Chapter 7
The γ-Aminobutyric Acid (GABA) Towards Abiotic Stress Tolerance

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Abstract The frequent exposure of plants to several environmental constraints (abiotic and biotic stress) limit plant growth and yield globally. These constraints are managed by plants through morphological, physiological and molecular alteration to resume the loss underway. Amongst, the priming with chemicals including GABA is a promising approach. GABA (γ-aminobutyric acid) is a non-protein amino acid produced through GABA-shunt, and usually accumulates in several plant species when subjected to any environmental stress (salt, drought, heat, etc.). Its accumulation or exogenous application leads to adjustments at many levels under stress conditions, to maintain the usual plant growth and development and therefore may provide better outcome in terms of productivity. The present chapter offers understanding of GABA metabolism and its significance towards promoting abiotic stress tolerance in plants.

Keywords Abiotic stress · Cold · Drought · GABA · Heavy Metal · Heat · Metabolism

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7.1 Introduction

The plants being sessile are frequently exposed to various environmental constraints both naturally or under agricultural set-up. These limitations are majorly unpredictable and lead to significant loss in crop productivity. Amongst such constraints, the abiotic factors/stress (salinity, drought, flooding, heat, cold, freezing, excess light, UV radiation, and heavy metal toxicity) play higher participation and majorly limit the global crop yields (Wang et al. 2003; Jain 2013). This majorly involves oxidative stress mediated by ROS, which may impact the plant by regulating several developmental features (Mishra et al. 2017). In certain instances, abiotic stress also provides ways to invite several biotic stress (Vijayakumari et al. 2016), thereby further promotes crop losses. To cope with these limitations, plants have developed methods that mainly involve participation of stress-related genes. Such genes remain silent during the normal course of plants' life and get up-regulated during stress conditions (Gao et al. 2007, Atkinson and Urwin 2012). Despite their direct relevance in stress tolerance, the transgenic for such genes many times exhibited compromise of desired traits; therefore, the development of methodologies that can better address the plant stress tolerance along with maintaining plant productivity is essentially required.

Plant priming (sensitization or hardening) is considered as one of the effective strategies which activate faster and/or stronger protective responses, when stress (biotic or abiotic) pressure is encountered. The strategy is originally devised for biotic stress, where a non-pathogenic microbe can boost plant immunity, thereby providing a strong defence, when the plant encounters any pathogenic agent in subsequent life. In recent past, the exogenous application of chemicals that can mitigate stress conditions (chemical priming) was found effective to better manage plants encountered to stress. In the 'primed' state, plants attain a unique physiological condition, which generates mild stress, and thus let plants to withstand further strong stress conditions (Savvides et al. 2016). Some of the important priming agents are sodium nitroprusside, hydrogen peroxide, sodium hydrosulfide, melatonin, polyamines, GABA, BABA, etc. (Vijayakumari et al. 2016; Savvides et al. 2016).

The γ-aminobutyric acid (4-aminobutyric acid, GABA), is a non-protein amino acid, which possesses an amino group at γ-carbon rather than α-carbon, therefore does not integrate into proteins. It contributes significantly to the free amino acid pool and exists in unbound form (Shelp et al. 1999). It exhibits zwitterionic features at physiological pH, high solubility in water and can attain many conformations in solution, including cyclic structure like proline (Christensen et al. 1994). The metabolism behind GABA is known as GABA shunt which bypasses two steps of the tricarboxylic acid cycle (Bouche and Fromm 2004). GABA has a wide distribution in prokaryotes and eukaryotes. The discovery of GABA in plants was reported by Steward et al. (1949); however, its occurrence is conserved from bacteria to plants and to vertebrates (Bouche and Fromm 2004). In animals, the study mainly focuses GABA as a signalling molecule and found to be accumulated in brain and functions in neurotransmission (Kinnersley and Turano 2000; Bouche and Fromm 2004). In crayfish stretch receptor neurons, it was reported to suppress impulses (Awapara et al. 1950; Elliott and Jasper 1959).

