

# Role of HDAC in Mediating Homeostasis in Plants during Stress - A Review

Drishya Mukherjee<sup>1</sup>, Nirjhar Dasgupta<sup>2</sup>

<sup>1</sup>Department of Life Science, Guru Nanak Institute of Pharmaceutical Science and Technology, 157/f, Nilgunj Rd, Panihati, Kolkata, West Bengal, India

<sup>2</sup>Biotechnology Department, Techno India University, EM-4/1, Sector-V, Salt Lake, Kolkata – 700091, West Bengal, India  
Corresponding Author Email: [dr.nirjhardg\[at\]gmail.com](mailto:dr.nirjhardg[at]gmail.com)

**Abstract:** *Crop yield is directly impacted by plant growth and development as well as their ability to respond to changing climatic circumstances. Histone deacetylation is an epigenetic alteration that regulates a number of genes important for biological processes including stress reactions and development. The implications of histone Deacetylation dynamics on vegetative growth, fawn development, fruit ripening, and biotic and abiotic stress responses have been the primary focuses of this study. Histone acetylation dynamics is one of the best-studied PTM processes. Like the majority of other PTMs, acetylation is reversible, and its dynamic management depends on the activity of histone acetyltransferases (HATs) and histone deacetylases (HDACs). Typically, HATs bind acetyl groups (CH<sub>3</sub>COO<sup>-</sup>) to lysine residues in both the globular and N-terminal tails of histones to activate genes. However, by restoring the histones to their basal state, which largely results in gene repression, the removal of these acetyl groups by HDACs serves to offset the actions of HATs. In exceedingly rare instances, HATs and HDACs may, respectively, induce the activation and repression of genes. HATs and HDACs both target the histone lysine residues H3K9, H3K14, H3K36, H4K5, H4K8, H4K12, and H4K16 in order to preserve the dynamics of histone acetylation. Hyper- and hypo-acetylation, which are often associated with the activation and repression of certain genes, are the results of the dynamics of histone acetylation. We have also emphasized the information gaps that need to be researched in order to completely understand the role of histone deacetylation dynamics in plants. Finally, a thorough understanding of the dynamics of histone deacetylation might help increase stress resistance and lessen production losses in a variety of crops caused by environmental changes.*

**Keywords:** HDACs, HATs, Epigenetic Modification, Stress Response, Homeostasis

## 1. Introduction

DNA is wrapped up into chromatin in eukaryotes by the key histone proteins histone H2A, H2B, H3, and H4. Acetylation, methylation, phosphorylation, ubiquitination, sumoylation, and ADP ribosylation are just a few of the post-translational changes that histone proteins can undergo [1] (Z. Wang et al., 2014a). The mechanism of histone acetylation involves the covalent addition of an acetyl moiety to the lysine ε-amino group on the histone protein tails, and it is mediated by the counteracting action of two enzymes, HAT (histone acetyltransferase) and HDACs (histone deacetylase). Histone deacetylase activity was described first in peas and the first RPD3-HDAC gene reported in plants was ZmRPD3 in maize [2] (Rossi et al., 1998). Three families can be used to group HDACs. The most well-researched member of the first family is the yeast Reduced Potassium Deficiency 3 (RPD3), which is found in all eukaryotes. The second family, known as HD2, was first discovered in maize and is thought to exist only in plants. A nicotinamide adenine dinucleotide (NAD)-dependent enzyme from the yeast Silent Information Regulator 2 (Sir2) is homologous to the structurally different third family of sirtuins [3] (Hollender & Liu, 2008). HDACs and HATs can function in protein complexes as co-repressors and co-activators of transcription. They can be connected to chromatin remodelers to regulate the accessibility of DNA to various machinery [4] (Tai et al., 2005). Histone acetylation is a crucial developmental signal in the seed germination process, as demonstrated by GeneChip arrays showing trichostatin A (TSA), an inhibitor of HDACs, can activate or repress the expression of numerous genes during seed

germination [5] (Chang & Pikaard, 2005). The best-described RPD3-like HDACs in Arabidopsis are AtHDA19 and AtHDA6, which have distinct and overlapping roles in seed development and seed performance [6] (Z. Wang et al., 2014b). Inferring potential roles during seed development and germination, microarray research revealed that HDA716 showed a significant expression in developing endosperm and germinating seeds, whereas HDA710 and HDA703 indicated greater expression in ingested and germinating seeds [7] (Hu et al., 2009a). Any change in the environment that has a detrimental impact on a plant's natural physiological state is referred to as stress. The ability of the plants to adapt allows them to survive in situations where normal growth is not possible. The majority of the time when stressed conditions exist, the unadapted plants die. Abiotic (non-living) and biotic (living) factors are the two main categories used to categorize plant stress factors (Mosa et al., 2017). Abiotic elements like light, water, temperature, and salinity are crucial, whereas biotic factors like pests, diseases, and other creatures have an impact on how plants grow and develop. Plant diseases are generally caused by pathogens such as fungi, bacteria, nematodes, and viruses. Fungi and bacteria can affect different plant organs and create symptoms such as leaf spots, vascular wilts, and cankers. Nematodes consume plant cell material and target every part of the plant. They can also make it easier for soil-borne diseases to enter the root system, which results in indications of nutrient insufficiency including stunting or wilting. Even though they frequently do not kill their hosts, viruses inflict local lesions and systemic harm that results in deformities, stunting, and chlorosis in different plant parts. On the other side, emphasis needs to be placed on insects

