cope with the world's demand for food. Along with this, according to the Food and Agriculture Organization of the United Nations (FAO) (2017), the world population will increase to 9700 billion people by 2050 and therefore the agricultural systems will have to produce almost 50% more food, fodder and biofuels than it did in 2012. It has been shown that plant productivity is strongly affected when stresses act in combination [3]. Thus, the heat waves combined with a serious drought episode that affected Europe in 2003 led to a 30% reduction of the total European agricultural production [4]. Plants respond to environmental stresses through a variety of biochemical and molecular mechanisms, including the selective absorption and exclusion of ions, the compartmentalization of ions into the central vacuole, the synthesis and accumulation of organic solutes in the cytoplasm, the changes in membrane composition and the alteration of plant hormone levels [3,5–7]. In this sense,

molecules such as phytohormones, nitric oxide (NO), hydrogen sulfide, and calcium (Ca2+), are directly involved in the plant's response to environmental stresses [8,9]. Recently, numerous studies have shown that a new and recent plant molecule, melatonin (MET), plays an important role in the response of plants to environmental stress, and its exogenous application has been shown to have a positive effect on the reduction of the impact of stress in plants [1,10], being cataloged as a phytohormone for its functions in plants [11].

2. Melatonin as an elicitor of plant stress response

MET (N-acetyl-5-methoxy-tryptamine) was first discovered in the bovine pineal gland in 1958 by Lerner et al. (1958) and it was not discovered in higher plants until 1995, simultaneously by Dubbels et al. (1995) and Hattori et al. (1995). MET has an indole ring structure, a low molecular weight, and is an evolutionarily-conserved pleiotropic molecule that exists ubiquitously in living organisms. MET has an amphiphilic or amphipathic molecular character, which allows the molecule to easily pass through the cell membrane and move into the cytosol, the nucleus, and/or the mitochondria [15,16]. In plants, 2-hydroxymelatonin (2-OHMET) is the most abundant MET derivative, and its intracellular concentration is about two orders of magnitude higher than that of MET [17]. Thus, it this thought that this MET derivative may be more efficient in the induction of plant stress tolerance than MET [18].

Starting with tryptophan, MET biosynthesis includes four enzymatic steps in all organisms; however, this varies among species [19]. In plants, tryptophan is first decarboxylated to tryptamine, which is then hydroxylated to serotonin, or the tryptophan is first hydroxylated to 5-hidroxytryphan, which is then decarboxylated to serotonin. Serotonin is either acetylated to N-acetylserotonin or it is methylated to form 5-methoxytryptamine; these products are either methylated or acetylated, respectively, to produce MET [20] (Figure 1). The content of MET in plants commonly differs between cultivars, species, growth and developmental periods, tissue types, and even in repetitions from a single experiment, and MET can be found in almost all the plant organs, from leaves to pistils [15,21]. Mitochondria and chloroplast are considered major sites of MET synthesis, although it can be also synthesized in the cytosol. MET is important because it provides protection against free radicals in the tissues or compartments where it is produced, as reactive oxygen species (ROS) are abundantly generated in these organelles [20,22]. Especially in plants, MET is maintained at a relatively constant level under normal conditions, just as with ROS, and it therefore believed that MET may mainly act as a regulator of ROS levels. Nevertheless, its synthesis and accumulation can be greatly and rapidly activated and upregulated in response to unfavorable conditions such as cold, heat, salt, drought, oxidative and nutrient stress, and bacterial infection [23,24]. On the other hand, it has been shown that under special circumstances, high levels of MET may be toxic to plants and may induce growth inhibition [25].
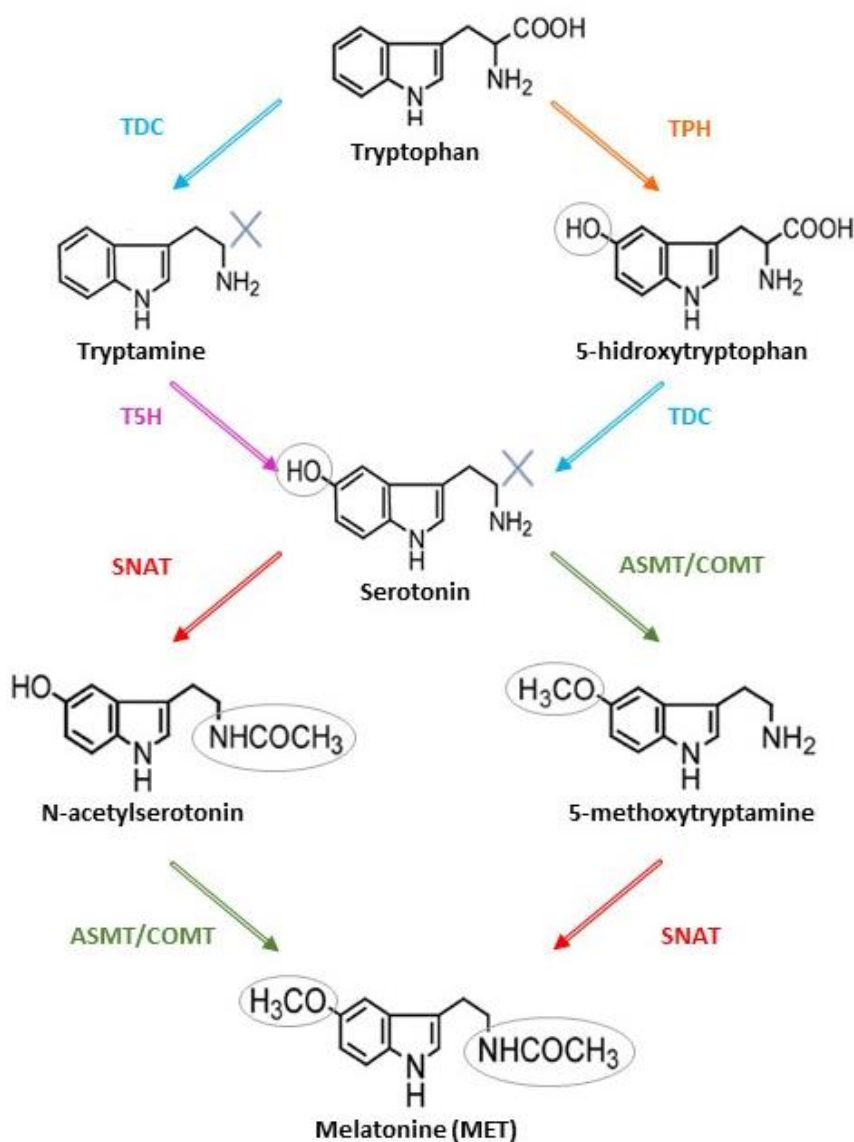
Figure 1. The four possible routes of melatonin (MET) biosynthesis. The enzymes that participate in the synthesis are: tryptophan decarboxylase (TDC), tryptophan hydroxylase (TPH), tryptamine 5-hydroxylase (T5H); serotonin N-acetyltransferase (SNAT); N-acetylserotonin methyltransferase (ASMT), and caffeic acid O-methyltransferase (COMT).

MET has been described as having many and important functions in plants. Several studies have reported that MET could be considered a growth regulator, as it plays a role in specific physiological processes in plants. MET regu¬lates the growth of leaves, shoots and explants, and plays a role in leaf senescence. MET can also regulate plant vegetative growth processes such as rooting, leaf aging, photosyn¬thetic yield, and biomass yield, and it plays a potential regulatory role in flowering processes and the formation and maturation of fruit and seeds [1,26,27]. Lastly, the evidence of the importance of MET in phytoremediation has been increasing [28]. But perhaps the most important function described for MET in living organisms is related to its role in non-receptor-mediated activities, such as scavenging of ROS and reactive nitrogen species (RNS) and improving the cell's antioxidant capacity, preventing cells, tissues, and organisms from suffering oxidative stress [15]. In this sense, MET modulates and quickly upregulates the activity of different antioxidant enzymes and stress-tolerance related genes, and activates downstream signaling transduction pathways when the plant is exposed to abiotic or biotic stress and the perception of MET [29,30]. In 2018 Dr. Chen's group first detected and characterized the phytoMET receptor PMTR1. PMTR1-phytoMET binding triggers the dissociation of Gγb and Gα, which activates NADPH oxidase-dependent H2O2 production,

enhancing Ca2+ influx and promoting K+ efflux, all of which results in stomatal closure [11,31]. In addition, MET can interact with unknown receptors in the activation of H2O2/NO signaling pathways, and further improve plant stress tolerance by regulating a variety of antioxidant enzymes, alleviating photosynthesis inhibition and modulating the activity of various transcription factors [32].

3. NO-plant mediated stress response and its relationship with melatonin.

Nitric oxide (NO) is another key signaling molecule in plant physiology. The most strongly described and evidenced NO production route involves the reduction of nitrite to NO via different non-enzymatic and/or enzymatic mechanisms in plants [33] (Figure 2). When high concentrations of nitrate are present in a low pH or high reducing environments, the reduction of nitrites to NO could efficiently and rapidly occur non-enzymatically [34] (Figure 2a). On the other hand, several proteins have been described as being able to catalyze the production of NO from nitrites, and one of them is nitrate reductase (NR). NR is a multifunctional cytoplasmic enzyme that is responsible for the reduction of nitrate to nitrite using NADH as an electron donor, and it is the first limiting step of nitrate assimilation [35]. This enzyme also has a nitrite:NO reductase activity (Ni- NR activity), from which NO is produced. However, this second reaction represents only 1% of the nitrate-reducing capacity of NR in normal conditions. Nevertheless, the reaction could be promoted by specific conditions such as anoxic conditions [36–38] (Figure 2c). Furthermore, in Arabidopsis thaliana, it has been shown that NR can interact with the partner protein NOFNiR (nitric oxide-forming nitrite reductase) to produce NO from nitrite. In contrast to the Ni-NR activity, the NO-producing activity occurs under normoxia and is not inhibited by nitrate [39] (Figure 2d). Also, NO can be produced from nitrite through the action of the mitochondrial electron transport chain (mETC) in plants, which requires anaerobic conditions and depends on the availability of nitrite [40,41] (Figure 2b). Apart from these reductive routes, several lines of evidence demonstrate the existence of an oxidative route for NO production in an arginine-dependent pathway in plants [33]. At present, it is evident that embryophyte transcriptomes do not have canonical nitric oxide synthases (NOSs). However, several pieces of evidence reported in various articles are in favor of the existence of NOS-like activity. This activity is dependent on arginine, or at least the arginine metabolic pathways (Figure 2e). The identification and description of the proteins and substrate/cofactors involved are necessary for a better understanding of NO formation in plants [33,42].
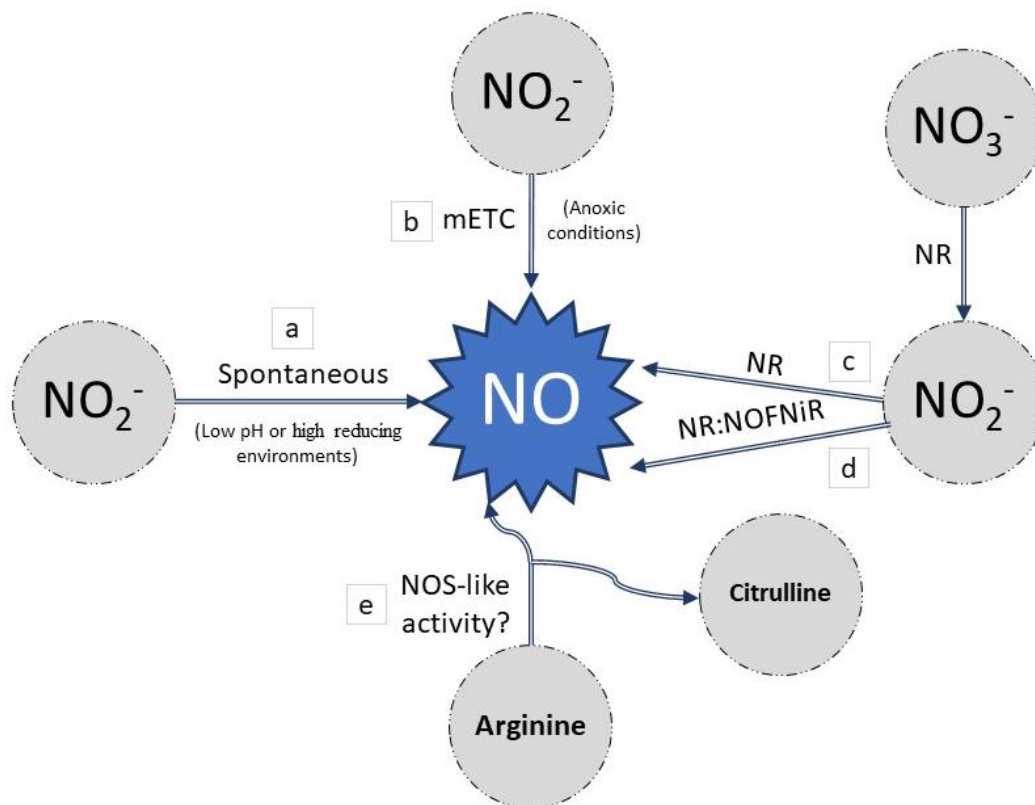
Figure 2. Nitric oxide (NO) synthesis in plants: a) the non-enzymatically mechanism, under low pH or high reducing environments. b) NO can be produced from nitrite through the action of the mitochondrial electron transport chain (mETC). c) nitrate reductase (NR) is responsible for the reduction of nitrate to nitrite using and then producing NO by Ni- NR activity. d) NR can interact with the partner protein NOFNiR (nitric oxide-forming nitrite reductase) to produce NO from nitrite. e) arginine-dependent pathway in plants forms NO by NOS (nitric oxide synthase) -like activity.

The main functions of NO in plant cells are related to its role in regulating the cellular redox balance in plants through post-translational modifications (PTMs) and/or through its binding to the prosthetic hemo group of some antioxidant enzymes. The PMTs induced by NO include S-nitrosylation, tyrosine nitration, and metal nitrosylation, although the first two are the most important at a physiological level [43]. S-nitrosylation is the covalent binding of NO to the thiol group of cysteines. In many antioxidant target proteins, S-nitrosylation leads to the regulation of the protein's function during stress [44,45]. Likewise, protein tyrosine nitration (NO2-Tyr) consists of the addition of a nitro (-NO2) group to one of the two equivalent ortho carbons of the aromatic ring of tyrosine residues [46]. This NO2-Tyr is considered a selective process, as under physiological conditions, the nitrotyrosine concentration is very low (from 1-5 NO2-Tyr among 10,000 molecules of tyrosine)[47]. In the same manner as S-nitrosylation, NO2-Tyr is able to alter protein functions through a gain, no change or loss of function, with the last one being the most common in plants [43,48]. Numerous data show an interrelationship between S-nitrosylation and NO2-Tyr in the regulation of the activity of some antioxidant proteins, being an important mechanism for maintaining the antioxidant capacity of the AsA/GSH (ascorbic acid/glutathione) cycle under nitro-oxidative conditions [49,50]. NO also regulates other important proteins, inducing other cellular processes. NO functions as a Ca2+-mobilizing messenger by promoting the rise in cytosolic Ca2+ concentrations. By increasing cytosolic Ca2+ concentration, NO modulates the activity of protein kinases and Ca2+-sensitive channels, which may be involved in the signaling cascade that leads to the expression of defense-related genes (adaptive response to biotic and abiotic stresses), stomatal

closure, or adventitious root formation and germination. These processes involve cyclic adenosine diphosphate (cADP) ribose, cyclic guanosine monophosphate (cGMP), and protein kinases [51].

