

Trehalose-6-phosphate: Biosynthesis, plant metabolism, and crop yields

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Abstract

Trehalose is a stress-response disaccharide commonly found in yeasts, bacteria, plants, and invertebrates. In plants, its purpose is uncertain, but some studies suggest it protects against abiotic stressors like chilling, heat, drought, and salinity. It is an osmoprotectant and a stabilizing agent for higher animals and plants. Some trehalose metabolism mutants show growth abnormalities, which could compromise plant physiology. Biotic stress causes contradictory results as well. It is also crucial for pathogen infectivity and plant defensive response. In our opinion, trehalose should not be considered only as a defensive sugar but rather as a molecule with two identities. It is an exceptional molecule that maintains the plant's vigor despite severe environmental conditions. *Arabidopsis* plants have been used to treat Alzheimer's, Parkinson's, and Huntington's diseases. There's no doubt that what we have just learned about this disaccharide will take us down many roads we've never been down before.

1. Introduction

Plants can convert carbon into a wide variety of monosaccharides, many of which are then used as building blocks in forming oligo and polysaccharides. Even though many carbohydrates have yet to be evaluated, the physiological function of many of them remains unknown (Loewus and Tanner 2012). Carbohydrates not only give plants energy, but they can also act as growth stimulants or growth regulators (Creelman and Mullet 1997). In 1998, scientists found a new way for plants to make carbohydrates (Blazquez et al. 1998; Vogel et al. 1998). Trehalose is a nonreducing disaccharide of two glucose molecules (-D-glucopyranosyl-1,1-D-glucopyranoside). It can be found in diverse organisms, i.e., prokaryotes and eukaryotes. Trehalose is a sugar found in insects and serves as a source of energy during flight (Elbein et al. 2003). It is well-known that anhydrobiotic organisms accumulate substantial amounts of this substance to protect their membranes in dry times. (Crowe et al. 1984; Drennan et al. 1993). This is done so that the microorganisms can endure complete dehydration. In yeast, trehalose has a role in tolerating osmotic stress, heat, and desiccation (Hounsa et al. 1998). Bacteria are reported to accumulate trehalose as a defense mechanism against osmotic pressure (Iordachescu and Imai 2008; Styrvold and Strøm 1991).

Resurrection plants were thought to be the only sources of trehalose because of the high concentrations [up to 10 mg/g fresh weight (F.W.)] of trehalose in these plants (Goddijn and van Dun 1999; Paul et al. 2008). Later, trehalose was found in the model plant *Arabidopsis* (*Arabidopsis thaliana*) using validamycin A, which blocks trehalase activity. Trehalase is involved in the breakdown of trehalose (Muller et al. 2001). Crops such as *Oryza sativa* and *Nicotiana tabacum* have recently been found to contain trehalose in 10 mg/g F.W. (Garg et al. 2002) (Karim et al. 2007). It is a disaccharide with unique characteristics. The glycosidic bond is formed by both the reducing and nonreducing ends of the molecule. So, it cannot be broken down by acidic hydrolysis and stays stable in acidic solutions at high temperatures (Fernandez et al. 2010; Richards et al. 2002).

Trehalose seems to be a suitable membrane and molecule stabilizer based on two different processes. The mechanics for replacing water and forming glass are as follows: It returns water during dehydration or freezing by creating electrostatic dipole-dipole interactions with macromolecules and membranes. Further, it remains in a glass-like condition after being thoroughly dried in the glass production process (Crowe 2007). Trehalose's glassy state prevents biomolecules from denaturing during dehydration, allowing them to maintain their functional activity when rehydrated. Multiple stresses affect plant physiology, growth, and development throughout their life cycle (Agrios 2005). Abiotic and biotic stresses are the two types of stress. Abiotic stress can be caused by a variety of environmental variables. They may be chemical or physical, such as low temperatures, high temperatures, salty water, famine, chemicals, or irradiation. Biotic stresses are caused by biological organisms like bacteria, fungi, viruses, etc. (Shilpi Mahajan 2005). The disruption of physiological processes can be caused by stress in various ways, ranging from halting standard critical approaches to the complete disintegration of tissue (Hirt and Shinozaki 2003). Plants are equipped with a wide range of defense mechanisms, some inherent and others activated only when a stress-specific signal is received. Both types of stress lead to the following reactions: (i) activating signal transduction pathways (Zhao and Qi 2008), (ii) triggering expression of downstream genes (Chinnusamy et al. 2007), (iii) activation of pathogenesis-related (P.R.) proteins (van Loon et al. 2006), and (iv) accumulation of compatible sugar intermediates, for example, proline and phytoalexins (Moore et al. 2009) (Hammerschmidt 1999) that showed in Fig. 1 as described by Paul et al. (2020).

Due to its unique chemical and physical properties and documented significance in managing stress in microorganisms, there is a rapidly increasing desire to identify whether trehalose or its precursor trehalose-6-phosphate (T6P) helps plants withstand stress (Cao et al. 2008; Purvis et al. 2005). For instance, the sweet mutant of *A. thaliana* was recently discovered to accumulate abnormally high trehalose levels. The abiotic stress response genes in this mutant are more often expressed. Plants that make trehalose have some of the same problems as other species with too many trehalose-producing genes (Crowe 2007; Fernandez et al. 2010).

Reviews or backgrounds

There are multiple established routes for trehalose biosynthesis in living organisms. However, the type of stress the organism is under will determine the pathway. Trehalose has several different uses, but they are all species-specific. Microorganisms, for instance, serve as an energy source during the germination of spores. Trehalose accumulation in fungus is well understood. Compared to other development stages, trehalose formation in fungus occurs more frequently during the vegetative and reproductive phases. The contribution of trehalose to the desiccation tolerance of bacterial species has received significant attention. Understanding the specific function of trehalose in abiotic stress and the signaling pathway would be easier with knowledge of each trehalose production gene. Therefore, additional research is required to comprehend the intricate process of trehalose metabolism to create stress-tolerant plants better able to withstand environmental adversity. One of the best osmoprotectants is the nonreducing disaccharide of glucose called trehalose. Genes of bacterial, yeast, and, more recently, plant origin have

been used in several techniques leading to its accumulation in model and crop plants. Transgenic plants can tolerate abiotic stress at significant levels of trehalose buildup. This review summarizes recent progress on the most biologically significant characteristics of trehalose, including its chemical and biological properties, presence and metabolism in organisms, special reference to plants, its protective role in stabilizing molecules, and its physiological role in plants, with emphasis on carbohydrate metabolism. However, the focus of this study will be on altering trehalose metabolism to increase plants' ability to withstand abiotic stress. Due to space restrictions, we make an effort to highlight significant viewpoints, particularly from systems biology, that have been used in recent research.