Though the contribution of GABA as a signalling molecule was considered quite early in animals, in plants, until recently, it was generally considered as a carbon-nitrogen metabolite (Shelp et al. 1999; Bouche et al. 2003; Bouche and Fromm 2004). In plants, the recent outlook suggested it as an endogenous signalling molecule for plant growth regulation and plant development (Carillo 2018). In plants, the accumulation of GABA is noticed under environmental stress conditions which facilitate plant chemical response to mitigate stress. Apart, it also has multiple functions under non-stressed conditions. It serves as a key metabolite of nitrogen metabolism and involves both primary and secondary metabolic pathways. Besides, it also provides source of carbon skeleton through GABA shunt for further down-stream metabolism (Ramos-Ruiz et al. 2019). Two mechanisms have been noticed for stress-induced GABA accumulation in plants viz. cytosolic acidification and Ca^{2+} rise. It has been noticed that stress resulted in cytosolic acidification which induces low pH-dependent activation on glutamate decarboxylase and therefore GABA biosynthesis and accumulation. Such acidic conditions are predominantly found under oxygen-deprived conditions as generated during flood stress. Further, other stresses (viz, cold, heat, salt, etc.) subsequently increase Ca^{2+} level in the cellular environment. These high cytosolic Ca^{2+} levels activate calmodulin-dependent glutamate decarboxylase activity and GABA biosynthesis (Kinnersley and Turano 2000).

The early decades of GABA research mostly considered it as metabolite, though argue exist regarding its functioning as signalling molecules (Bouche and Fromm 2004; Bown and Shelp 2016). However, there are certain observations that backed the signalling feature of GABA as highlighted in a review (Ramesh et al. 2015), which include features like rapid increase in response to biotic and abiotic stress, gradient of GABA concentration across plant tissues, inter- and intracellular compartmentation of GABA metabolism, discovery of GABA-binding site in plant cell membrane, and GABA-regulated ion channels in plants. Under several abiotic (hypoxia, heat, cold, drought, mechanical wounding) or biotic stress (wounding due to herbivory and infection), the quick accumulation of GABA was noticed (Shelp et al. 1999; Shelp et al. 2012). The accumulation promotes plant growth and can alleviate stress by up-regulating the anti-oxidant defence systems. Its metabolism is also involved in the nitrogen recycling and reallocation during leaf senescence in response to abiotic stress (Jalil et al. 2017; Jalil and Ansari 2020). Considering the diverse aspects of GABA in plant stress management, present chapter will provide judicial compilation on the representative studies of GABA as a stress alleviator and promises to combat the adverse situation.

7.2 GABA Shunt and GABA Metabolism

The biogenesis or metabolism of GABA involves a short pathway referred as GABA shunt which bypasses two steps of tricarboxylic (citric) acid cycle as mentioned in Fig. 7.1. Compared to TCA cycle, the shunt provides less energy as it directly converts α-ketoglutarate to succinate, and therefore does not produce high-energy

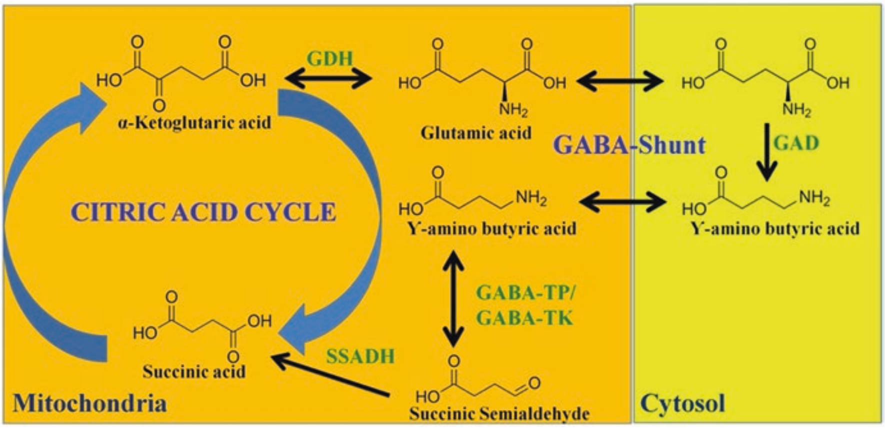

Fig. 7.1 Schematic representation of the metabolism of GABA via GABA-shunt and citric acid cycle regulation; enzymes involved are indicated in green bold, reversible reactions in arrow with both heads. Other abbreviations include GDH, glutamate dehydrogenase; GAD, glutamate decarboxylase; GABA-TP, GABA: pyruvate transaminase; GABA-TK, GABA: α-ketoglutarate transaminase; SSADH, succinic semi-aldehyde dehydrogenase