Also, NO can be used commercially in postharvest fruit programs for the improvement of antioxidant and defense systems, the inhibition of ethylene biosynthesis, the activation of the C-repeat-binding factors (CBFs) pathway, and the regulation of sugar and energy metabolisms [52]. The signaling role of NO in plants has also been reported to modulate plant growth in normal and stress conditions [53]. Treatment with exogenous NO prevents damage from stress, promotes disease resistance, delays fruit ripening and enriches the nutritional quality of fruits [54]. In normal growth conditions, Wen et al. (2016) suggests that elevated NO levels resulting from the upregulated expression of NR, the down-regulation of S-nitrosoglutathionereductase (GSNOR), and auxin signaling were involved in the MET-induced adventitious root formation in tomato (Solanum lycopersicum L.) plants.

MET acts together with NO in plant growth and mediates plant abiotic stress tolerance through the improvement of the antioxidant system [56] (Figure 3). Just as MET, NO can directly scavenge free radicals and reduce oxidative damage in a receptor-independent manner under external stimuli and developmental signals [57]. MET can induce NO production or scavenge excess NO, and can promote the accumulation of NO by increasing the activity of NOS-like protein (arginine metabolic pathway), as MET up-regulates the expression of related genes [58,59]. In the presence of oxygen, MET can be easily converted to N-Nitrosomelatonin (NOMET) by NO nitrosation under different pH conditions. However, under the presence of serotonin and its derivatives, NOMET is an effective NO donor in cell cultures [60,61]. On the other hand, through a cGMP-dependent pathway, NO induces the expression of TDC, T5H, SNAT, and COMT (genes of the enzymes from the MET biosynthesis pathway) to increase the MET levels [56]. The interaction between NO and MET shows a certain degree of intricacy, as they interact independently and through multiple signaling pathways [62].
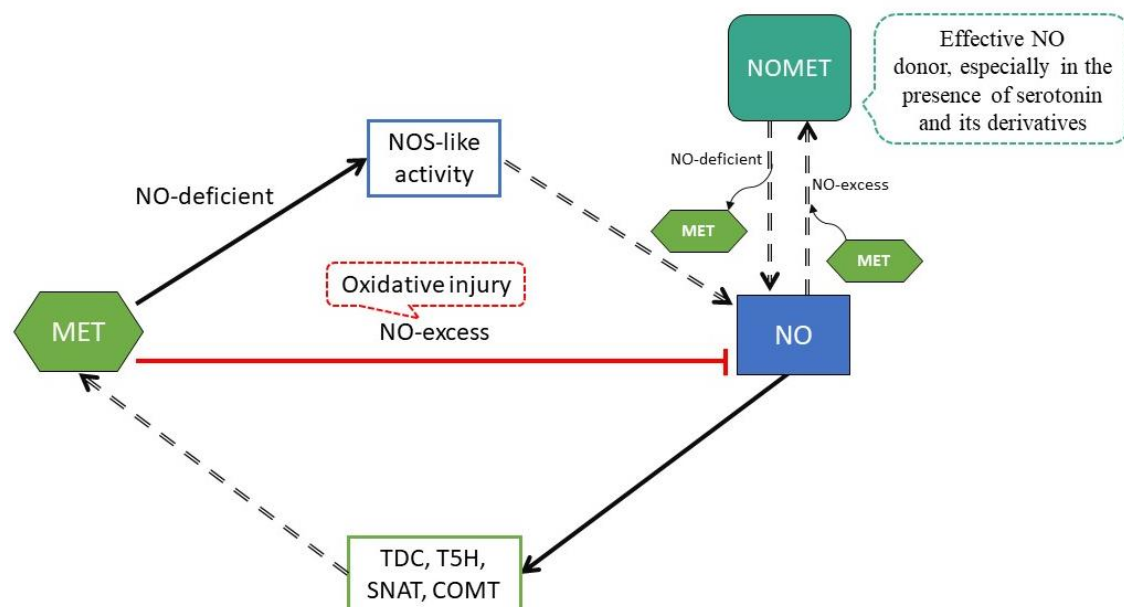

Figure 3. Interaction between melatonin (MET) and nitric oxide (NO). MET promotes the accumulation of NO by increasing the activity of NOS (nitric oxide synthase)-like since MET up-regulates the expression of related genes. MET scavenges excess NO, as it produces oxidative injury (red arrow). In the presence of oxygen, MET can be easily converted to N-Nitrosomelatonin (NOMET) by NO nitrosation under different pH conditions. As well, NOMET is an effective NO donor in cell cultures under the presence of serotonin and its derivatives. On the other hand, through a cyclic guanosine monophosphate (cGMP)-dependent pathway, NO induces the expression of TDC, T5H, SNAT, and COMT (genes of the enzymes of the MET biosynthesis pathway) to increase MET levels.

Taking into consideration the new progress in MET studies in recent years, the activity of MET in plants has been comprehensively and intensely explored. Here we compile the updated research works conducted on the relationship of MET with the stress tolerance mechanisms of plants, and the elucidated interaction between MET, ROS, and NO in the induction of this tolerance under different environmental stresses.

4. Coexistence and interaction of ROS, RNS and MET under environmental stress

Plants live in constantly changing environments that are often unfavorable or stressful for their growth and development. These adverse environmental conditions include biotic stress and abiotic stress. Some of the most important abiotic stresses are drought, salinity, and high/low temperatures which affect and ultimately determine the geographical distribution of plants in nature, limit plant productivity in agriculture and threaten food security. Moreover, the adverse effects of these abiotic stresses are aggravated by the inevitable effects of climate change, which has been predicted to result in an increased frequency of extreme weather [63,64]. Thus, improving plant stress resistance is critical for ensuring agricultural productivity and also for environmental sustainability, as it has also been shown that crops with poor stress resistance consume too much water and fertilizers [64].

Plant responses to abiotic stress are dynamic and complex. Different experiments have revealed the kinetics of stress responses through the identification of multiple response phases that involve core sets of genes and condition-dependent changes. In many examples, abscisic acid (ABA) signaling mediates the plant's responses to abiotic stress [65]. To decrease damage due to stress, plants have evolved different pathways. Reactive species increase is one of the first responses to stress. The formation of ROS and RNS is especially important, as they can cause electron leakage, lipid peroxidation, and subsequent membrane damage, as well as damage to nucleic acids and proteins [66]. In response to their elevated cellular concentration, plants initiate efficient detoxification through a network that coordinates antioxidant enzymes and non-enzymatic compounds. Well-known antioxidant enzymes include superoxide dismutase (SOD), catalase (CAT), peroxidase (POD), ascorbate peroxidase (APX) and glutathione peroxidase (GPX), while representative non-enzymatic compounds include glutathione (GSH), ascorbic acid (AsA), proline (Pro), carotenoids, α-tocopherols, etc. Moreover, a plethora of metabolites, including carbohydrates and amino acids, are generally accumulated to protect plants against abiotic stress[67–69]. Other antioxidant molecules that improve plant tolerance in plant tissues are different phenolic [70] and flavonoid compounds [71], although in the present review we will only focus on the increasingly recognized and important antioxidant, MET.

3.1. Salinity stress

Salinity stress is one of the main environmental stresses that limits plant growth and productivity in many agricultural areas in the world, notably in arid and semi-arid areas [72]. From the start, salt stress increases inter- and intracellular accumulation of sodium ions (Na+), inhibits protein synthesis and enzyme activities, damages cellular organelles, and uncouples photosynthesis and respiration. Next, salinity decreases nutrient uptake and/or transport to the shoot, resulting in a nutrient imbalance; and lastly, salinity decreases soil osmotic potentials which impedes water uptake by roots, leading to physiological drought in plants [73,74]. The osmotic stress, together with the overproduction of ROS generated under these conditions, causes the peroxidation of membrane lipids and proteins, destruction of cellular membrane structures, and ultimately cell death [75]. While several publications have confirmed the beneficial roles of exogenous MET in the enhancement of salinity tolerance in plants, which will be described in detail here, more studies are still needed to elucidate the involvement of endogenous MET in the mechanisms implicated in saline stress tolerance of plants [76].

Firstly, Zhou et al. (2016) verified that MET improves the photosynthetic activities of tomato (Solanum lycopersicum cv. Jin Peng Yi Hao) seedlings under salinity stress. These authors demonstrated that MET controlled ROS levels and prevented the damage caused by the high cellular concentration of ROS caused by salinity stress, promoting the recovery of the photosynthetic electron transport chain (PET) and D1 protein synthesis. In this sense, MET enhanced the photosynthetic activities and the repair of the light reaction-related proteins under salinity stress [77].

Although soil alkalization is often associated with soil salinity, the first is considered much more hazardous to plants. More specifically, this was studied by Yang et al. (2020), providing new insights on the beneficial effects of exogenous MET on saline-alkaline stress tolerance in mycorrhizal Leymus chinensis (Trin.) Tzvel through the regulation of the antioxidant systems, the protection of photosynthetic activity, and the promotion of associated arbuscular mycorrhizal fungal growth, without changing soil salinity and alkalinity. In tomato (S. lycopersicum L.) seedlings, Liu et al. (2015b) also observed that the exogenous application of MET resulted in a marked alleviation of alkalinity-associated inhibition of plant growth, a slower decline in chlorophyll (ChI) contents, and in the maximum photochemistry efficiency of photosystem II (PSII). MET also alleviated lipid peroxidation and reduced oxidative damage in S. lycopersicum L. seedlings under alkaline stress. Lastly, MET also improved the capacity of the AsA –GSH cycle and maintained the balance of K+ and Na+ (increased K+ content and decreased Na+ content in tomato leaves). Tolerance to salt stress and the homeostatic balance of Na+ and K+ promoted by MET has also been reported in potato (Ipomoea batatas (L.) Lam.) [80]. Also, a different study with S. lycopersicum L plants under salinity stress showed the overexpression of the enzyme involved in the synthesis of 5-methoxytryptamine/MET through the methylation of serotonin/Nacetylserotonin, COMT1 [19], resulting in increased MET levels, which allowed for the maintenance of ionic homeostasis, the protection of the photosynthetic system and the reduction of oxidative stress [81].

Gong et al. (2017) discovered the beneficial role of MET treatment in the response of alkaline conditions in Malus hupehensis Rehd. MET supplementation was associated with a reduction in cell membrane damage, maintenance of a normal root system architecture and a decrease in ROS due to the enhanced scavenging activity of the antioxidant enzymes SOD, POD and CAT. Transcript levels of six genes involved in polyamine (PA) synthesis were upregulated in response to MET application. These authors showed that an exogenous application of MET provided an increase in salinity stress tolerance through the regulation of the biosynthesis of PAs [82].

Similarly, a pretreatment with MET of watermelon seedlings (Citrullus lanatus L. cv. 04-1-2) alleviated NaCl-induced in roots through the inhibition of stomatal closure and thus, through the protection of the photosynthesis apparatus. It was also shown that MET improved light energy absorption, PET in PSII and redox homeostasis coupled with the enhanced activities of antioxidant enzymes [83]. Cen et al. (2020) confirmed that MET performed its primary function as an antioxidant, positively improving the salt tolerance of alfalfa (Medicago sativa L. cv. Zhongmu No. 2) through ROS scavenging and the enhancement of the activities of antioxidant enzymes.   Lastly, Zahedi et al. (2020) indicated that the effects of MET application were associated with a boost in leaf antioxidant enzymes and ABA, and provided support that the application of MET was a promising tool for mitigating salt stress in strawberry (Fragaria × ananassa Duch., cv. 'Camarosa').

For the first time, Zhao et al. (2018) presented genetic and pharmacological evidence demonstrating the involvement of NO in MET signaling for salinity tolerance. The salt stress tolerance in rapeseed (Brassica napus L. zhongshuang 11) was related to increased MET, which triggered a signaling cascade that resulted in the induction of nitrate reductase- (NR) and NO associated 1- (NOA1) dependent NO concentration. They demonstrated in rapeseed that the removal of NO did not alter endogenous MET content in roots supplemented with NaCl alone or together with MET; thus, NO was not responsible for MET production. Zhao et al. (2018) also discovered that NaCl-induced S-nitrosylation was intensified by MET and sodium nitroprusside (SNP), although decreased by the

removal of NO. In brief, pharmacological, molecular, and genetic data have provided solid evidence that NO operates downstream of MET enhancing salinity tolerance, which opens a new door for future research on the signaling mechanisms involved in plant stress tolerance.

Current results show evidence of an interaction between MET and NO on sunflower (Helianthus annuus L. var. KBSH 54) seedlings grown under salinity stress, with a differential modulation of two SOD isoforms (Cu/Zn SOD and Mn SOD). Presumably, MET is transported in the form of a metabolic signal (NOMET) from the roots, across the hypocotyl, until reaching the cotyledon cells within a time frame of 48 hours after radical emergence, leading to a reduction in both oxidative and nitrosative stress in seedlings under salt stress. That is, NO plays a role as a positive modulator of MET accumulation in seedling cotyledons in a long-distance signaling response [87]. Also, MET and NO differentially and coordinately ameliorate the salt stress effect by modulating glutathione reductase (GR) activity and GSH content in sunflower cotyledons (H. annuus L. cv. KBSH 53) seedlings. MET content in these organs was also modulated by NO, which upregulated the activity of hydroxyindole-O-methyltransferase - a regulatory enzyme in MET biosynthesis - in response to salt stress [88].

More specifically, under alkaline-saline stress it was also observed that exogenous MET treatment elevated NO levels in tomato (S. lycopersicum L.) roots, increasing their tolerance to alkaline stress. The treatment with MET and NO reduced damage caused by alkaline stress through the reduction of Na+ accumulation, activating the expressions of genes from the defense response signal pathway, and improving the uptake of K+, antioxidant enzyme activity and ASA–GSH detoxification capacity. These findings strongly suggest that NO, acting as a downstream signal, is involved in the MET–induced tomato tolerance to alkaline stress [89].

3.2. High temperature

Heat stress is considered one of the main limiting factors for plant growth, and it causes an important decrease in crop yield worldwide [90]. Heat stress (5 °C above the optimal growth temperature) is commonly related to three types of damage: oxidative stress caused by ROS; dicarbonyl stress induced by methylglyoxal, which rapidly reacts with biomacromolecules (proteins, lipids, and nucleic acids); dehydration or desiccation of cells due to water deficit caused by osmotic stress; and, loss of biomembrane integrity [91–94]. In addition, heat stress boosts the endogenous levels of putrescine, spermidine and spermine, and increases the content of PAs, indicating a higher metabolic gene expression [95]. To cope with it, plant cells have evolved several mechanisms, among them MET and its involvement on the heat-tolerant response has recently gained the interest of researchers. In kiwifruit (Actinidia deliciosa), it has been observed that MET exerts a protective effect against heat-related damage via the regulation of antioxidant pathways by reducing H_2O_2 content and increasing Pro content. Moreover, MET application has increased AsA levels and the activity of several antioxidant enzymes. These changes have been shown to be accompanied by an increase in the activity of enzymes related to the AsA-GSH cycle, such as APX, monodehydroascorbate reductase (MDHAR), dehydroascorbate reductase (DHAR), and GR. Furthermore, MET application increases the expression of 28 out of 31 glutathione S-transferase genes, which drive to the reduction of the oxidative stress generated under heat stress [96].