2. Trehalose Biosynthesis And Metabolism

There are at least five ways for trehalose to be produced in nature (Fig. 2). Numerous creatures, including eubacteria, archaea, fungi, insects, and plants, share the most prevalent route (the TPS-TPP pathway). When glucose is transformed through this pathway from UDP-glucose to glucose-6-phosphate (G6P), the enzyme trehalose-6-phosphate synthase (TPS) (OtsA in *Escherichia coli*) catalyzes the reaction and generates the intermediate trehalose-6-phosphate (T6P). An enzyme from *E. coli* called trehalose-6-phosphate phosphatase (TPP) dephosphorylates T6P to produce trehalose (Elbein et al. 2003). The thermophilic archaea of the genus *Sulfolobus* contain the TreZ-TreY route, the second metabolic pathway. Maltooligosaccharides or starch are converted to trehalose in this pathway by the enzymes maltooligosyl trehalose synthase (TreY) and maltooligosyl trehalose trehalohydrolase (TreZ). The trehalose synthase isomerizes the 1–4 linkage of maltose into the 1–1 linkage of trehalose (TreS). In *Pimelobacter* sp., the TreS route was discovered for the first time [5] (Elbein et al. 2003). The catalyzes for reversible trehalose synthesis from glucose and glucose-1-phosphate in fungi like *Agaricus bisporus* and protists like *Euglena gracilis* (Avonce et al. 2004; Avonce et al. 2006) are done by Trehalose phosphorylase (TreP). Trehalose glycosyl-transferring synthase (TreT), a component of the TreT pathway, catalyzes the conversion of glucose and ADP-glucose into trehalose. This approach is used by extremophiles like *Thermococcus litoralis* and *Thermotoga maritima* (Niehaus et al. 1999). Some organisms, including those in the genus *Mycobacterium*, convert TPS/TPP UDP-glc + G6P using the TreY-TreZ pathway, the TreS pathway, and the TPS-TPP path. Maltooligosyl trehalose ADP-GLC + GLC in TreY Maltose, also known as TPS T6P Maltooligosaccharides or starch TreS G1P with TreS Glc TreT, TreP, TreS, and TRE 2 Glc. TreP TPP TreZ TreZ Trehalose in Fig. 1 depicts the biosynthesis of trehalose. Trehalose synthase, maltooligosyl trehalose synthase, maltooligosyl trehalose trehalohydrolase, trehalose glycosyl transferring synthase, and trehalose phosphorylase are all denoted by the letters TreS, TreY, TreZ, TreT, and TreP, respectively (TRE). Trehalose can therefore build up in response to abiotic stimuli without causing the substrate to become depleted. Trehalose is hydrolyzed by trehalase into two units of glucose (TRE). This has been observed in many organisms, including bacteria, fungi, plants, animals, and mammals, that don't produce trehalose (Elbein et al. 2003). Some species of trehalase have a range of isoforms. *Saccharomyces cerevisiae*, for instance, possesses three trehalase genes. While the exterior environment and vacuoles work with an acid trehalase (Ath1), the neutral trehalase genes Nth1 and Nth2 encode two cytosolic trehalases (Nwaka et al. 1996). In *E. coli*, TreA and TreF encode

periplasmic and cytosolic trehalases, respectively. The Attre1-1 deletion mutant, however, lacked any discernible trehalase activity, indicating that just one gene (AtTRE1) in *Arabidopsis thaliana* encodes a functional trehalase. Eukaryotes use trehalose6phosphate synthase (TPS), which converts UDP glucose to glucose6phosphate (G6P) to produce trehalose, which is then dephosphorylated by trehalose6phosphate phosphatase (TPP) to produce trehalose. The OtsA-OtsB pathway (also known as the TPS-TPS pathway) is the sole trehalose biosynthesis pathway in higher plants. At the same time, bacteria, fungi, yeast, and algae have five distinct ways (Avonce et al. 2006; Goddijn and van Dun 1999). Trehalase is an enzyme that degrades trehalose into two glucose residues by breaking it down. All organisms that produce trehalose have been found to have this mechanism. Trehalase has been found in a variety of forms in both yeast and bacteria (Jules et al. 2008) (Fig. 3).

3. Genes Involved In Trehalose Synthesis

Arabidopsis has 11 putative TPS genes that code for TPS and TPP, respectively, based on their similarity to *S. cerevisiae* TPS1 and TPS2 genes (Leyman et al. 2001). Class I contains four genes (including AtTPS1), and Class II includes seven. It has only been established that the AtTPS1 gene encodes a TPS-active protein, not a TPP-active protein (Zentella et al. 1999). Although they are expressed, TPS and TPP activity appear absent in two class II homologs (Vogel et al. 2001). In *S. cerevisiae*, a holoenzyme complex is responsible for trehalose production (Bell et al. 1998). Plant proteins that do not have catalytic properties may have TPS and TPP domains because they are involved in forming a complex. However, it is unknown if such a structure exists in plants. Ten TPP homologs (class III) in *Arabidopsis* lack a TPS domain. The *S. cerevisiae* mutant *tps2D* has multiple copies of two class-III proteins responsible for the heat stress sensitivity (Vogel et al. 1998). *Glycine max* and *Arabidopsis* have single copies of the trehalase gene, and both are also functionally characterized (Aeschbacher et al. 1999). As the trehalase inhibitor validamycin A makes trehalose buildup, it is probably the only way plants can break down trehalose (Muller et al. 2001).

4. Trehalose In Abiotic Stress

Resurrection plants like *Selaginella tamariscina*, *Myrothamnus flabellifolius*, and *Selaginella lepidophylla* were the first to demonstrate the significance of trehalose in abiotic stress tolerance. These plants can tolerate severe dehydration and recover normal viability upon water availability (Liu 2008). These species were declared trehalose-rich plants. There is only a modest rise in the concentration of trehalose after dehydration, which magnificently helps maintain the stability of both proteins and cell membranes. The significance of trehalose has been reviewed in almost all organisms under stress conditions because it is reported to stave off the negative impacts on plants' growth and development under saline, desiccation, and extreme temperature conditions (Iordachescu and Imai 2008; Tapia and Koshland 2014). Nowadays, a significant amount of work is being done at various institutions to shed light on the function of trehalose in plants cultivated under stress conditions.

4.1. Desiccation:

Water scarcity is a significant factor in crop productivity declines worldwide (Rasheed et al. 2020; Rasheed et al. 2017; Rasheed et al. 2019; Richards et al. 2002; Rollins et al. 2013). Recent climate change has led to an intensification of drought stress, which poses a considerable risk to agricultural productivity and international peace and stability (Hassan et al. 2021; Neha et al. 2021; Rasheed et al. 2021). Therefore, to boost crop yields, it is imperative to critically examine the mechanisms of drought stress (Singh and Laxmi 2015). As the world's population grows, we must find ways to increase crop productivity to secure global food security.

The modifications in plants' physiology and biochemistry induced by drought stress highly depend on the duration and intensity of desiccation and the plant growth stage (Ahmad et al. 2018; Hassan et al. 2017; Hassan et al. 2019; Hassan et al. 2021). In such conditions, the photosynthetic activity, chlorophyll synthesis, and nutrient uptake badly affect the survival of any plant (Wahab et al. 2022). Photosynthetic efficiency is severely affected due to reduced chlorophyll content and inhibition of ribulose-1,5-bisphosphate carboxylase/oxygenase (RuBisco) activity (Perdomo et al. 2017). Furthermore, reactive oxygen species (ROS) are also responsible for lipids' destruction and configurational changes in enzyme structure, ultimately leading to cell death (Khan et al. 2020; Waszczak et al. 2018). Furthermore, to defend themselves against the damaging effects of ROS, plants have developed a system of antioxidant defense (Hasanuzzaman et al. 2019; Sewelam et al. 2016) (Fig. 4). Despite this, abiotic stress disrupted this antioxidant system, which led to an imbalance in the redox homeostasis of plant cells (Talaat et al. 2015). Likewise, the plant system started to produce more soluble sugars and other osmolytes to maintain its proper growth and development. Trehalose helps plants withstand stressful cues by shielding the cell membranes and photosystem-II from oxidative stress and over-excitation (Kosar et al. 2018; Zulfiqar et al. 2021). Because trehalose exhibits several desirable qualities, researchers are actively working to produce transgenic plants with enhanced trehalose levels that confer resistance against the negative effects of stress.

