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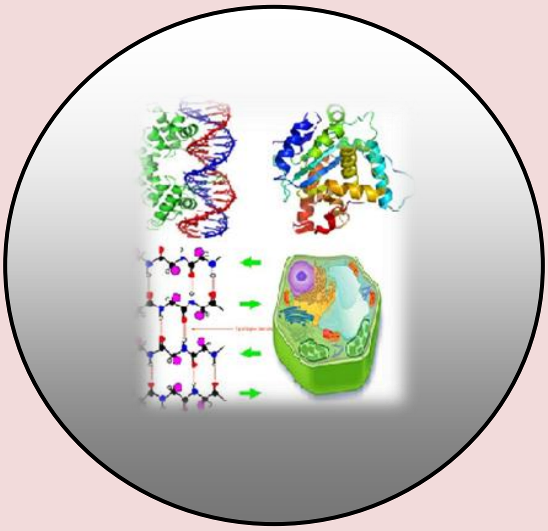

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Tremendous Role of GABA Shunt Metabolic Pathway in Plant System

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ABSTRACT

GABA shunt is an important pathway in plants that comprise of three key enzymes glutamate dehydrogenase that involve in the conversion of glutamate into γ-aminobutyric acid (GABA) that catalyzed via GABA transaminaseto succinic semialdehyde that further converted to succinate using succinic semialdehyde dehydrogenase then consequently goesto tricarboxylic acid cycle. GABA is an important component of GABA shunt pathway that may involve in different mechanism of plant but specific role of GABA is not clear in plants, but it involved in neurotransmission in central nervous system of invertebrates. GABA shunt approached to produce carbons through glutamate and to make carbon and a nitrogen flue that goes into tricarboxylic acid (TCA) cycle that is significant for various metabolic and developmental process of plants including senescence and plant development. In plants, GABA involve as metabolites and signaling component in various system of plant cell, it increases under different stresses that are regulated by GABA shunt pathway. The potential studies on GABA shunt may facilitate in agricultural benefits that help in the increment of crop productivity.

Key words: GABA shunt, Plants, Abiotic stress, Plant defence and Plant development.

INTRODUCTION

The GABA shunt pathway found in all species, the pathway comprises of three important enzymes: GAD, GABA-T, and SSADH. The GABA shunt is metabolic pathway and compartmentalized ineukaryotes; the synthesis occurs in the cytoplasm whereas the enzymes degradedin the mitochondria. In *Saccharomyces cerevisiae,* the whole pathway completed in cytoplasm. GABA is metabolised in plants via GABA shunt pathway but it is also reported that some polyamines such as spermidine and putrescine are also involved in the synthesis of GABA (Bouchereau et al. 1999; Shelp et al. 2012). Glutamate is decarboxylated into GABA via catalytic enzyme GAD in cytoplasm. GADs found in various organisms; the enzymatic activity regulated post translationally by binding of cofactor in mammals or binding with calmoduline (CaM) in plants (Baum et al. 1996; Baum et al. 1993). Non-protein, four-carbon amino acid GABA is ubiquitous and present from Yeast and vertebrates to bacteria. GABA investigated in plants about sixty years ago (Stewart, 1949) but mainly research done on vertebrates because of it involved in the mammalian nervous system as neurotransmitter (Ribak and Yan 2000).

Plants can metabolise high concentration of GABA in various stress conditions *viz.* hypoxia, mechanical stress, chilling injury, darkness, heat stress, and water lodging (Shelp, 1999; Wallace et al. 1984). GABA-T involved in metabolism of carbon and nitrogen in leaf senescence process. When the leaf senescence initiated, protein started to degrade and remobilized into the developing parts of the plants (Smart 1994). Metabolism of proteins releases ammonia and amino acids that changed into glutaminevia substrate of glutamate with the help of glutamine synthetase enzyme. It has been reported that the senescence-related genes increased the expression of glutamine syntheta seen coded genes (Miflin and Habash, 2002; Kamachi et al. 1992). Moreover, during leaf senescence the activity of asparagine syntheta seen coded gene also increased in asparagus (King et al. 1995). Asparagine as well as glutamine arekey amino acids present in cells that mobilized via leaf senescence (Feller and Fischer 1994). Throughout senescence process, proteolytic and transamination activities increases using aspartate and alanine that enhanced the production of glutamate which used as substrate for GAD. Due to increased availability of the glutamate, the conversion of glutamate to GABA by GAD was also increased. Therefore, the GABA shunt accommodates carbon flux to furnish carboxylic acids of the tricarboxylic acid cycle in the mitochondria (Ansari et al. 2005).