In tall fescue (Festuca arundinacea Schreb.) Alam et al. (2018) also found that MET effectively improved thermotolerance through a decrease of ROS levels, electrolyte leakage (EL) and a product of membrane lipid peroxidation, malondialdehyde (MDA), and also increased Chl contents, total protein and antioxidant enzyme activities under heat stress conditions, resulting in improved plant growth. Moreover, heat-tolerance related genes including FaHSFA3, FaAWPM and FaCYTC2 were significantly upregulated by the MET treatment, indicating that these genes may function as the implied target genes of MET. Li et al. (2019) also demonstrated that MET enhanced the

thermotolerance of maize (Zea mays L.) seedlings by reducing the MDA and EL levels. In the same manner, the exogenous application of MET stimulated the antioxidant defense system (GR, CAT, AsA, and GSH), MG detoxification (system glyoxalase I and glyoxalase II), and the osmoregulation system (Pro, trehalose and total soluble sugar) in maize seedlings under normal growing conditions and maintained under heat stress as compared to control conditions. These authors also reported that MET could enhance the thermotolerance of maize seedlings by adjusting the antioxidant defense, MG detoxification, and osmoregulation systems.

Ahammed et al. (2019) generated MET-deficient tomato plants (S. lycopersicum cv. Ailsa Craig) by silencing the COMT1 gene involved in MET biosynthesis to try to understand the role of endogenous MET in plant thermotolerance. Endogenous MET deficiency aggravated high temperature-induced oxidative stress as evidenced by the increased EL percentage, MDA concentration, oxidized and insoluble protein accumulation in tomato leaves. Additionally, silencing of COMT1 altered redox balance as shown by the significantly-decreased GSH:GSSG and AsA:DHA ratios under high temperature stress. Furthermore, a significant reduction in the activity of APX and CAT was observed, two key antioxidant enzymes that play prominent roles in plant thermotolerance. These results pointed out that endogenous MET was critical for both its self-antioxidant capacity and for maintaining and efficient enzymatic antioxidant system and redox homeostasis under heat stress. Similar works conducted by Wang et al. (2020) demonstrated that high temperature induced MET biosynthesis as a result of the accumulation of heat-induced Heat-sock factors (Hsfs) and heat shock proteins (HSPs) in tomato plants (S. lycopersicum L. cv. Micro-Tom). The accumulation of Hsfs stimulated the transcription of SNAT, an enzyme involved in MET biosynthesis. Simultaneously, HSP40 interacted with SNAT, avoiding natural SNAT degradation which occurs under heat stress. Upregulated SNAT also improved the transcription of Hsfs and HSPs under heat stress [100]. Increased MET synthesis in response to heat may help tomato plants maintain a balance of ROS and avoid the ROS-induced decrease in RuBisCo activity [100]. Lastly, in tomato (S. lycopersicum L. cv. Micro-Tom), it has also been shown that the irrigation treatment with MET effectively ameliorated high temperature-induced inactivation of pollen and inhibition of pollen germination in tomato plants [101]. MET decreased ROS accumulation in the anthers by inducing the activities of the different antioxidant enzymes. As the authors pointed out, the high temperature-induced pollen abortion decreased with the MET treatment, as it provided protection against the degradation of organelles by enhancing the expression of heat shock protein genes to refold unfolded proteins and the expression of autophagy-related genes and formation of autophagosomes to degrade denatured proteins [101].

Another molecule involved in heat stress tolerance is NO. In several plants, NO is a key signaling molecule needed for regulating responses such as photosynthesis, oxidative defense, osmolyte accumulation, gene expression, and protein modifications under heat stress. In addition, the NO interactions with other signaling molecules and phytohormones (such as MET) have been shown to achieve heat tolerance [102]. A research study with tomato (S. lycopersicum L. Cv. Hezuo 903) seedlings demonstrated that heat stress-induced damage was suppressed by MET, which coordinated with the PAs and NO biosynthesis pathways. The exogenous MET treatment improved their antioxidant defense mechanisms, inducing the AsA-GSH cycle, and reprogramed the PAs metabolic pathway (further increasing levels of PAs and upregulating transcript abundance, which coincided with the suppression of catabolic-related gene expression), and the NO biosynthesis pathway (increasing endogenous NO content, nitrate reductase and NO synthase-related activities, and the expression of their related genes). Consequently, the cellular membrane stability and the alleviation of heat-induced oxidative stress increased by the enhanced scavenging of excess ROS. Therefore, the cross-talk that exists between MET, PAs, and NO is related with the inhibition of thermal stress effects [95].

3.3. Cold stress

As described previously for high temperatures, low temperatures can also compromise growth and development in crops, causing a considerable yield loss   all over the world [64]. In plants, cold stress exerts various effects, resulting in physiological, biochemical and molecular changes [103,104]. Cold stress directly affects the photosynthetic machinery, principally by inducing photoinhibition at both PSI and PSII levels [105]. As described previously for other abiotic stresses, the defects in the PET in chloroplasts cause an excessive generation of ROS [106,107]. An overaccumulation of ROS induces an increase in membrane lipid peroxidation, as well as damage to vital biomolecules [92]. In recent years, the application of MET has gained considerable attention as a safe procedure for alleviating chilling injury in plants [108,109].

Firstly, Bajwa et al. (2014) indicated that MET protects Arabidopsis thaliana plant cells from cold stresses through the upregulation of specific cold-responsive genes. MET upregulated the expression of CBFs/Drought Response Element Binding factors, COR15a, a cold responsive gene, CAMTA1, a transcription factor involved in freezing and drought-stress tolerance, and transcription activators of ROS-related antioxidant genes ZAT10 and ZAT12, following cold stress. MET-treated plants had substantially higher fresh weight, primary root length, and shoot height in contrast with the non-treated plants.

In addition, Zhao et al. (2016) found that chilling stress led to serious chloroplast damage due to the over-accumulation of ROS, as evidenced by the high levels of O_2^- and H_2O_2. However, a pretreatment with MET increased the chilling tolerance of chloroplasts in cucumber (Cucumis sativus L.) seedlings by enhancing the levels of AsA and GSH, and increased the activity of total SOD, APX, MDHAR, DHAR, GR in the AsA–GSH cycle to increase the ROS scavenging capacity. MET also decreased the production of ROS in chloroplasts by balancing the distribution of the photosynthetic electron flux. On the other hand, Marta et al. (2016) conducted the first work that investigated and documented MET influences on redox state during seed germination in an in vivo plant model, specifically in cucumber (C. sativus L. var Odys) seeds, which are very sensitive to chilling. They provided evidence that MET could protect cucumber seeds and young seedlings against oxidative stress by directly and indirectly detoxifying ROS.

Additionally, it has been shown that exogenous MET and ABA have the ability to alleviate cold stress in Elymus nutans Griseb. Fu et al. (2017) investigated that the exogenous application of MET enhanced cold tolerance via the induction of endogenous MET production, which may serve as a secondary messenger, activating downstream cold-responsive genes. Their results indicated that both ABA-dependent and ABA-independent pathways may contribute to MET-induced cold tolerance in E. nutans. Nevertheless, more studies are needed to elucidate the interrelation between MET and other signaling molecules in response to cold stress.

The unprecedented early spring frost that causes cold stress adversely affects growth and productivity of tea (Camellia sinensis L.); therefore, it is indispensable to develop approaches to improve the cold tolerance of tea [114]. Li et al. (2018) is the first article that describes the beneficial role of MET in the cold tolerance of C. sinensis cv. Longjing 43. The treatment of tea with MET mitigated cold-induced reductions in photosynthetic capacity by reducing oxidative stress through enhanced antioxidant potential and redox homeostasis.

On the other hand, Wang et al. (2020) generated MET-deficient tomato (S. lycopersicum L. cv. Micro-Tom) plants using the virus-induced gene silencing approach and MET-rich tomato plants by the foliar application of MET. In this way, MET deficiency increased the accumulation of ROS and aggravated lipid peroxidation in chilling-stressed tomato leaves, while the exogenous application of MET had the opposite effect. Thus, they demonstrated that MET is critical for antioxidant capacity and redox balance and is in favor of photosynthesis in tomato plants under chilling stress [67].

Under cold stress, various plants respond with the formation of NO, and afterwards, a series of proteins targeted by NO are changed through post-translational modifications. Furthermore, key cold-regulated genes have been described as NO-dependent, suggesting the crucial importance of NO signaling for cold-responsive gene expression [115]. For this reason, it was thought that there could be a relationship between MET and NO in tolerance to cold stress. In tomato (Lycopersicon esculentum cv. Izmir) fruits, the application of exogenous MET conferred chilling tolerance. MET treatment produces higher arginine pathway activity in tomato fruits, therefore, a higher endogenous PAs accumulation and higher endogenous NO accumulation arising from higher NOS gene expression and enzyme activity may be responsible for maintaining safe membrane integrity by lowering electrolyte leakage and MDA accumulation during chilling stress [58].

3.4. Drought

Drought stress is a major problem that restricts crop growth and production, as it adversely effects many different physiological and biochemical processes in plant cells [116]. The main deleterious effects of drought stress are the reduction in relative water content, reduction in water potential of the leaf, loss of turgor, and cell enlargement reduction, which further results in the decrease of photosynthetic pigments, disturbance of different metabolic processes, and lastly plant death [117,118]. Drought stress also disrupts redox homeostasis, causing an imbalance on the production and scavenging of ROS, which reduces photosynthesis and stomatal closure, and alters the activities of enzymes [66]. To decrease these damages, plants have evolved different pathways such as increasing antioxidant compounds such as non-enzymatic antioxidants or enzymatic antioxidants [68].

Various results suggest that the adverse effects of water stress can be minimized by the application of MET. Zhang et al. (2013) showed that water-stressed cucumber (C. sativus L.) seedlings treated with MET clearly had a higher photosynthetic rate, thus reversing the effect of water stress. MET treatment significantly reduced Chl degradation, increased antioxidant levels and enhanced the activities of ROS scavenging enzymes such as SOD, POD, and CAT [119]. In naked oat (Avena nuda L.), the effects of exogenous MET on the antioxidant capacity of the plants under drought stress has also been shown. The results showed that a MET pretreatment reduced the levels of H_2O_2 and O_2-. and enhanced SOD, POD, CAT and APX activities in the leaves of naked oat seedlings under drought stress. Similarly, MET upregulated the expression levels of the mitogen-activated protein kinases (MAPKs) Asmap1 and Aspk11, and the transcription factor (TF) genes (except for NAC), WRKY1, DREB2, and MYB. These authors demonstrated that MET could induce the expression of MAPKs and TFs and therefore regulate the expression of downstream stress-responsive genes, thereby increasing the plant's drought tolerance [120]. Moreover, genetic analyses in A. thaliana Columbia (Col-0) suggested that in the plant defense response, MET as a signaling molecule functioned downstream of ROS and upstream of MAPK cascades [32].

In maize plants (Z. mays L. cv. Zhengdan 958) the mitigating potential of MET application against drought stress was demonstrated by the enhancement of the photosynthetic efficiency and the activities of antioxidants enzymes, as well as by the increases in the concentration of soluble proteins and Pro, which function as osmoprotectants under drought [121]. In addition, Huang et al. (2019) confirmed that MET application to maize (Z. mays L.) seedlings in the irrigation solution and in direct contact with the roots, showed a more effective protective role under drought stress than the leaf-spraying method. The signals from the exogenous MET received by the roots could affect the stress responses of the leaves, and the MET signals perceived by the leaves could also result in changes to different physiological metabolic processes of the roots under the stress. Therefore, the different organs of the seedlings acted in coordination, resulting in the systemic acclimation against drought stress. In this sense, Zhang et al. (2019) observed that the application of exogenous MET at the

seedling and flowering stages of soybean (Glycine max L. Merrill) was effective for alleviating plant damage caused by water deficit stress. MET enhanced PSII efficiency and the leaf area index, slowed down oxidative stress and damage to leaves by increasing the activity of antioxidant enzymes (SOD, POD, and CAT) and reduced the content of MDA. In addition, their results also showed that the application of exogenous MET through the root system was more effective than the foliar spraying [123].

Another more detailed study in grafted Chinese hickory (Carya cathayensis) plants revealed that exogenously-applied MET successfully recovered the growth of plants and improved photosynthetic efficiency [124]. The results of this work showed that the exogenously-applied MET resulted in enhanced ROS scavenging and the accumulation of compatible solutes such as total soluble sugars and Pro. Moreover, the analyses using metabolomics demonstrated that drought-stressed plants treated with MET showed differentially-regulated key metabolic pathways such as phenylpropanoid, Chl and carotenoid biosynthesis, carbon fixation, and sugar metabolism. It was also observed that MET cross talked with other hormones (zeatin, gibberellin A14, 24-epibrassinolide, jasmonic acid, and ABA) to regulate these physiological processes [124]. The role of MET in improving Moringa oleifera L. growth and yield under sandy soil conditions, which retains little water, has also been demonstrated [118]. MET improved photosynthetic pigments, the contents of phenolics and some elements, and antioxidant enzyme systems, whereas it decreased the content of MDA as compared with their corresponding untreated controls [118]. Lastly, in a different study, the authors overexpressed ASMT, an enzyme that synthesizes MET, in transgenic A. thaliana plants. The transgenic A. thaliana plants had an increased MET concentration and a significant decrease in ROS as compared to wild type plants, and therefore these plants exhibited greater tolerance to drought stress than their wild types [125].

Other results revealed that the rhizospheric application of MET remarkably enhanced the drought tolerance of alfalfa (Medicago sativa L.) plants through nitro-oxidative homeostasis through the regulation of reactive oxygen (SOD, GR, CAT, APX) and nitrogen species (NR, NADH dehydrogenase) metabolic enzymes at the enzymatic and/or transcript level. MET pre-treatment was correlated with the latter significant down-regulation of NR transcript levels, which is the key biosynthetic enzyme for NO generation in plants [126].

3.5. High light stress

Light is essential for photosynthesis but, on the other hand, high light plays a role as an environmental stressor that elicits ROS production in plants, resulting in extensive photooxidative damage [127]. Specifically, natural levels of UV-B (280–315 nm wavelength) play important roles in the regulation of plant growth and development. Nevertheless, elevated UV-B doses can induce deleterious effects, including disruption of the integrity and function of important macromolecules (DNA, lipids and proteins), oxidative damage, and photosynthesis deficiency [128]. Extended exposure to UV-B may also negatively affect growth and productivity and may produce photomorphogenic effects on plants [129,130]. As described previously for other types of abiotic stresses, high light stress also induced the cell's antioxidant system to cope with the excess ROS generated under these conditions. In this sense, flavonoids and related phenolic compounds can absorb UV-B radiation, acting as a protective shield in leaves [71]. In addition, it has been shown that MET is also related to tolerance to light stress. As evidence of this, MET levels have been shown to be more elevated in Alpine and Mediterranean plant species, which are exposed to more ultraviolet light than their lower-latitude counterparts [131].