and mites. Plants are harmed by them when they lay eggs or feed. Insects with piercing suckers can serve as vectors. According to research on abiotic stress, one of the main environmental stresses that have an impact on plant growth and development is salt stress (Ding et al., 2009). Salt stress can lead to a hazardous build-up of sodium and an increase in intracellular osmotic pressure. Drought is another such frequent environmental stress which affects plant physiology. More than cell division, environmental stress limits cell expansion. It inhibits several physiological and biochemical activities, including photosynthesis, respiration, translocation, ion uptake, carbohydrates, nutrition metabolism, and growth promoters, which all contribute to lessening plant growth (Liu et al., 2008). While temperature pressures are undoubtedly limiting factors for crops grown in marginal areas, agricultural yield is frequently subject to arbitrary climatic changes everywhere. Current rumors regarding worldwide (Iba, 2002). Plants respond to biotic and abiotic stresses through intricate signaling mechanisms. More and more evidence points to the frequent involvement of many defense genes as common or generic stress-responsive genes in the response to diverse biotic and abiotic stimuli. Despite significant overlap in response pathways to many environmental challenges, plants coordinate extensive transcriptional reprogramming and exhibit a unique pattern of transcript response when faced with multiple stresses. Numerous studies found interactions between combined stress therapy's synergistic and antagonistic effects. Notably, abiotic challenges can increase plant vulnerability to biotic stresses and detrimental to biotic stress resistance. According to studies employing microarrays on the genetic response of *A. thaliana* to concurrent drought stress and infection with the plant-parasitic worm *Heterodera schachtii*, drought stress increased *A. thaliana*'s susceptibility to nematode infection (Liu et al., 2008). A distinct response that was especially activated by the combination of biotic/abiotic stress was also visible in the induction patterns of differentially expressed genes following these stress treatments, in addition to a specific response to each stress.

### Types of HDACs in Plant

There are 19 HDACs found in rice. Inferring potential roles during seed development and germination, microarray research revealed that HDA716 showed significant expression in developing endosperm and germinating seeds, whereas HDA710 and HDA703 indicated greater expression in ingested and germinating seeds [8] (Hu et al., 2009b). Artificial micro RNA (amiRNA)-induced down regulation of HDA703 in plants resulted in partial or total sterility and awn seeds that were associated with higher levels of histone H4 acetylation, indicating that HDA703 In addition to mediating the interaction between histone acetylation and other histone modifications, histone deacetylases can aid in the development of epigenetic states. Histone deacetylase HD1's enzymatic activity in *Z. mays* was demonstrated to be low in the dry embryo and to grow throughout germination, whereas HD2 was demonstrated to be the major enzyme in the dry embryo and to virtually completely vanish at later germination [9] (Georgieva et al., 1991). Additionally, it was discovered that the genes for three Rpd3-type histone deacetylases (ZmHDA101, ZmHDA102, and ZmHDA108) had comparable expression patterns and accumulated more in the endosperm [10] (Varotto et al., 2003). All of these

findings point to possible roles for HDACs in the growth and germination of maize seeds.

In addition to mediating the interaction between histone acetylation and other histone modifications, histone deacetylases can aid in the development of epigenetic states. Our prior research demonstrated that HDA6 regulates DNA methylation and histone deacetylation in *Arabidopsis* via interacting with the DNA methyltransferase MET1 [11] (Luo, Yu, et al., 2012). Additionally, a protein complex containing HDA5 and HDA6 directly interacts with the histone demethylase FLD. This implies that there is regulatory interference between histone deacetylation and demethylation [12] (Yu et al., 2011). To silence transposons, histone methyltransferases SUVH4/5/6 and HDA6 remove the acetyl group from histone H3 and add the methyl group to histone H3K9 [13] (Yu et al., 2017). The finding that the specific histone acetylation site H3K14, which is connected to transcription activation, is propionylated and butyrylated *in vivo* [14] (Kebede et al., 2017), provides additional proof that histone acetylation and other modifications may cooperate to influence chromatin condensation and transcription outputs. In the soybean genome, 28 HDAC coding genes have been found. We have identified 28 HDAC-coding genes in YFP-tagged transient expression tests that demonstrated the subcellular localization of the soybean genome [15] (Yang et al., 2018a). GmHDACs' subcellular localization was confirmed by YFP-tagged transient expression experiments. In addition to analysing the levels of histone acetylation and methylation in response to cold and heat treatments, quantitative RT-PCR was utilised to discover the tissue-specific and stress-responsive expression patterns for nine representative genes [16] (Liew et al., 2013). Insight into the function of GmHDAC genes in several facets of plant growth and development, including the reaction to abiotic stress, is provided by our collective research. GmHDACs. While quantitative RT-PCR was used to identify the tissue-specific and stress-responsive expression patterns of nine representative genes. Additionally, the amounts of histone acetylation and methylation under cold and heat treatments were examined [17] (Yang et al., 2018b). Our findings together offer insight on the function of GmHDAC genes in several facets of plant development and growth, including the response to abiotic stress. Both HATs and HDACs selectively target the histone lysine residues H3K9, H3K14, H3K36, H4K5, H4K8, H4K12, and H4K16 in order to maintain the dynamics of histone acetylation [18] (Bjerling et al., 2002). For instance, the histone acetylase/deacetylase complex, histone methylase/demethylase chromatin remodelling complex, and DNA methylase/demethylase complex combinations all have an effect on the transcriptional state of the genomic locus of transcription as a result of histone acetylation dynamics [19] (Hung et al., 2019). Because of this, the effects of HATs and HDACs are often combinatorial rather than linear, and they must be understood in the context of the full "histone code." Additionally, histones can go through a variety of additional alterations other from acetylation and deacetylation [20] (Nie et al., 2019). The various combinations of specific alterations at different chromatin-local amino acid residues inside nucleosomes have differing effects on the local chromatin structure and have the ability to either activate or