The trehalose biosynthetic genes of microbial origin have been introduced into various plants, including tobacco, rice, *Arabidopsis*, and tomato, to produce stress-resistant plants. An osmoprotectant (Zulfiqar et al. 2021) is significant in stabilizing cell membranes' and proteins' integrity (Crowe et al. 1984). These genes have been used by various groups to create plants that are more resistant to stress. In pilot experiments, trehalose accumulation was observed in tobacco and *Arabidopsis* plants expressed with bacterial *OtsA* and yeast *TPS1*. However, its expression was deficient with aberrant phenotypes, but the plants showed tolerance in drought conditions. The altered phenotypes were observed due to the accretion of T6P in those plants (Goddijn et al. 1997; Pilon-Smits et al. 1998; Romero et al. 1997). This limitation was addressed using two strategies; (i) expression of a fusion gene (TPP-TPS) under a stress-inducible promoter to direct the expressed protein to the plastid genome (Garg et al. 2002; Jang et al. 2003; Karim et al. 2007), and (ii) utilization of different biosynthetic genes that overcome the requisition of T6P (Park et al. 2003). There observed 25 µg/g and 170 µg/g F.W. trehalose in resultant transgenics. Similarly, *A. thaliana* also demonstrated a rise in T6P content, which was 3 µg/g F.W., as opposed to the

wild type, which was recorded to be 0.75 µg/g F.W. (Nelson Avonce 2004). Moreover, rice and tobacco also studied bifunctional fusion gene expression (ScTPS-ScTPP and OtsA-OtsB) (Ajay K. Garg et al. 2002).

It is known that trehalose biosynthetic genes have a mandatory role in conferring resistance to plants against stress. TPS and TPP received worldwide attention due to their functions in trehalose biosynthesis (Delorge et al. 2015; Van Dijck et al. 2002). These genes function as essential growth regulators when the plant is subjected to a stressful environment and improve crop yield. For example, *AtTPS1* expression in *Arabidopsis* increases both trehalose and T6P levels, contributing to increased drought tolerance (Avonce et al. 2004). According to another finding, genetic modification in the trehalose metabolism remarkably increases the RuBisCO concentration, subsequently improving the photosynthetic potency (Pellny et al. 2004). Upon lyophilization, the stability of liable proteins was disclosed, describing how candidate proteins remain preferentially hydrated during the stress conditions in response to trehalose (Kreilgaard et al. 1998). Further, it was also observed that trehalose stabilizes RNase A in solution form by increasing surface tension in the surrounding environment (Lin and Timasheff 1996; Xie and Timasheff 1997).

AtTPP1 regulates trehalose levels in plants and improves their productivity while subjected to drought stress. Similarly, other genes like *ScTPS1* and *SCTPS2* boosted their expression and generated better adaptability in transgenic lines (Lin et al. 2019). Additionally, *BvMTSH*, *TPP*, *OsTPS1*, and *OsTPP3* over-expression led to yield improvement even in water scarcity (Joo et al. 2014; Li et al. 2011; Nuccio et al. 2015). Among these, transgenic plants expressed with *OsTPP3* grew more quickly and were more tolerant to drought. *OsTPS1* elevated the proline concentration and imparted tolerance against abiotic stresses (Li et al. 2011). Over-expression of *AtDREB1D* genes in soybean plants improved the relative water content (RWC), decreased water loss, and increased the plant's drought tolerance by boosting endogenous trehalose concentration (Guttikonda et al. 2014). Increased levels of *AtTPP1* gene expression in transgenic plants resulted in improved resistance to drought. Genotypes having a lower expression of *AtTPP1* and abscisic acid (ABA) caused stomata to close in these plants to deal with water loss during transpiration. Compared to genotypes with a mild expression of *AtTPP1*, over-expression of *AtTPP1* in drought-stressed plants leads to improvements in stomatal opening and closing, root development, and water use efficiency (WUE) (Lin et al. 2020). The drought-inducible TPS1 gene resides in the roots and leaves of *Gossypium hirsutum* (Sotirios A. Kosmas 2006), while the same gene is hyper-expressed in maize ears (Yunlong Zhuang 2007). Another drought-responsive gene (*TPP*) is suppressed in the tassels of *Zea mays* (Yunlong Zhuang 2007). In *Oryza sativa*, two genes, *TPP1* and *TPP2*, were briefly expressed to fight against abiotic stresses like salinity, drought, and abscisic acid (ABA) application to seedlings. Thus, current findings suggest that genetic engineering of trehalose biosynthetic genes is potent for enhancing the performance of plants developed under drought conditions.

4.2. Salinity:

Salinity is a severe ecological barrier to agricultural output. It interferes with numerous essential metabolic processes in plant cells, resulting in profoundly negative consequences for the growth and development of plants. High salinity negatively impacts plants, like oxidative stress, osmotic stress,

metabolic alterations, ionic imbalance, ionic toxicity, nutrient problems, membrane disruption, retarded cell division and expansion, genotoxicity, and other detrimental effects (Kamran et al. 2019). Photosynthesis may be badly affected by high salt concentration due to abnormalities in chloroplasts' size and shape, reduced number of functional chloroplasts, and lipid and starch deposition (Kamran et al. 2019) (Fig. 5). The activation of stress-related signaling pathways enables plants to respond to minor alterations in their environmental conditions. Salinity stimulates osmotic homeostasis and protects or repairs the plant cell from stress-induced damage. Sometimes it even detoxifies the stress-induced environment in the plant cell (Parida and Das 2005). Trehalose concentration in a plant cell is correlated with the degree of salt stress. *In vitro* findings showed that it protects membranes and proteins from abiotic stress by preventing protein denaturation and membrane fusion by creating a hydrogen bond with polar amino acids (Magazù et al. 2012). The trehalose deposition prevented the preliminary signs of misfolding and aggregation of proteins from appearing because it functioned as a scavenger for free radicals. Because of this, trehalose accumulation in strained cells is necessary to avert the formation of reaction oxygen species (ROS) in cell organelles.

Significant leaps in our understanding of the trehalose signaling pathway were made possible by research conducted in molecular genetics on the *Arabidopsis thaliana* system. It was found that apart from the nucleus, T6P-metabolizing enzymes also resided in cytosol and chloroplast of *A. thaliana*. Research also suggests that the chloroplast-localized *AtTPPD* regulates glucose metabolism and salt tolerance through redox reactions (Krasensky et al. 2014). AGPase was boosted within 15 minutes following the treatment of 100 μ M T6P to intact chloroplasts (Kolbe et al. 2005). Because of its low atomic mass, trehalose can easily pass through the peroxisomal membrane. Due to their small size, peroxisomes have easy access to the cytoplasm's small metabolites (Antonenkov and Hiltunen 2012). Peroxisomes are responsible for the oxidation of fatty acids and glycerol production. The regulation of sugar transporters is disrupted when plants are subjected to salt stress, which leads to abnormal sugar transport and an inability to absorb energy (Hummel et al. 2010).

