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Review

Interaction of glucose and phytohormone signaling in plants

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ABSTRACT

Energy acts as a primary prerequisite for plant growth like all the other organisms. Soluble sugars function in providing enough supply of nutrients which further helps in building macromolecules and energy to carry out specific and coordinated development. Sugars functions as nutrient as well as signaling molecule to promote cell division and differentiation in plants. Intriguingly, glucose has emerged as a crucial signaling molecule where hexokinase1 acts as the conserved glucose sensor. On the molecular scale, an extensive crosstalk between glucose and phytohormone signaling has been observed where glucose signals trigger multiple hexokinase1-dependent as well as hexokinase1-independent pathways to mediate diverse developmental, physiological and molecular mechanisms. Taken together, these findings this review focused on the glucose crosstalk with several classical plant hormonal-signaling pathways and the crucial role of hexokinase1 in modulating plant physiological processes.

1. Introduction

Sugar sensing and signaling play an important role to balance the requirement of nutrient, hormone and environmental signals in plants. In this context, glucose (Glc) occupies an enviable place in mediating diverse process, such as seed germination, development, photosynthesis, flowering and senescence (Gibson, 2005; Sami et al., 2016). Rapid advances in the area of Glc signaling have helped to shed light on the developmental process with great intricacies where hexokinase1 (HXK1) acts as a conserved evolutionary Glc sensor. Glc-mediated effect under abiotic stress (water stress, heat stress, dehydration stress and low-temperature stress) in plants is still lacking (Hu et al., 2009, 2012; Jiang et al., 2012; Huang et al., 2013). In general, phytohormones act as crucial players in altering growth, development and functioning in plants. Recent studies focused on Glc and phytohormone crosstalk exploring the hidden interconnectivity between Glc and hormonal signaling where HXK1 functions as Glc sensor. Glc crosstalk with auxins (Aux) displays extremely positive results by promoting cell proliferation, cell expansion and seed development and root growth (Mishra et al., 2009; Booker et al., 2010; Wang and Ruan, 2013). A positive crosstalk was observed between Glc and cytokinins (CKs) that modulate hypocotyl growth, anthocyanin production and root growth (Kushwah et al., 2011). Glc and gibberellins (GA) also modulate seed germination (Li et al., 2013). Glc negatively interacts with ethylene (ET) facilitating EIN3 degradation (Yanagisawa et al., 2003). Glc and abscisic acid (ABA) interact to modulate root meristem growth (Yuan et al., 2014). Several researches demonstrate Glc and brassinosteroids (BRs) crosstalk and functions in facilitating hypocotyl elongation, root growth direction, lateral root direction and emergence (Singh et al., 2014; Gupta et al. 2014, 2015). More recently, Glc and strigolactones (SLs) interact to facilitate seedling development and bud outgrowth (Barbier et al., 2015a,b; Li et al., 2016). The back-breaking decades of long work revealed that Glc teamed up with several phytohormones to modulate the expression of diverse genes. Moreover, via whole genome transcript profiling it has come in to view that out of 604 IAA-regulated genes, 377 (62%) genes are modulated by Glc (Gupta et al., 2009). Out of 377 genes, 68% genes are agonistically regulated by Glc and 32% genes are antagonistically regulated by Glc (Gupta et al., 2009). Glc and CK act in combination to alter the expression of 713 (76%) genes on the total of 941 CK-regulated genes (Kushwah and Laxmi, 2014). Intriguingly, Glc alters the expression of 63% of BR-regulated genes in plants.

The intent of this review is to explain the crosstalk of Glc with several phytohormones in modulating diverse physiological and developmental processes. Also, this crosstalk alters the expression of diverse phytohormone-regulated genes. This review also aims to evaluate recent progress on the regulatory role of Glc and phytohormone signaling via HXK1-dependent as well as HXK1-independent pathways.

