



Mini Review

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Phytoeffectors: A Non-transgenic Strategy to Improve Drought Tolerance of Crop Plants



Tatiana Bilova^{1,2,†}, Maria Cherevatskaya^{2†}, and Andrej Frolov^{1*}

¹Laboratory of Analytical Biochemistry and Biotechnology, K. A. Timiryazev Institute of Plant Physiology, Botanicheskaya ul. 35, Moscow, Russia

²Department of Plant Physiology and Biochemistry, St. Petersburg State University, 199034 St. Petersburg, Russia

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***Corresponding author:** Andrej Frolov, Laboratory of Analytical Biochemistry and Biotechnology, K. A. Timiryazev Institute of Plant Physiology, Botanicheskaya ul. 35, Moscow, Russia

†These authors contributed equally to the manuscript

Abstract

Due to the oncoming climate changes, drought became the principal challenge for sustainable agriculture. Indeed, today, water deficit becomes common even in the northern part of Europe and results in continuously increasing tremendous crop losses. Therefore, development of new strategies to improve plant stress tolerance is one of the principal tasks for the current agricultural research. In this context, application of the transgenic approach proved to be an efficient tool in establishment of new highlyproductive drought-tolerant crops. However, the practical implementation of this strategy is under the strict control of national governments and, typically, requires a special legal approval. Due to this, application of drought-protective agrochemicals might be a promising alternative strategy to establish drought tolerance in crops. Most often, these agrochemicals represent small molecules with molecular weights below 1000Da, which typically act as inhibitors of essential plant enzymes and are referred to as phytoeffectors. The phytoeffector strategy assumes identification of the major players (on both protein and metabolite levels) involved in the deleterious effects of the plant stress response. Based on this knowledge, specific receptors or/and enzymatic activities, which are essential for inhibition or modulation of the targeted specific deleterious aspect(s) of the stress response, need to be identified. Thereby, an increase in stress tolerance and sustaining of crop productivity are recognized as the principal outputs of the phytoeffector application. However, not only crop productivity, but also crop quality and nutritional safety need to be considered when establishing new drought-protective phytoeffectors. Importantly, all these criteria need to be combined for efficient implementation of the phytoeffector approach. As the concept of drought-protective phytoeffectors is new and develops rapidly, here we provide an overview of the current progress and key directions in the evolution of this approach.

Keywords: Drought tolerance; Environmental stress; Functional genomics; Plant stress tolerance; Phytoeffectors; Small molecules

Introduction

The oncoming global climate changes, manifested as the increase of average temperatures, duration and severity of storms, droughts and floodings, dramatically affect plant growth and development that results in tremendous crop yield losses worldwide [1]. Therefore, improvement of the plant stress tolerance is one of the primary aims of plant physiologists, biochemists, geneticists and breeders working with crops. From the agricultural point of view, two aspects are of the principal importance in terms of the stress tolerance of the crop plants: (i) sustaining crop productivity and (ii) preserving crop quality (that ultimately affects nutritional properties of the foods, manufactured from these crops). Unfortunately, in the absolute majority of

cases, only the first aspect is properly addressed, whereas the importance of the second one is often underestimated. Indeed, it is well-known, that even a short-term exposure to environmental stresses results in characteristic phenotypic changes, i.e. clearly visible changes in plant appearance and biochemical status [2-4]. In respect to various stresses (drought, heat, cold, high salt and heavy metal contents in the environment), these changes are often underlied by essentially common physiological and biochemical mechanisms of the plant stress response [5]. Many of these mechanisms are most comprehensively characterized for the plant response to drought.

At the earlier steps of its development, the drought stress response is usually manifested by activation of protective

mechanisms preventing excessive tissue dehydration. The primary plant response at this step is the abscisic acid (ABA)-dependent stomata closure. This key event ultimately causes the overload of the electron-transport chains (ETCs) in chloroplasts and mitochondria that is accompanied by enhanced transfer of electrons to molecular oxygen by the intermediate players of the ETCs [6,7]. Under these conditions, reactive oxygen species (ROS) are generated with the rates essentially overwhelming the cellular capacities for their detoxification, i.e. oxidative stress develops [8]. At the further step of the dehydration avoidance strategy, the plant accumulates osmoprotective proteins and metabolites (predominantly amino acids and sugars) [2,9]. The accompanying rearrangement of the cellular metabolism is usually referred to as metabolic adjustment [10,11].