Trace amounts of trehalose are now known to be metabolized by the enzyme TPP. Salinity stress was more difficult for plants that lacked *AtTPPD* than those that overexpressed the gene (Krasensky et al. 2014). *AtTPPD* may function in modulating sugar metabolism under saline environments based on the elevated stress tolerance of *AtTPPD* and the high accumulation of soluble sugars and starch. When maize plants were grown in a saline environment, T6P levels in the kernels, leaves, and cobs increased, while the sucrose levels remained constant. Compared to leaves, T6P has a specific role in roots, shoots, and seeds, implying that osmotic stress-induced kernel abortion is due to an inability to utilize these reserves. By lowering ROS and improving chlorophyll, RWC, and redox status, the incubation of plants with 10mM trehalose for two days significantly reduced salt-induced deleterious effects. Plants treated with trehalose before being exposed to salt stress were still active in the biochemical pathways of salt stress. Trehalose may help prevent salt-induced oxidative damage by boosting antioxidants and activating glyoxalase while also building up low levels of ROS. Trehalose administration also significantly reduced apoptosis, ionic, and ROS stress in *Arabidopsis* seedlings caused by high salinity (Yang et al. 2014).

Trehalose degradation in various plant organs could also regulate its concentration under stress. Evidence shows that when salt stress is applied to *Medicago truncatula*'s nodules, the trehalose gene (*MtTRE1*) is silenced, leading to an upsurge in trehalose levels (Miguel López et al. 2008). It has been found that many of the genes accountable for trehalose metabolism are susceptible to a variety of abiotic stimuli, like ultraviolet light, cold, and salt (Iordachescu and Imai 2008). Thus, it provides direct evidence that trehalose and T6P might be vital in inducing metabolic changes against abiotic stresses.

Both degradation reactions and synthesis processes are part of sugar metabolism, a dynamic process that happens simultaneously with stress conditions like salinity. The expression of genes is controlled by several kinases and phosphatases in response to each sugar signal. They include HEXOKINASE1, Sucrose nonfermenting Related Kinase-1 (SnRK1), TOR KINASE, and the C/S1 bZIP factors studied the most. Salt stress alters the uptake of CO₂, carbon partitioning between the sources and sinks, and other vital processes (Hilal et al. 1998). Due to this, they tend to have a more substantial signaling capacity to endure high salt concentration.

The synthesis of T6P as a signaling molecule may constitute most of the trehalose biosynthesis pathway instead of its accumulation as an osmoprotectant (Iturriaga et al. 2009). T6P is used in many plants to indicate carbon storage, although its role in salt stress response has not yet been fully characterized. T6P and hexokinase-dependent signaling pathways have not been proven to have a direct connection. Many researchers, however, have postulated that T6P and SnRK1 may be associated with it (Baena-González et al. 2007). Sugar-controlled gene expression can be controlled by trehalose (Wingler et al. 2000). T6P may affect plant growth and yield by suppressing the SNF1-related protein kinase, SnRK1. Other sugar phosphates, such as glucose1phosphate (G1P) and G6P, can inhibit SnRK1 when combined with T6P (Nunes et al. 2013). According to numerous studies, plants' sucrose metabolism is also linked to T6P.

Phytohormones are essential in controlling plant growth and the responses to environmental stresses, keeping homeostasis, and allowing plants to adapt to changing conditions. During adverse conditions, phytohormones are activated, and they become more resistant to environmental stress (Nunes et al. 2013). Stunted plant growth due to salinity damages plants' ability to produce certain hormones (Kaya et al. 2003). Plants' phytohormone levels can be affected negatively or positively by salt stress and trehalose signaling (Kaya et al. 2003). In plants, salt stress tolerance is tightly monitored by auxins, gibberellins, ethylene, and abscisic acid signaling (Mishra et al. 2022). Research has indicated that phytohormones and T6P can alter SnRK1 and TOR regulatory pathways. It describes how these sugars affect plant sustainability under adverse situations (Fichtner and Lunn 2021; Gorjanc C and VODNIK 2018; Schepetilnikov and Ryabova 2017; Wurzinger et al. 2018). Apart from raising T6P and trehalose concentrations, the upregulation of *AtTPS1* in Arabidopsis has improved glucose sensitivity and ABA signaling gene levels [67]. Although trehalose metabolism is critical in *Arabidopsis thaliana* to control stomatal conductance, its relationship to ABA signaling is still unclear (Figueroa et al. 2016). *TPS5* decreased ABA signaling in *Arabidopsis thaliana* (Tian et al. 2019). Since both trehalose and T6P have been demonstrated to influence ROS formation in studies, it is reasonable to assume that both sugars are involved in ABA-signaling processes that lead to stomatal closure (Gamm et al. 2015). Plant development

and physiological functions such as embryogenesis, seed germination, and stomatal aperture size can be affected by trehalose or T6P on ABA signaling (Gómez et al. 2010).

4.3. Extreme temperatures:

Plant yield is negatively impacted by exposure to too high and too low temperatures (John et al. 2017). There have been reports of trehalose synthesis in microorganisms under low-temperature stress (Kandror et al. 2002; Petitjean et al. 2015). Under abiotic stress, plants other than resurrection can accumulate trehalose. For instance, *Arabidopsis thaliana* can withstand heat stress (40°C) by doubling the trehalose concentration within four hours, whereas during chilling (4°C), its concentration is elevated up to eight times (Fatma Kaplan 2004). The transcriptional activation of trehalose-producing genes is correlated with the stress-induced aggregation of trehalose. When roots of rice plants are exposed to freezing stress, the TPP activity and trehalose content rise as expected, these genes are not expressed equally during salt stress; only TPP1 is activated in their shoots (Imai 2005). Trehalose level and cell survival rate were recovered when mutants having *otsA/otsB* genes were transduced at 4°C (Kandror et al. 2002). A rise in cellular osmotic pressure caused by trehalose aggregation in heat-stressed *Saccharomyces cerevisiae* activated the protein kinase C1 pathway. A study on *S. cerevisiae* found that trehalose deposition activates the kinases C1 and C2 pathways when the yeast cells are subjected to osmotic potential (Mensonides et al. 2005). T6P has been proven to act as a sucrose sensor, which can alter the ambient immediately as the environment changes (Delorge et al. 2015). T6P production or degradation and trehalose hydroxylation can boost crop production and biomass by altering the trehalose biosynthesis pathways. This is due to the importance of trehalose in plant development. Modifying the levels of T6P and/or trehalose can result in greater stress tolerance, in addition to various phenotypic changes that were not expected. According to the reports that have been discussed previously, trehalose appears to perform a potentially adaptive role in plants that are subjected to stressful events.

5. Trehalose In Biotic Stress

Since there are standard processes implicated in abiotic stresses, it is possible to anticipate that trehalose plays an indispensable role in response to biotic interactions (Miki Fujita 2006). Nevertheless, very little evidence is available, but some reports suggest that trehalose may play mutually exclusive positions.

5.1. Trehalose as an inducer of plant defensive response

Plant defense genes were upregulated in *A. thaliana* through transcriptome analysis when cultivated on a 30 mM trehalose-supplemented medium. There is an increase in the expression of genes encoding for defense-responsive transcription factors and P.R. proteins, such as WRKY6 and β -1,3-glucanase. According to a recent study, therapy with trehalose can protect wheat from *Blumeria graminis* (Fernandez et al. 2010).

The catalytic activity of phenylalanine ammonia-lyase or ROS formation at infection sites was linked to protection. Surprisingly, when added to the solution, trehalose has a negligible impact on the disease-causing agent. The inoculant hypothesis is supported since it does not alter the lipid composition of the pathogen membrane (Jérôme Muchembled 2006) or conidia formation (Delphine Renard-Merliera 2007). At least for some of these outcomes, trehalose was sprayed at an extremely high concentration, much outside the normal range of trehalose concentrations in humans. This begs the question of whether osmotic stress or elicitation induces defenses.