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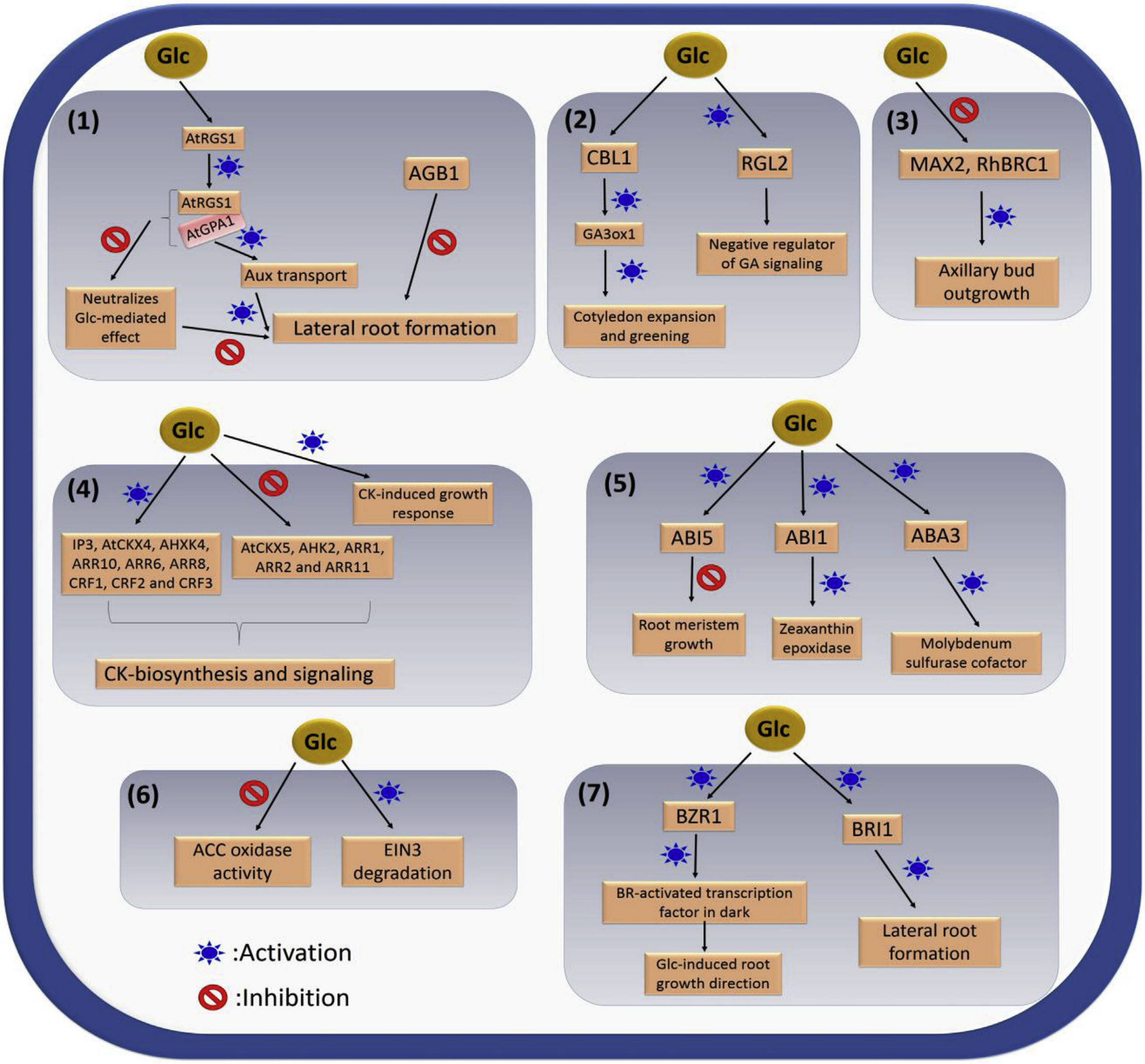

Fig. 1. The role of Glc-mediated functions in plants. (1) Glc interacts with Aux to facilitate lateral root formation where Glc signaling is linked to heteromeric G-protein that constitutes AtGPA1 (α subunit), AGB1 (β subunit), AGG (ϒ subunit) and AtRGS1 (GTPase accelerating protein). Glc binds to AtRGS1 to facilitate ATRGS and AtGPA1 interaction that promotes lateral root formation and AGB1 inhibits lateral root formation. (2) Glc up-regulates the expression of CBL1 which further affects cotyledon expansion and greening and promotes RGL2 expression that is the negative regulator of GA signaling. (3) Glc down-regulates the expression of root hair specific genes and also down-regulates the expression of *MAX2* and *RhBRC1* that activates axillary bud outgrowth. (4) Glc activates the expression of *IP3, AtCKX4, AtHXK4, ARR10, ARR6, ARR8, CRF1, CRF2* and *CRF3* and inhibits the expression of *AtCKX5, AHK2, ARR1, ARR2* and *ARR11* to modulate CK biosynthesis and signaling. Glc response enhances CK-induced growth response. (5) Glc inhibits root meristem growth via ABA insensitive 5, upregulates *ABI1* that activates zeaxanthin epoxidase and upregulates the expression of ABA3 regulating molybdenum sulfurase cofactor. (6) Glc facilitates EIN3 degradation that further inhibits the expression. (7) Glc upregulates the expression of BZR1 that up-regulate BR activated transcription factor in dark that further mediates Glc-induced root growth direction and also up-regulates the expression of BRI1 that activates lateral root formation.

