



Trehalose: A Key Organic Osmolyte Effectively Involved in Plant Abiotic Stress Tolerance

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Abstract

Trehalose is a natural non-reducing sugar that is found in the vast majority of organisms such as bacteria, yeasts, invertebrates and even in plants. Regarding its features, it is considered as a unique compound. It plays a key role as a carbon source in lower organisms and as an osmoprotectant or a stabilizing molecule in higher animals and plants. Although in plants it is present in a minor quantity, its levels rise upon exposure to abiotic stresses. Trehalose is believed to play a protective role against different abiotic stressful cues such as temperature extremes, salinity, desiccation. Moreover, it regulates water use efficiency and stomatal movement in most plants. Detectable endogenous trehalose levels are vital for sustaining growth under stressful cues. Exogenously applied trehalose in low amounts mitigates physiological and biochemical disorders induced by various abiotic stresses, delays leaf abscission and stimulates flowering in crops. External application of trehalose also up-regulates the stress responsive genes in plants exposed to environmental cues. The genetically modified plants with trehalose biosynthesis genes exhibit improved tolerance against stressful conditions. An increased level of trehalose has been observed in transgenic plants over-expressing genes of microbial trehalose biosynthesis. However, these transgenic plants display enhanced tolerance to heat, cold, salinity, and drought tolerance. Due to multiple bio-functions of this sugar, it has gained considerable ground in various fields. However, exogenous use of this bio-safe sugar would only be possible under field conditions upon adopting strategies of low-cost production of trehalose. In short, trehalose is a unique chemical that preserves vitality of plant life under harsh ecological conditions. Certainly, the new findings of this disaccharide will revolutionize a wide array of new avenues.

Keywords Trehalose · Abiotic stress · Osmoprotectants · Antioxidant · Plants

Introduction

Sugars perform key roles in a myriad of metabolic processes throughout the plant life span, that is, from the juvenile stage up to reproductive stage. There is an interplay between sugar signaling and phyto-hormone signaling such as that of ethylene, gibberellins, auxins and abscisic acid. This phenomenon is important for transitions of plant growth processes. Trehalose, a disaccharide, was first discovered by Wiggers

(1832) in a parasitic fungus (*Claviceps* spp.) mycelium of rye. This sweet disaccharide was isolated in abundant quantities from nests and cocoons of the insects *Larinus acutatus* and *L. nidificans* by a French chemist Marcellin Berthelot in the mid of nineteenth century. Its old name “trehalo manna” is known due to cocoons of the beetles (Feofilova 1992; Luyckx and Baudonin 2011). In the past, it was also recognized as “mycos” (Richards et al. 2002). It is extensively found in different organisms ranging from bacteria to invertebrates and in lesser amounts in higher plants. The spores of mycelial fungi and yeasts contain the compound in higher amounts from 16 to 30% (Sols et al. 1971). Trehalose occurs in white powder form having no odor, but is 45% sweeter than that of sucrose (Jain and Roy 2009). This sugar has diversified roles in both animals and plants. During growth and development in organisms, it acts as an energy source as in the case of spore sprouting (Elbein et al. 2003). In resurrection plants such as *Myrothamnus flabellifolius*, it

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was reported to accumulate in higher levels during extreme water scarcity, and it played a significant role in conserving *M. flabellifolius* (Gechev et al. 2012). In some cases, it stimulates the stress-related signaling pathways (John et al. 2017). It also acts as an osmoprotectant during stress adversities (Paul et al. 2008). In angiosperms, naturally a minute quantity of trehalose is synthesized, but upon exposure to stress levels rise in the plant (Kempa et al. 2008). GC-FID and GC-MS have been commonly used to quantify trehalose concentration in wild-type *Arabidopsis* plant extracts 37 ng g⁻¹ dry weight/plant and 100 ng g⁻¹ dry weight/flower (Suzuki et al. 2008; Schluepmann and Paul 2009). Trehalose is a low-calorie sweetener, and it remains stable against hydrolysis (Walmagh et al. 2015). It withstands a diverse pH range and is non-carcinogenic. It is also used in processed foods and now has more market shares (Nakakuki 2005). During digestion, it is catalyzed into glucose by the trehalase enzyme in the small intestine and then taken up in the villi (Teramoto et al. 2008). Endogenous trehalose stabilizes microbial cells, membranes, enzymes, and even DNA (Jain and Roy 2010). It is also used in manufacturing heat-resistant vaccines (Ohtake et al. 2011). Because it is an effective antioxidant, it prolongs the shelf lives of cosmetic products and inhibits ingredient degradation. It is used as an ingredient in sweet delicacies (Ohtake and Wang 2011). A review of the literature indicates that trehalose is effective in regulating various physio-biochemical processes in plants, which may have a direct or indirect role in stimulating plant growth and yield production. Furthermore, the primary focus of this review is to uncover trehalose-induced changes in plants subjected to different environmental stresses and examine the putative mechanisms and metabolite profiles involved in stress tolerance.