For the first time, Afreen et al. (2006) provided proof of the presence of MET in the roots of mature Glycyrrhiza uralensis plants grown under white, blue, and red light, showing that the concentration

varied depending on the wavelength of the light spectrum utilized, in the following order: red ⊚⊚ blue ⊚ white light. The increase in MET concentration was proportional to the intensity of UV exposure and may function to protect the G. uralensis plant from oxidative damage from the production of ROS as a response to UV irradiation.

Various genetic pieces of evidence have demonstrated that MET synthesis is induced under high light stress in A. thaliana, which confers high light stress tolerance by scavenging ROS or inducing various antioxidant enzymes. The first evidence found was that MET-deficient snat1 A. thaliana was vulnerable to high light stress. Second, the complementation of the snat1 mutant with SNAT1 genomic DNA confirmed that the high light-susceptible phenotype was caused by the loss of SNAT1, preventing MET induction. Third, SNAT1 overexpression enabled high light stress tolerance in A.thaliana. The same work verified that MET was involved in efficient $1O_2$ detoxification in combination with other antioxidant molecules, such as carotenoids, tocopherol and plastoquinones [131]. Moreover, exogenous MET reduced the negative effect of excess light by increasing the efficiency of the photosystems and rearranging the expression of chloroplast- and nuclear-encoded genes (housekeeping genes involved in maintaining transcriptional activity and the functional state of chloroplasts) in detached A. thaliana leaves [133].

The influence of exogenous MET was also studied in Malus hupehensis Rehd. seedlings under two levels of UV-B radiation. In general, the MET solution alleviated the reduction in plant growth, biomass production, and root system under UV-B stress, especially at the higher dose of UV-B radiation. The inhibitory effects of UV-B radiation on photosynthetic parameters, Chl fluorescence parameters, stomatal apertures, Chl levels, and leaf membrane damages were also markedly alleviated with MET application. This treatment was also associated with a higher activity and expression of genes encoding antioxidant enzymes (APX, CAT and POD) and a greater decline of H_2O_2 content in leaves exposed to UV-B. Moreover, exogenous MET treatment and UV-B stress increased the concentration of endogenous MET and several phenolic compounds, including chlorogenic acid, phloridzin and quercetin-3-galactoside [130].

Currently there are no studies that link MET with NO in the response to high light stress. However, different studies have shown that NO is involved in the tolerance to high light stress [134]. Kim et al. (2010) demonstrated that NO was involved in the high light tolerance of maize (Zea mays L.) leaves of seedlings. The NO donor permitted the survival of more green leaf tissue than in non-treated controls under UV-B stress. Moreover, NO-treated seedlings had an increased concentration of flavonoids and anthocyanins, UV-B absorbing compounds, and MDA. Lastly, the NO donor under UV-B stress increased the CAT and APX activities to a greater degree [135]. In the same way, UV-B strongly induced NO production, which protected the green alga Chlorella pyrenoidosa against UV-B-induced oxidative damage [136].

On the other hand, it has been observed that in the response to stress due to high light, NO interacts with other molecules. For example, the interplay between NO and inositol signaling can be involved in the mediation of UV-B-initiated oxidative stress in A. thaliana cells [137] or the causal and interdependent relationship between NO and H_2O_2 induces stomatal closure in broad bean (Vicia faba L.) under UV-B [138]. Similarly, it is considered that salicylic acid, SNP, and especially their combination, could alleviate UV-B stress in dwarf polish wheat (Triticum polonicum L.) [139]. Ultimately, Cassia et al. (2019) showed that UV-B perception triggers an increase in ABA concentration, which increases H_2O_2 and induces NO. Therefore, it is probable that there could be a relationship between MET and NO for combating high light stress.

3.6. Waterlogging

Waterlogging has been suggested as a major environmental stress that affects crop survival, growth, and productivity in those areas prone to heavy rainfall, poor soil drainage, and high water table

fluctuations [141,142]. At the early stage during waterlogging, the elevated ROS molecules function as an important second messenger in signaling for a response. Following a prolonged period of waterlogging, the increased anaerobic respiration of roots and the stomata closure response in leaves induces a burst of excessive ROS production. If the excessive ROS is not migrated properly, it will cause plant oxidative damage, and finally resulting in rotting of roots and the wilting of leaves [143,144]. Plants have defense mechanisms against waterlogging that are both enzymatic and non-enzymatic, although it has later been shown that perhaps one of the most effective mechanisms may be MET.

For instance, Zheng et al. (2017) showed that MET significantly improved the tolerance of Malus baccata (Linn.) Borkh. seedlings against waterlogging stress. To maintain aerobic respiration, MET preserved photosynthesis and reduced the oxidative damage of the plants under waterlogging stress. MET application also enhanced the gene expression of its synthesis enzymes (MbT5H1, MbAANAT3, MbASMT9) increasing its concentration. Lastly, when exogenous MET meets the requirement of the plants it was found that the synthesis of the MbASMT9 protein was suppressed.

In the same manner, in alfalfa plants (Medicago sativa L.) an exogenous application of MET also had a significant involvement in mitigating waterlogging stress[146]. The researchers observed that first, MET suppressed ethylene production through the downregulation of the ethylene biosynthesis-related genes and the mitigation of waterlogging-induced growth reduction, chlorosis, and premature senescence in plants. Subsequently, MET increased PA content by enhancing the activity and gene expressions of the PA metabolism enzymes. Thus, MET mitigated waterlogging stress through cross-talk with or by directly modulating the metabolic pathways of PAs and ethylene in alfalfa [146].

Additionally, in mitochondria, NO generation is a significant process at low oxygen conditions, as nitrite acts as an electron acceptor, maintaining the recycling of NADH and restricting the amount of ATP [147]. Later, at low O2 concentrations, the ubiquitous proteins called "class 1 hemoglobins" or "phytoglobins" scavenge NO and thus contribute to the regeneration of NAD and nitrate. Moreover, the induction of phytoglobins genes alleviated flooding stress by allowing the correct functioning of photosynthesis and limiting ROS-induced damage [148,149]. For example, the overexpression of class 1 phytoglobin enhanced NO scavenging activity and increased tolerance to hypoxic stress in Lotus japonicus plants under flooding stress [150].

In soybeans (Glycine max L.), Khan et al. (2019) observed that the application of a NO donor could mitigate the negative effects of short-term flooding stress through the reduction of the oxidative stress. More specifically, Salas et al. (2019) demonstrated that NO is produced in the nodules of soybean plants grown in flooded soils that contain nitrates. In addition, in two varieties of wheat (Triticum aestivum L. cv. Dogankent and T. aestivum cv. Ducula-4). the application of waterlogging and waterlogging + NO increased antioxidant enzyme activity as well as the expression of the genes that were studied, i.e. Myb2, PDPK, and SST1, specifically during the early hours of treatment, although this was higher in the Wt + NO condition [153]. On the other hand, Chen et al. (2016) have provided support to the hypothesis that NO increases waterlogging tolerance by increased adventitious root formation and endogenous NO production via the upregulation of NOS activity in Suaeda salsa L. [154]. Lastly, three tree species Alnus glutinosa L., Populus tremula L. and Quercus rubra L. have different flooding tolerance and not the same NO production under waterlogging stress. Copolovici and Niinemets (2010) demonstrated that the tolerance to flood stress was proportionally related to the amount of NO emitted during longer-term condition under this stress. At present, studies on the relationship of MET with NO in response to waterlogging stress, have not been found. However, as with most stresses, this relationship must exist in the response to this particular stress.

3.7. Nutrient Deficiency

For the normal growth of the plants, chemical elements such as N, K, Ca, P, Fe and S, among others, are necessary. Along the same line as the other abiotic stresses described previously, the positive role of MET against soil mineral deficiency has been described in several studies [156,157]. In the same manner, another key molecule in the response to changes in nutrient availability is NO. The rate of NO synthesis or NO degradation is normally affected by nutrient imbalances. In turn, changes in the level of NO modify plant morphology and/or regulate the nutrient homeostasis, through its interaction with reactive oxygen species and phytohormones, and through the post-translational modification of proteins [158].

In seedlings of A. thaliana under Fe deficiency, exogenous MET significantly increased the soluble Fe content of shoots and roots, and decreased the levels of root cell wall Fe bound to pectin and hemicellulose, allowing for the remobilization of cell wall Fe and the alleviation of Fe deficiency-induced chlorosis. Additionally, Fe deficiency quickly induced MET biosynthesis, acting synergistically with exogenous treatments [159]. On the other hand, NO also acts to enhance iron nutrition in plants under Fe-deficient stress. NO is related to the reduction of Fe^{3+} to Fe^{2+} and it could be one of the key process involved in iron homeostasis [160,161]. NO also seems to be involved in the formation of dinitrosyl–iron complexes (DNICs) perhaps linked to glutathione, which could facilitate iron transport through cell membranes [160]. In addition, NO could modulate the expression and activity of specific transporters. In short, all of these evidences relate NO to the tolerance against Fe starvation stress [162].

In winter wheat (Triticum aestivum L., cv. Changhan58) grown in a N deficient medium, the application of MET to the hydroponic solution significantly improved seedling growth. The MET treatment produced higher N contents and nitrate levels in shoots under N deficient conditions and also maintained higher nitrogen content in the shape of nitrate in roots. Furthermore, nitrate reductase and glutamine synthetase activities were higher under these conditions. Thus, MET improved assimilation through the upregulation of the activities of N uptake and N metabolism-related enzymes [157]. In addition, low N increased auxin transport from the shoot to the root, which stimulated the production of NO and afterwards, promoted the synthesis of strigolactones to accelerate cell division, ultimately enhancing the elongation of the primary root [163,164]. Also, Sun et al. (2015) found that in rice (Oryza sativa L.), NO participated in the enhancement of N uptake capacity through the regulation of lateral root formation and inorganic N uptake.

Regarding the deficiency of S in the soil, researchers have observed that the application of MET in tomato (S. lycopersicum L. cv. Ailsa Craig) seedlings decreased ROS content and alleviated growth inhibition as a result of a reduced chlorophyll content, photosynthesis, and biomass accumulation. MET promoted S uptake and its assimilation by regulating the expression of genes encoding the enzymes involved in S transport and metabolism, supporting the role of MET as a molecule that improves primary metabolism and redox homeostasis [156].

In brief, both MET and NO are involved in the regulation of nutrient deficiency tolerance. Nevertheless, there is still much to study, as there could be an interaction between MET and NO that could be important in the response of plants under this stress.

3.8. Abiotic stress combination

Recent studies have shown that the plant's response to the combination of two or more abiotic stresses is highly specific and therefore cannot be extrapolated/deduced from the responses obtained when these stresses are applied individually [166–172].

In the same manner, MET does not act in the same manner against an individual stress as against combined stresses, and our research group has already shown how MET can also help improve the negative effects of abiotic stress combination. Thus, Martinez et al. (2018) described how tomato plants (S. lycopersicon cv. Boludo) grown under the combination of salinity and heat, and previously treated with exogenous MET, showed a different modulation in the expression on specific antioxidant-related genes and their related enzymes. More specifically, APX, GR, GPX and phospholipid hydroperoxide glutathione peroxidase showed an antagonistic regulation as compared to plants that did not receive MET. This translated into a better antioxidant capacity and to a lesser ROS accumulation under stress combination. The performance of the photosynthesis parameters and the photosystems was also increased in plants treated with exogenous MET under the combination of salinity and heat at physiological and biochemical levels [10].

Similarly, in rice seeds (Oryza sativa cv. Dongjin), 2-OHMET alleviated the combined effects of cold and drought stresses via the actions of multiple TFs, including Myb4 and AP37, whereas no tolerance was observed in seedlings treated with either MET or water (control). The tolerance phenotype was associated with the induction of several transporter proteins, including a proton transporter (UCP1), a potassium transporter (HKT1), and a water channel protein (PIP2;1). Treatment with 2-OHMET also increased the content of the osmoprotectant Pro and maintained mitochondrial structure when plants were subjected to a combination of cold and drought stress [18].

As we previously described for nutrient deficiencies, MET application helped plants to improve nutrient absorption and transport. Ding et al. (2018) observed that under stress combining high light and N deficiency in Haematococcus pluvialis, MET induced the accumulation of astaxanthin, which was associated with the activation of the cyclic adenosine monophosphate (cAMP) signaling pathway and the signaling cascade of NO-mediated MAPK [173]. In this sense, in pepper (Capsicum annuum L. cv Semerkand) plants, the tolerance to Fe deficiency or salinity stress, applied individually, induced by MET, was shown to involved the downstream signal crosstalk between NO and H2S. However, MET was not very effective when Fe deficiency and salinity stress were applied together [174]. Consequently, more studies are necessary to elucidate a possible role of MET and NO in the tolerance mechanisms induced by field conditions.

Table 1. Some relevant studies about   roles melatonin plays in response to abiotic stresses in plants