repress the relevant genomic loci [21] (B. Wang et al., 2018). For instance, the transcriptional state of the genomic locus of transcription is influenced by the interactions of the histone acetylase/deacetylase complex with the histone methylase/demethylase chromatin remodelling complex and the DNA methylase/demethylase complex [22] (Li et al., 2020). A histone deacetylase is the "eraser," removing an acetyl group from the acetylated lysine residues of the core histones that the HATs added. Deacetylation often causes gene repression to regulate a number of biological processes. Similar to HATs, the amount of HDACs varies between plant species. Arabidopsis, as an example, contains 18 HDACs (Pandey, 2002). 30 in upland cotton (Avci et al., 2013), 28 in soybean (Yang et al., 2018c), 14 in tomato (AieseCigliano et al., 2013), 11 in litchi (Peng et al., 2017), 13 in grape (Aquea et al., 2010), and 18 in rice (Fu et al., 2007) [23-29].

### Functions in Biotic Stress Response

Various diseases can cause biotic stress, which can damage the host plants and reduce yield. Numerous studies have demonstrated the importance of a number of HATs and HDACs in biotic stress responses that increase plant immunity to the causative infections. Hormones including ethylene, jasmonic acid, and salicylic acid (SA) play a significant role in how plants respond to biotic and abiotic stresses [30] (Kumar et al., 2021). According to a recent research in Arabidopsis [31] (S. Kim et al., 2020), the GCN5 controls SA-responsive genes by raising the quantity of H3K14ac on their promoters in response to pathogen stress. However, it has been found that HDA19 controls genes linked to ethylene and JA signalling in response to pathogen attack [32] (Zhou et al., 2005). Additionally, HDA19 interacts with WRKY38 and WRKY62 to modify the fundamental defensive reactions by inhibiting SA signalling [33]. The plant-specific histone deacetylase HD2B is phosphorylated by MPK3 (MITOGEN- (K.-C. Kim et al., 2008a) ACTIVATED PROTEIN KINASE 3) to move from the nucleolus to the nucleoplasm when the pathogen *Pseudomonas syringae* pv. tomato DC3000 (Pst DC3000) infects a plant [34] (Latrasse et al., 2017). The HD2B-MPK3 module maintains a basal level of several defense-related genes in order to keep the innate immunity at its base level. Therefore, the pathogen is more likely to attack the hd2b mutant plants. The CBP/p300-type histone acetyltransferases AtHAC1/5 form a coactivator complex with NPR1 (NON-EXPRESSER OF PR GENES 1) and TGA (TGACG-BINDING FACTOR) to activate the transcription of PATHOGENESIS RELATED (PR) genes [35] (Jin et al., 2018a). The outcome of this acetylation-mediated epigenetic reprogramming is the development of Pst DC3000 immunity in the host plants. On the other hand, a histone deacetylase by the name of HDA9 reduces innate immunity by physically interacting with HOS15 [36] (L. Yang et al., 2020a). During the infection of Pst DC3000 by a pathogen, the HDA9-HOS15 complex inhibits the expression of the NLR (NOD-LIKE RECEPTOR) and SNC1 (SUPPRESSOR OF npr1-1, CONSTITUTIVE 1) by H3K9 deacetylation. GCN5 controls the expression of the wax biosynthesis-related gene CER3 (ECERIFERUM3) in Arabidopsis by acetylating H3K9/14 lysine residues [37] (T. Wang et al., 2018). To encourage the transcription of the ECR (ENOYL-COA REDUCTASE) gene, which is

responsible for a critical component of cuticular wax, in wheat, GCN5 connects with ADA2 and EPBM1 [38] (Kong et al., 2020a). During Bgt infection, a repressor complex composed of HDA6 and HOS15 suppresses the expression of the defense-related genes TaPR1, TaPR2, TaPR5, and TaWRKY45. These genes are crucial for the plant's defense against Bgt [39] (J. Liu et al., 2019a). Another HDAC, TaHDT701, works with the HDA6-HOS15 complex during Bgt infection to suppress the PR1/2/5 genes [40] (Zhi et al., 2020). These investigations demonstrate that the histone deacetylases HDA6 and HDT701 are antagonistic regulators of innate immunity in wheat. By deacetylating histone H4 on its promoter, HDT701 also reduces innate immunity in rice and defense-related genes including PRR (PSEUDO-RESPONSE REGULATOR) [41] (Ding et al., 2012a). HDACs have a number of defense-related activities in plants against bacterial and fungal invaders, but they are seldom linked to plant susceptibility to viral infection.