Trehalose Distribution

Trehalose occurs ubiquitously in almost all organisms, and it plays a key role in vitro and in vivo (López-Gómez and Lluch 2012). In microorganisms, it serves as an energy source as well as a key compatible osmolyte. In the fungal cell wall, it initiates chitin formation. Different bacteria such as nitrogen fixing *Rhizobium* sp. (Maruta et al. 1996) and pathogenic *Escherichia coli* (Kaasen et al. 1994) possess this sugar as a cell wall component or a carbon source or as an osmoprotectant. In the animal kingdom, especially in insects, trehalose is consumed as a carbon source during flight activity (Becker et al. 1996; Carpinelli et al. 2006). Ascospores under severe stress conditions have higher levels of mannitol and trehalose (Dijksterhuis et al. 2002). The asexual spores such as conidia having abundant trehalose and mannitol can germinate on a growth medium supplied with a low amount of water but rich in nutrients (Wang et al.

2012). Conidia deficient in trehalose were reported to be stress sensitive (Sakamoto et al. 2008). Trehalose also mitigates the harmful effects of hydrocarbons such as ethanol and toluene (Wen et al. 2016). In the nematode *Aphelenchus avenae*, trehalose accumulation is stimulated during desiccation conditions (Madin and Crowe 1975). So, in a nutshell, trehalose is a natural versatile disaccharide with has a bio-preservative role in metabolic machinery during abiotic stress conditions.

Structural Properties of Trehalose

Trehalose is a non-reducing disaccharide sugar composed of two glucose subunits linked by an alpha, alpha-1,1 glycosidic bond (Fig. 1).

Trehalose has unique properties compared to other disaccharides, because both reducing subunits are involved in making the glycosidic bond (Jain and Roy 2009). It resists acid hydrolysis and remains durable even in soluble form at elevated temperatures despite acidic pH conditions (Teramoto et al. 2008). The α - α linkage of trehalose is very stable (Richards et al. 2002). Trehalose has high hydrophilicity due to its inability for internal hydrogen bonding (Paul and Paul 2014). Due to these properties, it is a useful molecular, membranous and protein preservative (López-Gómez and Lluch 2012). It has dehydrating and vitrification ability (Sakurai et al. 2008). In the case of dehydration or freezing states, trehalose forms hydrogen bonding with surrounding macromolecules and membranes by replacing water molecules (Crowe 2007). Upon extreme dehydration, it crystallizes into a glass-like appearance (Einfalt et al. 2013); thus, it is a particular trait of trehalose (Cesaro et al. 2008). This glassy formation preserves biomolecules from denaturation even under extreme dehydration, and it recovers their functional activity upon rehydration (Fernandez et al. 2010). Trehalose has a very low bond energy (1 kcal mol⁻¹) and a chemically inert sugar (Schwarz and Van Dijk 2017). In contrast, sucrose has 27 kcal mol⁻¹ bond energy. It does not break down into reducing monosaccharide components unless it is exposed to the action of trehalase or extreme hydrolytic conditions (López-Gómez and Lluch 2012).

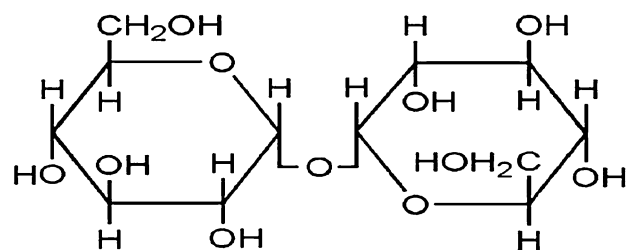


Fig. 1 Structure of trehalose

Trehalose Biosynthesis in Plants

Two molecules, uridine-diphospho-glucose (UDP-Glc) and glucose-6-phosphate (Glc-6-P), are consumed for trehalose biosynthesis in plants. The enzyme trehalose phosphate synthetase (TPS) catalyzes UDP-Glc and Glc-6-P into trehalose-6-phosphate (Blazquez et al. 1998; Zentella et al. 1999). The enzyme trehalose-6-phosphate phosphatase (TPP) then catalyzes trehalose-6-phosphate into the final product, trehalose (Vogel et al. 1998) (Fig. 2).