Abiotic stress	Plant specie	Regulated element	Reference
Salinity with alcalinity	*Leymus chinensis*	antioxidant systems, photosynthetic activity, arbuscular mycorrhizal fungal growth	[78]
Salinity	Tomato (*S. lycopersicum* L.)	photosynthetic activity, lipid peroxidation, capacity of the AsA –GSH cycle, balance of K+ and Na+	[79]
	Potato (*Ipomoea batatas* L.)	homeostatic balance of Na + and K +	[80]
	Malus hupehensis	cell membrane damage, root system architecture, SOD, POD, CAT, PAs synthesis	[82]
	Tomato (*Solanum lycopersicum* L.)	ROS levels, PET, D1 protein.	[77]
	Watermelon (*Citrullus lanatus*)	stomatal closure, light energy absorption, PET in PSII, activities of antioxidant enzymes	[83]
	Alfalfa (*Medicago sativa*)	scavenging ROS, activities of antioxidant enzymes	[84]
	(*Fragaria × ananassa*)	antioxidant enzymes, ABA	[85]
	Rapeseed (*Brassica napus* L.)	NR and NOA1- dependent NO concentration	[86]
	Sunflower (*Helianthus annuus* L.)	SOD isoforms (Cu/Zn SOD and Mn SOD), NO	[87]
	Sunflower (*H. annuus* L.)	GR activity, GSH content	[88]
	Tomato (*S. lycopersicum* L.)	Na^+ accumulation, uptake K^+, antioxidant enzyme activity, ASA–GSH detoxification capacity, NO	[89]
High temperature	Kiwifruit (*Actinidia deliciosa*)	H_2O_2 and Pro content, AsA levels, activity of several antioxidant enzymes, GST	[96]
	Tall fescue (*Festuca arundinacea*)	ROS level, EL, membrane lipid peroxidation, MDA, Chl, total protein, antioxidant enzyme activities	[97]
	Maize (*Zea mays* L.)	MDA and EL levels, GR, CAT, AsA, GSH, MG detoxification, osmoregulation system	[98]
	Tomato (*S. lycopersicum* L.)	activity of APX and CAT	[99]
	Tomato (*S. lycopersicum* L.)	ROS levels, RuBisCo activity	[100]
	Tomato (*S. lycopersicum* L.)	ROS accumulation in the anthers, activity of antioxidant enzymes, heat shock protein	[101]
	Tomato (*S. lycopersicum* L.)	antioxidant defense mechanisms, AsA-GSH cycle, polyamines metabolic pathway, NO	[95]
Low temperature	*Arabidopsis thaliana*	CBFs/DREBs, COR15a, CAMTA1, ZAT10, ZAT12.	[110]
	Cucumber (*Cucumis sativus* L.)	levels of AsA and GSH, SOD, APX, MDHAR, DHAR, GR in the AsA–GSH cycle	[111]
	Cucumber (*C. sativus* L.)	antioxidant enzymes especially SOD and GSSG-R, synthesis of glutathione, GSH/GSSG ratio	[112]
	Elymus nutans	ABA, downstream cold-responsive genes such as *EnCBF9*, *EnCBF14*, and *EnCOR14a*	[113]
	Tea (*Camellia sinensis* L.)	photosynthetic capacity, antioxidant potential, redox homeostasis	[103]
	Tomato (*S. lycopersicum* L.)	accumulation of ROS, lipid peroxidation	[67]
	Tomato (*Lycopersicon esculentum*)	arginine pathway activity, polyamines, electolyte, MDA, NO accumulation	[58]
Drought	Cucumber (*C. sativus* L.)	photosynthetic rate, Chl degradation, SOD, POD, CAT	[119]
	Naked oat (*Avena nuda* L.)	levels of H_2O_2 and O_2^-, SOD, POD, CAT and APX activities, MAPKs,TFs (WRKY1, DREB2 and MYB)	[120]
	Maize plants (*Z. mays* L.)	photosynthetic efficiency, activities of antioxidants enzymes, soluble proteins, Pro	[121]
	Maize (*Z. mays* L.)	D1 protein, photosynthesic activities, antioxidantive defense system	[122]
	Soybean (*Glycine max* L.	PSII efficiency, leaf area index, activity of SOD, POD, CAT, MDA.	[123]
	Chinese hickory (*Carya cathayensis*)	ROS scavenging activity, photosynthetic activity, soluble sugars, Pro	[124]
	Moringa oleifera L.	photosynthetic pigments phenolic, antioxidant enzyme systems, MDA content	[118]
	Alfalfa (*Medicago sativa* L.)	SOD, GR, CAT, APX, NR, NadDe	[126]
	A. thaliana	scavenging ROS, antioxidant enzymes	[131]
	A. thaliana	photosystems efficiency, oxidative damage	[133]
	Malus hupehensis	photosynthetic parameters, Chl fluorescence parameters, stomatal apertures, APX, CAT, POD	[130]
Waterlogging stress	*Malus baccata*	photosynthesis, oxidative damage	[145]
	Alfalfa plants (*Medicago sativa* L.)	ethylene production, polyamine content	[146]
Fe deciency	*A. thaliana*	remobilizing cell wall Fe, chlorosis	[159]
N deficiency	Winter wheat (*Triticum aestivum* L.)	N contents and nitrate levels, NR and GS activities	[157]
S deficiency	Tomato (*S. lycopersicum* L.)	ROS content, chlorophyll content, photosynthesis, enzymes involved in S transport and metabolism	[156]
Salinity+high temperatre stress combination	Tomato (*S. lycopersicon*)	antioxidant capacity, photosynthesis parameters, APX, GR, GPX, Ph-GPX	[10]
Low temperature+ droght stress combination	Rice (*Oryza sativa*)	several transporter proteins, Pro content, mitochondrial structure	[18]
High light + N deficiency stress combination	*Haematococcus pluvialis*	astaxanthin, cAMP signaling pathway, signaling cascade of NO-mediated MAPK.	[173]
Fe deficiency + salinity stress combination	Pepper (*Capsicum annuum* L.)	NO, H_2S	[174]

4. Conclusions and future perpectives

Melatonin (MET) seems to play a relevant role in alleviating abiotic stress directly through scavenging ROS and RNS, and indirectly through enhancing antioxidant activities and photosynthetic capacity, regulating plant growth regulators, increasing osmotic metabolites, and downregulating or upregulating stress-related genes in plants. Recent research studies have also shown that MET treatment increases the stress tolerance of plants. Wei et al. (2018) have discovered the receptor of MET, CAND2/PMTR1, in Arabidopsis, although the transduction mechanism is not well understood, and whether or not more types of MET receptors exist, is unknown. In addition, relatively few research studies have been focused on the genes and core pathways that are precisely regulated by MET. On the other hand, NO is also a signaling molecule involved in numerous physiological functions, and therefore plays essential roles in the responses to various abiotic stresses. Some studies have demonstrated that MET is involved in the signaling pathway that is directly mediated by NO, even though their relationship is still unclear. Most research studies on endogenous MET and NO are also necessary, as most works have only focused on exogenous MET. Moreover, it is fundamental to understand the different responses depending on the type of stress, and if all of these responses operate through MET and NO. Lastly, S-nitrosation target proteins have not yet been identified, and the NO signaling pathway is not well understood. Ultimately, MET and NO are potentially important molecules in the regulation of ROS and RNS under abiotic stress conditions, but there is still much to understand about how they interact with each other and the nature of their mechanisms of action.

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References

1.   1.   Kul, R.; Esringü, A.; Dadasoglu, E.; Sahin, Ü.; Turan, M.; Örs, S.; Ekinci, M.; Agar, G.; Yildirim, E. Melatonin: Role in Increasing Plant Tolerance in Abiotic Stress Conditions. Abiotic and Biotic Stress in Plants 2019, doi:10.5772/intechopen.82590.

2.   2.   Piao, S.; Liu, Q.; Chen, A.; Janssens, I.A.; Fu, Y.; Dai, J.; Liu, L.; Lian, X.; Shen, M.; Zhu, X. Plant phenology and global climate change: Current progresses and challenges. Global Change Biology 2019, 25, 1922–1940, doi:10.1111/gcb.14619.

3.   3.   Zandalinas, S.I.; Sengupta, S.; Burks, D.; Azad, R.K.; Mittler, R. Identification and characterization of a core set of ROS wave-associated transcripts involved in the systemic acquired acclimation response of Arabidopsis to excess light. The Plant Journal 2019, 98, 126–141, doi:10.1111/tpj.14205.

4.   4.   Ciais, P.; Reichstein, M.; Viovy, N.; Granier, A.; Ogée, J.; Allard, V.; Aubinet, M.; Buchmann, N.; Bernhofer, C.; Carrara, A.; et al. Europe-wide reduction in primary productivity caused by the heat and drought in 2003. Nature 2005, 437, 529–533, doi:10.1038/nature03972.

5.   5.   Bailey-Serres, J.; Parker, J.E.; Ainsworth, E.A.; Oldroyd, G.E.D.; Schroeder, J.I. Genetic strategies for improving crop yields. Nature 2019, 575, 109–118, doi:10.1038/s41586-019-1679-0.

6.   6.   Miller, G.; Schlauch, K.; Tam, R.; Cortes, D.; Torres, M.A.; Shulaev, V.; Dangl, J.L.; Mittler, R. The Plant NADPH Oxidase RBOHD Mediates Rapid Systemic Signaling in Response to Diverse Stimuli. Sci. Signal. 2009, 2, ra45, doi:10.1126/scisignal.2000448.

7.   7.   Suzuki, N.; Miller, G.; Salazar, C.; Mondal, H.A.; Shulaev, E.; Cortes, D.F.; Shuman, J.L.; Luo, X.; Shah, J.; Schlauch, K.; et al. Temporal-Spatial Interaction between Reactive Oxygen Species and Abscisic Acid Regulates Rapid Systemic Acclimation in Plants. Plant Cell 2013, 25, 3553, doi:10.1105/tpc.113.114595.

8.   8.   Fichman, Y.; Miller, G.; Mittler, R. Whole-Plant Live Imaging of Reactive Oxygen Species. Molecular Plant 2019, 12, 1203–1210, doi:10.1016/j.molp.2019.06.003.

9.   9.   Nguyen, C.T.; Kurenda, A.; Stolz, S.; Chételat, A.; Farmer, E.E. Identification of cell populations necessary for leaf-to-leaf electrical signaling in a wounded plant. Proc Natl Acad Sci USA 2018, 115, 10178, doi:10.1073/pnas.1807049115.

10.   10.   Martinez, V.; Nieves-Cordones, M.; Lopez-Delacalle, M.; Rodenas, R.; Mestre, T.C.; Garcia-Sanchez, F.; Rubio, F.; Nortes, P.A.; Mittler, R.; Rivero, R.M. Tolerance to Stress Combination in Tomato Plants: New Insights in the Protective Role of Melatonin. Molecules 2018, 23, 535, doi:10.3390/molecules23030535.

11.   11.   Arnao, M.B.; Hernández-Ruiz, J. Is Phytomelatonin a New Plant Hormone? Agronomy 2020, 10, 95, doi:10.3390/agronomy10010095.

12.   12.   Lerner, A.B.; Case, J.D.; Takahashi, Y.; Lee, T.H.; Mori, W. ISOLATION OF MELATONIN, THE PINEAL GLAND FACTOR THAT LIGHTENS MELANOCYTES1. J. Am. Chem. Soc. 1958, 80, 2587–2587, doi:10.1021/ja01543a060.

13.   13.   Dubbels, R.; Reiter, R.J.; Klenke, E.; Goebel, A.; Schnakenberg, E.; Ehlers, C.; Schiwara, H.W.; Schloot, W. Melatonin in edible plants identified by radioimmunoassay and by high performance liquid chromatography-mass spectrometry. Journal of Pineal Research 1995, 18, 28–31, doi:10.1111/j.1600-079X.1995.tb00136.x.

14.   14.   Hattori, A.; Migitaka, H.; Iigo, M.; Itoh, M.; Yamamoto, K.; Ohtani-Kaneko, R.; Hara, M.; Suzuki, T.; Reiter, R.J. Identification of melatonin in plants and its effects on plasma melatonin levels and binding to melatonin receptors in vertebrates. Biochem. Mol. Biol. Int. 1995, 35, 627–634.

15.   15.   Debnath, B.; Islam, W.; Li, M.; Sun, Y.; Lu, X.; Mitra, S.; Hussain, M.; Liu, S.; Qiu, D. Melatonin Mediates Enhancement of Stress Tolerance in Plants. International Journal of Molecular Sciences 2019, 20, 1040, doi:10.3390/ijms20051040.

16.   16.   Hardeland, R.; Cardinali, D.P.; Srinivasan, V.; Spence, D.W.; Brown, G.M.; Pandi-Perumal, S.R. Melatonin—A pleiotropic, orchestrating regulator molecule. Progress in Neurobiology 2011, 93, 350–384, doi:10.1016/j.pneurobio.2010.12.004.

17.   17.   Byeon, Y.; Tan, D.-X.; Reiter, R.J.; Back, K. Predominance of 2-hydroxymelatonin over melatonin in plants. Journal of Pineal Research 2015, 59, 448–454, doi:10.1111/jpi.12274.

18.   18.   Lee, H.-J.; Back, K. 2-Hydroxymelatonin promotes the resistance of rice plant to multiple simultaneous abiotic stresses (combined cold and drought). J. Pineal Res. 2016, 61, 303–316, doi:10.1111/jpi.12347.

19.   19.   Zhao, D.; Yu, Y.; Shen, Y.; Liu, Q.; Zhao, Z.; Sharma, R.; Reiter, R.J. Melatonin Synthesis and Function: Evolutionary History in Animals and Plants. Front Endocrinol (Lausanne) 2019, 10, doi:10.3389/fendo.2019.00249.

20.   20.   Back, K.; Tan, D.-X.; Reiter, R.J. Melatonin biosynthesis in plants: multiple pathways catalyze tryptophan to melatonin in the cytoplasm or chloroplasts. Journal of Pineal Research 2016, 61, 426–437, doi:10.1111/jpi.12364.

21.   21.   Erland, L.A.E.; Murch, S.J.; Reiter, R.J.; Saxena, P.K. A new balancing act: The many roles of melatonin and serotonin in plant growth and development. Plant Signaling & Behavior 2015, 10, e1096469, doi:10.1080/15592324.2015.1096469.

22.   22.   Wang, L.; Feng, C.; Zheng, X.; Guo, Y.; Zhou, F.; Shan, D.; Liu, X.; Kong, J. Plant mitochondria synthesize melatonin and enhance the tolerance of plants to drought stress. Journal of Pineal Research 2017, 63, e12429, doi:10.1111/jpi.12429.

23.   23.   Ma, Y.; Jiao, J.; Fan, X.; Sun, H.; Zhang, Y.; Jiang, J.; Liu, C. Endophytic Bacterium Pseudomonas fluorescens RG11 May Transform Tryptophan to Melatonin and Promote Endogenous Melatonin Levels in the Roots of Four Grape Cultivars. Front. Plant Sci. 2017, 7, doi:10.3389/fpls.2016.02068.

24.   24.   Zhang, N.; Sun, Q.; Zhang, H.; Cao, Y.; Weeda, S.; Ren, S.; Guo, Y.-D. Roles of melatonin in abiotic stress resistance in plants. J. Exp. Bot. 2015, 66, 647–656, doi:10.1093/jxb/eru336.

25.   25.   Posmyk, M.M.; Kuran, H.; Marciniak, K.; Janas, K.M. Presowing seed treatment with melatonin protects red cabbage seedlings against toxic copper ion concentrations. Journal of Pineal Research 2008, 45, 24–31, doi:10.1111/j.1600-079X.2007.00552.x.

26.   26.   Arnao, M.B.; Hernández-Ruiz, J. Melatonin: plant growth regulator and/or biostimulator during stress? Trends in Plant Science 2014, 19, 789–797, doi:10.1016/j.tplants.2014.07.006.

27. 27. Nawaz, M.A.; Huang, Y.; Bie, Z.; Ahmed, W.; Reiter, R.J.; Niu, M.; Hameed, S. Melatonin: Current Status and Future Perspectives in Plant Science. Front Plant Sci 2016, 6, doi:10.3389/fpls.2015.01230.

28. 28. Arnao, M.B.; Hernández-Ruiz, J. Role of Melatonin to Enhance Phytoremediation Capacity. Applied Sciences 2019, 9, 5293, doi:10.3390/app9245293.

29. 29. Arnao, M.B.; Hernández-Ruiz, J. Functions of melatonin in plants: a review. Journal of Pineal Research 2015, 59, 133–150, doi:10.1111/jpi.12253.

30. 30. Wang, Y.; Reiter, R.J.; Chan, Z. Phytomelatonin: a universal abiotic stress regulator. J Exp Bot 2018, 69, 963–974, doi:10.1093/jxb/erx473.

31. 31. Wei, J.; Li, D.-X.; Zhang, J.-R.; Shan, C.; Rengel, Z.; Song, Z.-B.; Chen, Q. Phytomelatonin receptor PMTR1-mediated signaling regulates stomatal closure in Arabidopsis thaliana. Journal of Pineal Research 2018, 65, e12500, doi:10.1111/jpi.12500.

32. 32. Lee, H.Y.; Back, K. Melatonin is required for H2O2- and NO-mediated defense signaling through MAPKKK3 and OXI1 in Arabidopsis thaliana. Journal of Pineal Research 2017, 62, e12379, doi:10.1111/jpi.12379.

33. 33. Astier, J.; Gross, I.; Durner, J. Nitric oxide production in plants: an update. J. Exp. Bot. 2018, 69, 3401–3411, doi:10.1093/jxb/erx420.