molecule viz., reduced nicotinamide adenine dinucleotide phosphate (NADH) molecule and guanosine triphosphate (GTP) molecule (Singh and Roychoudhary 2020). The precursor molecule of this shunt is α-ketoglutarate, which in mitochondria undergoes oxidative deamination and is converted to glutamate by glutamate dehydrogenase (GDH). Glutamate is then transported to cytosol and subsequently processed by GABA shunt enzymes.

The metabolism further involves participation of enzymes, comprising of one cytosolic (Glutamate decarboxylase, GAD) and two mitochondrial (GABA transaminase, GABA-T and Succinic semi-aldehyde dehydrogenase, SSADH) enzymes. The first enzyme (GAD) converts glutamate to GABA, along with a co-product carbon dioxide. In *Arabidopsis,* it was reported that GAD isoforms are expressed in tissue-dependent manner and their activity is modulated by Ca^{2+}–CaM (Zik et al. 1998a, b). However, this feature of Ca^{2+}–CaM is not mandatory as in rice, here GAD isoform lacks CaM-binding domain (Akama et al. 2001).

The GABA is then transported (through mediation of gamma-aminobutyric acid permease, GABAP; Michaeli et al. 2011) and metabolized in mitochondria to produce succinic semi-aldehyde (SSA). The GABA-T (GABA transaminase) facilitates this conversion, using either α-ketoglutarate (GABA-TK) or pyruvate (GABA-TP) as amino acid acceptors in plants, producing glutamate or alanine, respectively (Shelp et al. 1999). The succinic semi-aldehyde is then converted to succinic acid by the activity of succinic semi-aldehyde dehydrogenase (SSADH) (Ham et al. 2012). The association of GABA shunt with tricarboxylic acid cycle links carbon and nitrogen metabolism in plants. Beside this, SSA can also be transported to cytosol, where it produces γ-hydroxybutyric acid (GHB), through the activity of succinic semi-aldehyde reductase (SSR) (Singh and Roychoudhary 2020). Addition to this polyamine (spermidine and putresscine) catabolism and proline under oxidative stress can also produce GABA (Fait et al. 2008; Signorelli et al. 2015).

7.3 GABA: Significance Under Abiotic Environmental Constraints

During environment stress such as drought (Hanower and Brzozowsak 1975), heat (Mayer et al. 1990), cold (Wallace et al. 1984), there is high production of GABA; the intensity of increase is so high, as the cellular level of this non-protein amino acid exceeds the amino acid involved in protein synthesis (Shelp et al. 1999; Kinnersley and Turano 2000). It was observed that large amount of GABA is produced during biotic and abiotic stress and its metabolism was found connected with many features viz., C:N balance, regulation of cytosolic pH, osmoregulation, defence against oxidative stress, etc. (Bouche and Fromm 2004; Ham et al. 2012).

The endogenous production of GABA or its exogenous application has very high implication on plant stress mitigation. During this, the GABA is proposed to function as signalling molecule and found associated with nitrogen metabolism, cytosolic pH regulation, and offer protection against oxidative damage generated in response to several abiotic stresses (AL-Quraan et al. 2013). The priming using different chemicals has been observed as an effective strategy for the enhancement of abiotic stress tolerance. Vijayakumari et al. (2016) has recently reviewed the priming potential for non-protein amino acid-GABA along with BABA (β-amino butyric acid). Rapid γ-Aminobutyric acid (GABA) accumulation was observed, when plants are exposed to stress, which either exhibit the metabolism regulation in response to stress or an adaptive response for stress mitigation (Bown and Shelp 2016).