### Functions in Abiotic Stress Response

#### Salt and Drought Stress:

It seems that HDAC plays a more nuanced function in the reaction to salt stress. Recent data suggest that the salt-stress response is significantly regulated by HDAC genes. According to the research, HDAC inhibition affects both the ability to tolerate salt stress and its ability to decline. By activating the endogenous promoter activity of AREB1 (ABA-RESPONSIVE ELEMENT BINDING PROTEIN 1) by the CRISPRa dCas9 HAT approach, it was shown that AtHAC1 had a favourable influence on gene transcription. Increased drought tolerance was observed in Arabidopsis in transgenic plants harbouring the CRISPRa dCas9HAT gene due to the upregulation of RD29A (RESPONSIVE TO DESICCATION 29A) expression [42] (Roca Paixão et al., 2019). By lowering the H3K9ac level of the stress-responsive genes, HDA9 lessens the plant's sensitivity to salinity and drought conditions [43] (Zheng et al., 2016). This activity inhibits the activity of WRKY53 [44] (Zheng et al., 2020). In Arabidopsis, HDA6 interacts with HD2C to modulate H3K9ac and H3K14ac lysine residues to control the ABA- and salt-stress-responsive genes [45] (Luo, Wang, Liu, Yang, Lu, et al., 2012a). HDA6 also regulates JA signaling to control the drought-responsive network [46] (J.-M. Kim et al., 2017). Under high salt and drought conditions, microarray research of rice showed that the expression of OsHDA703 and OsHDA710 was elevated, whereas the expression of numerous other HDAC genes was inhibited (Hu et al., 2009c) [47]. Additionally, the stressors of ABA, salt, and PEG had an impact on the expression of OsHDT701 and OsHDT702 (Zhao et al., 2015) [48]. It's interesting to note that high salt levels suppressed OsHDA709 and OsSRT702, while drought therapy induced them. Using H3K9 deacetylation, genome-wide acetylation and binding study revealed that OsSRT701 may directly control the expression of stress-related genes (Zhong et al., 2013) [49]. *Magnaporthe oryzae* and *Xanthomonas oryzae* pv. *oryzae* (Xoo) resistance were increased as a result of overexpressing OsHDT701 in transgenic rice (Ding et al., 2012b) [50]. By deacetylating H3K9 marks on the promoter and suppressing WRKY33, a suppressor of the drought responses in cotton, GhHDT4D, a cotton homolog of HD2D, regulates drought responses [51] (L. Wang et al.,

2015). Additional rice HDACs involved in responses to salt and drought stress have been discovered through molecular research. ABA and drought tolerance are negatively regulated by a co-repressor complex that includes HDA702 and TOPLESS-RELATED3 (OsTPR3) [52] (Zhao et al., 2016a). The negative regulatory domain D of OsbZIP46 limits OsbZIP46 function and is necessary for physical interaction with the Mediator of OsbZIP46 deactivation and degradation (MODD) [53] (X. Cheng et al., 2018a). The drought tolerance mediated by ABA signaling is positively regulated by OsbZIP46. Additionally, MODD interacts with the OsTPR3-HDA702 complex to prevent OsbZIP46 target genes from being transcribed, negatively affecting ABA signaling and drought tolerance. In addition to the co-repressor complex's function in the drought stress response, HDA702 and TOPLESS-RELATED1 (TPR1) together create a transcriptional repression complex that adversely controls salt tolerance. The main factors influencing salt tolerance The transcription factor OsIDS1, which is encoding for the proteins LATE EMBRYOGENESIS ABUNDANT PROTEIN1 (LEA1) and SALT OVERLY SENSITIVE1 (SOS1), suppresses the expression of these genes in rice through H3 deacetylation. Because of this, rice with an OsIDS1 deletion has greater salt tolerance [54] (S. Cheng et al., 2018). Our molecular studies show that HDA702 performs dual roles in drought and salt stress responses via distinct processes by producing a number of co-repressor complexes. Along with the model plant Arabidopsis, other plants and trees have also been studied for their histone deacetylases. Common beans' HDA6 levels rise in response to cold stress, suggesting that it likely contributes to the plant's capacity to survive abiotic stress [55] (Hayford et al., 2017a). The overexpression of the Populus histone deacetylase, 84KHDA903, increased the expression of the drought-responsive genes DREB3, DREB4 (DEHYDRATION-RESPONSIVE-ELEMENT-BINDING 3/4), and LEA5, which in turn improved the stress responses to drought in transgenic tobacco (LATE EMBRYOGENESIS ABUNDANT 5) [56] (Ashraf & Harris, 2004a). The over-expression of PtHDT902, a plant-specific HD2 gene, led to the activation of genes involved in the production of gibberellic acid (GA), including ENT-KAURENE OXIDASE (KO), ENT-KAURENOIC ACID HYDROXYLASE (KAO), and GIBBERELLIN 20-OXIDASE (GA20ox) [57] (Ma et al., 2020). As a consequence, transgenic Populus did not generate adventitious roots, but transgenic Arabidopsis had increased main root growth. On the other hand, the salt-responsive genes HIGH-AFFINITY K<sup>+</sup> TRANSPORTER 1 (HKT1) and GALACTINOL SYNTHASE 4 (GOLS4) were overexpressed in the transgenic lines, which resulted in a reduction in their expression [58] (S.-W. Li, 2021). PtHDT902 is an interesting example of a histone deacetylase that may control numerous signalling pathways in different ways.