34. 34. Bethke, P.C.; Badger, M.R.; Jones, R.L. Apoplastic Synthesis of Nitric Oxide by Plant Tissues. The Plant Cell 2004, 16, 332–341, doi:10.1105/tpc.017822.

35. 35. Campbell, W.H. Structure and function of eukaryotic NAD(P)H:nitrate reductase. CMLS, Cell. Mol. Life Sci. 2001, 58, 194–204, doi:10.1007/PL00000847.

36. 36. Rockel, P.; Strube, F.; Rockel, A.; Wildt, J.; Kaiser, W.M. Regulation of nitric oxide (NO) production by plant nitrate reductase in vivo and in vitro. J Exp Bot 2002, 53, 103–110, doi:10.1093/jexbot/53.366.103.

37. 37. Yamasaki, H.; Sakihama, Y.; Takahashi, S. An alternative pathway for nitric oxide production in plants: new features of an old enzyme. Trends Plant Sci. 1999, 4, 128–129, doi:10.1016/s1360-1385(99)01393-x.

38. 38. Yamasaki, H.; Sakihama, Y. Simultaneous production of nitric oxide and peroxynitrite by plant nitrate reductase: in vitro evidence for the NR-dependent formation of active nitrogen species. FEBS Letters 2000, 468, 89–92, doi:10.1016/S0014-5793(00)01203-5.

39. 39. Chamizo-Ampudia, A.; Sanz-Luque, E.; Llamas, Á.; Ocaña-Calahorro, F.; Mariscal, V.; Carreras, A.; Barroso, J.B.; Galván, A.; Fernández, E. A dual system formed by the ARC and NR molybdoenzymes mediates nitrite-dependent NO production in Chlamydomonas. Plant, Cell & Environment 2016, 39, 2097–2107, doi:10.1111/pce.12739.

40. 40. Gupta, K.J.; Igamberdiev, A.U. The anoxic plant mitochondrion as a nitrite: NO reductase. Mitochondrion 2011, 11, 537–543, doi:10.1016/j.mito.2011.03.005.

41. 41. Planchet, E.; Gupta, K.J.; Sonoda, M.; Kaiser, W.M. Nitric oxide emission from tobacco leaves and cell suspensions: rate limiting factors and evidence for the involvement of mitochondrial electron transport. The Plant Journal 2005, 41, 732–743, doi:10.1111/j.1365-313X.2005.02335.x.

42. 42. Corpas, F.J.; Barroso, J.B. Nitric oxide synthase-like activity in higher plants. Nitric Oxide 2017, 68, 5–6, doi:10.1016/j.niox.2016.10.009.

43. 43. Nieves-Cordones, M.; López-Delacalle, M.; Ródenas, R.; Martínez, V.; Rubio, F.; Rivero, R.M. Critical responses to nutrient deprivation: A comprehensive review on the role of ROS and RNS. Environmental and Experimental Botany 2019, 161, 74–85, doi:10.1016/j.envexpbot.2018.10.039.

44. 44. Fares, A.; Rossignol, M.; Peltier, J.-B. Proteomics investigation of endogenous S-nitrosylation in Arabidopsis. Biochemical and Biophysical Research Communications 2011, 416, 331–336, doi:10.1016/j.bbrc.2011.11.036.

45. 45. Romero-Puertas, M.C.; Campostrini, N.; Mattè, A.; Righetti, P.G.; Perazzolli, M.; Zolla, L.; Roepstorff, P.; Delledonne, M. Proteomic analysis of S-nitrosylated proteins in Arabidopsis thaliana undergoing hypersensitive response. PROTEOMICS 2008, 8, 1459–1469, doi:10.1002/pmic.200700536.

46. 46. Gow, A.J.; Farkouh, C.R.; Munson, D.A.; Posencheg, M.A.; Ischiropoulos, H. Biological significance of nitric oxide-mediated protein modifications. American Journal of Physiology-Lung Cellular and Molecular Physiology 2004, 287, L262–L268, doi:10.1152/ajplung.00295.2003.

47. 47. Bartesaghi, S.; Radi, R. Fundamentals on the biochemistry of peroxynitrite and protein tyrosine nitration. Redox Biology 2018, 14, 618–625, doi:10.1016/j.redox.2017.09.009.

48.   48.   Radi, R. Nitric oxide, oxidants, and protein tyrosine nitration. PNAS 2004, 101, 4003–4008, doi:10.1073/pnas.0307446101.

49.   49.   Begara-Morales, J.C.; Sánchez-Calvo, B.; Chaki, M.; Mata-Pérez, C.; Valderrama, R.; Padilla, M.N.; López-Jaramillo, J.; Luque, F.; Corpas, F.J.; Barroso, J.B. Differential molecular response of monodehydroascorbate reductase and glutathione reductase by nitration and S-nitrosylation. J Exp Bot 2015, 66, 5983–5996, doi:10.1093/jxb/erv306.

50.   50.   Begara-Morales, J.C.; Sánchez-Calvo, B.; Chaki, M.; Valderrama, R.; Mata-Pérez, C.; López-Jaramillo, J.; Padilla, M.N.; Carreras, A.; Corpas, F.J.; Barroso, J.B. Dual regulation of cytosolic ascorbate peroxidase (APX) by tyrosine nitration and S-nitrosylation. J Exp Bot 2014, 65, 527–538, doi:10.1093/jxb/ert396.

51.   51.   Besson-Bard, A.; Pugin, A.; Wendehenne, D. New Insights into Nitric Oxide Signaling in Plants. Annual Review of Plant Biology 2008, 59, 21–39, doi:10.1146/annurev.arplant.59.032607.092830.

52.   52.   Zhang, W.; Cao, J.; Fan, X.; Jiang, W. Applications of nitric oxide and melatonin in improving postharvest fruit quality and the separate and crosstalk biochemical mechanisms. Trends in Food Science & Technology 2020, 99, 531–541, doi:10.1016/j.tifs.2020.03.024.

53.   53.   Baudouin, E.; Hancock, J. Nitric oxide signaling in plants. Front. Plant Sci. 2014, 4, doi:10.3389/fpls.2013.00553.

54.   54.   Palma, J.M.; Freschi, L.; Rodríguez-Ruiz, M.; González-Gordo, S.; Corpas, F.J. Nitric oxide in the physiology and quality of fleshy fruits. J. Exp. Bot. 2019, 70, 4405–4417, doi:10.1093/jxb/erz350.

55.   55.   Wen, D.; Gong, B.; Sun, S.; Liu, S.; Wang, X.; Wei, M.; Yang, F.; Li, Y.; Shi, Q. Promoting Roles of Melatonin in Adventitious Root Development of Solanum lycopersicum L. by Regulating Auxin and Nitric Oxide Signaling. Front. Plant Sci. 2016, 7, doi:10.3389/fpls.2016.00718.

56.   56.   He, H.; He, L.-F. Crosstalk between melatonin and nitric oxide in plant development and stress responses. Physiologia Plantarum 2020, 170, 218–226, doi:10.1111/ppl.13143.

57.   57.   Aydogan, S.; Yerer, M.B.; Goktas, A. Melatonin and nitric oxide. J Endocrinol Invest 2006, 29, 281–287, doi:10.1007/BF03345555.

58.   58.   Aghdam, M.S.; Luo, Z.; Jannatizadeh, A.; Sheikh-Assadi, M.; Sharafi, Y.; Farmani, B.; Fard, J.R.; Razavi, F. Employing exogenous melatonin applying confers chilling tolerance in tomato fruits by upregulating ZAT2/6/12 giving rise to promoting endogenous polyamines, proline, and nitric oxide accumulation by triggering arginine pathway activity. Food Chemistry 2019, 275, 549–556, doi:10.1016/j.foodchem.2018.09.157.

59.   59.   Liu, J.; Yang, J.; Zhang, H.; Cong, L.; Zhai, R.; Yang, C.; Wang, Z.; Ma, F.; Xu, L. Melatonin Inhibits Ethylene Synthesis via Nitric Oxide Regulation To Delay Postharvest Senescence in Pears. J. Agric. Food Chem. 2019, 67, 2279–2288, doi:10.1021/acs.jafc.8b06580.

60.   60.   Berchner-Pfannschmidt, U.; Tug, S.; Trinidad, B.; Becker, M.; Oehme, F.; Flamme, I.; Fandrey, J.; Kirsch, M. The impact of N-nitrosomelatonin as nitric oxide donor in cell culture experiments. Journal of Pineal Research 2008, 45, 489–496, doi:10.1111/j.1600-079X.2008.00622.x.

61.   61.   Kopczak, A.; Korth, H.-G.; Groot, H. de; Kirsch, M. N-nitroso-melatonin releases nitric oxide in the presence of serotonin and its derivatives. Journal of Pineal Research 2007, 43, 343–350, doi:10.1111/j.1600-079X.2007.00484.x.

62.   62.   Zhu, Y.; Gao, H.; Lu, M.; Hao, C.; Pu, Z.; Guo, M.; Hou, D.; Chen, L.-Y.; Huang, X. Melatonin-Nitric Oxide Crosstalk and Their Roles in the Redox Network in Plants. International Journal of Molecular Sciences 2019, 20, 6200, doi:10.3390/ijms20246200.

63.   63.   Fedoroff, N.V.; Battisti, D.S.; Beachy, R.N.; Cooper, P.J.M.; Fischhoff, D.A.; Hodges, C.N.; Knauf, V.C.; Lobell, D.; Mazur, B.J.; Molden, D.; et al. Radically Rethinking Agriculture for the 21st Century. Science 2010, 327, 833–834, doi:10.1126/science.1186834.

64.   64.   Zhu, J.-K. Abiotic Stress Signaling and Responses in Plants. Cell 2016, 167, 313–324, doi:10.1016/j.cell.2016.08.029.

65.   65.   Cramer, G.R.; Urano, K.; Delrot, S.; Pezzotti, M.; Shinozaki, K. Effects of abiotic stress on plants: a systems biology perspective. BMC Plant Biology 2011, 11, 163, doi:10.1186/1471-2229-11-163.

66.   66.   Sharma, A.; Zheng, B. Melatonin Mediated Regulation of Drought Stress: Physiological and Molecular Aspects. Plants 2019, 8, 190, doi:10.3390/plants8070190.

67.   67.   Wang, M.; Zhang, S.; Ding, F. Melatonin Mitigates Chilling-Induced Oxidative Stress and Photosynthesis Inhibition in Tomato Plants. Antioxidants (Basel) 2020, 9, doi:10.3390/antiox9030218.

68.   68.   Elhamid, E.M.A.; Sadak, M.S.; Tawfik, M.M. Alleviation of Adverse Effects of Salt Stress in Wheat Cultivars by Foliar Treatment with Antioxidant 2—Changes in Some Biochemical Aspects, Lipid Peroxidation, Antioxidant Enzymes and Amino Acid Contents. Agricultural Sciences 2014, 05, 1269, doi:10.4236/as.2014.513135.

69.   69.   Dreyer, A.; Dietz, K.-J. Reactive Oxygen Species and the Redox-Regulatory Network in Cold Stress Acclimation. Antioxidants 2018, 7, 169, doi:10.3390/antiox7110169.

70.   70.   Dawood, M.G.; Sadak, M.S. Physiological Role of Glycinebetaine in Alleviating the Deleterious Effects of Drought Stress on Canola Plants (Brassica napus L.). 2014, 12.

71.   71.   Sullivan, J.H. Possible impacts of changes in UV-B radiation on North American trees and forests. Environmental Pollution 2005, 137, 380–389, doi:10.1016/j.envpol.2005.01.029.

72.   72.   Shrivastava, P.; Kumar, R. Soil salinity: A serious environmental issue and plant growth promoting bacteria as one of the tools for its alleviation. Saudi J Biol Sci 2015, 22, 123–131, doi:10.1016/j.sjbs.2014.12.001.

73.   73.   Parida, A.K.; Das, A.B. Salt tolerance and salinity effects on plants: a review. Ecotoxicology and Environmental Safety 2005, 60, 324–349, doi:10.1016/j.ecoenv.2004.06.010.

74.   74.   Ruiz-Lozano, J.M.; Porcel, R.; Azcón, C.; Aroca, R. Regulation by arbuscular mycorrhizae of the integrated physiological response to salinity in plants: new challenges in physiological and molecular studies. J Exp Bot 2012, 63, 4033–4044, doi:10.1093/jxb/ers126.

75.   75.   Julkowska, M.M.; Testerink, C. Tuning plant signaling and growth to survive salt. Trends Plant Sci. 2015, 20, 586–594, doi:10.1016/j.tplants.2015.06.008.

76.   76.   Chen, Z.; Xie, Y.; Gu, Q.; Zhao, G.; Zhang, Y.; Cui, W.; Xu, S.; Wang, R.; Shen, W. The AtrbohF-dependent regulation of ROS signaling is required for melatonin-induced salinity tolerance in Arabidopsis. Free Radical Biology and Medicine 2017, 108, 465–477, doi:10.1016/j.freeradbiomed.2017.04.009.

77.   77.   Zhou, X.; Zhao, H.; Cao, K.; Hu, L.; Du, T.; Baluška, F.; Zou, Z. Beneficial Roles of Melatonin on Redox Regulation of Photosynthetic Electron Transport and Synthesis of D1 Protein in Tomato Seedlings under Salt Stress. Front Plant Sci 2016, 7, doi:10.3389/fpls.2016.01823.

78.   78.   Yang, Y.; Cao, Y.; Li, Z.; Zhukova, A.; Yang, S.; Wang, J.; Tang, Z.; Cao, Y.; Zhang, Y.; Wang, D. Interactive effects of exogenous melatonin and Rhizophagus intraradices on saline-alkaline stress tolerance in Leymus chinensis. Mycorrhiza 2020, doi:10.1007/s00572-020-00942-2.

79.   79.   Liu, N.; Jin, Z.; Wang, S.; Gong, B.; Wen, D.; Wang, X.; Wei, M.; Shi, Q. Sodic alkaline stress mitigation with exogenous melatonin involves reactive oxygen metabolism and ion homeostasis in tomato. Scientia Horticulturae 2015, 181, 18–25, doi:10.1016/j.scienta.2014.10.049.

80.   80.   Yu, Y.; Wang, A.; Li, X.; Kou, M.; Wang, W.; Chen, X.; Xu, T.; Zhu, M.; Ma, D.; Li, Z.; et al. Melatonin-Stimulated Triacylglycerol Breakdown and Energy Turnover under Salinity Stress Contributes to the Maintenance of Plasma Membrane H+–ATPase Activity and K+/Na+ Homeostasis in Sweet Potato. Front. Plant Sci. 2018, 9, doi:10.3389/fpls.2018.00256.

81.   81.   Sun, S.; Wen, D.; Yang, W.; Meng, Q.; Shi, Q.; Gong, B. Overexpression of Caffeic Acid O-Methyltransferase 1 (COMT1) Increases Melatonin Level and Salt Stress Tolerance in Tomato Plant. J Plant Growth Regul 2019, doi:10.1007/s00344-019-10058-3.

82.   82.   Gong, X.; Shi, S.; Dou, F.; Song, Y.; Ma, F. Exogenous Melatonin Alleviates Alkaline Stress in Malus hupehensis Rehd. by Regulating the Biosynthesis of Polyamines. Molecules 2017, 22, doi:10.3390/molecules22091542.