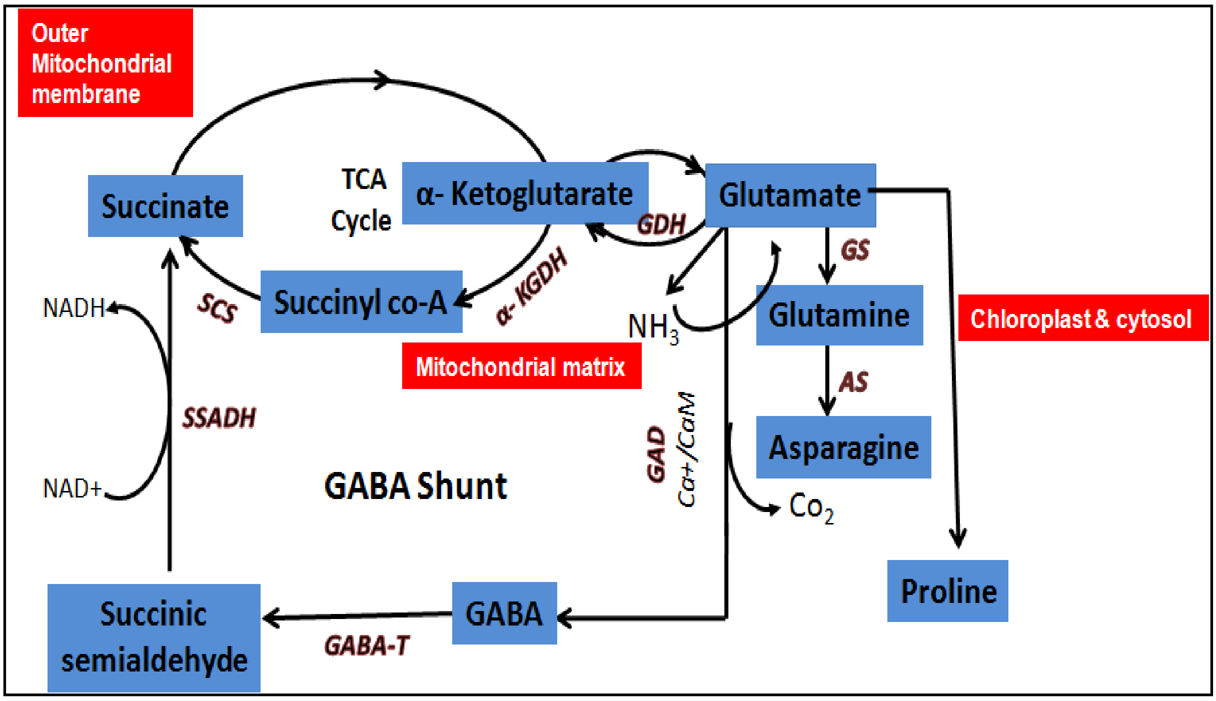

Figure 1. Metabolism of GABA shunt pathway.

Metabolism of GABA shunt components

GABA metabolism occurs in two compartments of cell; synthesis of GABA takes place in the cytosol whereas degradation of GABA in the mitochondria by different reactions cooperatively called the GABA shunt pathway. The reactions in the GABA shunt are:

In first reaction, glutamate is irreversibly decarboxylated by enzyme GAD to form GABA. In second step, reversible transamination of GABA takes place by enzyme GABA-T that utilized α-ketoglutarate for transferring of amino group in mammalian cells, while GABA-T used pyruvate to form SSA and either alanine or glutamate in plant. The third reaction starts with the irreversible oxidation of SSA by enzyme SSADH to acquiesce the succinate in Kreb's cycle (Bown and Shelp, 1997). GAD enzyme existed in cytosol (Breitkreuz and Shelp, 1995) and specifically for glutamate, acquires an auto inhibitory CAM-binding domain, and has an optimum pH of 5.8. GABA-T and SSADH are present in mitochondria (Breitkreuz and Shelp, 1995) by optimum pH of 8 to 10.

Synthesis of GABA occurs in the cytosol by GAD and transferred to the mitochondrion to convert into succinate via GABA-T and SSADH as in Fig. 1.

The GABA metabolism utilized the activities of three enzymes via GABA shunt. GABA shunt components and GABA has performs various functions, depending upon species to species on the basis of the compartment in the cell where they active. The functions of GABA and GABA shunt components in bacteria, yeast, vertebrates as well as in plants are well documented.

Mechanism and function of GABA shunt in plants

Studies in plants stressed principally on the mechanism of GABA metabolism, generally in the perspective of stress effect, till some finding were reported o indicate a signalling function of GABA in plants.

Carbon and nitrogen metabolism

GABA accumulation increases in plant tissues in response to various stress conditions. Furthermore, *Arabidopsis thaliana* develops properly on GABA rich media mainly for carbon and nitrogen source. Thus, GABA is intricate in the carbon and nitrogen metabolism and in the transport and storage of N_2 in fruits. The GABA shunt assimilates carbons from glutamate and to produce C/Nflux, which moved in the tricarboxylic acid cycle (Ansari et al. 2014).

Regulation of cytosolic pH

GABA shunt is involved in acid resistance in bacterial cell. During acidic condition, GAD activity is increases in *E. coli*, thus eliminating protons via decarboxy latingglutamate that formed GABA that disseminated from the cells. Carroll et al. (1994) reported that GAD is stimulated by acidic environment then GABA produced in cytosolic acidification, therefore it is probable that GAD activity involved in the pH regulation in cytoplasm of plant species (Crawford et al. 1994).