#### Temperature (Heat and Cold stress):

By controlling the expression of genes that are responsive to cold stress, HDA6 is essential for cold tolerance [59] (To et al., 2011). Additionally, HDA6 interacts with the cold signaling attenuator HOS1 and is prevented from binding to FLC chromatin, delaying flowering under short-term cold stress [60] (Jung et al., 2013). Han found that transgenic

Arabidopsis that overexpressed HD2D was more resilient to cold stressors [61] (Han et al., 2016). In plants subjected to heat treatment, HD2C regulates heat-activated genes negatively by interacting with the chromatin remodeling protein BRAHMA (BRM) [62] (Buszewicz et al., 2016a). Luo suggested that HD2-type HDACs functionally engage with RPD3-type HDACs in the multiprotein complex to control stress response genes in plants [63] (Luo, Wang, Liu, Yang, & Wu, 2012). PvHDA6 expression in common bean (*Phaseolus vulgaris* Linn.) increased in response to cold treatment, suggesting that PvHDA6 is a cold response gene that regulates plant abiotic stress tolerance [64] (Hayford et al., 2017b). The transcriptional patterns of ZmHDACs, such as ZmHDAC1, ZmHDAC2, ZmHDAC3, ZmHDAC6, ZmHDAC8, and ZmHDAC110, were changed in response to low temperature in the maize (*Zea mays*). After exposure to cold, histone H3K9ac, H4K5ac, and H4 levels dropped [65] (Hu et al., 2011). Through interaction with other activators like HsfB1, which promotes heat stress tolerance in tomatoes, HAC1 has been discovered to maintain or restore the expression level of various viral and housekeeping genes [66] (Bharti et al., 2004). Banana fruits held at 7°C started to exhibit indications of chilling injury after just one day of cold storage, as opposed to the control banana fruits stored at 22°C. Fruit peels' epidermis turned dark green and eventually turned brown as cold storage duration increased, indicating that the fruit had suffered significant damage. Malondialdehyde (MDA) level and relative membrane conductivity were also significantly higher in the cold-stored fruits, which supports the chilling injury caused by cold stress [67] (Song et al., 2019a). The identification of MaFADs and the patterns of their expression in response to cold stress FADs are critical components of the metabolic pathways for fatty acid desaturation. We discovered 14 MaFADs genes altogether using the banana genome and transcriptome data. The o-3 desaturase group and the o-6 desaturase group are the two different forms of FADs found in plants [68] (KAWAGUCHI et al., 2000). Following the construction of a phylogenetic tree of FADs from bananas, tomatoes, and Arabidopsis, banana MaFADs were classified in accordance with their evolutionary relationship. For instance, six MaFADs were identified as MaFAD6-1/2/3/4/5/6, which belong to the o6-desaturase group, as opposed to seven MaFADs that were termed MaFAD3-1/2/3/4/5/6/7 and are members of the o3-desaturase group. MaFAD4, the sole remaining gene, is a member of the FAD4 family. These o-3 MaFADs from bananas responded differentially to cold stress, according to quantitative real-time PCR (qRT-PCR) research. Three of them (MaFAD3-1, MaFAD3-3, MaFAD3-4, and MaFAD3-7) were clearly upregulated during cold stress, notably at the beginning of the fruit's response to low temperature. Notably, MaFAD3-1, MaFAD3-3, and MaFAD3-4 belong to the FAD3 homologous group, but MaFAD3-7 belongs to the FAD7/8 homologous group. This indicates that MaFAD3-1/3/4 and MaFAD3-7 may serve similar roles to AtFAD3 and AtFAD7/8, respectively, by promoting the conversion of LA (C18: 2) to ALA (C18: 3). These four o-3 MaFADs were chosen for additional research because of this [69] (Song et al., 2019b).

**ABA Signalling**

The hormone ABA is essential for stress tolerance, and plants may respond to stimuli in a number of ways thanks to its signalling. The ROP (RHO OF PLANTS) family of proteins, which includes ROP6, ROP10, and ROP11, regulates ABA signalling in the early phases of stress [70] (Lee & Seo, 2019). The HDA15-MYB96 protein complex silences these genes by deacetylating the appropriate histone H3 and H4 sites. Via repressing the ABA receptor-encoding genes *PYL1*, *PYL4*, *PYL5*, and *PYL6* (PYRABAC-TIN RESISTANCE 1 (PYR1)-LIKE 1/4/5/6) by H3K9 deacetylation, HDA19 and MSI1 (MULTICOPY SUPPRESSOR OF IRA1) modulate ABA signalling in Arabidopsis [71] (Mehdi et al., 2016a). The Arabidopsis *hda19* mutants showed increased ABA accumulation in young seedlings and better tolerance to a variety of stresses [72] (Ueda et al., 2017). By suppressing the drought-responsive genes through deacetylation of H3K9ac lysine residues, BdHD1, a homolog of HDA19 in Brachypodium, controls ABA signalling and drought tolerance [73] (Ashraf & Harris, 2004b). CYP707A1/2 promotes hydroxylation, which makes ABA inactive, under typical conditions. During drought stress, the HDA9-PWR-ABI4 histone deacetylase complex inhibits the CYP707A1/2 genes and