Importantly, the simultaneous increase in the tissue ROS equilibrium concentrations and carbohydrate contents triggers oxidative degradation of cellular hydroxyl carbonyls and fatty acids, most typically associated with monosaccharide autoxidation [12,13] and lipid peroxidation [14], respectively, which ultimately result in so-called carbonyl stress, i.e. enhancement of reactive carbonyl compound (RCC) production [15]. These highly-reactive species readily modify cellular biopolymers, compromising their functions and nutritional properties. Specifically, on one hand, the reactions of the sugar-derived RCCs with proteins yield advanced glycation end products (AGEs). On the other hand, due to enhanced ROS generation and production of reactive intermediates of lipid peroxidation (GO, MGO, hydroxyaldehydes and ketoaldehydes), formation of advanced lipoxidation products (ALEs) is observed as well [16]. Both AGEs and ALEs are known to be toxic due to their pro-inflammatory properties, clearly exposed in mammals [17]. Generation of AGEs is well-characterized in animal tissues, and was recently confirmed in plants on the amino acid and proteome levels [18,19]. Moreover, the patterns of AGE-modified proteins were comprehensively characterized under the conditions of moderate osmotic stress [2]. Thus, stress-induced oxidative and carbonyl stresses might impact dramatically on nutritional properties of plant proteins. This aspect is often underestimated when new strategies to improve stress tolerance of crop plants are designed. Therefore, here we addressed different strategies to stimulate plant stress tolerance mechanisms including those which directed on simultaneous prevention of glyco- and lipotoxins formation and crop quality preservation.

Transgenic strategies to improve plant drought tolerance

Obviously, the physiological and molecular mechanisms behind the plant stress tolerance need to be addressed before consideration of the agricultural strategies, which might be employed in the reduction of the deleterious effects associated with drought. Such stress-protective mechanisms might rely on (i) antioxidative enzymes, (ii) proteins responsive to stress-induced ROS-mediated signals (e.g. enzymes of ABA synthesis and signaling), (iii) enzymes attenuating deleterious effects of

oxidative stress (e.g. carbonyl and ROS scavengers), and (iv) proteins involved in recognition, repair and selective degradation of damaged polypeptides. Therefore, the key players of the related metabolic pathways might represent prospective molecular targets for different strategies to improve crop yields and quality.

Unfortunately, despite these obvious considerations, the most of the classical breeding strategies target exclusively higher crop yields without considering the underlying physiological mechanisms, which might negatively affect crop properties without any decrease of productivity [20,21]. Moreover, the breeding-based approaches are associated with several serious challenges, such as high time and labor investments, transfer of non-desired genes and genetic barriers [20].

These limitations can be, at least partly, overcome by marker-assisted selection (MAS) [22,23] and genetic engineering (i.e. the transgenic approach) [24]. The first strategy represents a powerful tool for efficient identification of DNA markers for economically important and stress-related crop traits: mapping for quantitative trait loci (QTL) [25], identification of the single nucleotide polymorphism (SNP) [26] and simple sequence repeat (SSR) markers [27], as well as those associated with randomly amplified polymorphic DNA (RAPD) [28]. In particular, combination of conventional breeding strategies with MAS can be applied for introgression of stress tolerance to crop cultivars from wild predecessors (i.e. from the donors of the target genes associated with the plant stress tolerance) [20]. The MAS approach can be also employed for building of genetic maps, which are required for localization of the stress-dependently regulated genes [24]. In contrast to the classical approaches, the transgenic methods allow incorporation or silencing of the target genes in the recipient organism without the simultaneous transfer of undesirable genes from the donor one [24].