Further, the exogenous GABA application bestows stress tolerance by modulation of the genes associated with plant signalling, transcriptional regulation, hormone biosynthesis, reactive oxygen species production, and polyamine metabolism (Podlešáková et al. 2019). The accumulation and metabolism of GABA itself are regulated by several other biological molecules. Many evidence has also suggested the cross-talk between GABA and polyamines/ hormones (viz. abscisic acid, cytokinins, auxins, gibberellins and ethylene), where one affects the signalling pathway and metabolism of others (Podlešáková et al. 2019). Recently, the contribution of GABA in alleviation of salts stress, salinity-alkalinity stress, drought stress, heat stress, chromium stress etc., has been reported in a number of studies using different plants (Table 7.1). Few of the relevant stress studies are as follows:

Table 7.1 Response of exogenously supplied GABA to various abiotic stresses

S. No	Crop	Concentration	Response to abiotic stress	References
1	*Agrostis stolonifera*	0.5 mM	Induced tolerance to heat stress	Li et al. (2016a)
2	*A. stolonifera*	0.5µmol	Enhanced tolerance against heat stress	Li et al. (2019a)
3	*A. stolonifera*	0.5 mM	Induced drought tolerance	Li et al. (2019b)
4	*A. stolonifera*	0.5 mM	Improved tolerance to drought and heat stress	Li et al. (2018)
5	*A. stolonifera*	0.5 mM	Improved tolerance to drought/heat stress	Li et al. (2016)
6	*Brassica juncea L.*	125µM	Confers tolerance to chromium stress	Mahmud et al. (2017)
7	*Camellia sinensis L.*	5.0 mM	Improved tolerance to cold	Zhu et al. (2019a, b)
8	*Cucumis melo L.*	50 mM	Enhanced resistance to salinity-alkalinity stress	Xiang et al. (2016)
9	*C. melo L.*	50 mM	Increased tolerance to salinity-alkalinity	Chen et al. (2018)
10	*C. melo L.*	50 mM	Enhanced tolerance to salinity alkalinity	Jin et al. (2019)
11	*C. melo L .*	50 mM	Enhanced tolerance to calcium nitrate stress	Hu et al. (2015)
12	*H. vulgare L.*	0.5 mM	Increased tolerance against salinity stress	Ma et al. (2018)
13	*Lactuca sativa L.*	25µM	Enhanced salt tolerance	Kalhor et al. (2018)
14	*Lolium perenne*	50 mM	Promote tolerance against drought stress	Krishnan et al. (2013)
15	*Nigella sativa L.*	2.0 mg L^{-1}	Improved tolerance to drought stress	Rezaei-Chiyaneh et al. (2018)
16	*Oryza sativa L.*	0.5 mM	Enhance tolerance to arsenite stress	Kumar et al. (2019)
17	*O. sativa L.*	1 mM	Partially enhanced tolerance against heat stress	Nayyar et al. (2014)
18	*Solanum lycopersicum L.*	5 mM	Improved resistance against salinity stress	Wu et al. (2020)
19	*Trifolium repens L.*	1µM	Increased resistance against salinity stress	Cheng et al. (2018)
20	*Triticum aestivum L.*	0.5 mM	Increased tolerance against salinity stress	Li et al. (2016c)
21	*T. aestivum L.*	50 mg/L	Promoted tolerance to salinity stress	Wang et al. (2017a)

(continued)

Table 7.1 (continued)

S. No	Crop	Concentration	Response to abiotic stress	References
22	*Vigna radiate L.*	1 mM	Improved tolerance against heat stress	Priya et al. (2019)
23	*Zea mays L.*	25 and 50µM	Confered tolerance against cadmium stress	Seifikalhor et al. (2020)
24	*Z. mays L.*	0.5 mM	Improved tolerance against salinity stress	Wang et al. (2017a, b)