5.2. Trehalose in response to pathogen attack

Trehalose formation in response to pathogenic infection has not been extensively studied. After infecting the roots and hypocotyls of *A. thaliana* with *Plasmodiophora brassicae*, up to 10 mg/g D.W. of trehalose was collected in response to successful interaction (David Brodmann 2002).

Armillaria ostoyae infection has also been linked to trehalose deposition in the roots of Scots pine (*Pinus sylvestris*) (Valery A. Isidorov 2008). Plants and pathogenic fungi share the disaccharide, making it difficult to determine which one is responsible for trehalose production. In addition to its function as a defender against plant stress, it is a versatile sugar in fungus. It plays a significant part in mycelium production and infection (Carlos Gancedo and Flores 2004) *Magnaporthe grisea*'s reduced pathogenicity in the *tps1* deletion mutant demonstrates the importance of trehalose in disease (Foster et al. 2003). In the *A. thaliana*-*Plasmodiophora brassicae* pathosystem, an analysis of both host and parasite metabolic genes reveals that the pathogen produces trehalose as one of its virulence weapons (David Brodmann 2002). At the beginning of the infection, *PbTPS*, the pathogen's *PbTPS* gene, is activated, resulting in an increase in the trehalose concentration in the host. This shows that trehalase may be an essential aspect of a plant's defensive system against trehalose accumulation in infected tissue. To put it another way, trehalose overaccumulation is bad for plants. Thus, trehalose might have a deleterious influence on plants in some areas in specific quantities.

5.3. Trehalose and plant-pathogen symbiosis

Legumes and mycorrhizal interactions generally benefit from the production of rhizobia nodules, which results in higher biomass and improved stress tolerance. However, the beginning of the plant-pathogen interaction is similar to that of a pathogen attack in that plants engage in innate immunity later overcome by the parasite (Mithöfer 2002). Trehalose appears to be a key player in these associations. It was first discovered in *Glycine max* nodules in the early 1980s (J. G. Streeter 2006) and has since been detected in a variety of legumes at quantities ranging from 0.1–14 mg/g dry weight (D.W.) (Rodolfo Farías-Rodríguez 1998). Most trehalose is found within host plant cells, although the synthesis happens in bacteria. These relationships may involve trehalose at two levels. Host sensitivity to stress may be enhanced by trehalose in nodules, as indicated by the rise in trehalose production in nodules during desiccation (Rodolfo Farías-Rodríguez 1998). A *rhizobium etli* strain (*ReOtsA*) that overexpresses the *E. coli otsA* gene was used to further demonstrate this trehalose activity (Ramón Suárez 2008). *ReOtsA*-inoculated common bean (*Phaseolus vulgaris*) produced 27 percent more nodules, 38 percent higher nitrogenase activity, and 25

percent more biomass than the wild-type strain. Nodule count was reduced by 26%, nitrogenase efficiency was reduced by 45%, and biomass by 40% when the *R. etli* TPSKO mutant was inoculated on beans. The *ReOtsA*-inoculated plants could fully recover after three weeks of stress induction, whereas the wild-type and *R. etli* TPSKO mutants could not survive (Ramón Suárez 2008). Another theory is that the symbiont's trehalose accumulation could help it endure the host's innate immunity that were produced at the start of the interaction. Trehalose breakdown is impaired in the *thuB* mutants of the two *Sinorhizobium* species, leading to an increase in the number of nodules and accumulation of the disaccharide (Osei Yaw Ampomah 2008).

Trehalose plays a significant role in both mycorrhizal and ectomycorrhizal symbioses (Nehls 2008). An increase in the transcriptome of genes encoding for fungal trehalose-producing enzymes was identified in a study that investigated the relationship between *Amanita muscaria* and *Populus tremula tremuloides*. Following this, trehalose was aggregated in the Hartig net, a hyphal network that serves as a location for an extensive exchange of nutrients between the organisms (Mónica Fajardo López 2007). It has been thought that trehalose can increase the number of photoassimilates by acting as a carbon sink for the symbiont.

6. Trehalose As A Compatible Solute

Compatible solutes are non-toxic, cytoplasm-accumulating compounds. They maintain turgor and prevent macromolecular structures from anhydrobiotic destabilization (Y. Gibon et al. 1997). Saccharides, such as trehalose, are included in this category because of their extensive scope (David Gagneul 2007). It is a more effective membrane and biomolecule stabilizer in many species than other sugars (Elbein et al. 2003) and a compatible solute in others (Avonce et al. 2006). The genetically engineered plants containing trehalose have been shown to have an aberrant morphology, which may result from the toxicity induced by high concentrations of trehalose and indicates that trehalose is not a suitable solute (Henriette Schluemann 2003; Romero et al. 1997). However, many plants store trehalose in stressful conditions in particular organs (Ajay K. Garg et al. 2002; Tarek El-Bashitia 2005). For example, the transformation of *A. thaliana* with the chloroplast-specific ScTPS1 gene results in plants being more resistant to drought without causing growth abnormalities (Sazzad Karim 2007). These findings show that trehalose might function as a compatible solute in particular cells and organelles.

7. Trehalose As An Antioxidative Agent

The production of ROS by plants in response to stressful conditions caused by either abiotic or biotic agents is a frequent plant response (Gad Miller 2008). Its overproduction can cause the oxidation of plant cell membranes and biomolecules (Gad Miller 2008; Mittler 2002), which might result in the activation of antioxidant processes, of which the biosynthesis of trehalose could be a component. It has been demonstrated that trehalose can remove ROS in a concentration-determined method, with the highest neutralizing impact occurring at 50 mM in wheat (*Triticum aestivum*) subjected to heat stress (Yin Luo 2008). A similar response was recorded when yeast cells were treated with trehalose at a concentration of

10% (Déborada Costa Morato Nery 2008). The yeast cells became more resistant to the effects of H_2O_2 . Although it produces trehalose, it may inhibit ROS signaling, which in turn may influence the eventual plant defensive response.

8. Trehalose As A Signaling Molecule

It is commonly known that sucrose effectively transmits signals. However, there is still debate over the function of trehalose in signaling, and there is a possibility that trehalose and T6P have mutually antagonistic roles. Only limited evidence suggests that trehalose plays a direct role as a signaling molecule. It interacts with proteins and lipids [133], indicating that it may be a component of signal transduction cascades. Trehalase is a membrane protein found in *A. thaliana*. The active hydrolase domain of this protein is situated on the apoplastic side of the cell membrane (Mathieu Frison 2007), suggesting that it may have a role in sugar sensing. There is strong reason to assume that T6P is responsible for cell signaling actions. In yeast, hexokinase can be inhibited by T6P (Lunn; et al. 2006; Paul et al. 2008). It was first hypothesized that T6P acts as a vital indicator in plants for survival (Henriette Schluemann 2003; Pellny et al. 2004). Recent research suggests that T6P inhibits SnRK1, a transcriptional regulator that responds to carbon source availability (Yuhua Zhang et al. 2009). Interactions of trehalose with protein kinases and the 14-3-3 protein suggest that its biosynthetic machinery might have regulatory functions. (Jean E. Harthill 2006). Kinase activity by T6P may indicate plant stress responses (Andrea Pitzschke 2009). Another question that needs to be answered is whether trehalose and T6P are signaling molecules that trigger stress-related defensive reactions. Still, no experimental evidence for the mechanism exists.