Role in oxidative stress tolerance

SSADH mutants of *Arabidopsis thaliana* are oversensitive to stress conditions because of defective scavenging ability for hydrogen peroxide. In the final reaction, the GABA shunt pathway provided succinate and NADH to electron transport chain. Thus, it proposed that deprivation of GABA can restrict the generation of ROS during oxidative stress that limits some of the enzymes of the tri carboxylic acid cycle. It has been reported that GABA shunt genes knocked out mutants of Yeast show more sensitivity to hydrogen peroxide (Coleman et al. 2001; Bouche´ et al. 2003).

Defence against biotic stress

GABA is act as neurotransmitter in mammals; it also observed that plants that inhibit insect feeding could able to accumulate GABA (Morse et al. 1979). It has been studied that GABA content increased by mechanical stress, and by creeping of insects on leaves, because it was possibility that, consumed GABA interrupts the growth process of insects (Bown et al. 2002). Moreover, transformed tobacco plants with enhanced GABA contents were observer to confer resistance against root-knot nematode and tobacco budworm larvae. Similarly, it was observed that the GABA level was enhanced in Asparagus cells that were exposed to pathogen-induced oxidative stress (Shelp et al. 2003; Shelp et al. 2006).

GABA involve in osmoregulation

GABA also transported via proline transporters from AtProT2 of *Arabidopsis thaliana* and LeProT1 of tomato. During water or salinity stress, AtProT2 is highly activated. Proline-GABA transporters also play protective role during osmotic stress by transporting organic osmolytes (Breitkreuz et al. 1999).

Role in plant signalling

GABA acts as a neurotransmitter in vertebrates and mammals by serve its role in signalling. Correspondingly, GABA known to be a signalling substance in plants. Some reports indicated that plants have GABA receptors or plant glutamate receptors utilized GABA as signalling molecules. An analysis of *Arabidopsis thaliana pop2* mutants revealed that a GABA communicated signals for accurate targeting of the pollen tube in the female tissues for the release of sperm cells (Palanivelu et al. 2003). Pollen tube germinated by the appropriate contact of the pollen grain and the stigma. The germinating pollen tube access path for the sperm cells to arrive and fused with the egg cell and the central cell of the ovary in female part of the ovule. Therefore, pollen tube guided several female tissues for the sperm cells to reach the egg and central cell.

Role of GABA in pollen tube growth

GABA involved in defence and development mechanisms, as well as other stress responses in plant system. Moreover, *pop 2* mutants are involved in growth and guidance of pollen tubes of *Arabidopsis thaliana* (Palanivelu et al. 2003).

GABA play key role in this process, because *pop 2* mutants encodes a GABA-T that involves in catabolism of GABA (Palanivelu et al. 2003, Renault et al. 2010, Ansari et al. 2011). GABA level enhanced along the passage via pollen tubes transportable to female tissues, therefore producing GABA gradient in the pistil of wild type plant. The gradient is defective in *pop 2* plants since they produced GABA in flowers. Therefore, the pollen tube precisely battered to the ovule uncertainty GABA degraded with an active GABA-T enzyme by the pistil or by the pollen tube.

Role in leaf senescence

In plant life cycle, leaf senescence is an integral event, which recognized as the last stage of plant development. It has been considered to be an unintended and programme aging, which involves decline in photosynthesis, reduction of complex molecules such as nucleic acid, carbohydrates, proteins, and lipids, disassembles of cellular structures and remobilisation of supplements from senescing leaves to the developing plants' organs, growing seeds and fruits (Smart et al. 1994; Nam et al. 1997; Lim et al. 2003; Thomas 2013; Ansari et al. 2014).Nitrogen is an essential supplement to be mobilized in senescence process. It has been reported that in the leaf senescence, nitrogen that is subsistin macromolecules was breakdown into glutamine and asparagine and these amino acids was transferred via phloem to the developing organs of the plant (Ansari et al. 2014).Though, premature senescence can cause the negative effect to the plants. The lack of assimilatory limits as leaf senescence progress get restricted yield of crop (Nooden, 1988) and thuslate senescence can positively effect on crop production (Lee et al. 2001). Many senescence-associated genes (*SAG*s) were characterized from various plants to elucidate the molecular mechanisms involved in foliar senescence (He and Gan, 2002; Park et al.1998; Oh et al. 1996; Buchanan-Wollaston, 1997; Al-Quraan, 2015; Al-Quraan and Al-Share, 2016).

GABA shunt assimilates carbons through glutamate and to generate nitrogen and carbon flues, which enter into the TCA cycle (Breitkreuz et al. 1999; Ackay et al. 2012).During foliar senescence, proteins present in leaves were transformed into α-amino acid by proteases and transaminase enzyme converts this α-amino acid to glutamate and α-keto acids that releases ammonia. The released ammonia was used in the conversion of glutamate into glutamine using glutamine synthetase (GS) that further change into asparagine viaasparagine synthetase (AS) (Miflin and Habash, 2002). Some glutamate is converts into GABA by GAD. The conversion of GABA to glutamate acceleratesby inhibiting protein synthesis (Satya Narayan and Nair 1990). The GABA metabolism associated with the metabolism of glutamate in senescence that allows glutamate to goes into GABA shunt pathway. In mitochondria GABA is converted into succinate via SSADH. Therefore, GABA shunt pathway involved in the conversion of glutatmate into succinate through GABA (Shelp et al. 1999) in leaf senescence.