In terms of the biochemical mechanisms, stress tolerance can be reliably established for the cultivars featuring enhanced production of non-toxic natural stress protectors. In the most easy and straightforward way these stress protectors can act as low- or high-molecular weight antioxidants. For example, highly tolerant lines, featured with the over-expression of the genes encoding antioxidant enzymes were designed for some crop plants. Thus, transgenic lines, over-expressing superoxide dismutase were reported for rice, potato and alfalfa, whereas monodehydroascorbate reductase was successfully overexpressed in tobacco plants [29]. Other important players involved in plant stress response (osmoprotectors such as glycine betaine [30], proline [31], and trehalose [32]; late embryogenesis abundant (LEA) proteins, various molecules of ABA-biosynthesis and signaling) can be considered as the targets for the transgenic approach as well [33].

Unfortunately, despite their obvious efficiency, suggestions for agricultural application of transgenic plants still have not met an ultimate approval from the consumers, researchers and the members of national food safety control boards. Indeed, the

phenomenon of gene pleiotropy (which is manifested by multiple effects of individual genes on diverse plant traits) might affect biochemical homeostasis of a plant organism in a complex and often unpredictable way [34,35]. In this context, transgenic plants can be a potential source of toxicity, allergenicity and genetic hazards [36]. Relatively low ecological and physiological flexibility of transgenic crops might be another problem. Indeed, a permanent character of the genetically induced stress tolerance might result in high investment of growth energy even under a favorable water regimen [37]. Also, agricultural approaches, relying on a broad selection of cultivars, or even crops, are preferred in commercial application. This requirement is, however, incompatible with the transgenic approach.

Non-transgenic strategies to improve plant drought tolerance

Due to the above listed disadvantages of the transgenic strategy, several non-transgenic approaches were recently proposed to improve plant tolerance to drought. These alternative strategies do not rely on genetic engineering tools, but employ informational resources of functional genomics - transcriptomics, proteomics and metabolomics. To date, the most established non-transgenic concepts are the "molecular strengthening (MOST) treatment" [23] and the "phytoeffector approach" [38]. At the principal level, these concepts appear to be similar as they both are based on the comprehensive understanding of underlying molecular mechanisms affecting particular plant traits. This mechanistic information is necessary for adequate selection of potential targets, which can be activated or inactivated upon interaction with appropriate natural or synthetic molecular effectors. At this point, these strategies are analogous to the pharmaceutical approach for targeted delivery of medicines for therapy of human diseases. However, in this aspect the MOST treatment and the phytoeffector approach have different focusing.

Thus, the MOST treatment strategy assumes deep understanding of gene functions or/and molecular pathways [23]. It targets expression of specific traits, which impact essentially on general plant performance, e.g. improvement of yield stability under environmental stress conditions, modulation of plant development or morphology and reduction in fertilizer input [23]. In contrast, phytoeffector approach is focused exclusively at improvement of the plant stress tolerance traits with a special attention on preserving of crop productivity under unfavorable environmental conditions [39]. In the latter case, analysis of the related transcriptomics, proteomics and metabolomics data allows selection of the most promising proteins (stress enhancers), critically impacting on the deleterious effects accompanying the plant stress response. For these prospective targets, appropriate low molecular weight effectors (most often termed as phytoeffectors) can be selected and synthetically optimized. These small molecules might suppress development of oxidative stress and stress-related metabolic adjustment by affecting specific

enzymes, preventing, thereby, productivity losses, enhancement of the toxicity related to specific metabolites, as well as glyco- and lipotoxins.