promotes ABA accumulation. [74] (Baek et al., 2020a). These results claim that when stress is present, HDA9, HDA15, and HDA19 collaborate to alter ABA signalling at different phases [75] (Khan et al., 2020). The MaHDA2-MaMYB4 repressor complex recruits the promoters of the three fatty acid desaturase genes MaFAD3-1, MaFAD3-3, MaFAD3-4, and MaFAD3-7 in bananas to suppress transcription during cold stress [76] (Song et al., 2019c). As a result, the signalling cascades that underpin the stress responses are significantly impacted by changes to histone acetylation caused by different HAT and HDAC. In rice, an RPD3-type histone deacetylase named HDA1 that interacts with IDS1 (INDETERMINATESPIKELET1) and TPR1 (TOPLESS-RELATED PROTEIN1) suppresses the expression of salt stress-responsive genes including SOS1 (SALT OVERLY SENSITIVE1) and LEA1 (LATE EMBRYOGENESIS ABUNDANT PROTEIN1) [77] (X. Cheng et al., 2018b). OsHDA705, a different RPD3-type histone deacetylase, regulates the genes that cause the production of GA and ABA during rice seed germination. During seed germination in rice, OsHDA705 over expression lowers ABA levels and salt stress tolerance. Osmotic resistance, however, rises throughout the seedling stage [78] (Zhao et al., 2016b).

**Table 1:** Summary of known HAT and HDAC protein complexes have a vital role in different biotic and abiotic stress responses in plants

HATs/HDACs Complex	Target Genes	Associated histone marks	Functions	Plant	Reference
<b>Biotic Stress Responses</b>					
HDA19-WRKY38/62	<i>PR1</i>		Fine-tuning of basal defense-responses	<i>Arabidopsis</i>	[79] (K.-C. Kim et al., 2008b)
HAC-NPR1-TGA	<i>PR</i>	H3ac	IMMUNITY	<i>Arabidopsis</i>	[80] (Jin et al., 2018b)
HDA9-HOS15	<i>SNCI</i>	H3K9ac	immunity	<i>Arabidopsis</i>	[81] (L. Yang et al., 2020b)
GCN5-ADA2-EPBM1	<i>ECR</i>	H3K4/K9/K14/K27ac and H4K5ac	Cuticular wax biosynthesis	wheat	[82] (Kong et al., 2020b)
TaHDA6-TaHOS15-TaHDT701	<i>TaPR1, TaPR2, TaPR5 and TaWRKY45</i>	H3K9/H4K16ac	Defence-responses against <i>Blumeriagraminis</i>	wheat	[83] (J. Liu et al., 2019b)
<b>Abiotic Stress Responses</b>					
GCN5-ADA2b-AREB1	<i>NAC6/7/120, ZmEXPB2 AND ZmXET1</i>	H3K9ac	Drought responses	Populus	[84] (S. Li et al., 2019)
ZmGCN5-ZmHATB		H3K9ac	Salt stress responses	maize	[85] (H. Li et al., 2014)
HDA15-MYB96	<i>ROP6/10/11</i>	H3 and H4ac	ABA signalling and early stage stress responses	<i>Arabidopsis</i>	[86] (Lewkowicz & Way, 2019)
HDA19-MSI1	<i>PYL1, PYL4, PYL5, PYL6</i>	H3K9ac	ABA signaling	<i>Arabidopsis</i>	[87] (Mehdi et al., 2016b)
HDA9-AB14-PWR	<i>CYP707A1/2</i>		ABA homeostasis	<i>Arabidopsis</i>	[88] (Baek et al., 2020b)
HDA9-PWR	<i>PIF4, YUCCA8</i>	H3K9ac	Thermogenesis	<i>Arabidopsis</i>	[89] (Tasset et al., 2018)
HDA15-HFR1	<i>PIF4, HB2, XTR7</i>	H3K14ac	HEAT STRESS	<i>Arabidopsis</i>	[90] (Shen et al., 2019)
HDA6-HD2C	<i>ABII/2</i>	H3K9/K14ac	ABA and salt response	<i>Arabidopsis</i>	[91] (Luo, Wang, Liu, Yang, Lu, et al., 2012b)
SRT1/2-ENAP1	<i>ETHYLENE RESPONSIVE GENES</i>	H3K9ac	Ethylene signalling	<i>Arabidopsis</i>	[92] (Zhang et al., 2018)
HD2C-HOS15	<i>CORs</i>	H3ac	Cold stress-responses		[93] (Park et al., 2018)
HD2C-BRAHMA	<i>HSP101 and HSFA3</i>	H4K16ac	Stress-responsive	<i>Arabidopsis</i>	[94] (Buszewicz et al., 2016b)
HDA1-IDS1-TPR1	<i>SOS1, LEA1</i>	H3ac	Salt stress-responses	rice	[95] (X. Cheng et al., 2018c)
MaHDA2-MaMYB4	<i>MaFAD3-1, MaFAD3-7</i>	H3 and HDac	Cold stress responses	banana	[96] (Xu et al., 2013)