Trehalose Metabolism in Higher Plants

In plants, endogenous trehalose plays a direct role as a signaling molecule associated with carbon allocation and subsequently in dehydration stress (Schluepmann et al. 2003). Trehalose presence in plants has been detected in angiospermic herbaceous plants such as *Selaginella lepidophylla* and *Myrothamnus flabellifolius* (Gechev et al. 2014). Subsequently, this sugar was also revealed in tobacco and rice plants but in very low amounts ($10 \mu\text{g g}^{-1}$) (Kretovich 1980). Recently, research has been focused on elucidation of trehalose metabolism particularly in transgenic crops with stress tolerance (Schwarz and Van Dijck 2017). A low concentration of trehalose is not solely due to the action of trehalase, but also due to tight regulation of TPS and TPP gene expression and enzyme activity (Delorge et al. 2014). The addition of validamycin A to the growth medium promoted trehalose accumulation by inhibiting trehalase, but it did not stimulate the biosynthesis of trehalose (Goddijn et al. 1997). The regulation of trehalose genes although resulted in a limited increase in trehalose, transgenic plants conferred abiotic stress tolerance (Delorge et al. 2014). The expression of *E. coli* and yeast derived trehalose genes in different plant species made them more tolerant against salinity, water deficit and cold stress (Iordachescu and Imai 2008). For example, in rice, the higher expression of various trehalose phosphate synthetase genes produced acclimation to drought, cold and salt stress (Li et al. 2011). The up-regulation of *AtTPS1* (*Arabidopsis* trehalose-6-P synthase) in *Arabidopsis* plants caused a little increase in T6P as well as trehalose, but TPP activity induced transiently increased trehalose levels under low temperature stress (Suzuki et al.

2008). Exposure to high temperature (40°C) in *A. thaliana* induced a twofold increase in trehalose levels within 4 h and its levels became eightfold more after four days when treated with cold stress (4°C) (Kaplan et al. 2004). The expression of trehalose transgenes activates the biosynthetic pathway in organs exposed to stressful environments. For example, in cotton plants, the induced *TPS1* genes were expressed only in roots and leaves (Kosmas et al. 2006). In maize, the *TPP* gene was repressed in tassels whereas *TPS1* was over-expressed in ears under drought conditions (Zhuang et al. 2007). Sometimes, degradation of trehalose regulates its levels in different plant tissues. For example, in *Medicago truncatula* under salt stress, the expression of the trehalase gene *MtTRE1* was blocked and trehalose concentrations increased in its nodules (López et al. 2008). A microarray analysis showed that in *A. thaliana* the instance of abiotic stress induced a marked expression of relevant genes involved in trehalose metabolism (Iordachescu and Imai 2008). From these findings, it is clear that trehalose or T6P is effectively involved in stress tolerance of plants. The transgenic plants support the logic that activated trehalose metabolism triggers acclimation against stress conditions (Bae et al. 2005).

Trehalose and Abiotic Stress Resistance

The role of trehalose has been investigated in both simple and complex organisms exposed to stressful cues. Trehalose averts the adverse effects of salinity, dehydration, cold and high temperature on plants (Iordachescu and Imai 2008; Tapia and Koshland 2014). Currently, considerable efforts are underway at different institutions for elucidating the role of trehalose in different plants grown in a variety of stresses including drought, salinity, and temperature.

Drought Stress

Drought stress is a globally widespread and ever-growing environmental problem (Nezhadahmadi et al. 2013). Anhydrobiotic organisms tolerate extreme water deficiency. Such organisms include *Saccharomyces cerevisiae* and some desert plants (Ambastha and Tiwari 2015). Among animals, invertebrate rotifers, brine shrimps, tardigrades, and nematodes can endure water scarcity (Barnett and Facey 2016). These organisms possess elevated trehalose levels during adverse desiccated conditions. The main role of trehalose is to preserve membrane stability under such conditions (Iordachescu and Imai 2011). Trehalose even in small quantities prevents membrane vesicle fusions and retains lipids in the liquid crystalline state (Ohtake et al. 2006). Trehalose has high hydration potential during desiccation or freezing; it stabilizes dry proteins and biological membranes

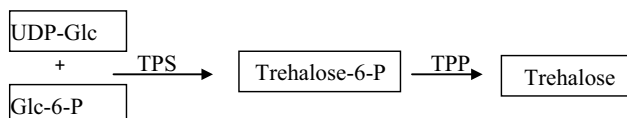


Fig. 2 Trehalose biosynthesis in plants (partially adopted from Winger 2002)

by replacing surface bound water of biological structures (Luzardo et al. 2000). Moreover, it makes hydrogen bonding between its OH groups and polar groups of proteins and phosphate groups of membranes. Current molecular findings revealed that trehalose is a potent source for stress survival in baker yeast (Tapia et al. 2015). The microbial trehalose derived transgenic plants although have low amounts of trehalose, they are stress tolerant (Cortina and Culianez-Macia 2005).