Therefore, GABA shunt is participated in the metabolism of nitrogen that transported in foliar senescence and ultimately goes into TCA cycle (Barbosa et al. 2010; Akcay et al. 2012).It concluded that, the formation of succinate via GABA shunt is significant process, in the time if TCA cycle does not supply enough succinate. Thus GABA shunt is significantin foliar senescence (Bouche et al. 2003).

Role in plant development

The GABA shunt is required for normal plant development. Transgenic tobacco plants expressed a truncated petunia GAD by lacking the CaM-binding domain showed abnormal morphology with extremely high levels of GABA due to an abnormal regulation of GAD activity (Baum et al. 1996). The GAD knockout mutant prevented GABA accumulation in Arabidopsis in normal growth conditions and under heat stress condition; however, abnormal development was not observed (Bouche et al. 2004). The Arabidopsis T-DNA knockout mutants of SSADH demonstrated that the ssadh mutants were sensitive to UV and heat which were associated with increased hydrogen peroxide and causes cell loss. A study in double mutants of genes encoding GABA-T and SSADH (pop2 ssadh mutants) revealed accumulation of the GABA shunt intermediates (SSA and GHB) caused accumulation of peroxides and impaired development (Ludewig et al. 2008). These findings suggested a role of GABA shunt in restricting the accumulation of ROS (Bouche et al., 2003). Arabidopsis SSR knockout mutants showed significant accumulation of GBH in SSR-deficient mutants and vigabatrin VGB, a GABA-T inhibitor, reduced GHB levels and improved plant growth by preventing the accumulation of hydrogen peroxide and cell death (Fait et al. 2005).GABA identified as a key pollen-tube guidance signal (Bouche et al. 2003; Palanivelu et al. 2003).

GABA concentrations are higher at the position closer to the ovaries, thus GABA degradation is required to maintain GABA gradient in order to guide the pollen to the ovule. Arabidopsis POP2 gene, encoding GABA-T, was shown to be involved in the formation of GABA gradient, which provided appropriate targeting for pollen tubes. The POP2 mutant showed elevated GABA levels, which in turn eliminated the GABA gradient resulting in the fertility defect in the mutant (Palanivelu et al. 2003). A study in soybean hypocotyl tissue demonstrated that the rapid GABA synthesis under mechanical stress was associated with the rapid growth inhibition (Bown and Zhang, 2000). NMR analysis in root cultures of *Daturastramonium* suggested that de-differentiation of root tissue was accompanied by the increased levels of GABA. This change can also be induced by other factors such as phytohormone treatment and Ca2+ deficiency (Fliniaux et al. 2004). GABA also stimulated ethylene biosynthesis. Exogenous GABA was found to increase the rate of ethylene production in excised sunflower tissues, which was associated with increases in ACC synthase mRNA levels, ACC levels, ACC oxidase levels, and ACC oxidase acitivity (Kathiresan et al. 1997). Biochemical studies of tomato fruit development found that GABA accumulated in tomato fruit before the breaker phase and then declined shortly after the breaker phase (Mounet et al. 2007; Akihiro et al. 2008; Saito et al., 2008). Akihiro et al. (2008) also stated the positive correlation between GABA concentrations and expression of SlGAD2 and SlGAD3, and the negative correlation between GABA concentrations and α-ketoglutarate-dependent GABA-T activity.

Role in abiotic stress tolerance

The GABA is non-protein, ubiquitous, and one of the special interest of molecule that found in all organisms (Shelp et al. 1999). In plants, GABA involved in C/N metabolism and essential for plant development (Ansari et al. 2014). The accumulation of GABA in plants is rapidly enhanced due to different stress conditions such as low temperature, γ radiation, low pH, hypoxia, and darkness including leaf senescence process (Lane and Stiller 1970; Wallace et al. 1984; Ansari et al. 2009;Shelp et al. 2012). GABA in plants acts as an active osmolyte devoid of harmful effects under the salinity-induced desiccation and had the free radicals scavenging activity in stress conditions(Carillo2018). It has been considered that during environmental stress conditions, GABA shunt pathway can potentially involve in the regulation of GABA metabolism as shown in Fig. 1 (Al-Quraan et al.2016; Jalil et al. 2016; Jalil et al.2017). Moreover, the application of GABA encourage plant development, antioxidant metabolism, and expression of antioxidant genes in dose dependent manner, thus reducing stress induced oxidative harm in plants (Shi et al. 2010; Vijayakumari et al. 2016; Li et al. 2017). Application of GABA likewise directs the osmo regulation in plant adding to the upgrade of stress resistance (Yu et al. 2014; Vijayakumari and Puthur, 2015). More prominently, exogenous GABA successfully hindered the generation of free radicals and decreased oxidative harm through controlling the expression of important genes of free radical generation and genes encoding antioxidant enzyme in salinity stress (Shi et al. 2010). The treatment of GABA on seed also improved seed germination rate and diminished the salinity-induced damage during seeds germination of *Triticum aestivum* and *Zea mays* (Luo et al. 2011; 2019).The exogenous application of GABA improves the tolerance in several plants against abiotic stresses. GABA and sensitivity of plants to stresses GABA accumulates in response to many stresses including salinity, anoxia, hypoxia, drought, heat, and chilling (Wallace et al. 1984; Mayer et al., 1990; Zushi and Matsuzoe, 2007; Renault et al. 2010). The possible correlation between GABA metabolism and tolerance of plants to stresses is still unclear. However, studies on GABA in frost-resistant and frost-sensitive cultivars in barley and wheat reveal differences between the two groups (Mazzucotelli et al. 2006). GABA-related amino acids were higher in frost-resistant cultivars. An increase in GAD activity caused glutamate depletion in frost-sensitive cultivars, while glutamate levels were retained in frost-resistant cultivars. In addition, GABA degradation via the GABA shunt only occurred in a frost-resistant genotype. A recent study on salinity stress in tomatoes demonstrates that the effect on GABA promoting was greatest in the sensitive cultivar, and the effect of the stress on its accumulation did not occur during the early development stages (Saito et al. 2008).