7.3.1 Salt Stress

The salinity in soil has been reported to severely devastate plant growth, thereby crop productivity, due to its negative impact on several metabolic and physiological processes. This impact mostly includes photosynthesis inhibition, ROS, and other metabolism. It has been reported that in salt-sensitive variety, there is inhibition of growth and development, reduction in respiration, photosynthesis, and protein synthesis (Parida and Das 2005; Munns and Tester 2008; Hussain et al. 2013). In addition to the above effects, the salt stress also causes generation of reactive oxygen species in chloroplast and mitochondria that lead to oxidative damage in plants (Masood et al. 2006). To deal with the stress, plant produces various metabolites that offer stress tolerance including GABA. Like other stresses, the GABA accumulates during salt stress, which maintains the pH and carbon/nitrogen metabolism for Kreb's cycle and scavenges free radicals through anti-oxidant systems (Jalil and Ansari 2020). Jalil and Ansari (2020) have described the salt tolerance mechanism by GABA, which includes promotion of photosynthesis and chlorophyll fluorescence, regulation of oxidative stress, and up-regulation of anti-oxidant activity and osmotic regulation through osmolyte accumulation.

The exogenous GABA application exhibited improvement in photosynthetic capacity and anti-oxidant enzyme activities and decreased MDA content and electrolyte conductivity, thereby mitigating the impact of salinity on the wheat seedlings (Li et al. 2016). The exogenous root-drenching-based GABA application to salt-stressed (moderate-150 mM to severe- 300 mM) maize seedlings exhibited an increase in endogenous GABA concentration, improves seedling growth, and demonstrates reduced GAD activity (Wang et al. 2017a, b). The exogenous applications offered attributes such as alleviation of membrane damage, accumulation of proline and soluble sugars in leaves, reduction in water loss, along with reduced oxidative damage (particularly of superoxide anion ($O_2^{\cdot -}$) and malondialdehyde content) and increased anti-oxidant enzyme activity. Thus, the exogenous application of GABA enhanced the salt tolerance of maize seedlings (Wang et al. 2017a, b). Under saline condition, GABA improves seed germination and plant growth in lettuce, by reducing the effects of salt stress on photosynthetic performance and salt stress–induced oxidative stress (Kalhor et al. 2018). In *Triticum aestivum* and *Hordeum vulgare*, the abundance of GABA shunt metabolites (GABA, glutamate, and alanine) was observed along with the increasing concentration of salt (Al-Quraan et al. 2019) which signify its importance during stress.

Many times, salt along with other stresses were also studied and this part of the chapter also describes some of few such instances. The NaCl treatment in *Arabidopsis* up-regulates GABA metabolism. Precisely, GABA-T (first step of its catabolism) was found to play a crucial function in salt tolerance, as the loss-of-function of its corresponding gene mutant (*pop2–1* mutant) was oversensitive to ionic stress but not to osmotic stress (Renault et al. 2010). In a study, Al-Quraan et al. (2013) have reported a significant increase in GABA, MDA, and GAD mRNA levels under salt and osmotic stress in the five wheat cultivars (Hurani 75, Sham I, Acsad 65, Um Qayes and Nodsieh). The study suggested key contribution of GABA shunt, which permits salt stress management in wheat. Sheteiwy et al. (2019) have demonstrated that the high tolerance to OS+S (PEG + NaCl) involves the GABA potentiality to regulate ROS level, secondary metabolism, and transcription. Jin et al. (2019), while working on salinity-alkalinity stress in muskmelon, have observed that the stress increased MDA content, relative electrical conductivity, and the activities of many anti-oxidant enzymes including SOD, APX, and DHAR. Along with that, it decreases shoot weight (dry and fresh), leaf area, and antioxidant metabolites. The pre-treatment with GABA, H_2O_2, GSH, or AsA was found effective and reduces the salinity-alkalinity-induced effects. Further, the mitigation effect of GABA involves the surplus accumulation of chl and its precursors to evade photo-oxidation injury. In this study, it was also demonstrated that GABA stimulates the free polyamine contents (PAs), which in turn reduces Na^+/K^+ ratio and alleviates membrane lipid peroxidation, under salinity-alkalinity stress in muskmelon (Xu et al. 2019).