9. Trehalose As An Antiapoptotic Agent

PCD can occur in plants after pathogen assaults and environmental changes (Theresa J. Reape 2008). In tobacco, PCD is induced by *Pseudomonas syringae* pv. *phaseolicola* (Olgadel Pozo 1998) and UV-C light (Danon et al. 2004). Trehalose has antiapoptotic properties in animals. Antiapoptotic activity improves stem cell and platelet preservation after freezing (Qi Liu 2009; Sasnoor 2005). Only once trehalose-affected plant PCD has been reported till now. Florets stored in trehalose-supplemented water wilted later and had less PCD (Tetsuya Yamada 2003). Trehalose degradation seems significant during senescence, which is linked to PCD (Theresa J. Reape 2008). The investigator V3 tool (Tomas Hruz et al. 2008) shows that *AtTRE* is substantially increased during senescence. It implies that trehalose breakdown is essential for PCD as it has an antiapoptotic action in plants.

Antiapoptotic characteristics can seem contradictory in pathogen attacks. A hypersensitive response (H.R.) is induced in many plant diseases when the host plant detects a parasite that suppresses immune response (Jonathan et al. 2006). H.R. causes cell death at the wound surface, limiting pathogen development. Trehalose accumulation at the sites of infection can hinder H.R. AvrRpm1 increased *AtTRE* when applied to *A. thaliana* leaves compared to DC3000 (Tomas Hruz et al. 2008). H.R. is activated by *P.*

syringae (AvrRpm1). Theoretically, trehalose could be secreted by some pathogens to counteract PCD, but there is no evidence to support this.

10. Conclusion

Stress response and stress tolerance are dependent on trehalose and T6P. Sugar metabolism and signaling have been revolutionized by their discovery. Trace amounts of trehalose can help plants cope better with the effects of salt, drought, and extremes in temperature. Even in nonhalophytic plants, this chemical serves as an osmotic protector and an important signaling molecule. Studying several genes involved in the trehalose biosynthetic pathway can reveal their roles under stress and may help us design novel techniques to increase biotic and abiotic stress tolerance. Two areas need more research. First, despite a significant association between trehalose and abiotic stress tolerance, excessive quantities of trehalose in mutant or genetically engineered plants typically contribute to developmental abnormalities, demonstrating that trehalose is a multi-functional chemical. More research is needed on Trehalose and T6P in pathogen resistance. In specific instances, plant-pathogen interactions may enhance trehalose production. Antitumor trehalose may hinder plant defenses. The presence of trehalose in most viruses makes studying this interaction difficult. Trehalose can be used in experiments to start defense processes, but it's unclear if it's part of a plant's natural defense against infections.

Trehalose's effect on plant physiology is still being studied, and more research on higher plants is needed to discover its role in plant protection. A wide range of molecular techniques would clarify the trehalose function in plants. Optimizing trehalose and T6P assays will assist in correlating levels with phenotypes. It may be possible to better understand trehalose's role in stress defense systems by examining *A. thaliana* mutant lines with defects in the synthesis or breakdown of the trehalose sugar.

Declarations

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Figures

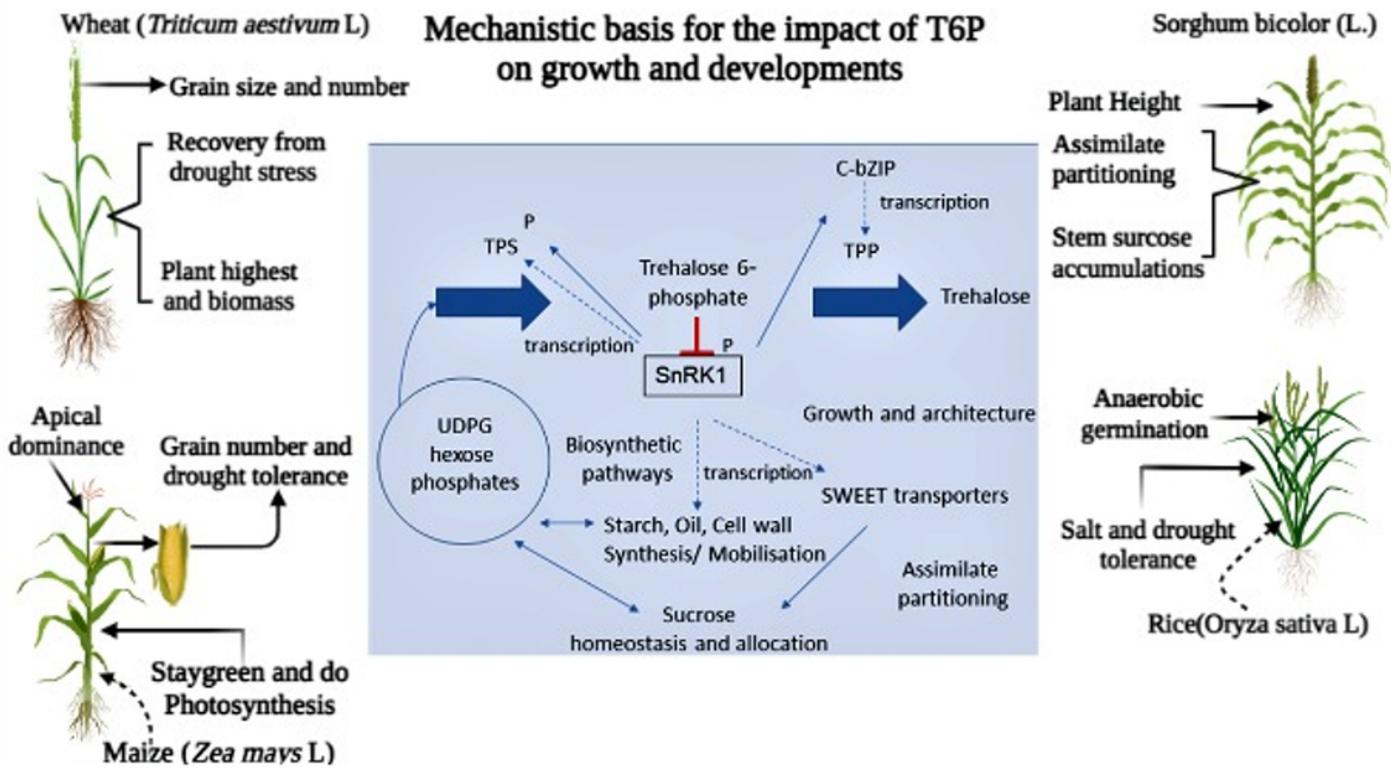


Figure 1

The mechanistic basis for the impact of T6P on growth and development.