Role in post harvest management

Little is known about GABA in response to postharvest stresses. However, an increase in GABA was observed in cold stored cherimoya fruits during the last stage of storage (Escribano and Merodio, 2001), in CO_2 treated cherimoya fruit (Merodio et al. 1998), in tomatoes stored in customized atmospheres (Makino et al., 2008), and in controlled atmosphere stored pears (Franck et al. 2007; Pedreschi et al. 2009). In post-harvest citrus fruit GABA shunt catabolised organic acid and associated with organic acid metabolism and amino acid synthesis that causes inorganic nitrogen assimilated mainly into four amino acids such as aspartic acid, glutamic acid, asparagine and, glutamine from that glutamine and asparagine required for plant metabolism (Katz et al. 2011 and Sun et al. 2013).

Additionally, exogenous application of GABA improved cold tolerance of zucchini fruit in postharvest storage (Palma et al. 2019).There is various studies reported that regulating the functional GABA shunt pathway is vital for tolerance to postharvest chilling stress by increasing ATP, dropping NADH and decreasing reactive oxygen species (ROS). Furthermore, it has been studied that anthurium flowers are highly sensitive to chilling stress; its optimum storage temperature is 12.5–20 °C. It has been investigated that the application of salicylic acid by postharvest stem-end dipping enhanced the GABA shunt pathway activities of anthurium flowers that regulated the storage of the flowers at below optimum temperature (Aghdam et al. 2016).

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REFERENCES

Al-Quraan, N.A. (2015). GABA shunt deficiencies and accumulation of reactive oxygen species under UV treatments: insight from Arabidopsis thaliana calmodulin mutants. *Acta. Physiol. Plant.* 37, 1-11.

Al-Quraan., N.A. and Al-Share, A.T. (2016). Characterization of the γ-aminobutyric acid shunt pathway and oxidative damage in Arabidopsis thaliana pop 2mutants under various abiotic stresses**.** *Biologia Plantarum.* 60 (1), 132-138.

Aghdam, M.S., Naderi, R., Malekzadeh, P. and Jannatizadeh, A. (2016). Contribution of GABA shunt to chilling tolerance in anthurium cut flowers in response to postharvest salicylic acid treatment. *Scientia Horticulturae*, 205: 90-96.

Akçay, N., Bor, M., Karabudak, T., Özdemir, F. and Türkan, I. (2012). Contribution of gamma amino butyric acid (GABA) to salt stress responses of Nicotiana sylvestris CMSII mutant and wild type plants. *J. Plant. Physiol.* 169, 452-458.

Akihiro, T., Koike, S., Tani, R., Tominaga, T., Watanabe, S., et al. (2008). Biochemical Mechanism on GABA Accumulation During Fruit Development in Tomato. *Plant Cell Physiol.* 49(9): 1378–1389.

Ansari, M.I. and Chen, S.C.G. (2011). Leaf Senescence-An Overview. *Int. J. of Recent. Trends in Sci. Technol.* 1, 110-114.

Ansari, M.I. and Chen, S.C.G. (2009). Biochemical characterization of gamma-aminobutyric acid (GABA): pyruvate transaminase during rice leaf senescence. *Inter. J. Integ. Biol.* 16, 27-32.

Ansari, M.I., Lee, R.H. and Chen, S.C.G. (2005). A novel senescence- associated gene encoding g-aminobutyric acid (GABA): pyruvate transaminase is upregulated during rice leaf senescence. *Physiol. Plant.* 123, 1–8.

Ansari, M.I., Hasan, S. and Jalil, S.U. (2014). Leaf Senescence and GABA Shunt. *Bioinformation,* 10, 730-732.

Barbosa, J.M., Singh, N.K., Cherry, J.H. and Locy, R.D. (2010). Nitrate uptake and utilization is modulated by exogenous gamma-aminobutyric acid in Arabidopsis thaliana seedlings. *Plant Physiol Biochem.* 48, (6), 443-50.