7.3.2 *Drought Stress*

In nature, the combined interplay of less rainfall, reduced groundwater table, and insufficient water availability lead to drought stress (Singh and Laxmi 2015; Singh et al. 2015). The drought stress affects different physiological and metabolic processes of plant and significantly reduced growth, water content, chlorophyll content, and change in different fluorescence parameters (Levitt 1980; Ahmed et al. 2017). It also results in the production of reactive oxygen species, which in turn causes damage to cellular constituent such as lipids, nucleic acids, carbohydrates, and proteins (Waraich et al. 2011). Besides, the drought stresses also regulate genes associated with stress response (Mishra et al. 2015).

The possible contribution of hypoxia and drought stress on GAD in vivo activity was reported by Serraj et al. (1998). The analysis of GABA suggested its six-fold accumulation after 6 h hypoxia exposure to soybean nodules and no changes after PEG treatment. The GABA application in drought-stressed perennial ryegrass (*Lolium perenne*) demonstrated higher relative water content, turf quality, and peroxidise activity. However, lowering of wilt rating, canopy temperature depression, electrolyte leakage, and lipid peroxidation were also observed as compared to untreated plants. No significant impact of GABA application was observed in the activity of superoxide dismutase and catalase in this study (Krishnan et al. 2013). Vijayakumari and Puthur (2016) have reported the contribution of GABA priming for the enhancement of osmotic stress tolerance in *Piper nigrum* Linn, stressed with PEG. In leaves of white clover (*Trifolium repens*), the drought (15% PEG)-induced damage can be effectively managed by exogenous application of GABA. The physiological features include behind this alleviation are higher relative water content, lower electrolyte leakage, lipid peroxidation, and leaf wilting. This improvement of GABA-mediated drought tolerance was observed in white clover, which involves participation of GABA-shunt, polyamines, and proline metabolism (Yong et al. 2017). In order to further understand the specificity and GABA functioning, Mekonnen et al. (2016) have investigated the *gad1/2* (with GABA depletion) to drought stress. The GAD (glutamate decarboxylase) performs primary function of GABA biosynthesis and decarboxylate glutamate. In *A. thaliana*, five copies of GAD are available in genome. Amongst these, *GAD1* and *GAD2* are highly expressed and responsible for significant reduction of GABA content in knockouts. The *gad1/2* mutant phenotypically exhibited reduced shoot growth and early wilting after prolonged drought stress, mainly because of defect in stomata functioning (closure). This over-sensitivity can be reversed by functional complementation, which increases GABA content in leaves (Mekonnen et al. 2016).

7.3.3 Temperature Stress

Any variation to plants' optima temperature is considered as 'Temperature stress', which can be of two types: heat stress (above optima) and chilling/cold (Below optima) stress. The application of GABA in mitigation of temperature has been demonstrated in both cold and heat stress (Nayyar et al. 2014; Li et al. 2016a; Wang et al. 2016). High temperature or heat stress (HT) is one of the major environmental stresses that limit the growth, development, and productivity of plant globally (Hasanuzzaman et al. 2013). Plant responses to HT vary with type of plant, duration, and degree of high temperature. Plants are generally susceptible to high temperature in almost every development stage, but reproductive stage is most sensitive stage (Hasanuzzaman et al. 2013). Heat-triggered morphological, physiological, biochemical, and molecular changes in plants limit plant growth and development. HT inhibits seed germination, scoring of stems and leaves, root and shoot growth inhibition, senescence, and abscission of leaf (Vollenweider and Gunthardt-Goerg 2005; Wassie et al., 2019). It has also been reported that HT reduces relative water content, impaired photosynthesis, and increases accumulation of reactive oxygen species which in turn results in oxidative stress. It is responsible for lipid peroxidation, disturbing the stability of membrane and enzymes and nucleic acid denaturation (Hasanuzzaman et al. 2013; Wassie et al. 2019). The heat stress was also demonstrated to regulate the transcript of stress-related genes including heat shock transcription factors and heat shock proteins, specifically characterised for heat stress, though they may also have some other applications (Mishra et al. 2019). Further, it has been reported that application of exogenous osmolytes, signalling molecules, polyamines, and phytohormones, can alleviate heat stress (Mishra et al. 2020).