This phytoeffector strategy was proposed recently, and it is already established in the Wessjohann's lab for poly-(ADP-ribose)-polymerase (PARP) inhibitors [38]. This group demonstrated that inhibition of the PARP enzymes and related prevention of NADH depletion could give access to sustaining of plant crop productivity under the conditions of short-termed moderate drought. Later on, Marshall and co-workers proposed that receptor-like kinases (RLKs) could be another promising target for low-molecular weight phytoeffectors [40]. Due to its pronounced impact on the plant drought response, this protein family attracted a special attention of researchers [41]. Due to their involvement in various signaling cascades and dependence on small molecules (peptide ligands), the activity of RLKs can be easily modulated. This fact provides a unique opportunity for improvement of plant tolerance to drought (and, probably, to other stresses) [40]. Indeed, modulation of the RLK activity by synthetic molecules (phytoeffectors) can be readily expected. Such interactions would activate or repress the regulatory proteins and thus might be a powerful chemical tool to affect the relevant signaling pathways.

In general, the phytoeffector strategy includes the following steps: comprehensive search for target proteins acting as stress enhancers in plant experiment-based databases, confirmation of adverse impact of the proteins on the plant stress physiology, modeling of the protein structure, construction of corresponding chemicals (phytoeffectors), *in vivo* validation of their efficiency and field trials to confirm the applicability of the phytoeffectors used. Ideally, the potent phytoeffectors need to be designed as a universal tool, which can be applied to various crops at desired times and locations. These molecules must demonstrate high bioavailability, i.e. readily penetrate cell membranes and participate in the intracellular metabolism. Moreover, they need to be easy in application, e.g. via foliar spraying, root infiltration and/or pre-sowing treatment of seeds.

At the level of the seed pre-treatment, the phytoeffector approach can also be employed to establish so-called priming-mediated plant tolerance. In general, priming is considered to be an adaptive strategy to stimulate and maintain an "alertness" state of the plant without exposure it to severe stress [42]. This leads to pre-activation of the tolerance mechanisms. Due to this, the full-scale response to the post-activation stress exposure would be developed faster. In terms of this concept, the effect of the phytoeffector might be associated with the enhanced production of the key cellular regulators, such as ABA and nitric oxide (NO).

Targeting phytohormone-related signaling is another field of the phytoeffector application. Thereby, phytoeffectors might enhance phytohormone synthesis and slow down their degradation. It is well known, that application of exogenic ABA as a natural phytoeffector molecule appeared to be inefficient as no

enhancement of stress tolerance mechanisms could be observed in field-grown plants [43]. Kim et al. attributed this failure to isomerization of the ABA aliphatic side chain. Under natural field conditions, high rates of this process might yield high amounts of physiologically inactive 2-trans ABA isomer [44]. However, several synthetic ABA analogs (sulfonamide-based compounds ABA mimic 1, 2, 3 (AMs 1-3) and pyrabactin [45]) which are able to trigger signaling cascades and to activate, thereby, tolerance mechanisms, appeared to be promising phytoeffectors. The potential use of these and several other synthetic ABA signaling pathway modulators in managing agronomic and post-harvest traits was comprehensively discussed recently [46,47].

Due to well-known importance of NO as a potent modulator of plant stress response [48-50], NO donors are currently recognized as promising stress-protective phytoeffectors. The most commonly used synthetic NO donors are sodium nitroprusside, S-nitrosoglutathione, S-nitroso-N-acetylpennicillamine and 3,3-bis(aminoethyl)-1-hydroxy-2-oxo-1-triazene [48,49,51]. Thus, it was shown that NO applied exogenously in the form of inorganic sodium nitroprusside and organic S-nitroso-N-acetylpennicillamine suppressed drought stress in wheat leaves. On the other hand, exogenous NO (also applied as sodium nitroprusside) showed good results in enhancement of drought tolerance in *Tradescantia sp.*, *Salpichroa organifolia*, *Vicia faba* [52] and *Medicago sativa* [53]. The characteristics of NO release and some metabolic responses induced by the NO-donors are reviewed in the works of Ederli et al. (2009) [49] and Murgia et al. (2004) [50].