**Salinity Stress Responses:**

Chemical inhibition of HDAC proteins is a promising approach that has to be examined for its ability to increase

salt stress tolerance in plants under field conditions. Research on HDAC gene mutations revealed that salt stress response might be positively and negatively impacted by

HDAC suppression in a recessive mutation. Salinity stress tolerance improved following multiple disruptions of class I (HDA19) and class II HDAC genes, showing that hierarchical regulation allows the inhibition of even nonclass selective HDACs to enhance stress tolerance [97] (Ueda et al., 2017b). The screening of 13 different selective HDIs (class I selective HDIs FK228, Ky-2, MC1293, MGCD-0103, and MS-275; class II selective HDIs MC1568, TMP195, TMP269, and Tubastatin A; and nonclass selective HDIs JNJ-26481585, LBH-589, sodium butyrate (NaBT), and trichostatin A (TSA)) revealed that 8 of the HD HDIs have been looked into as a way to improve cassava's capacity to endure salt stress. When fed with SAHA, a kind of HDI, cassava plants were less stressed by the high salt conditions. How the SAHA treatment was able to lessen salt stress in cassava plants is still a mystery [98] (Patanun et al., 2017).

Treatment of plants with HDI chemicals is considered to be a potentially effective way for enhancing salt stress resistance in crops when it is difficult to add unique, commercially important traits through genetic modification or conventional breeding techniques. Additionally, using HDIs at the right time to reduce environmental challenges might be beneficial since it could limit the growth inhibition brought on by the expression of stress-responsive genes. Before using chemical approaches to improve stress tolerance can become a workable management strategy, the majority of present HDIs share targets (HDACs) in both plants and animals, which raises substantial safety issues. This calls for the development of a plant-specific HDI. Finding a mechanism to stop the inhibitory action of HDIs on non-plant HDACs is both feasible and worthwhile (Sako et al., 2016), especially now that the HDAC that must be inhibited in order to improve salt-stress tolerance has been identified. We must address the critical global requirement of improving salt-stress tolerance in crops if we are to provide enough food for a growing global population.

Under salinity stress conditions, the expression of the ABA and abiotic stress-responsive genes ABI1, ABI2, KAT1, KAT2, DREB2A, RD29A, and RD29B was reduced, which resulted in a salt-sensitive phenotype in *axe1-5* and HDA6 RNA-interfering plants (Chen et al. 2010, 100). Since their complex formation with HDA6 was established and their single and double mutants display elevated histone H3K9K14 acetylation [101] (Luo, Wang, Liu, Yang, Lu, et al., 2012c), research by Luo suggests that HD2C and HDA6 proteins collaborate to govern the response to salt stress. HD2C overexpression resulted in increased resistance to salt stress, which is consistent with the *hd2c* phenotype [102] (Sridha & Wu, 2006). Together, HDA6 and HD2C's interaction has a beneficial regulatory impact on how the body responds to salt stress.

In the Col-0 background, two *hda19* recessive alleles have shown resistance to salt stress [103] (Ueda et al., 2017c).

### Heavy Metal Stress Response

Heavy metal toxicity in the soil is very common in industrial areas that cause lethal effects on crop growth, development, and productivity by modifying their physiological and metabolic processes (Gupta et al., 2014). Metals like iron, copper, zinc and manganese are required by plants in very

low amount as they act as cofactors of several enzymatic reactions. Higher concentrations of these metals become toxic to plants' physiology (Gielen et al., 2012).

Histone acetylation and DNA methylation work together to regulate gene expression. Histone acetylation is a different chromatin modification associated with transcriptional activity. Histone acetylation homeostasis is maintained through the interaction of histone acetyl transferases (HATs) and histone deacetylases (HDACs) [104] (Shafiq et al., 2020a). Histone deacetylation is essential for plant growth and development, blooming, the production of seeds, and the control of biotic and abiotic stresses, such as the impacts of salt, cold, and drought. The relevance of Pb, Cd, and Zn in other crops is suggested by the fact that these metals influence the gene expression of HATs and HDACs in cotton. The maize HDACs have an effect on plant growth. There hasn't been much research done on the effects of heavy metals on histone acetylation in agricultural plants, notably the function of maize histone deacetylases in the tolerance of metal stress. The possible interactions and coordination of Zn, Pb, and Cd for their absorption and/or translocation, as well as the potential involvement and epigenetic regulation of ZIP transporters in this particular interaction, have also received limited attention. We expected that divalent metals (Pb, Cd, and Zn) would interfere with one another's absorption and translocation due to the non-specific nature of divalent Zn transporters. Furthermore, we put forth the theory that heavy metals alter the epigenetic profiles of maize plants, which in turn regulates the expression of Zn transporters.