2. Glucose signaling and its crosstalk with several hormonal-signaling pathways in plants

2.1. Glucose and auxin

In general, Glc and Aux mediate endless process of growth and development in plants. Interestingly, Glc signaling is coupled via heteromeric G-protein that composed of α subunit (AtGPA1), β subunit (AGB1), γ subunit (AGG) and GTPase accelerating protein (AtRGS1, regulator of G protein 1 protein) that regulates Aux transport (Chen et al. 2003, 2004, 2006; Johnston et al., 2007; Grigston et al., 2008) (Fig. 1). Glc directly binds to AtRGS1 to permit AtRGS1-AtGPA1 interaction (Johnston et al., 2007) (Fig. 1). Deletions of AtGPA1 or AtRGS1 neutralize Glc effect on Aux-induced lateral root formation. However, deleting Gβ subunit enhance Aux-induced lateral root formation (Booker et al., 2010) suggesting the role of G-protein in Glc signaling pathway. Exogenous application of 0–1% Glc promotes lateral roots maximally up to 0.3 μM Aux. However, at high concentrations (3% Glc and 3 μM Aux) reduced the number of lateral root formation in Arabidopsis (Booker et al., 2010) (Table 1).

Several studies demonstrate that Glc and Aux alters root length, root hairs, lateral root number and root growth direction in Arabidopsis (Mishra et al., 2009) (Fig. 2). In 5-day old wild type (WT) seedlings of Arabidopsis, exogenous application of 0–3% Glc significantly enhances root length and lateral root number. However, root length and lateral root number was declined at 5% Glc. Furthermore, root growth

Table 1
Summary of exogenous application of Glc and phytohormones in mediating diverse physiological processes.

Phytohormones	Glc-mediated effects	Plant species	Reference(s)
Auxin	Exogenous application of 1% Glc + 0.3 μM Aux enhance lateral root formation	*Arabidopsis*	Booker et al. (2010)
	Exogenous application of 3% Glc + 3 μM Aux reduce lateral root formation and lateral root primordium		
	Exogenous application of 1–3% Glc increase root length	*Arabidopsis*	Mishra et al. (2009)
	Exogenous application of 1–3% Glc increase the number of lateral roots		
	Exogenous application of 1–5% Glc enhance root deviation from vertical		
Cytokinin	Exogenous application of 1–3% Glc + 10^{-7} M, 5×10^{-7} M and 10^{-6} M benzylaminopurine enhance root length	*Arabidopsis*	Kushwah and Laxmi (2014)
	Exogenous application of 0–1% Glc + 10^{-7} M, 5×10^{-7} M and 10^{-6} M benzylaminopurine promotes hypocotyl elongation		
	Exogenous application of 0–3% Glc significantly increase chlorophyll content and 10^{-7} M, 5×10^{-7} M and 10^{-6} M benzylaminopurine significantly decrease chlorophyll content per gram fresh weight		
	Exogenous application of 1–5% Glc + 10^{-7} M, 5×10^{-7} M and 10^{-6} M benzylaminopurine significantly increase anthocyanin content per gram fresh weight		
Gibberellin	Exogenous application of 0.5 μM paclobutrazol inhibits cotyledon greening	*Arabidopsis*	Li et al. (2013)
	Exogenous application of 0.5 μM paclobutrazol + 1 μM GA3 restores cotyledon greening		
Ethylene	Exogenous application of 2 mM and 10 mM Glc leads to the repression of EBS-LUC activity	*Zea mays*	Yanagisawa et al. (2003)
	Exogenous application of 20 mM Glc escalated EIN3 degradation		
	Exogenous application of 6% Glc + ACC overcome Glc-induced development arrest	*Arabidopsis*	Zhou et al. (1998)
	Glc application inhibits ACC oxidase activity	*Lycopersicum esculentum*	Hong et al. (2004)
Abscisic acid	Exogenous application of 1, 3 and 5% Glc represses primary root growth by shortening root meristematic zone	*Arabidopsis*	Yuan et al., 2014
	Exogenous application of 1, 3 and 5% Glc elevates ABI5 transcript level that reduces PIN protein accumulation that limits Aux activity results in shortening of root meristematic zone		
	Exogenous application of 2 and 6% Glc upregulates the expression of ABA biosynthetic genes	*Arabidopsis*	Cheng et al. (2002)
Brassinosteroid	Exogenous application of 1% Glc stimulates hypocotyl elongation 5% Glc inhibits the same	*Arabidopsis*	Gupta et al. (2015)
	Exogenous application of 1–3% Glc +10 μM BR decrease hypocotyl elongation		
	Exogenous application of 1–3% Glc + 1 μM BR leads to even more decrease in hypocotyl elongation		
	Exogenous application of 1, 3 and 5% Glc leads to root deviation from vertical	*Arabidopsis*	Singh et al. (2014)
	Exogenous application of 0.5%, 1%, 3%, 4% and 5% Glc prompted lateral root emergence and lateral root direction	*Arabidopsis*	Gupta et al. (2014)
	Exogenous application of 1–5% Glc +100 nM BR increase the number of emerged lateral roots/seedling		
	Exogenous application of 1–5% Glc + 1 μM BR leads to less increase in number of emerged lateral roots/seedling		
Strigolactone	Exogenous application of 10, 50, 100 and 250 mM sucrose enhance bud length	*Rosa hybrida*	Barbier et al. (2015a,b)
	Exogenous application of 2% Glc + 2 μM GR24 increase radical emergence	*Arabidopsis*	Li et al. (2016)
	Exogenous application of 1% Glc + 2 μM GR24 decrease cotyledon expansion		