83.   83.   Li, H.; Chang, J.; Chen, H.; Wang, Z.; Gu, X.; Wei, C.; Zhang, Y.; Ma, J.; Yang, J.; Zhang, X. Exogenous Melatonin Confers Salt Stress Tolerance to Watermelon by Improving Photosynthesis and Redox Homeostasis. Front Plant Sci 2017, 8, 295, doi:10.3389/fpls.2017.00295.

84.   84.   Cen, H.; Wang, T.; Liu, H.; Tian, D.; Zhang, Y. Melatonin Application Improves Salt Tolerance of Alfalfa (Medicago sativa L.) by Enhancing Antioxidant Capacity. Plants 2020, 9, 220, doi:10.3390/plants9020220.

85.   85.   Zahedi, S.M.; Hosseini, M.S.; Abadía, J.; Marjani, M. Melatonin foliar sprays elicit salinity stress tolerance and enhance fruit yield and quality in strawberry (Fragaria × ananassa Duch.). Plant Physiology and Biochemistry 2020, 149, 313–323, doi:10.1016/j.plaphy.2020.02.021.

86.   86.   Zhao, G.; Zhao, Y.; Yu, X.; Kiprotich, F.; Han, H.; Guan, R.; Wang, R.; Shen, W. Nitric Oxide Is Required for Melatonin-Enhanced Tolerance against Salinity Stress in Rapeseed (Brassica napus L.) Seedlings. International Journal of Molecular Sciences 2018, 19, 1912, doi:10.3390/ijms19071912.

87.   87.   Arora, D.; Bhatla, S.C. Melatonin and nitric oxide regulate sunflower seedling growth under salt stress accompanying differential expression of Cu/Zn SOD and Mn SOD. Free Radical Biology and Medicine 2017, 106, 315–328, doi:10.1016/j.freeradbiomed.2017.02.042.

88.   88.   Kaur, H.; Bhatla, S.C. Melatonin and nitric oxide modulate glutathione content and glutathione reductase activity in sunflower seedling cotyledons accompanying salt stress. Nitric Oxide 2016, 59, 42–53, doi:10.1016/j.niox.2016.07.001.

89.   89.   Liu, N.; Gong, B.; Jin, Z.; Wang, X.; Wei, M.; Yang, F.; Li, Y.; Shi, Q. Sodic alkaline stress mitigation by exogenous melatonin in tomato needs nitric oxide as a downstream signal. Journal of Plant Physiology 2015, 186–187, 68–77, doi:10.1016/j.jplph.2015.07.012.

90.   90.   Wilson, R.A.; Sangha, M.K.; Banga, S.S.; Atwal, A.K.; Gupta, S. Heat stress tolerance in relation to oxidative stress and antioxidants in Brassica juncea. Journal of environmental biology 2014.

91.   91.   Bechtold, U.; Field, B. Molecular mechanisms controlling plant growth during abiotic stress. J Exp Bot 2018, 69, 2753–2758, doi:10.1093/jxb/ery157.

92.   92.   Gill, S.S.; Tuteja, N. Reactive oxygen species and antioxidant machinery in abiotic stress tolerance in crop plants. Plant Physiology and Biochemistry 2010, 48, 909–930, doi:10.1016/j.plaphy.2010.08.016.

93.   93.   Hasanuzzaman, M.; Nahar, K.; Alam, M.M.; Roychowdhury, R.; Fujita, M. Physiological, Biochemical, and Molecular Mechanisms of Heat Stress Tolerance in Plants. International Journal of Molecular Sciences 2013, 14, 9643–9684, doi:10.3390/ijms14059643.

94.   94.   Wahid, A.; Gelani, S.; Ashraf, M.; Foolad, M.R. Heat tolerance in plants: An overview. Environmental and Experimental Botany 2007, 61, 199–223, doi:10.1016/j.envexpbot.2007.05.011.

95.   95.   Jahan, M.S.; Shu, S.; Wang, Y.; Chen, Z.; He, M.; Tao, M.; Sun, J.; Guo, S. Melatonin alleviates heat-induced damage of tomato seedlings by balancing redox homeostasis and modulating polyamine and nitric oxide biosynthesis. BMC Plant Biol. 2019, 19, 414, doi:10.1186/s12870-019-1992-7.

96.   96.   Liang, D.; Gao, F.; Ni, Z.; Lin, L.; Deng, Q.; Tang, Y.; Wang, X.; Luo, X.; Xia, H. Melatonin Improves Heat Tolerance in Kiwifruit Seedlings through Promoting Antioxidant Enzymatic Activity and Glutathione S-Transferase Transcription. Molecules 2018, 23, doi:10.3390/molecules23030584.

97.   97.   Alam, M.N.; Zhang, L.; Yang, L.; Islam, Md.R.; Liu, Y.; Luo, H.; Yang, P.; Wang, Q.; Chan, Z. Transcriptomic profiling of tall fescue in response to heat stress and improved thermotolerance by melatonin and 24-epibrassinolide. BMC Genomics 2018, 19, doi:10.1186/s12864-018-4588-y.

98.   98.   Li, Z.-G.; Xu, Y.; Bai, L.-K.; Zhang, S.-Y.; Wang, Y. Melatonin enhances thermotolerance of maize seedlings (Zea mays L.) by modulating antioxidant defense, methylglyoxal detoxification, and osmoregulation systems. Protoplasma 2019, 256, 471–490, doi:10.1007/s00709-018-1311-4.

99.   99.   Ahammed, G.J.; Xu, W.; Liu, A.; Chen, S. Endogenous melatonin deficiency aggravates high temperature-induced oxidative stress in Solanum lycopersicum L. Environmental and Experimental Botany 2019, 161, 303–311, doi:10.1016/j.envexpbot.2018.06.006.

100.   100.   Wang, X.; Zhang, H.; Xie, Q.; Liu, Y.; Lv, H.; Bai, R.; Ma, R.; Li, X.; Zhang, X.; Guo, Y.-D.; et al. SlSNAT Interacts with HSP40, a Molecular Chaperone, to Regulate Melatonin Biosynthesis and Promote Thermotolerance in Tomato. Plant Cell Physiol. 2020, 61, 909–921, doi:10.1093/pcp/pcaa018.

101.   101.   Qi, Z.-Y.; Wang, K.-X.; Yan, M.-Y.; Kanwar, M.K.; Li, D.-Y.; Wijaya, L.; Alyemeni, M.N.; Ahmad, P.; Zhou, J. Melatonin Alleviates High Temperature-Induced Pollen Abortion in Solanum lycopersicum. Molecules 2018, 23, doi:10.3390/molecules23020386.

102.   102.   Parankusam, S.; Adimulam, S.S.; Bhatnagar-Mathur, P.; Sharma, K.K. Nitric Oxide (NO) in Plant Heat Stress Tolerance: Current Knowledge and Perspectives. Front Plant Sci 2017, 8, 1582, doi:10.3389/fpls.2017.01582.

103.   103.   Li, X.; Wei, J.-P.; Scott, E.R.; Liu, J.-W.; Guo, S.; Li, Y.; Zhang, L.; Han, W.-Y. Exogenous Melatonin Alleviates Cold Stress by Promoting Antioxidant Defense and Redox Homeostasis in Camellia sinensis L. Molecules 2018, 23, doi:10.3390/molecules23010165.

104.   104.   Xiong, L.; Schumaker, K.S.; Zhu, J.-K. Cell Signaling during Cold, Drought, and Salt Stress. The Plant Cell 2002, 14, S165–S183, doi:10.1105/tpc.000596.

105.   105.   Jiang, Y.-P.; Huang, L.-F.; Cheng, F.; Zhou, Y.-H.; Xia, X.-J.; Mao, W.-H.; Shi, K.; Yu, J.-Q. Brassinosteroids accelerate recovery of photosynthetic apparatus from cold stress by balancing the electron partitioning, carboxylation and redox homeostasis in cucumber. Physiologia Plantarum 2013, 148, 133–145, doi:10.1111/j.1399-3054.2012.01696.x.

106. 106. Allen, D.J.; Ort, D.R. Impacts of chilling temperatures on photosynthesis in warm-climate plants. Trends in Plant Science 2001, 6, 36–42, doi:10.1016/S1360-1385(00)01808-2.

107. 107. Asada, K. Production and Scavenging of Reactive Oxygen Species in Chloroplasts and Their Functions. Plant Physiology 2006, 141, 391–396, doi:10.1104/pp.106.082040.

108. 108. Aghdam, M.S.; Fard, J.R. Melatonin treatment attenuates postharvest decay and maintains nutritional quality of strawberry fruits (Fragaria×anannasa cv. Selva) by enhancing GABA shunt activity. Food Chemistry 2017, 221, 1650–1657, doi:10.1016/j.foodchem.2016.10.123.

109. 109. Sharafi, Y.; Aghdam, M.S.; Luo, Z.; Jannatizadeh, A.; Razavi, F.; Fard, J.R.; Farmani, B. Melatonin treatment promotes endogenous melatonin accumulation and triggers GABA shunt pathway activity in tomato fruits during cold storage. Scientia Horticulturae 2019, 254, 222–227, doi:10.1016/j.scienta.2019.04.056.

110. 110. Bajwa, V.S.; Shukla, M.R.; Sherif, S.M.; Murch, S.J.; Saxena, P.K. Role of melatonin in alleviating cold stress in Arabidopsis thaliana. Journal of Pineal Research 2014, 56, 238–245, doi:10.1111/jpi.12115.

111. 111. Zhao, H.; Ye, L.; Wang, Y.; Zhou, X.; Yang, J.; Wang, J.; Cao, K.; Zou, Z. Melatonin Increases the Chilling Tolerance of Chloroplast in Cucumber Seedlings by Regulating Photosynthetic Electron Flux and the Ascorbate-Glutathione Cycle. Front Plant Sci 2016, 7, 1814, doi:10.3389/fpls.2016.01814.

112. 112. Marta, B.; Szafrańska, K.; Posmyk, M.M. Exogenous Melatonin Improves Antioxidant Defense in Cucumber Seeds (Cucumis sativus L.) Germinated under Chilling Stress. Front Plant Sci 2016, 7, doi:10.3389/fpls.2016.00575.

113. 113. Fu, J.; Wu, Y.; Miao, Y.; Xu, Y.; Zhao, E.; Wang, J.; Sun, H.; Liu, Q.; Xue, Y.; Xu, Y.; et al. Improved cold tolerance in Elymus nutans by exogenous application of melatonin may involve ABA-dependent and ABA-independent pathways. Sci Rep 2017, 7, doi:10.1038/srep39865.

114. 114. Shen, J.; Wang, Y.; Chen, C.; Ding, Z.; Hu, J.; Zheng, C.; Li, Y. Metabolite profiling of tea (Camellia sinensis L.) leaves in winter. Scientia Horticulturae 2015, 192, 1–9, doi:10.1016/j.scienta.2015.05.022.

115. 115. Puyaubert, J.; Baudouin, E. New clues for a cold case: nitric oxide response to low temperature. Plant, Cell & Environment 2014, 37, 2623–2630, doi:10.1111/pce.12329.

116. 116. Okçu, G.; Kaya, M.D.; Atak, M. Effects of Salt and Drought Stresses on Germination and Seedling Growth of Pea (Pisum sativum L.). Turk J Agric For 2005, 29, 237–242.

117. 117. Boyer, J.S. Plant Productivity and Environment. Science 1982, 218, 443–448, doi:10.1126/science.218.4571.443.

118. 118. Sadak, M.Sh.; Abdalla, A.M.; Abd Elhamid, E.M.; Ezzo, M.I. Role of melatonin in improving growth, yield quantity and quality of Moringa oleifera L. plant under drought stress. Bulletin of the National Research Centre 2020, 44, 18, doi:10.1186/s42269-020-0275-7.

119. 119. Zhang, N.; Zhao, B.; Zhang, H.-J.; Weeda, S.; Yang, C.; Yang, Z.-C.; Ren, S.; Guo, Y.-D. Melatonin promotes water-stress tolerance, lateral root formation, and seed germination in cucumber (Cucumis sativus L.). Journal of Pineal Research 2013, 54, 15–23, doi:10.1111/j.1600-079X.2012.01015.x.

120. 120. Gao, W.; Zhang, Y.; Feng, Z.; Bai, Q.; He, J.; Wang, Y. Effects of Melatonin on Antioxidant Capacity in Naked Oat Seedlings under Drought Stress. Molecules 2018, 23, doi:10.3390/molecules23071580.

121. 121. Ahmad, S.; Kamran, M.; Ding, R.; Meng, X.; Wang, H.; Ahmad, I.; Fahad, S.; Han, Q. Exogenous melatonin confers drought stress by promoting plant growth, photosynthetic capacity and antioxidant defense system of maize seedlings. PeerJ 2019, 7, e7793, doi:10.7717/peerj.7793.

122. 122. Huang, B.; Chen, Y.-E.; Zhao, Y.-Q.; Ding, C.-B.; Liao, J.-Q.; Hu, C.; Zhou, L.-J.; Zhang, Z.-W.; Yuan, S.; Yuan, M. Exogenous Melatonin Alleviates Oxidative Damages and Protects Photosystem II in Maize Seedlings Under Drought Stress. Front Plant Sci 2019, 10, doi:10.3389/fpls.2019.00677.

123. 123. Zhang, M.; He, S.; Zhan, Y.; Qin, B.; Jin, X.; Wang, M.; Zhang, Y.; Hu, G.; Teng, Z.; Wu, Y. Exogenous melatonin reduces the inhibitory effect of osmotic stress on photosynthesis in soybean. PLOS ONE 2019, 14, e0226542, doi:10.1371/journal.pone.0226542.

124. 124. Sharma, A.; Wang, J.; Xu, D.; Tao, S.; Chong, S.; Yan, D.; Li, Z.; Yuan, H.; Zheng, B. Melatonin regulates the functional components of photosynthesis, antioxidant system, gene expression, and metabolic pathways to induce drought resistance in grafted Carya cathayensis plants. Science of The Total Environment 2020, 713, 136675, doi:10.1016/j.scitotenv.2020.136675.

125. 125. Zuo, B.; Zheng, X.; He, P.; Wang, L.; Lei, Q.; Feng, C.; Zhou, J.; Li, Q.; Han, Z.; Kong, J. Overexpression of MzASMT improves melatonin production and enhances drought tolerance in transgenic Arabidopsis thaliana plants. Journal of Pineal Research 2014, 57, 408–417, doi:10.1111/jpi.12180.

126.   126. Antoniou, C.; Chatzimichail, G.; Xenofontos, R.; Pavlou, J.J.; Panagiotou, E.; Christou, A.; Fotopoulos, V. Melatonin systemically ameliorates drought stress-induced damage in Medicago sativa plants by modulating nitro-oxidative homeostasis and proline metabolism. J. Pineal Res. 2017, 62, doi:10.1111/jpi.12401.

127.   127. Yokawa, K.; Koshiba, T.; Baluška, F. Light-dependent control of redox balance and auxin biosynthesis in plants. Plant Signaling & Behavior 2014, 9, e29522, doi:10.4161/psb.29522.