Salinity Stress

High accumulation of salts referred to as salt or salinity stress interferes with vital plant metabolites (Ashraf and Akram 2009). In response to salt stress, plants adopt a strategy to adjust osmotic potential of the cell by generating osmotica/osmoprotectants/compatible solutes such as sugars including trehalose (Shahbaz et al. 2017). It is now well evident that trehalose-6-phosphate phosphatase (TPP) catalyzes the final step of trehalose metabolism. Investigating the sub-cellular localization of TPP family members of *Arabidopsis thaliana*, it has been found that AtTPPD is a chloroplast-localized enzyme. Plants deficient in AtTPPD were sensitive, whereas plants over-expressing AtTPPD were more tolerant to salinity stress (Krasensky et al. 2014). Elevated stress tolerance of AtTPPD over-expressors associated with high accumulation of soluble sugars and starch levels suggest a putative role for AtTPPD in regulating sugar metabolism under saline conditions. Recently, Henry et al. (2015) observed an increase in the level of trehalose-6-phosphate in kernels at silking, leaf and cob of maize plants under saline regime, but it decreased gradually even if the sucrose level continued to increase. They found that both source and sink strength were reduced by salt, and the data indicated that T6P may have different roles in source and sink tissues, so the kernel abortion under osmotic stress may be due to inability to utilize these energy reserves. In another study with rice, Mostofa et al. (2015) reported that pre-treatment with trehalose at the rate of 10 mM for two days significantly suppressed salt-induced adversities by suppressing ROS and MDA, whereas chlorophyll contents, AsA, GSH, RWC and redox status were improved substantially. Trehalose-pre-treated salt-stressed rice seedlings maintained CAT, GST, GPX, and GR activities under salt stress. They suggested that trehalose is involved in protecting against salt-induced oxidative damage by accumulating low amounts of ROS, increasing in non-enzymatic antioxidants, and activation of the glyoxalase and antioxidative systems. Furthermore, trehalose application (0.5–5 mM) largely alleviated ionic imbalance, ROS burst, and programmed cell death (PCD) occurrence induced by high salinity (150–250 mM NaCl) in *Arabidopsis* seedlings (Yang et al. 2014).

Temperature Stress

Temperature stress (high/low) adversely affects plant growth and yield production (John et al. 2016). Trehalose accumulation under low temperature stress has been reported in microorganisms (Attfield 1987; Kandror et al. 2002; Petitjean et al. 2015). It was observed that transduction of a mutant with the *otsA/otsB* genes, responsible for trehalose synthesis, restored trehalose content and cell viability at 4 °C (Kandror et al. 2002). In another study with *Saccharomyces cerevisiae*, it was observed that activation of the protein kinase C1 pathway is triggered by an intracellular increase in osmolarity due to trehalose accumulation under heat stress (Mensonides et al. 2005). Recent studies indicate that trehalose metabolism is important for normal plant growth and development. The intermediate compound, trehalose-6-phosphate, has been widely shown to act as a sensor for available sucrose, thereby directly influencing the type of response to the changing environmental conditions (Delorge et al. 2014; Krasensky et al. 2014). Due to its influence on plant growth and development, alteration in trehalose biosynthesis pathways, either at the level of T6P synthesis, T6P hydrolysis, or trehalose hydrolysis, can be utilized to improve crop yield and biomass production. It is clear that alteration of the amounts of either T6P and/or trehalose may result in increased stress tolerance along with many unexpected phenotypic alterations (Fig. 3). The above-cited reports depict that trehalose plays a promising adaptive role in plants exposed stressful cues.

Exogenous Trehalose Application and Abiotic Stress Tolerance

Trehalose has been applied through different modes such as through the rooting medium, as a foliar spray or as a pre-sowing seed treatment so as to tailor plants to thrive well under stressful cues (Table 1). For example, trehalose was

Abiotic stresses (Drought, Salinity and Temperature)

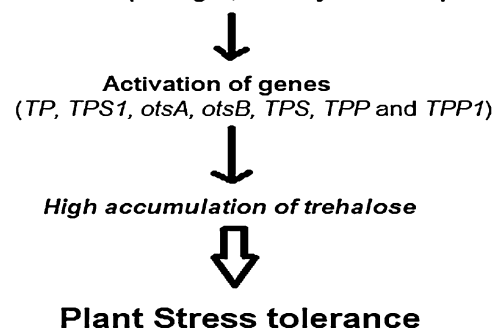


Fig. 3 Involvement of number of genes in trehalose accumulation and abiotic stress tolerance in plants

Table 1 Exogenously applied trehalose-induced improvement in growth and different physiological processes in different plants subjected to stressful environments