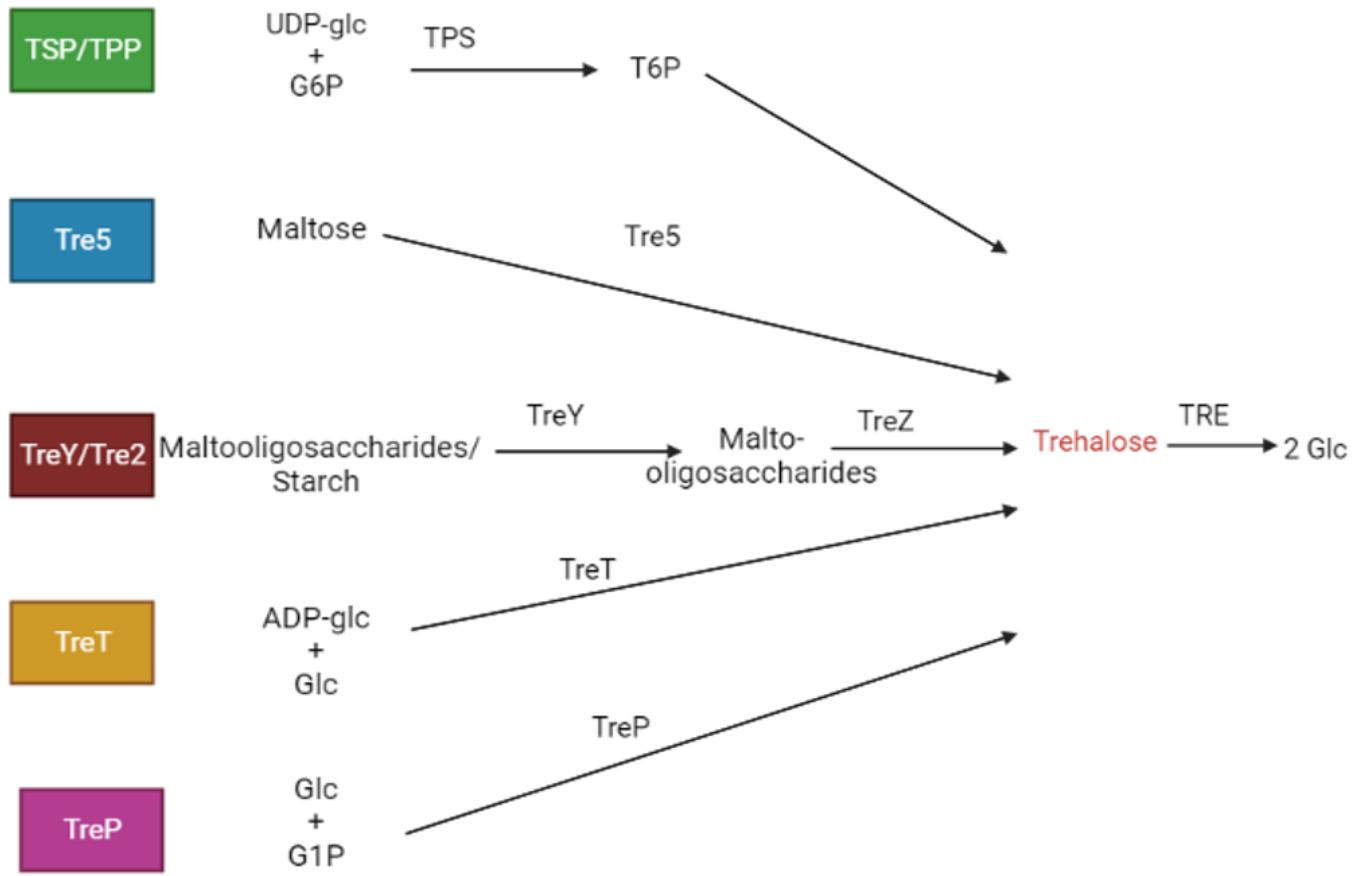


Figure 2

Genes involved in trehalose biosynthesis

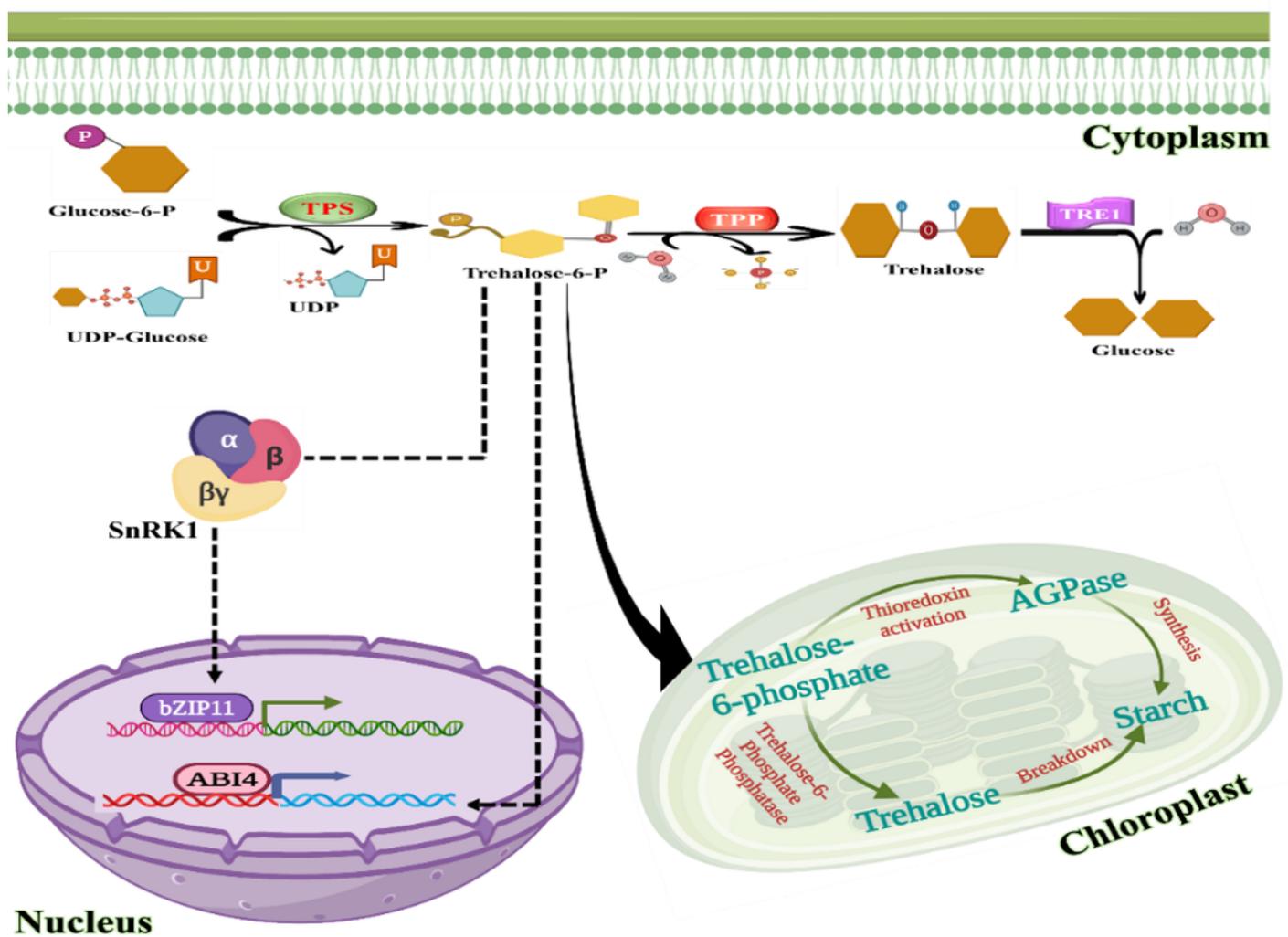


Figure 3

Biosynthesis pathway of trehalose and its function during carbohydrate metabolism.