Recently, a new type of heterocyclic NO-donors, such as sydnone imines, have emerged recently. Sydnone imines represent a class of mesoionic heterocyclic compounds [54] exhibiting a broad range of biological activities and in this regard they are successfully applicable in medicine. Due to their improved hydrolytic stability and low toxicity (which were comprehensively confirmed in multiple pharmacokinetic studies [55]), these compounds present a promising alternative to the conventional NO-donating agents. Since 2017, several reports demonstrated a pronounced ability of selected sydnone imine derivatives to act as plant growth stimulants, herbicide antidotes, retardants, germination inhibitors (herbicides), and inducers of plant tolerance to environmental stresses [56-60]. Recently, we summarized available *state of the art* information on sydnone imine application to various crop plants (*Triticum aestivum* L., *Zea mays* L., *Brassica napus* L., *Helianthus annuus*), with a special emphasis on the structure-activity relationships (SAR) in the context of the growth modulating activity of the effector compounds [61]. Our search showed that 4-(α -hydroxybenzyl) sydnone imine derivatives containing an alkyl substituent in the position N-3 demonstrated pronounced growth-stimulating or antidote effects. The activity profiles of individual sydnone imines might be also affected by structure of the substituent at position N-6 [56,57,61]. However, despite the achieved progress, further investigations are necessary to characterize the structure-

activity relationships (SAR) completely. This would be absolutely mandatory to understand the potential of sydnone imines as a new class of promising phytoeffectors.

Conclusion

To summarize, despite the stress tolerance mechanisms act under the finely tuned control of multiple plant regulatory systems [4,62], the activities of individual stress-protective enzymes and even the whole adaptive pathways can be efficiently modulated by the application of low-molecular weight synthetic phytoeffectors. Most often, these plant-targeted effector molecules act as the inhibitors of enzymes, which are critical in manifestations of the deleterious effects accompanying plant stress response or as enhancers of stress-protective signaling. Inhibition of targeted enzymes or modulation of specific regulatory pathways results in improved plant survival under stressed conditions. Thus, the main goal of the phytoeffector application is improvement of stress tolerance and preserving the quality of crop production.

In general, application of these agrochemicals follows the logics behind the idea of targeted delivery of pharmaceuticals to diseased human tissues. Accordingly, the overall success of the phytoeffector application completely relies on the comprehensive understanding of the molecular mechanisms underlying the plant stress tolerance. Therefore, the functional genomics data acquired in comprehensive transcriptomics, proteomics, metabolomics and phenomics experiments serve as the starting point for selection of the specific phytoeffector strategy. The information, which can be extracted from these data by well-established bioinformatics tools, might give access to the appropriate phytoeffector targets, i.e. the proteins, most strongly involved in the deleterious effects accompanying the plant stress response. Further, by a combination of chemoinformatic and biochemical methods appropriate inhibitors can be selected and synthetically optimized to yield promising active phytoeffectors. Thus, depending on the specific enzymes targeted by these small molecules, the phytoeffectors can suppress development of oxidative stress, prevent formation of glyco- and lipotoxins, protect functional proteins from molecular damage and functionality loss and modulate stress-related metabolic adjustment, reducing stress-induced deleterious effects on crop productivity. Thus, undoubtedly, phytoeffector strategy allows targeting different manifestations of the drought stress response in crop plants. Highly likely, combining differentially targeted phytoeffectors within one application scheme might essentially improve the induced drought protective effect. Importantly, one needs to take into account, that application of phytoeffectors is a quite new field in plant stress physiology research. Therefore, multiple aspects still require more detailed and comprehensive investigations, in particular potential development of adverse effects in treated plants.