Nature of stress	Mode of application	Concentrations	Plant species	Metabolic processes	References
Salinity	Pre-soaking treatment	10 mM	Maize	Increased photosynthetic pigments, nucleic acids content, K/Na ions decreased lipid peroxidation and ion leakage	Zeid (2009)
Heat	Pretreatment	1.5 mM	Wheat	Reduction in electrolyte leakage, H ₂ O ₂ , MDA, superoxide anion, and lipoygenase activity	Luo et al. (2010)
Cadmium stress	Foliar spray	0.5, 1, 2, and 5 mM	Duckweed	Reduced proline contents, MDA levels, and accumulation of Cd while SOD, CAT and APX, activities improved under heavy metal stress	Duman et al. (2011)
Drought	Foliar spray	30 mM	Maize	Improved water relation attributes, photosynthetic and antioxidant defense mechanism	Ali and Ashraf (2011)
Salinity	Pretreatment	10 mM	Rice	Reduced Na ⁺ /K ⁺ ratio, proline contents, decreased SOD and POX activities, whereas APX increased	Nounjan et al. (2012)
Salinity	Foliar spray	10 mM	<i>Catharanthroseus</i>	Increase in soluble sugars, free amino acids, control water loss, leaf gas exchange and ionic flow	Chang et al. (2014)
Heat stress	Foliar spray	0, 5, 10, 15, 20, and 25 mM	Maize	Increased internal trehalose levels with decreased MDA contents and ions leakage due to stress conditions	Li et al. (2014)
Drought	Pre-sowing seed treatment and foliar spray	25 and 50 mmol/L	Radish	Useful in enhancing the both enzymatic and non-enzymatic antioxidant activities	Shafiq et al. (2015)
Drought	Foliar spray	25 and 50 mM	Radish	External fortification with trehalose enhanced growth and shoots P and reduced relative membrane permeability	Akram et al. (2015)
Drought stress	Foliar spray	1.5 mM	Wheat	Enhanced activities of POD, phenylalanine ammonia lyase and ascorbic acid oxidase along with limited activity of polyphenol oxidase	Aldesuquy and Ghanem (2015)
Copper stress	Pretreatment	10 mM	Rice	Increased concentrations of AsA, proline, antioxidants, glutathione and decreased Cu absorption, MDA and limited aggregation of ROS	Mostofa et al. (2015a, b)

Table 1 (continued)

Nature of stress	Mode of application	Concentrations	Plant species	Metabolic processes	References
Salt stress	Pretreatment	10 mM	Rice	Improved relative water content, AsA, chlorophyll pigments but decreased MDA, lipoxygenase activity	Mostofa et al. (2015)
Drought	Foliar spray	250 or 500 μ M	Fenugreek	Increases in growth parameters, flavonoids, carbohydrate, total phenolics, photosynthetic pigments, and protein contents	Sadak (2016)
Drought	Pre-sowing and foliar	25 mmol/L	Radish	External use of trehalose via both methods was useful in stimulating leaf anatomical changes under water stress and non-stress conditions	Akram et al. (2016)
Drought	Foliar spray	10 mM	Wheat	Significant and positive effect on most growth parameters and biochemical components	Ibrahim and Abdellatif (2016)
Drought	Pre-treatment	25 mM	<i>Raphanus sativus</i>	Significant increase in chlorophyll <i>a</i> , total soluble sugars, free proline, water use efficiency and activity of SOD enzyme	Akram et al. (2016a, b, c)
Drought	Foliar spray	25 and 50 mM	Radish	Foliar trehalose spray improved AsA, phenolics and catalase activity under drought conditions	Akram et al. (2016)
Salt stress	Foliar spray	0, 50, 100, and 150 mM	Rice	Increased biomass, GB, proteins levels, superoxide dismutase and yield parameters	Shahbaz et al. (2017)

applied through the rooting medium of rice plants grown under saline stress (Garcia et al. 1997). The authors reported trehalose-induced conservation of root cell integrity, cell division, and keeping out Na from the chloroplast (Garcia et al. 1997). In the same experiment, they also applied trehalose as a foliar spray and showed that foliar-applied trehalose neutralized the adverse effects of salinity by reducing Na⁺ accumulation, chlorophyll loss, and growth retardation as well as by conserving root integrity. In the same crop, Nounjan et al. (2012) showed that exogenous application of trehalose through leaves decreased the Na⁺/K⁺ ratio, endogenous proline levels and up-regulated antioxidant genes. Chang et al. (2015) showed that 10 mM trehalose application as a foliar spray on *Catharanthus roseus* increased alkaloid compounds in plants grown under salinity stress.