Baum, G., Lev-Yadun, S., Fridmann, Y., Arazi, T., Katsnelson, H., Zik, M. and Fromm, H. (1996). Calmudulin binding to glutamate decarboxylase is required for regulation of glutamate and GABA metabolism and normal development in plants. *Embo. J.* 15, 2988-96.

Bouché, N., Fait, A., Bouché, D., Moller, S.G. and Fromm, H. (2003). Mitochondrial succinate-semialdehyde dehydrogenase of the gamma-aminobutyrate shunt in required to restricts levels of reactive oxygen intermediates in plants. *Proc. nat. Acad. Sci.* USA 100, 6843-6848.

Bouche´, N. and Fromm, H. (2004). GABA in plants: just a metabolite? *Trends Plant Sci*. 9, 110–115.

Bouchereau, A., Aziz, A., Larher, F. and Martin-Tanguy, J. (1999). Polyamines and environmental challenges: recent development. *Plant Sci.* 140,103–125.

Bown, A.W. and Shelp, B.J. (1997). The metabolism and function of gamma aminobutyric acid. *Plant Physiol*. 115, 1-5.

Bown, A.W., Hall, D.E. and Mac Gregor, K.B. (2002). Insect footsteps on leaves stimulate the accumulation of 4-aminobutyrate and can be visualized through increased chlorophyll fluorescence and superoxide production. *Plant Physiol.* 129, 1430-40.

Bown, A. W. and Zhang, G. (2000). Mechanical stimulation, 4-aminobutyrate (GABA) synthesis and growth inhibition in soybean hypocotyl tissue. *Can. J. Bot* 78: 119–123.

Breitbreuz, K.E. and Shelp, B.J. (1995). Subcellular compartmentation of the 4-aminobutyric shunt in protoplast from developing soybean cotelydons. *Plant Physiol.* 108, 99-103.

Breitkreuz, K.E., Shelp, B.J., Fischer, W.N. and Rentsch, D. (1999). Identification and characterization of GABA, proline and quaternary ammonium compound transporters from *Arabidopsis thaliana***.** *FEBS Lett.* 450, 280.

Buchanan-Wollaston, V. (1997). The molecular biology of leaf senescence. *J. Exp. Bot.* 48(1), 81-199.

Caroll, A.D., Fox, G.G., Laurie, S., Phillips, R., Ratcliffe, R.G. and Stewart, G.R. (1994). Ammonium assimilation and the role of [gamma]-Aminobutyric Acid in pH homeostasis in carrot cell suspensions. *Plant Physiol.* 106, 513-520.

Coleman, S.T., Fang, T.K., Rovinsky, S.A, et al. (2001). Expression of a glutamate decarboxylase homologue is required for normal oxidative stress tolerance in *Saccharomyces cerevisiae*. *J. Biol. Chem*. 276: 244–250.

Crawford, L.A., Bown, A.W., Breitkreuz, K.E. and Guinel, F.C. (1994). The synthesis of [gamma]-Aminobutyric Acid in response to treatment reducing cytosolic pH. *Plant Physiol.* 104, 865-871.

Escribano, M.I. and Merodio, C. (2001). Limited ammonium assimilation in cherimoya fruit stored at chilling temperature. *Acta Horticulturae* 553: 311- 312.

Fait, A., Yellin, A. and Fromm, H. (2005). GABA shunt deficiencies and accumulation of reactive oxygen intermediates: insight from Arabidopsis mutants. *FEBS Lett* 579, 415–420.

Feller, U., and Fischer, A. (1994). Nitrogen metabolism in senescing leaves. *Critical Rev. Plant Sci.* 13, 241-273.

Fliniaux, O., Mesnard, F., Raynaud, S., Baltora, S., Robins, R.J. and Fliniaux, M.A. (2001). Use of heteronuclear multiple bond coherence NMR spectroscopy to monitor nitrogen metabolism in a transformed root culture of Daturastramonium. Comptes Rendus de l'AcadeÂmie des Sciences, Paris, *Chimie/Chemistry* 4, 775±778.

Franck, C., Lammertyn, J., Tri Ho, Q., Verboven, P., Verlinden, B. and Nicolaï, B.M. (2007). Browning disorders in pear fruit. *Postharvest Biol. Technol.* 43, 1–13.

He, Y. and Gan, S.A. (2002). Gene encoding an acyl hydrolase is involved in leaf senescence in Arabidopsis. *Plant Cell.* 14, 805–815.

Jalil, S.U., Ahmad, I. and Ansari, M.I. (2016). Screening of Arabidopsis thaliana GABA – Transaminase Mutant and its Root Pattern Analysis. *J Biol Chem Research* 33: 909-917.

Jalil, S.U., Ahmad, I. and Ansari, M.I. (2017). Functional loss of GABA transaminase (GABA-T) expressed early leaf senescence under various stress conditions in Arabidopsis thaliana. *Curr Plant Biol* 9-10: 11-22.

Kamachi, K., Yamaya, T., Hayakawa, T., Mae, T. and Ojima, K. (1992). Changes in cytosolic glutamine synthetase polypeptide and its mRNA in leaf blade of rice plants during natural senescence. *Plant Physiol.* 98, 1323–1329.