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References

1. Bibi F, Rahman A (2023) An Overview of Climate Change Impacts on Agriculture and Their Mitigation Strategies. *Agriculture* 13(8): 1508.
2. Paudel G, Bilova T, Schmidt R, Uta G, Berger R, et al. (2016) Osmotic stress is accompanied by protein glycation in *Arabidopsis thaliana*. *J Exp Bot*, 2016. 67(22): 6283-6295.
3. van der Weele CM, Spollen WG, Sharp RE, Baskin TI (2000) Growth of *Arabidopsis thaliana* seedlings under water deficit studied by control of water potential in nutrient-agar media. *Journal of Experimental Botany* 51(350): 1555-1562.
4. Oguz MC, Aycan M, Oguz E, Poyraz I, Yildiz M (2022) Drought Stress Tolerance in Plants: Interplay of Molecular, Biochemical and Physiological Responses in Important Development Stages. *Physiologia* 2(4): p. 180-197.
5. Saharan BS, Brar B, Duhan JS, Kumar R, Marwaha S, et al. (2022) Molecular and Physiological Mechanisms to Mitigate Abiotic Stress Conditions in Plants. *Life* 12(10): 1634.
6. Scarpeci TE (2008) Generation of superoxide anion in chloroplasts of *Arabidopsis thaliana* during active photosynthesis: a focus on rapidly induced genes. *Plant Molecular Biology* 66(4): 361-378.
7. Turrens JF (2003) Mitochondrial formation of reactive oxygen species. *J Physiol* 552(Pt 2): 335-44.
8. Kar RK (2011) Plant responses to water stress: role of reactive oxygen species. *Plant Signal Behav* 6(11): 1741-5.
9. Frolov A, Bilova T, Paudel G, Breger R, Gerd UB, et al. (2017) Early responses of mature *Arabidopsis thaliana* plants to reduced water potential in the agar-based polyethylene glycol infusion drought model. *J Plant Physiol* 208: 70-83.
10. Dichio B, Cristos X, Sofo A, Montanaro G (2006) Osmotic regulation in leaves and roots of olive trees during a water deficit and rewatering. *Tree Physiol* 26(2): 179-85.
11. Zhang H, Zhu J, Gong Z, Zhu JK (2022) Abiotic stress responses in plants. *Nat Rev Genet* 23(2): 104-119.
12. Shumilina J, Alena K, Tsarev A, Henry CJ, Sergei M, et al. (2019) Glycation of Plant Proteins: Regulatory Roles and Interplay with Sugar Signalling? *Int J Mol Sci* 20(9): 2366.
13. Wolff SP, Dean RT (1987) Glucose autooxidation and protein modification. The potential role of 'autoxidative glycosylation' in diabetes. *Biochem J* 245(1): 243-50.
14. Halliwell B, Chirico S (1993) Lipid peroxidation: its mechanism, measurement, and significance. *Am J Clin Nutr* 57(5 Suppl): 715S-724S.
15. Mano J (2012) Reactive carbonyl species: their production from lipid peroxides, action in environmental stress, and the detoxification mechanism. *Plant Physiol Biochem* 59: 907.
16. Vistoli G, Maddis D, Cipak A, Zarkovic N, Carini M, et al. (2013) Advanced glycoxidation and lipoxidation end products (AGEs and ALEs): an overview of their mechanisms of formation. *Free Radical Research* 47(sup1): 3-27.
17. Poulsen MW, Rikke VH, Andersen JM, Courten B, Bugel S, et al. (2013) Advanced glycation endproducts in food and their effects on health. *Food Chem Toxicol* 60: 10-37.
18. Bilova T, Elena L, Dominic B, Uta G, Paudel G, et al. (2016) A Snapshot of the Plant Glycated Proteome: STRUCTURAL, FUNCTIONAL, AND MECHANISTIC ASPECTS. *J Biol Chem*, 2016. 291(14): p. 7621-36.