The external fortification of trehalose in plants is believed to counteract the adverse effects of drought stress (Aldesuquy and Ghanem 2015). Upon exposure of plants

to dehydrated conditions, trehalose plays a role in balancing metabolic processes in plants (Ilhan et al. 2015). Ali and Ashraf (2011) applied trehalose to the leaves of drought stressed maize plants and showed the regulation of photosynthesis, osmotic potential and ROS scavenging enzymes. In a latter study, the exogenous application of trehalose (30 mM + Tween 20) in maize during drought stress induced the accumulation of antioxidants such as flavonoids, phenolics as well as improvement in plant growth and seed composition (Ali et al. 2012). Similarly, Theerakulpisut and Gunnula (2012) reported that external application of trehalose ameliorated desiccation stress by improving water relations, growth, chlorophyll content, and antioxidant activity in maize. External application of trehalose has been shown to improve non-enzymatic and enzymatic antioxidants in the edible portion of radish under drought stress (Shafiq et al. 2015). In another study, wheat plants treated with trehalose showed enhanced membrane stability and increased

enzymatic and non-enzymatic antioxidant activities under water stress. Trehalose acts as a compatible osmoprotectant, and it also can effectively scavenge ROS in plants under stress conditions in particular drought stress (Dawood 2016). Using the pre-sowing treatment mode, Akram et al. (2016a, b, c) have shown that trehalose pre-treated radish seeds caused a significant improvement in water use efficiency, chlorophyll *a*, free proline contents, and SOD enzyme activity under water deficit stress.

Under high temperature stress, the protective effect of trehalose in *Myrothamnus flabellifolius* was shown to be due to its involvement in effective protein conformation (Doeblemann et al. 2006). In another study with wheat under heat stress, Luo et al. (2008) showed that pre-treated winter wheat seeds with trehalose protected the membranes from lipid peroxidation and photo-systems against heat stress.

From the fore-going reports, it is possible to infer that exogenous application through any of the three modes mentioned earlier plays a critical role in alleviating the adverse effects of various stresses such as drought, salinity, and temperature extremes by regulating a myriad of physio-biochemical plant processes. Furthermore, the external applications of trehalose can act as an elicitor of stress related genes in plants.

Trehalose a Compatible Solute (Osmoprotectant)

Compatible solutes are those that are produced in plant cells to preserve biological structures and retain turgidity upon exposure to an osmotic stress (López-Gómez and Lluch 2012). Occurrence of deleterious conditions of abiotic stresses in plants stimulates the formation of organic osmolytes including trehalose, which protect cellular structures from stress conditions. During imposition of desiccation and heat stress, trehalose shields both biological membranes and enzymes (Müller et al. 1995). For example, trehalose presence in the root nodules of *Phaseolus vulgaris* made them water stress resistant by elevating tissue osmotic potential (Farías-Rodríguez et al. 1998). Supplementation of *Arabidopsis* with trehalose elicits strong responses that are not generated by osmoticum controls such as sorbitol or mannitol. It has been reported that in *Arabidopsis* seedlings grown on 25 mM trehalose, carbon allocation is reversed due to massive accumulation of starch from carbon fixed in the cotyledons (Wingler et al. 2000). However, at the rate of 100 mM trehalose, seedlings not only germinate, but also produce extended cotyledons. However, this trehalose level failed to develop primary leaves and hindered primary root development particularly beyond 2–5 mm (Schluepmann et al. 2004). It is imperative to note that the root meristem is reduced in cell size and number along with swelling and

bursting of the extension zone. Trehalose helps the proteins to retain their conformation (Schiraldi et al. 2002). External application of trehalose raises its endogenous levels which help to counteract the adverse effects of salt stress (Chen and Murata 2002). Zeid (2009) reported that foliar application of trehalose in maize under salinity stress conserved chlorophyll contents and Hill reaction activity. Similarly, external use of trehalose in rice seedlings maintained root integrity, ionic balance and regulated expression of osmotic genes (Fernandez et al. 2010). In rice under salt stress, Theerakulpisut and Phongngarm (2013) reported the osmoprotectant role of trehalose in plant physiology. In the same crop, Abdallah et al. (2016) reported that application of trehalose improved sugar levels, carotenoid contents and scavenged free radicals in rice plants grown under saline regimes. In *Arabidopsis*, exogenous application of trehalose was reported to maintain ionic homeostasis, levels of soluble sugars, and the activity of the antioxidant mechanism, thereby nullifying salt-induced adverse effects (Yang et al. 2014). Trehalose can effectively inhibit the ROS induced signaling pathway under stress conditions (Fernandez et al. 2010). It also adjusts cellular osmotic potential which prevents loss of cellular water and retains integrity of cellular structures associated with sugar metabolism (Taiz and Zeiger 2003; Paul et al. 2008). Trehalose also takes part in flowering and embryo formation. It also regulates carbon metabolism in plants. The interaction between plant and microorganisms also depends upon trehalose presence (Iturriaga et al. 2009). Thus, the role of trehalose in metabolic processes might be preservation. However, it is not fully elucidated to what extent it could protect different biomolecules involved in stress tolerance in different plant species.