In rice seedlings, with the rise in temperature the length of roots and shoots were found inhibited and caused decrease in survival, especially at 42/37 °C (Nayyar et al. 2014). The contrasting fluctuation in endogenous GABA content was observed under moderately (35/25 °C) and severe stress (42/37 °C) conditions, with more than two-fold increase and seven-fold decrease as compared to moderately stressed plants (possible reason for reduction in growth and survival), respectively. With exogenous GABA application, the growth of survival of heat-stressed plants improved, which found associated with lowering of membrane damage, better cellular reducing feature, chlorophyll content, and shoots photochemical efficiency. Further, improvement in relative water content and stomatal content was also noticed, which was found associated with increase in osmolyte (proline and trehalose) accumulation. Moreover, the damage caused in anti-oxidant system (enzymatic: superoxide dismutase, catalase, ascorbate peroxidase, and glutathione reductase and metabolite /non-enzymatic: ascorbate and glutamate) under heat stressed condition was also improved with GABA application in rice (Nayyar et al. 2014).

In another study, Li et al. (2016) have observed that pre-treatment of GABA (0.5 mM), before heat stress, improved heat tolerance in creeping bentgrass (*Agrostis stolonifera*). The metabolic analysis suggested that GABA application leads to higher accumulation of amino acids (glutamic acid, aspartic acid, alanine, threonine, serine, and valine), organic acids (aconitic acid, malic acid, succinic acid, oxalic acid, and threonic acid), sugars (sucrose, fructose, glucose, galactose, and maltose), and sugar alcohols (mannitol and myo-inositol). The study suggested the involvement of photosynthesis and ascorbate-glutathione cycle enhancement, osmotic adjustment, and GABA shunt in GABA-induced heat tolerance. Further studies suggested that during heat stress, the exogenous GABA application enhances expression of stress genes viz., *ABF3*, *POD*, *APX*, *HSP90*, *DHN3*, and *MT1,* which could be the possible reason to offer heat tolerance (Li et al. 2018). The global investigation of mRNAs and miRNAs suggested about the important adaptive responses, triggered by GABA, which includes HSFs pathway regulation, increased carbon metabolism, and biosynthesis of amino acids and plant hormone signalling (Li et al. 2019a, b). This study also reported the close association of heat-survival with significant changes of *miR398s*, *cca-miR156b*, *aly-miR159c-3p*, and *ata-miR408-3p*. Along with the involvement of *vvi-miR845c*, *ama-miR156*, and other novel *miRNAs* such as *novel-24,223*, *novel-2964*, and *novel-10,098* was also observed in GABA-regulated heat tolerance. Over all, the GABA-mediated heat tolerance in creeping bentgrass involved physiological, transcriptional, and post-transcriptional regulation.

Besides, the contribution of GABA towards cold-stress, another variant of temperature stress was also observed, which also has many negative impacts on plant growth and development. The nitric oxide–mediated chilling tolerance in cold-stored banana involves GABA metabolism and increased glutamate decarboxylase and decreased GABA transaminase activity, resulting into GABA accumulation (Wang et al. 2016). The investigation of amino acid homeostasis in frost-resistant and sensitive barley and wheat seedling under cold or freezing stress conditions revealed the significant conversion of glutamate to GABA, which was proportional to stress severity. Cold acclimation resulted into amino acid pool and GABA shunt gene induction, suggesting their contribution in frost tolerance (Mazzucotelli et al. 2006). The Isobaric tags for relative and absolute quantification (iTRAQ) based analysis suggested the association of the GABA-induced physiological effects with cold tolerance in tea plants. Further protein-protein interaction studies suggested the endogenous GABA alteration and stress response factors during improvement of cold tolerance and were linked with stimulated interactions among photosynthesis, amino acid biosynthesis, and carbon and nitrogen metabolism (Zhu et al. 2019).