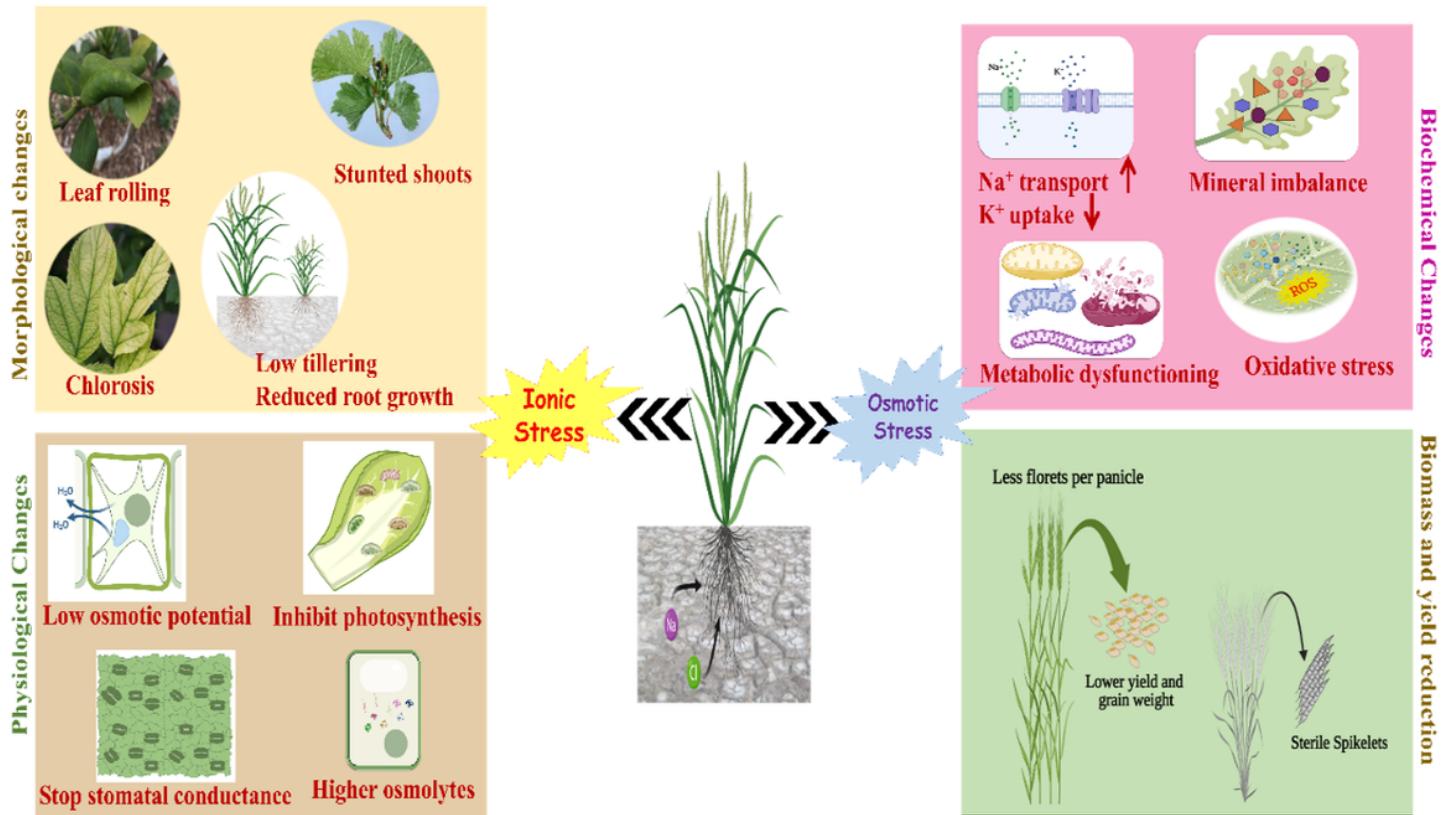


Figure 4

Changes in significant cell organelles and their collective effect on plant biomass and yield include salt-induced morphological, physiological, biochemical, and biochemical modifications.

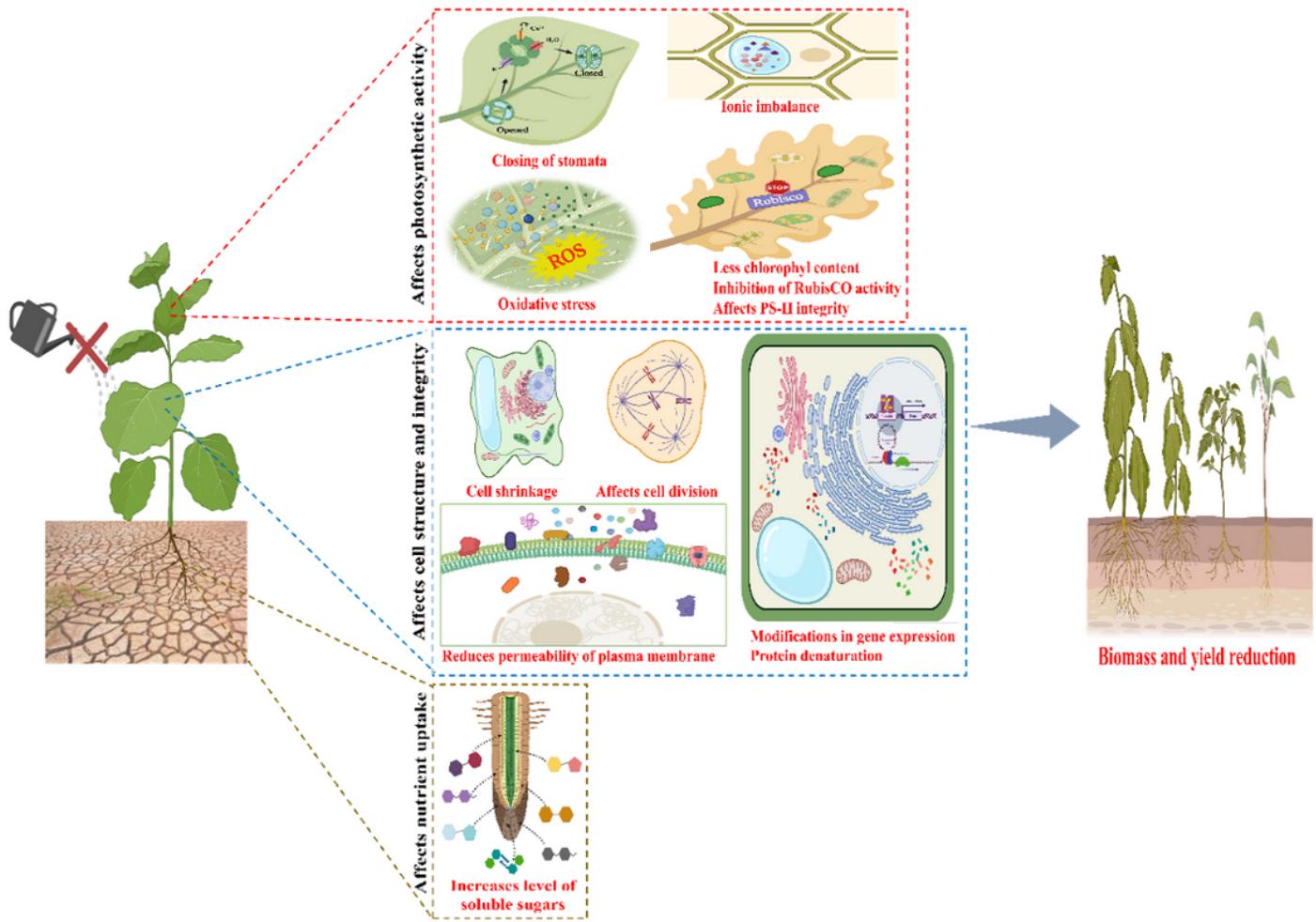


Figure 5

Impact of drought stress on the plant.