Trehalose as an Antioxidant as Well as a Stimulant of Other Antioxidants

In response to adverse conditions of ecological stresses, reactive oxygen species (ROS) are usually formed in plants (Miller et al. 2008). These toxic-free radicals deteriorate the macromolecules and biological membranes (Krumova and Cosa 2016). As a defense mechanism, plants produce a variety of enzymatic and non-enzymatic antioxidants (Yadav et al. 2008). Trehalose plays an important role in neutralizing ROS and conserving the protein anabolic machinery (Chang et al. 2014). Due to certain unique qualities such as lack of internal hydrogen bond formation, chemical stability, and more hydrophilicity, it plays a vital role during dehydrated conditions (Abdallah et al. 2016). Shahbaz et al. (2017) reported that trehalose is more effective than proline under water deficit conditions, because it shields biological molecules from xeric conditions (Rezvani and Shariati 2009). Increased carbohydrate levels correlate well with

accumulated amounts of trehalose (Garg and Chandel 2011; Shahbaz et al. 2017). During osmotic stress, one trehalose molecule stoichiometrically reacts with one *cis*-olefin double bond of an unsaturated fatty acid; consequently, a stable complex is formed which significantly reduces the oxidation process (Nery et al. 2008). In a study, it was reported that application of 50 mM trehalose in wheat neutralized the adverse effects of high temperature stress by reducing H₂O₂ and O₂⁻ radicals, and shielding SOD (Luo et al. 2008). External application of trehalose to salt stressed rice, although having no influence on catalase activity, significantly enhanced peroxidase and superoxide dismutase activities (Vaidyanathan et al. 2003). Luo et al. (2010) described that trehalose neutralizes free oxidative radicals rather than modifying superoxide dismutase activity. In another study, the presoaking treatment of wheat seedlings with trehalose stimulated catalase activity under salinity stress (Dolatbadian and Jouneghani 2009). Recently, Abdallah et al. (2016) have reported that in rice, trehalose treatment significantly increased proline, soluble sugars, and antioxidant enzymes as well as ameliorated the toxic effects of salinity. In rice plants, the external use of trehalose not only raised endogenous trehalose but also increased the activities of antioxidative enzymes such as superoxide dismutase, catalase, and peroxidase. Thus, trehalose not only acts as an antioxidant but also promotes the activities/levels of other key antioxidants.

Trehalose as a Biotechnological Tool/ Signaling Molecule

Based upon superior qualities of trehalose, efforts are being made to produce transgenic plants over-accumulating trehalose in plant tissues to confer stress tolerance. The introgression of bacterial or yeast-derived trehalose responsive genes in different plants like potato, *Arabidopsis*, and rice made them more stress tolerant (Karim et al. 2007). Recently, Sah et al. (2016) have described that over-expression of trehalose genes made transgenic plants more resistant to abiotic stresses. In another study, while transferring two trehalose biosynthesis genes, *otsA* and *otsB*, from *E. coli* to rice plants, Garg et al. (2002) found that these transformants had 3–10 times more trehalose levels than that in the control plants upon onset of stress conditions. The non-transformant plants showed wilting and leaf rolling after 8–12 h of withholding irrigation as compared to the transgenic lines. Han et al. (2005) engineered tobacco plants with the *TP* (trehalose pyrophosphate) gene from *Pleurotussajor-caju*. This gene can also be expressed in yeasts, fungi, and algae for trehalose synthesis from glucose-1-phosphate. The expression of *OsTPSI* gene in rice plants increased proline and trehalose levels under

stress conditions (Li et al. 2011). The expression of the yeast *TPSI* gene in tomato made it more tolerant to oxidative stress (Cortina and Culiáñez-Macià 2005). The transfer of the *AtTPSI* gene in tobacco from *Arabidopsis* made it more acclimated against multiple abiotic stresses (Almeida et al. 2007). The engineered *Arabidopsis* plants with yeast-originated *TPS* gene induced abiotic stress tolerance along with some phenotypical changes (Miranda et al. 2007). Tolerance against water scarcity in transgenic *Arabidopsis* was displayed by regulation of the homologous *AtTPSI* gene (Avonce et al. 2004). Transgenic melon and tobacco with yeast-based *TPSI* (trehalose-6-phosphate synthetase) gene showed improved multiple abiotic stress tolerance with many pleiotrophic effects on development processes (Serrano et al. 1998). The over-expression of the *TPSP* gene (a chimeric gene generated by fusing *TPS* and *TPP* enzymes) led to sugar signaling (production of trehalose) in transgenic rice and allocated the stress tolerance metabolic pathways (Redillas et al. 2012). Transgenic rice plants with over-expressed *OsTPSI* genes activated the signaling of other stress associated genes (Li et al. 2011). *Arabidopsis* has 10 *TPP* and 11 *TPS* putative genes, whereas rice contains nine *TPPs* and nine *TPSs* genes (Delorge et al. 2014). In transgenic rice plants, Ge et al. (2008) reported that over-expression of *OsTPP1* activated a series of stress-related genes which resulted in stress tolerance mechanisms. The aim of trehalose genetic engineering is not only to produce stress tolerant transgenes but also produce trehalose commercially at low cost (Zheng et al. 2015), so it can be utilized as a stabilizing agent for pharmaceuticals and other applied purposes. The trehalose engineering projects may also help discover advancement in plant metabolic machinery.