19. Bechtold U, Naila R, Philip MM, Paul JT (2009) Quantitative measurement of specific biomarkers for protein oxidation, nitration and glycation in *Arabidopsis* leaves. *Plant J* 59(4): 661-671.
20. Hikmet BH, Zaeema K, Neslihan ZO, Naimat U (2015) From Genetics to Functional Genomics: Improvement in Drought Signaling and Tolerance in Wheat. *Front Plant Sci* 6: 1012.
21. Yang S, Barbara V, Wan J, Huang Y (2010) Narrowing down the targets: towards successful genetic engineering of drought-tolerant crops. *Mol Plant* 3(3): 469-90.
22. Collard BC, Mackill DJ (2008) Marker-assisted selection: an approach for precision plant breeding in the twenty-first century. *Philos Trans R Soc Lond B Biol Sci* 363(1491): 557-72.
23. Hu S, Lübberstedt T (2015) Getting the 'MOST' out of crop improvement. *Trends Plant Sci* 20(6): 372-9.
24. Ashraf M (2010) Inducing drought tolerance in plants: recent advances. *Biotechnol Adv* 28(1): 169-83.
25. Nevo E, Chen G (2010) Drought and salt tolerances in wild relatives for wheat and barley improvement. *Plant Cell Environ* 33(4): 670-85.
26. Mondini L, Nachit MM, Pagnotta MA (2015) Allelic variants in durum wheat (*Triticum turgidum* L. var. durum) DREB genes conferring tolerance to abiotic stresses. *Mol Genet Genomics* 290(2): 531-44.
27. Noli E, Teriaca MS, Maria CCS, Conti SL (2008) Utilization of SSR and AFLP markers for the assessment of distinctness in durum wheat. *Molecular Breeding* 22(2): 301-313.
28. İlbi H (2003) RAPD markers assisted varietal identification and genetic purity test in pepper, *Capsicum annuum*. *Scientia Horticulturae* 97(3-4): 211-218.
29. Eltayeb AE, Kawano N, Badawi GH, Kaminaka H, Takeshi S, et al. (2007) Overexpression of monodehydroascorbate reductase in transgenic tobacco confers enhanced tolerance to ozone, salt and polyethylene glycol stresses. *Planta* 225(5): 1255-1264.
30. Khan M, Yu X, Akira K, Asahina M, Watanabe KN (2009) Genetic engineering of Glycine betaine biosynthesis to enhance abiotic stress tolerance in plants. *Plant Biotechnology* 26: 125-134.
31. Cvikrová M, Lenka G, Jana D, Olga M, Prasil IT, et al. (2012) Effect of heat stress on polyamine metabolism in proline-over-producing tobacco plants. *Plant Sci* 182: 49-58.
32. Jang IC (2003) Expression of a bifunctional fusion of the *Escherichia coli* genes for trehalose-6-phosphate synthase and trehalose-6-phosphate phosphatase in transgenic rice plants increases trehalose accumulation and abiotic stress tolerance without stunting growth. *Plant Physiol* 131(2): 516-524.
33. Saad AS (2013) A rice stress-responsive NAC gene enhances tolerance of transgenic wheat to drought and salt stresses. *Plant Sci* 203-204: 33-40.
34. Zhang CR, Wohlhueter, Zhang H (2016) Genetically modified foods: A critical review of their promise and problems. *Food Science and Human Wellness* 5(3): 116-123.
35. Rabara RCP, Tripathi, Rushton PJ (2014) The potential of transcription factor-based genetic engineering in improving crop tolerance to drought. *Omics* 18(10): 601-614.
36. Bawa AS, Anila Kumar KR (2013) Genetically modified foods: safety, risks and public concerns-a review. *J Food Sci Technol* 50(6): 1035-1046.
37. De Block M (2005) Poly(ADP-ribose) polymerase in plants affects energy homeostasis, cell death and stress tolerance. *Plant J* 41(1): 95-106.