7.3.4 Heavy Metal Stress

From a long time, heavy metals such as Mn, Fe, Cu, Cd, Zn, Hg, As, and Ni have been accumulated in the soil through industrial waste and sewage disposal. Though, some of these metals are essential micronutrient for growth and development of plant, however, their excess concentrations in the soil have detrimental effect on growth and development of plant (Ghori et al. 2019). Heavy metal stress cause denaturation or inactivation of enzymes which are important for many basic plant metabolic reaction associated with homeostasis, respiration, and photosynthesis (Hossain et al. 2012). It also triggers the production of reactive oxygen species such as hydrogen peroxide, superoxide radical, and hydroxyl radical which in turn cause oxidative damage to plant (Ahmad et al. 2012).

The contribution of GABA in reversing the negative effect of heavy metals (Cd, Cadmium; Cr, Chromium; As, Arsenic) on plant growth and physiological parameters has been shown (Mahmud et al. 2017; Kumar et al. 2017, 2019; Maryam et al. 2020). The improvement of physiological response in Cr-treated mustard seedlings was conferred by GABA (Mahmud et al. 2017). The supplementation of GABA on Cr-treated seedlings reversed most of the effect, which involves reduction of Cr uptake and reduction of oxidative damage by up-regulating non-enzymatic (ascorbate, AsA; glutathione, GSH) and enzymatic (ascorbate peroxidise, APX; monodehydroascorbate reductase, MDHAR; dehydroascorbate reductase, DHAR; glutathione reductase, GR etc.), anti-oxidant systems. Further, the application of GABA also increased leaf RWC and chl content and decreased proline and phytochelatin content. The GABA accumulation lowered the expression of *Lsi-1* and *Lsi-2* transporter expression, and hence reduced the As accumulation, along with reduction of oxidative stress marker TBARS and H_2O_2 with GABA accumulation.

The GABA-mediated modulation of physiological responses was noted, which exhibited better tolerance of *Oryza sativa* for As stress (Kumar et al. 2017). Kumar et al. (2019) have observed that the exogenous application of GABA (0.5 mM) against As(III) stressed rice seedlings, reduced the levels of H_2O_2 and TBARS, and improved the growth parameters. Further, its application along with As(III) enhanced level of unsaturated fatty acids (USFAs, particularly linolenic acid) as compared to saturated fatty acids (SFAs). The similar enhancement was also observed in case of amino acids (AA, proline, methionine, glutamic acid, and cysteine) and expression of genes associated with polyamine (PA) biosynthesis (*arginine decarboxylase, spermine* and *spermidine synthase*). This study cumulatively demonstrated that GABA at low concentrations provides solution for managing As(III) tolerance in rice, due to its positive effect on biosynthesis of USFA, AA, and PA (mainly putrescine) and negative effect on TBARS and H_2O_2. The application of GABA on Cd-treated maize plants demonstrated improvement of growth parameters. Further, its application conferred reduction in Cd uptake, increased activities of antioxidant enzymes (catalase and superoxide dismutase), along with induction of polyamine biosynthesis-responsive genes (*ornithine decarboxylase* and *spermidine synthase*), and suppression of *polyamine oxidase*, responsible for polyamine catabolism (Maryam et al. 2020). The contribution of GABA has also been observed during Cd stress in *Monoraphidium* sp. QLY-1, which resulted in higher protein, glutathione content, up-regulation of α-amylase activity, and reduction of starch, ROS, and Cd^{2+}. Further, GABA under Cd stress positively increases lipid production in this alga (Zhao et al. 2020).

7.4 Conclusion and Prospects

The present chapter addresses the significance of GABA in various types of environmental constraints mainly salt, drought, heat, cold, and heavy metals. The endogenous (one of the survival strategy) or exogenous GABA attributes advantages viz., reduction of photosynthesis inhibition, polyamine accumulation, reduction of ROS etc., and assists plant to maintain their normal growth and development. Though the investigations suggested its contribution in offering stress tolerance feature in plants, still the knowledge of its association in the management of several stress-related traits is not well understood at molecular level. Along with the transcriptional regulation of GABA-shunt genes under diverse conditions (developmental, hormonal, pathogenic, etc.) also would be an interesting area to work on. Further, their relations with transcriptionally modulated genes during stress, particularly transcription factors, also need attention, which will give better understanding to address combinatorial methods for stress management in crop plants to meet desired production.

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