128.   128. Jenkins, G.I. Signal Transduction in Responses to UV-B Radiation. Annual Review of Plant Biology 2009, 60, 407–431, doi:10.1146/annurev.arplant.59.032607.092953.

129.   129. Ballaré, C.L.; Caldwell, M.M.; Flint, S.D.; Robinson, S.A.; Bornman, J.F. Effects of solar ultraviolet radiation on terrestrial ecosystems. Patterns, mechanisms, and interactions with climate change. Photochem. Photobiol. Sci. 2011, 10, 226–241, doi:10.1039/C0PP90035D.

130.   130. Wei, Z.; Li, C.; Gao, T.; Zhang, Z.; Liang, B.; Lv, Z.; Zou, Y.; Ma, F. Melatonin increases the performance of Malus hupehensis after UV-B exposure. Plant Physiology and Biochemistry 2019, 139, 630–641, doi:10.1016/j.plaphy.2019.04.026.

131.   131. Lee, H.Y.; Back, K. Melatonin induction and its role in high light stress tolerance in Arabidopsis thaliana. Journal of Pineal Research 2018, 65, e12504, doi:10.1111/jpi.12504.

132.   132. Afreen, F.; Zobayed, S.M.A.; Kozai, T. Melatonin in Glycyrrhiza uralensis: response of plant roots to spectral quality of light and UV-B radiation. Journal of Pineal Research 2006, 41, 108–115, doi:10.1111/j.1600-079X.2006.00337.x.

133.   133. Bychkov, I.; Kudryakova, N.; Andreeva, A.; Pojidaeva, E.; Kusnetsov, V. Melatonin modifies the expression of the genes for nuclear- and plastid-encoded chloroplast proteins in detached Arabidopsis leaves exposed to photooxidative stress. Plant Physiology and Biochemistry 2019, 144, 404–412, doi:10.1016/j.plaphy.2019.10.013.

134.   134. Yemets, A.I.; Krasylenko, Y.A.; Blume, Y.B. Nitric Oxide and UV-B Radiation. In Nitric Oxide Action in Abiotic Stress Responses in Plants; Khan, M.N., Mobin, M., Mohammad, F., Corpas, F.J., Eds.; Springer International Publishing: Cham, 2015; pp. 141–154 ISBN 978-3-319-17804-2.

135.   135. Kim, T.-Y.; Jo, M.-H.; Hong, J.-H. Protective Effect of Nitric Oxide against Oxidative Stress under UV-B Radiation in Maize Leaves. Journal of the Environmental Sciences 2010, 19, 1323–1334, doi:10.5322/JES.2010.19.12.1323.

136.   136. Chen, K.; Feng, H.; Zhang, M.; Wang, X. Nitric oxide alleviates oxidative damage in the green algaChlorella pyrenoidosa caused by UV-B radiation. Folia Microbiol 2003, 48, 389, doi:10.1007/BF02931372.

137.   137. Lytvyn, D.I.; Raynaud, C.; Yemets, A.I.; Bergounioux, C.; Blume, Y.B. Involvement of Inositol Biosynthesis and Nitric Oxide in the Mediation of UV-B Induced Oxidative Stress. Front. Plant Sci. 2016, 7, doi:10.3389/fpls.2016.00430.

138.   138. He, J.-M.; Xu, H.; She, X.-P.; Song, X.-G.; Zhao, W.-M. The role and the interrelationship of hydrogen peroxide and nitric oxide in the UV-B-induced stomatal closure in broad bean. Functional Plant Biol. 2005, 32, 237–247, doi:10.1071/FP04185.

139.   139. Yan, F.; Liu, Y.; Sheng, H.; Wang, Y.; Kang, H.; Zeng, J. Salicylic acid and nitric oxide increase photosynthesis and antioxidant defense in wheat under UV-B stress. Biol Plant 2016, 60, 686–694, doi:10.1007/s10535-016-0622-6.

140.   140. Cassia, R.; Amenta, M.; Fernández, M.B.; Nocioni, M.; Dávila, V. The Role of Nitric Oxide in the Antioxidant Defense of Plants Exposed to UV-B Radiation. In Reactive Oxygen, Nitrogen and Sulfur Species in Plants; John Wiley & Sons, Ltd, 2019; pp. 555–572 ISBN 978-1-119-46867-7.

141.   141. Jackson, M.B.; Colmer, T.D. Response and Adaptation by Plants to Flooding Stress. Ann Bot 2005, 96, 501–505, doi:10.1093/aob/mci205.

142.   142. Xu, Q.T.; Yang, L.; Zhou, Z.Q.; Mei, F.Z.; Qu, L.H.; Zhou, G.S. Process of aerenchyma formation and reactive oxygen species induced by waterlogging in wheat seminal roots. Planta 2013, 238, 969–982, doi:10.1007/s00425-013-1947-4.

143.   143. Boru, G.; Vantoai, T.; Alves, J.; Hua, D.; Knee, M. Responses of Soybean to Oxygen Deficiency and Elevated Root-zone Carbon Dioxide Concentration. Ann Bot 2003, 91, 447–453, doi:10.1093/aob/mcg040.

144.   144. Hossain, Z.; López-Climent, M.F.; Arbona, V.; Pérez-Clemente, R.M.; Gómez-Cadenas, A. Modulation of the antioxidant system in citrus under waterlogging and subsequent drainage. Journal of Plant Physiology 2009, 166, 1391–1404, doi:10.1016/j.jplph.2009.02.012.

145. 145. Zheng, X.; Zhou, J.; Tan, D.-X.; Wang, N.; Wang, L.; Shan, D.; Kong, J. Melatonin Improves Waterlogging Tolerance of Malus baccata (Linn.) Borkh. Seedlings by Maintaining Aerobic Respiration, Photosynthesis and ROS Migration. Front Plant Sci 2017, 8, 483, doi:10.3389/fpls.2017.00483.

146. 146. Zhang, Q.; Liu, X.; Zhang, Z.; Liu, N.; Li, D.; Hu, L. Melatonin Improved Waterlogging Tolerance in Alfalfa (Medicago sativa) by Reprogramming Polyamine and Ethylene Metabolism. Front. Plant Sci. 2019, 10, doi:10.3389/fpls.2019.00044.

147. 147. Gupta, K.J.; Igamberdiev, A.U.; Manjunatha, G.; Segu, S.; Moran, J.F.; Neelawarne, B.; Bauwe, H.; Kaiser, W.M. The emerging roles of nitric oxide (NO) in plant mitochondria. Plant Science 2011, 181, 520–526, doi:10.1016/j.plantsci.2011.03.018.

148. 148. Dordas, C. Nitric Oxide and Plant Hemoglobins Improve the Tolerance of Plants to Hypoxia. In Nitric Oxide Action in Abiotic Stress Responses in Plants; Khan, M.N., Mobin, M., Mohammad, F., Corpas, F.J., Eds.; Springer International Publishing: Cham, 2015; pp. 115–128 ISBN 978-3-319-17804-2.

149. 149. Igamberdiev, A.U.; Bykova, N.V.; Hill, R.D. Nitric oxide scavenging by barley hemoglobin is facilitated by a monodehydroascorbate reductase-mediated ascorbate reduction of methemoglobin. Planta 2006, 223, 1033–1040, doi:10.1007/s00425-005-0146-3.

150. 150. Fukudome, M.; Watanabe, E.; Osuki, K.-I.; Uchi, N.; Uchiumi, T. Ectopic or Over-Expression of Class 1 Phytoglobin Genes Confers Flooding Tolerance to the Root Nodules of Lotus japonicus by Scavenging Nitric Oxide. Antioxidants (Basel) 2019, 8, doi:10.3390/antiox8070206.

151. 151. Khan, M.A.; Khan, A.L.; Imran, Q.M.; Asaf, S.; Lee, S.-U.; Yun, B.-W.; Hamayun, M.; Kim, T.-H.; Lee, I.-J. Exogenous application of nitric oxide donors regulates short-term flooding stress in soybean. PeerJ 2019, 7, e7741, doi:10.7717/peerj.7741.

152. 152. Salas, A.; Tortosa, G.; Hidalgo-García, A.; Delgado, A.; Bedmar, E.J.; Richardson, D.J.; Gates, A.J.; Delgado, M.J. The Hemoglobin Bjgb From Bradyrhizobium diazoefficiens Controls NO Homeostasis in Soybean Nodules to Protect Symbiotic Nitrogen Fixation. Front Microbiol 2019, 10, 2915, doi:10.3389/fmicb.2019.02915.

153. 153. Özçubukçu, S.; Ergün, N.; Ilhan, E. Waterlogging and nitric oxide induce gene expression and increase antioxidant enzyme activity in wheat (Triticum aestivum L.). Acta. Biol. Hung. 2014, 65, 47–60, doi:10.1556/ABiol.65.2014.1.5.

154. 154. Chen, T.; Yuan, F.; Song, J.; Wang, B. Nitric oxide participates in waterlogging tolerance through enhanced adventitious root formation in the euhalophyte Suaeda salsa. Funct. Plant Biol. 2016, 43, 244–253, doi:10.1071/FP15120.

155. 155. Copolovici, L.; Niinemets, U. Flooding induced emissions of volatile signalling compounds in three tree species with differing waterlogging tolerance. Plant Cell Environ. 2010, 33, 1582–1594, doi:10.1111/j.1365-3040.2010.02166.x.

156. 156. Hasan, M.K.; Liu, C.-X.; Pan, Y.-T.; Ahammed, G.J.; Qi, Z.-Y.; Zhou, J. Melatonin alleviates low-sulfur stress by promoting sulfur homeostasis in tomato plants. Scientific Reports 2018, 8, 10182, doi:10.1038/s41598-018-28561-0.

157. 157. Qiao, Y.; Yin, L.; Wang, B.; Ke, Q.; Deng, X.; Wang, S. Melatonin promotes plant growth by increasing nitrogen uptake and assimilation under nitrogen deficient condition in winter wheat. Plant Physiol. Biochem. 2019, 139, 342–349, doi:10.1016/j.plaphy.2019.03.037.

158. 158. Buet, A.; Galatro, A.; Ramos-Artuso, F.; Simontacchi, M. Nitric oxide and plant mineral nutrition: current knowledge. J. Exp. Bot. 2019, 70, 4461–4476, doi:10.1093/jxb/erz129.

159. 159. Zhou, C.; Liu, Z.; Zhu, L.; Ma, Z.; Wang, J.; Zhu, J. Exogenous Melatonin Improves Plant Iron Deficiency Tolerance via Increased Accumulation of Polyamine-Mediated Nitric Oxide. International Journal of Molecular Sciences 2016, 17, 1777, doi:10.3390/ijms17111777.

160. 160. Graziano, M.; Lamattina, L. Nitric oxide and iron in plants: an emerging and converging story. Trends Plant Sci. 2005, 10, 4–8, doi:10.1016/j.tplants.2004.12.004.

161. 161. Ramirez, L.; Zabaleta, E.J.; Lamattina, L. Nitric oxide and frataxin: two players contributing to maintain cellular iron homeostasis. Ann. Bot. 2010, 105, 801–810, doi:10.1093/aob/mcp147.

162. 162. Buet, A.; Simontacchi, M. Nitric oxide and plant iron homeostasis. Ann. N. Y. Acad. Sci. 2015, 1340, 39–46, doi:10.1111/nyas.12644.

163. 163. Sun, H.; Feng, F.; Liu, J.; Zhao, Q. Nitric Oxide Affects Rice Root Growth by Regulating Auxin Transport Under Nitrate Supply. Front. Plant Sci. 2018, 9, doi:10.3389/fpls.2018.00659.

164. 164. Sun, H.; Bi, Y.; Tao, J.; Huang, S.; Hou, M.; Xue, R.; Liang, Z.; Gu, P.; Yoneyama, K.; Xie, X.; et al. Strigolactones are required for nitric oxide to induce root elongation in response to nitrogen and phosphate deficiencies in rice. Plant, Cell & Environment 2016, 39, 1473–1484, doi:10.1111/pce.12709.

165. 165. Sun, H.; Li, J.; Song, W.; Tao, J.; Huang, S.; Chen, S.; Hou, M.; Xu, G.; Zhang, Y. Nitric oxide generated by nitrate reductase increases nitrogen uptake capacity by inducing lateral root formation and inorganic nitrogen uptake under partial nitrate nutrition in rice. J Exp Bot 2015, 66, 2449–2459, doi:10.1093/jxb/erv030.

166. 166. Choudhury, F.K.; Rivero, R.M.; Blumwald, E.; Mittler, R. Reactive oxygen species, abiotic stress and stress combination. The Plant Journal 2017, 90, 856–867, doi:10.1111/tpj.13299.

167. 167. Lopez-Delacalle, M.; Camejo, D.M.; García-Martí, M.; Nortes, P.A.; Nieves-Cordones, M.; Martínez, V.; Rubio, F.; Mittler, R.; Rivero, R.M. Using Tomato Recombinant Lines to Improve Plant Tolerance to Stress Combination Through a More Efficient Nitrogen Metabolism. Front. Plant Sci. 2020, 10, doi:10.3389/fpls.2019.01702.

168. 168. Martinez, V.; Mestre, T.C.; Rubio, F.; Girones-Vilaplana, A.; Moreno, D.A.; Mittler, R.; Rivero, R.M. Accumulation of Flavonols over Hydroxycinnamic Acids Favors Oxidative Damage Protection under Abiotic Stress. Front. Plant Sci. 2016, 7, doi:10.3389/fpls.2016.00838.

169. 169. Mittler, R. Abiotic stress, the field environment and stress combination. Trends in Plant Science 2006, 11, 15–19, doi:10.1016/j.tplants.2005.11.002.

170. 170. Rivero, R.M.; Mestre, T.C.; Mittler, R.; Rubio, F.; Garcia-Sanchez, F.; Martinez, V. The combined effect of salinity and heat reveals a specific physiological, biochemical and molecular response in tomato plants. Plant, Cell & Environment 2014, 37, 1059–1073, doi:10.1111/pce.12199.

171. 171. Rizhsky, L.; Liang, H.; Shuman, J.; Shulaev, V.; Davletova, S.; Mittler, R. When Defense Pathways Collide. The Response of Arabidopsis to a Combination of Drought and Heat Stress. Plant Physiology 2004, 134, 1683–1696, doi:10.1104/pp.103.033431.

172. 172. Suzuki, N.; Rivero, R.M.; Shulaev, V.; Blumwald, E.; Mittler, R. Abiotic and biotic stress combinations. New Phytologist 2014, 203, 32–43, doi:10.1111/nph.12797.

173. 173. Ding, W.; Zhao, Y.; Xu, J.-W.; Zhao, P.; Li, T.; Ma, H.; Reiter, R.J.; Yu, X. Melatonin: A Multifunctional Molecule That Triggers Defense Responses against High Light and Nitrogen Starvation Stress in Haematococcus pluvialis. J. Agric. Food Chem. 2018, 66, 7701–7711, doi:10.1021/acs.jafc.8b02178.

174. 174. Kaya, C.; Higgs, D.; Ashraf, M.; Alyemeni, M.N.; Ahmad, P. Integrative roles of nitric oxide and hydrogen sulfide in melatonin-induced tolerance of pepper (Capsicum annuum L.) plants to iron deficiency and salt stress alone or in combination. Physiologia Plantarum 2020, 168, 256–277, doi:10.1111/ppl.12976.