Kathiresan, A., Tung, P., Chinnappa, C. C. and Reid, D. M. (1997). γ-aminobutyric acid stimulates ethylene biosynthesis in sunflower. *Plant Physiol.* 115: 129–135.

Katz, E., Boo, K.H., Kim, H.Y., Eigenheer, R.A., Phinney, B.S.V., Shulaev, F., Negre-Zakharov, Sadka, A. and Blumwald, E. (2011). Label-free shotgun proteomics and metabolite analysis reveal a significant metabolic shift during citrus fruit development. *J Exp Bot.* 62, 5367-5384.

King, G.A., Davies, K.M., Stewart, R.J. and Borst, W.M. (1995). Similarities in gene expression during the post-harvest-induced senescence of spears and natural foliar senescence of asparagus. *Plant Physiol.* 108, 125–128.

Lane, T.R. and Stiller, M. (1970). Glutamic acid decarboxylation in Chlorella. *Plant Physiol*. 45, 558–562.

Li, Y., Fan, Y., Ma, Y., Zhang, Z., Yue, H., Wang, L., Li, J. and Jiao, Y. (2017). Effects of exogenous -aminobutyric acid(GABA) on photosynthesis and antioxidant system in pepper (Capsicum annuum L.) seedlings under lowlight stress. *J Plant Growth Regul* 36: 1–14.

Lim, P. O., Woo, H. R. and Nam, H. G. (2003). Molecular genetics of leaf senescence in Arabidopsis. *Trends Plant Sci.* 8, 272–278.

Ludewig, F., Hüser, A., Fromm, H., Beauclair, L. and Bouché, N. (2008). Mutants of GABA transaminase (POP2) suppress the severe phenotype of succinic semialdehyde dehydrogenase (ssadh) mutants in Arabidopsis. *PLoS One.* 3:e3383.

Luo, H.Y., Yang, L.W., Gao, H.B., Xiao-Lei, W.U. and Liu, H.H. (2011). Physiological mechanism of GABA soaking totomato seed germination and seedling development under NaCl stress. *Acta Bot Boreal-Occident Sin* 31: 2235–2242.

Luo, D., Zhou, Q., Wu, Y., Chai, X., et al. (2019). Full-length transcript sequencing and comparative transcriptomic analysis to evaluate the contribution of osmotic and ionic stress components towards salinity tolerance in the roots of cultivated alfalfa (*Medicagosativa* L.). *BMC Plant Biol* 19: 32.

Makino, Y., Soga, N., Oshita, S., Kawagoe, Y. and Tanaka, A. (2008). Stimulation of -aminobutyric acid production in vine-ripe tomato (Lycopersicon esculentum Mill.) fruits under modified atmospheres. *J. Agric. Food Chem*. 56, 7189–7193.

Mayer, R., Cherry, J. and Rhodes, D. (1990). Effect of heat shock on amino acid metabolism of cowpea cells. *Plant Physiol* 94: 7964310.

Mazzucotelli, E., Tartari, A., Cattivelli, L. and Forlani, G. (2006). Metabolism of γ-aminobutyric acid during cold acclimation and freezing and its relationship to frost tolerance in barley and wheat. *J. Exp. Bot.* 57, 3755-3766.

Merodio, C., Munoz, M.T., Cura, B.D., Buitrago, D. and Escribano, M.I. (1998). Effect of high CO2 level on the titres of -aminobutyric acid, total polyamines and some pathogenesis-related proteins in cherimoya fruit stored at low temperature. *J. Exp. Bot.* 49, 1339–1347.

Miflin, B.J. and Habash, D. (2002). The role of glutamine synthetase and glutamate dehydrogenase in nitrogen assimilation and possibilities for improvement in nitrogen utilization of crops. *J. Exp. Bot.* 53, 979–987.

Morse, D.E., Hooker, N., Duncan, H. and Jensen, L. (1979). ᵞ- Aminobutyric acid, a neurotransmitter, induces planktonic abalone larvae to settle and begin metamorphosis. *Science*. 204, 407-410.

Mounet, F., Lemaire-Chamley, M., Maucourt, M., Cabasson, C., Giraude, J.L., et al. (2007). Quantitative metabolic profiles of tomato flesh and seeds during fruit development: complementary analysis with ANN and PCA. *Metabolomics* 3: 273–288.

Nam, H.G. (1997). The molecular genetic analysis of leaf senescence, *Curr. Opin. Biotechnol.* 8(8), 200–207.

Nooden, L.D. (1988). Whole plant senescence. In Senescence and Aging in Plants, L.D. Nooden and S.C. Leopold, (San Diego, CA: Academic Press), 391-439.

Oh, S.A., Lee, S.Y., Chung, K.K., Lee, C.H. and Nam, H.G. (1996). A senescence- associated gene of Arabidopsis thaliana is distinctively regulated during natural and artificially induced leaf senescence. *Plant Mol. Biol.* 30, 739– 754.

Palanivelu, R., Brass, L., Edlund, A.F. and Preuss, D. (2003). Pollen Tube Growth and Guidance Is Regulated by POP2, an Arabidopsis Gene that Controls GABA Levels. *Cell.* 114 (1), 47-59.