We suggested that HDACs could also aid in the adaptation of plants to these metal stresses. The expression of each HDAC in maize in response to the administration of Pb, Cd, or Zn alone or in combination was therefore investigated. We found that each HDAC responds to metals in a unique way. In contrast to the control, Zn increased the expression of HD2a while decreasing the expression of HDA102, HD2b, HD2c, and HDA106. Every HDAC's expression was reduced in response to Pb compared to the control. The expression of all HDACs was elevated in response to Cd in contrast to the control, and HD2a was raised even more than Zn alone. These results show distinct impacts of Pb, Cd, and Zn on the regulation of HDACs, as well as distinct acetylation levels. For instance, Pb and Cd, respectively, may produce histone hyperacetylation and hypoacetylation. The expression of HDACs was then investigated in relation to the presence of Pb, Cd, and Zn. HDA102, HDA110, HD2a, HD2b, and HD2c expression increased in response to Cd + Zn compared to control, although it remained lower than that of Cd alone. In response to Cd + Pb, the expression of HD1b, HDA102, HDA110, HD2a, HD2c, and HDA106 increased in comparison to the control, although it was still less than that of Cd alone. This shows that Pb and Zn function to inhibit the increase of all HDAC expressions caused by Cd. In response to Pb + Zn, the expression of HDA102, HD2b, HD2c, and HDA106 dropped, falling below control levels to levels similar to Pb or Zn alone. The histone deacetylases RPD3, HDA1, or HDA108, on the other hand, did not appear to be expressed in maize roots exposed to Pb, Cd, or Zn alone or in combination [105] (Shafiq et al., 2020b). Similar to how Ni-induced

hypermethylation results from inhibiting H3K9 demethylation, it was discovered that Ni-induced decreased histone acetylation results from inhibiting histone acetyltransferase (HAT) activity, with no impact on histone deacetylases (HDAC; Kang et al., 2003). Ni might also cause histone ubiquitinations and phosphorylations in A549 cells, as shown by Ke et al. (2006, 2008a, 2008b). As a result of treatment with soluble NiCl<sub>2</sub> or insoluble Ni<sub>3</sub>S<sub>2</sub>, H2A and 2B ubiquitination levels in A549 cells rose in a dose-and time-dependent manner, suggesting that soluble and insoluble Ni compounds had similar epigenetic effects on cell ubiquitination of histones. Ni does not change the amount of non-histone ubiquitinated proteins in cells, indicating that the H2A and H2B ubiquitination is a distinct epigenetic response of the cells to Ni therapy (Ke et al., 2008a).

## 2. Conclusion

Global agricultural and food production is currently facing a number of issues due to a fast expanding population and climate change. If we can comprehend plant stress reactions and develop novel plant protection strategies, we might be able to achieve sustainable agricultural output. Plants may be able to respond to varying biotic and abiotic stress conditions through epigenetic changes. Under various stress situations, cellular modifications such as DNA methylation, chromatin changes, small RNA pathways, and DNA modifications all cooperate to control the expression of stress-responsive genes in plants. Today, a variety of abiotic stressors can be managed epigenetically to enable distinct plant species to adapt to various environmental conditions. Numerous crops have been subjected to epigenetic techniques. In plant species exposed to various environmental challenges, the use of epigenetics may be another way to build defense systems. To make this intriguing field feasible and broadly applicable, additional study is unquestionably required. To maximize its use in crop protection programs in the future, it will be crucial to develop markers to monitor epigenetic alterations, improve our understanding of how long priming lasts, and make technological advancements. According to recent investigations, HATs or HDACs can also acetylate or deacetylate non-histone proteins [106] (Kovacs et al., 2005). For instance, Arabidopsis HDA6 can enhance brassinosteroid (BR) signaling by directly deacetylating the GSK3-like kinase BR-INSENSITIVE 2 (BIN2) and preventing its kinase activity in the signaling pathway [107] (Hao et al., 2016). Additionally, the Arabidopsis c-Myc-Binding Protein-1 (AtMBP-1lysine) 's may be deacetylated by the NAD<sup>+</sup>-dependent HDAC SRT1 to significantly boost its stability in managing primary metabolism and stress response [108] (X. Liu et al., 2017). There is still a need for research into the acetylation and deacetylation of non-histone proteins during plant abiotic stress response. Environmental issues cause significant agricultural losses every year. Our knowledge of how plants adapt to environmental change would grow if we understood how HDACs function in plant responses to abiotic stress, which will boost agricultural productivity. HATs and HDACs are able to transition between permissive and restrictive chromatin in response to environmental and developmental signals thanks to histone acetylation dynamics, a gene-

regulatory epigenetic mechanism. Hormones, secondary messengers, and other signaling molecules initiate signaling cascades after the appropriate receptors pick up the inputs. The signaling pathways generate HATs and HDACs, which, respectively, activate and repress target genes to control processes downstream. In the end, these modifications to the metabolic pathways control how plants develop and respond to stress. Histone acetylation dynamics and other epigenetic alterations have been shown to be essential components of the transcription machinery that controls gene expression throughout plant growth and adaptation to challenging environments over the past 10 years. In this study, multiple HATs and HDACs have been discovered as epigenetic regulators of physiological and biological processes in various plants. The growth of seeds, leaves, roots, and flowers, fruit ripening and ageing, reactions to biotic and abiotic stress in plants, and many other developmental processes are all regulated by epigenetic regulators. Auxin, BRs, ethylene, JA, SA, and ABA are just a few of the several hormones whose production and signaling pathways they regulate to govern these functions. Despite substantial research in the area of epigenetics, many aspects, particularly in plants, are still not fully understood. For instance, it is currently unclear in many cases how these epigenetic modifications are produced, maintained, and transmitted. However, the modification of non-histone proteins by HATs and HDACs has not garnered much attention. A comparison of the processes that these HATs / HDACs targets and those that they do not target will be helpful to understand the function of these enzymes.

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