38. Geissler T, Wessjohann LA (2011) A Whole-Plant Microtiter Plate Assay for Drought Stress Tolerance-Inducing Effects. *Journal of Plant Growth Regulation* 30(4): 504-511.
39. Osmolovskaya N (2018) Methodology of Drought Stress Research: Experimental Setup and Physiological Characterization. *Int J Mol Sci* 19(12): 4089.
40. Marshall A (2012) Tackling drought stress: receptor-like kinases present new approaches. *Plant Cell* 24(6): 2262-2278.
41. Shiu SH, Bleecker AB (2001) Receptor-like kinases from Arabidopsis form a monophyletic gene family related to animal receptor kinases. *Proc Natl Acad Sci USA* 98(19): 10763-10768.
42. Conrath U (2009) Chapter 9 Priming of Induced Plant Defense Responses. *Advances in Botanical Research* 51: 361-395.
43. Davies WJ, Jones HG (1991) *Biology, Abscisic Acid: Physiology and Biochemistry*. Bios Scientific Publishers.
44. Kim BT (1992) Synthesis of New Abscisic Acid (ABA) Analogs Possessing a Geometrically Rigid Cyclized Side Chain. *Biosci Biotechnol Biochemistry* 56(4): 624629.
45. Cao M (2013) An ABA-mimicking ligand that reduces water loss and promotes drought resistance in plants. *Cell Res* 23(8): 1043-1054.
46. Hewage KAH (2020) Chemical Manipulation of Abscisic Acid Signaling: A New Approach to Abiotic and Biotic Stress Management in Agriculture. *Adv Sci (Weinh)* 7(18): 2001265.
47. Gupta MK (2020) Agonist, antagonist and signaling modulators of ABA receptor for agronomic and post-harvest management. *Plant Physiol Biochem* 148: 10-25.
48. Saddhe AA (2019) Reactive nitrogen species: Paradigms of cellular signaling and regulation of salt stress in plants. *Environmental and Experimental Botany* 161: 86-97.
49. Ederli L (2009) NO release by nitric oxide donors in vitro and in planta. *Plant Physiol Biochem* 47(1): 42-48.
50. Murgia I (2004) Comparative effects of various nitric oxide donors on ferritin regulation, programmed cell death, and cell redox state in plant cells. *J Plant Physiol* 161(7): 777-783.
51. Ziogas V (2015) Roles of sodium hydrosulfide and sodium nitroprusside as priming molecules during drought acclimation in citrus plants. *Plant Mol Biol* 89(4-5): 433-450.
52. García-Mata C, Lamattina L (2001) Nitric oxide induces stomatal closure and enhances the adaptive plant responses against drought stress. *Plant Physiol* 126(3): 1196-1204.
53. Zhao Y (2019) Identification of Exogenous Nitric Oxide-Responsive miRNAs from Alfalfa (*Medicago sativa L.*) under Drought Stress by High-Throughput Sequencing. *Genes (Basel)* 11(1): 30.
54. Cherepanov IA, Moiseev SK (2020) Chapter Two - Recent developments in the chemistry of sydnone and sydnone imines, in *Advances in Heterocyclic Chemistry*, E.F.V. Scriven and C.A. Ramsden, Editors Academic Press p: 49-164.
55. Fershtat LL, Zhilin ES (2021) Recent Advances in the Synthesis and Biomedical Applications of Heterocyclic NO-Donors. *Molecules* 26(18): 5705.
56. Olshevskaya V (2017) Herbicidal activity of carboranes, sydnone imine and ferrocene derivatives. *Agrokhimiya* 4: 16-21.
57. Cherepanov IA, Chichvarina OA, Samarskaya SA, Ponomaryov SKM (2018) Growth Stimulating Activity of Sydnoneimine Derivatives. *Agrochemistry* 9: 50-55.
58. Cherepanov IA (2021) 4-lithiosydnone imines: Generation and stability. Plant growth regulating activity of 4-hydroxymethyl derivatives of sydnone imines. *Journal of Organometallic Chemistry* 943: 121841.
59. Spiridonov YY (2022) A Comparative Study of Growth-Stimulating Effects of Sydnone Imine Derivatives on Corn, Sunflower, and Winter Wheat Plants. *Russian Agricultural Sciences* 48(1): S63-S68.
60. Lukatkin AS (2023) Sydnone Imines: A Novel Class of Plant Growth Regulators. *Agrochemicals* 2(2): 203-219.
61. Cherevatskaya M (2024) Sydnone Imines as a New Class of Promising Plant Growth and Stress Tolerance Modulators; A First Experimental Structure & Activity Overview. *Stresses* 4(1): 133-154.
62. Zhang A (2021) Research on the drought tolerance mechanism of *Pennisetum glaucum (L.)* in the root during the seedling stage. *BMC Genomics* 22(1): 568.



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