Palma, F., Carvajal, F., Jiménez-Muñoz, R., Pulido, A., Jamilena, M. and Garrido, D. (2019). Exogenous γ-aminobutyric acid treatment improves the cold tolerance of zucchini fruit during postharvest storage. *Plant Physiol Biochem.* 136:188-195.

Park, D.H., Mirabella, R., Bronstein, P.A., et al. (2010). Mutations in γ-aminobutyric acid (GABA) transaminase genes in plants or Pseudomonas syringae reduce bacterial virulence. *Plant J.* 64, 318–330.

Pedreschi, R., Franck, C., Lammerteyn, J., Erban, A., Kopka, J., Hertog, M., Verlinden, B. and Nicolaï, B. (2009). Metabolic profiling of 'Conference' pears under low oxygen stress. *Postharvest Biol. Technol.* 51, 123–130.

Renault, H., Roussel, V., El-Amrani, A., Arzel, M., Renault, D., Bouchéreau, A. and Deleu, C. (2010). The Arabidopsis pop2-1 mutant reveals the involvement of GABA transaminase in salt stress tolerance. *BMC Plant. Biol.* 10, 20.

Ribak, C.E. and Yan, X.X. (2000). GABA neurons in the neocortex. In: Martin DL, Olsen RW, editors. GABA in the nervous system: the view at fifty years. Philadelphia: Lippincott Williams and Wilkins. P. 357–368.

Saito, T., Matsukura, C., Sugiyama, M., Watahiki, A., Ohshima, I., et al. (2008). Screening for -aminobutyric acid (GABA)-rich tomato varieties. *J. Jpn. Soc. Hort. Sci.* 77: 242–250.

Satyanarayan, V. and Nair, P.M. (1990). Metabolism, enzymology and possible roles of 4-aminobutyrate in higher plants. *Phytochemistry*, 29, 367-375.

Shelp, B.J., Bown, A.W., et al. (1999). Metabolism and function of gamma aminobutyric acid. *Trends Plant Sci.* 4:446-452.

Shelp, B.J., Bown, A.W. and Faure, D. (2006). Extracellular γ-Aminobutyrate mediates communication between plants and other organisms. *Plant Physiol.* 142, 1350-1352.

Shelp, B. J., Bozzo, G. G., Trobacher, C. P., Zarei, A., Deyman, K. L. and Brikis C. J. (2012). Hypothesis/review: contribution of putrescine to 4-aminobutyrate (GABA) production in response to abiotic stress. *Plant Sci.* 193–194, 130–135.

Shelp, B.J., Van Cauwenberghe, O.R. and Bown, A.W. (2003). Gamma aminobutyrate: from intellectual curiosity to practical pest control. *Can. J. Bot.* 81, 1045-1048.

Shi, S. Q., Shi, Z., Jiang, Z.P., Qi, L.W., Sun, X.M., Li, C.X., Liu, J.F., Xiao, W.F. and Zhang, S.G. (2010). Effects of exogenous GABA on gene expression of Caraganainter media roots under NaCl stress: regulatory roles for H_2O_2 and ethylene production. *Plant, Cell and Environ.* 33, 149–162.

Smart, C.M. (1994). Gene expression during leaf senescence. *New Phytol.* 126: 419-448.

Steward, F. C., Thompson, J. F., and Dent, C. E. (1949). ᵞ-Aminobutyric acid a constituent of potato tubers? *Science*. 110, 439-440.

Sun, X., Zhu, A., Liu, S., Sheng, L., Ma, Q., Zhang, L., Nishawy, E.M., Zeng, Y., Xu, J., Ma, Z., Cheng, Y. and Deng, X. (2013). Integration of metabolomics and subcellular organelle expression microarray to increase understanding the organic acid changes in post-harvest citrus fruit. *J Integr Plant Biol.* 55, 1038-1053.

Thomas, H. (2013). Senescence, ageing and death of the whole plant. *New Phytol*. 197, 696–711.

Vijayakumari, K., Jisha, C. and Puthur, J.T. (2016). GABA/BABA priming: a means for enhancing abiotic stress tolerance potential of plants with less energy investments on defence cache. *Acta Physiol Plant* 38:230.

Vijayakumari, K. and Puthur, J.T. (2015). g-Aminobutyric acid (GABA) priming enhances the osmotic stress tolerance in piper *nigrumlinn*. plants subjected to PEG-induced stress. *Plant Growth Regul* 78: 1–11.

Wallace, W., Secor, J. and Schrader, L.E. (1984). Rapid accumulation of gamma-aminobutyric acid and alanine in soybean leaves in response to an abrupt transfer to lower temperature, darkness, or mechanical manipulation. *Plant Physiol.* 75, 170-175.

Yu, C., Zeng, L., Sheng, K., Chen, F., Zhou, T., Zheng, X. and Yu, T. (2014). g-Aminobutyric acid induces resistance against penicillium expansum by priming of defence responses in pear fruit. *Food Chem* 159: 29–37.

Zushi, K. and Matsuzoe, N. (2007). Salt stress-enhanced -aminobutyric acid (GABA) in tomato fruit. *Acta Hort*. 761, 431–435.

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