Plant interactions with *Rhizobium* bacteria, herbivorous insects, and pathogens show that trehalose acts as potent signaling molecule. For normal development and growth of plants, trehalose metabolism is necessary. Like in prokaryotes, biosynthesis of trehalose occurs in eukaryotes via a phosphorylated intermediate trehalose-6-phosphate (John et al. 2017). T6P acts as a signaling factor for maintaining the sucrose level (photosynthate) and particularly in sugar metabolism and sugar influx within plants. A meta-analysis indicated that the sucrose levels are associated with changes in T6P concentration. Along with varying environmental cues, T6P levels are sensitive to sucrose availability. It can happen due to T6P or trehalose or the interaction of biosynthetic enzymes with phyto-hormones as well as sugar-induced signaling routes (John et al. 2017). It has been identified that T6P at low concentrations such as μM has been involved in inhibition of SnRK1 (SNF1/AMPK group of protein kinases) *in vivo* and *in vitro*. From this, it can be concluded that the function of T6P acts as a sugar signaling molecule integrating development and metabolism in

Table 2 Transgenic plant species over-expresses trehalose related genes

Name of transgenic crop	Genes	Origin	Distinguished characters for adoption	References
Tobacco	<i>TPS1</i> and <i>TPS2</i>	<i>Saccharomyces cerevisiae</i>	When transgenic plants exposed to stress conditions, trehalose biosynthesis turned on	Karim et al. (2007)
Rice	<i>otsA</i> and <i>otsB</i>	<i>Escherichia coli</i>	Transformants had 3–10 times more trehalose levels than that in the control plants upon onset of stress conditions	Garg et al. (2002)
Tobacco	<i>PsTP</i>	Pleurotussajor-caju	Under water shortage conditions, the engineered plants had significant amount of trehalose	Han et al. (2005)
Tomato	<i>TPS1</i>	Yeast	Tomato plants showed adaptive behavior through trehalose biosynthesis without reducing yield under abiotic stress conditions	Cortina and Culianez-Macia (2005)
Tobacco	<i>T6P</i>	<i>Arabidopsis thaliana</i>	Showed tolerance against various abiotic conditions	Almeida et al. (2007)
<i>Arabidopsis thaliana</i>	<i>T6P</i> and <i>TPS</i>	Yeast	The transgenic plants confer abiotic stress conditions	Miranda et al. (2007)

relation to carbon supply (Schluepmann and Paul 2009) (Table 2).

Conclusions and Future Prospects

By virtue of being a versatile biomolecule, trehalose possesses a variety of functional characteristics that are beneficial for plants to thrive well under harsh environmental cues. Naturally, most plants synthesize/accumulate reasonably low amounts of trehalose, which may not be sufficient to optimally maintain the functioning of key metabolic processes involved in plant growth and development under stressful environments. Thus, efforts are currently underway to bio-engineer plants that must synthesize trehalose to desirable levels so as to counteract the stress-induced adverse conditions. The trehalose biosynthetic genes from ascospores and resurrection plants can be utilized for transforming plants against stressful conditions. There is a need to search convenient sources of trehalose biosynthetic genes other than bacteria and yeasts. Because improvement in trehalose levels through modern biotechnological tools is a cost-intensive approach, so most researchers recommend exogenous application of this vital biomolecule to plants. There is a need to assess which of the three modes is cost-effective and effective. Although pre-sowing seed treatment seems to be easy to handle and cost-effective, it is unclear whether its effect lasts up to terminal growth. Because pure synthetic trehalose is not a cheap commodity, there is a need to explore cheap sources of this vital sugar.

Although efforts have been made during the past few decades by different researchers to elucidate the role of trehalose in key plant physiological processes, the important role trehalose plays in plant protection is not fully uncovered. To assess the entire action of trehalose in plant metabolism starting from the cellular level to whole plant level,

extensive research is required. The information on compatibility between the trehalose-induced regulation of plant metabolites and resulting plant morphology will be helpful to optimize the amount of trehalose required. Similarly, the anatomical changes that take place in stressed plants due to trehalose treatment still need to be determined. The actual role of trehalose in mitigating the injurious effects of free radicals during stress-induced oxidative stress also needs to be investigated. The influence of trehalose application on different seed oil fatty acid profiles and their antioxidant activities must be explored. Further research on the role of trehalose in not only elucidating abiotic stress tolerance, but also in trehalose-induced signaling pathways and preservation from phenotypic aberrations is also required.

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Compliance with ethical standards

Conflict of interest All authors declare that they have no conflict of interest.

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