deviation from vertical significantly increased as 0% < 1% < 3% < 5% (Mishra et al., 2009) (Table 1). Furthermore, *glucose insensitive* (*gin2)* mutant (HXK1-dependent pathway) is very less sensitive towards Glc proving the fact that these responses are dependent on HXK1-mediated signaling (Mishra et al., 2009). In particular, Glc alters the expression of diverse genes, such as Aux biosynthetic *YUCCA (YUC)* gene, Aux efflux *PIN-FORMED1 (PIN1)* gene, *AUXIN BINDING PROTEIN1 (ABP1)* gene that mediate Aux transport and *TRANSPORT INHIBITOR* RESPONSE1 (*TIR1)* gene that mediate Aux-induced cell division and elongation (Mishra et al., 2009). Exogenous application of 1% Glc to *tir1* mutant (incapable of Aux-induced cell division and elongation), *auxin response protein (axr2)* mutant that shows agravitropic response and *solitary root 1 (slr1)* mutant that shows reduced Aux sensitivity and agravitropic response leads us to conclude the role of Aux signaling on gravitropic response (Mishra et al., 2009).

Mounting evidence suggests possible interplay between Glc and Aux signaling in mediating cell proliferation, cell expansion and seed development (Wang and Ruan, 2013). Noteworthy, Glc supplementation modulate the expression of cyclins (cycD2; 1, D3; 2, A3; 2, and B1; 2) where Glc-mediated cell division is a result of signaling and not nutrient availability (Hartig and Beck, 2006). In Arabidopsis, Glc signal initiates G2/M transition by supressing transcription of *TRP-domain suppressor of stimpy (TSS)* gene*,* a negative regulator of cell division. In Arabidopsis, a close correlation between Glc and Aux was observed where Glc supplementation alone is unable to prompt mitosis and requires the presence of Aux also indicating interplay of these two actors in G2/M regulation (Skylar et al., 2011).

2.2. Glucose and cytokinins

More recently, Glc and CKs display dual interaction where both these actors act in agonistic (Riou-Khamlichi et al., 1999, 2000; Hartig and Beck, 2006; Das et al., 2012) as well as antagonistic manner (Moore et al., 2003; Franco-Zorrilla et al., 2005). Moreover, it has also come to sight that Glc modulates the expression of genes associated with CK biosynthesis and signaling (Kushwah and Laxmi, 2014) (Figs. 1 and 2). In Arabidopsis, *6-benzylaminopurine (BAP)* regulates the expression of 941 genes where Glc alone regulate the expression of 713 (76%) genes. On total of 713 genes, the expression of 633 (89%) and 80 (11%) are agonistically and antagonistically regulated (Kushwah and Laxmi, 2014). In Arabidopsis, Glc up-regulate the expression of several genes i.e. *ISOPENTENYLTRANSFERASE 3 (IPT3)* gene that mediates CK biosynthesis, *CYTOKININ OXIDASE 4 (CKX4)* gene that mediates CK catabolism, *HISTIDINE KINASE 4 (HK4)* gene that mediates CK perception, *ARABIDOPSIS RESPONSE REGULATOR (ARR10)* gene that mediate CK signaling, *ARR6* and *ARR8* genes that mediate CK-early response and *CYTOKININ RESPONSE FACTOR (CRF1, CRF2 and CRF3)* genes that mediate the development of embryo, cotyledons and leaves (Werner et al., 2006; Rashotte et al., 2006; Kushwah and Laxmi, 2014) (Fig. 1). In contrast, Glc also down-regulate the expression of *AtCKX5* (CK-catabolism), *AHK2* (CK receptor), *ARR1, ARR2* and *ARR11* (CK-signaling) genes (Werner et al., 2006; Kushwah and Laxmi, 2014) (Fig. 1). Investigations reveal that exogenous application of Glc in the medium enhance CK-induced root growth response (Kushwah et al., 2011). A significant increase in root length was observed by the supplementation of 0–3% Glc but decline in root length was observed at 5% Glc. However all BAP concentrations (0, 10^{-7}, 5×10^{-7}, 10^{-6} M) results in

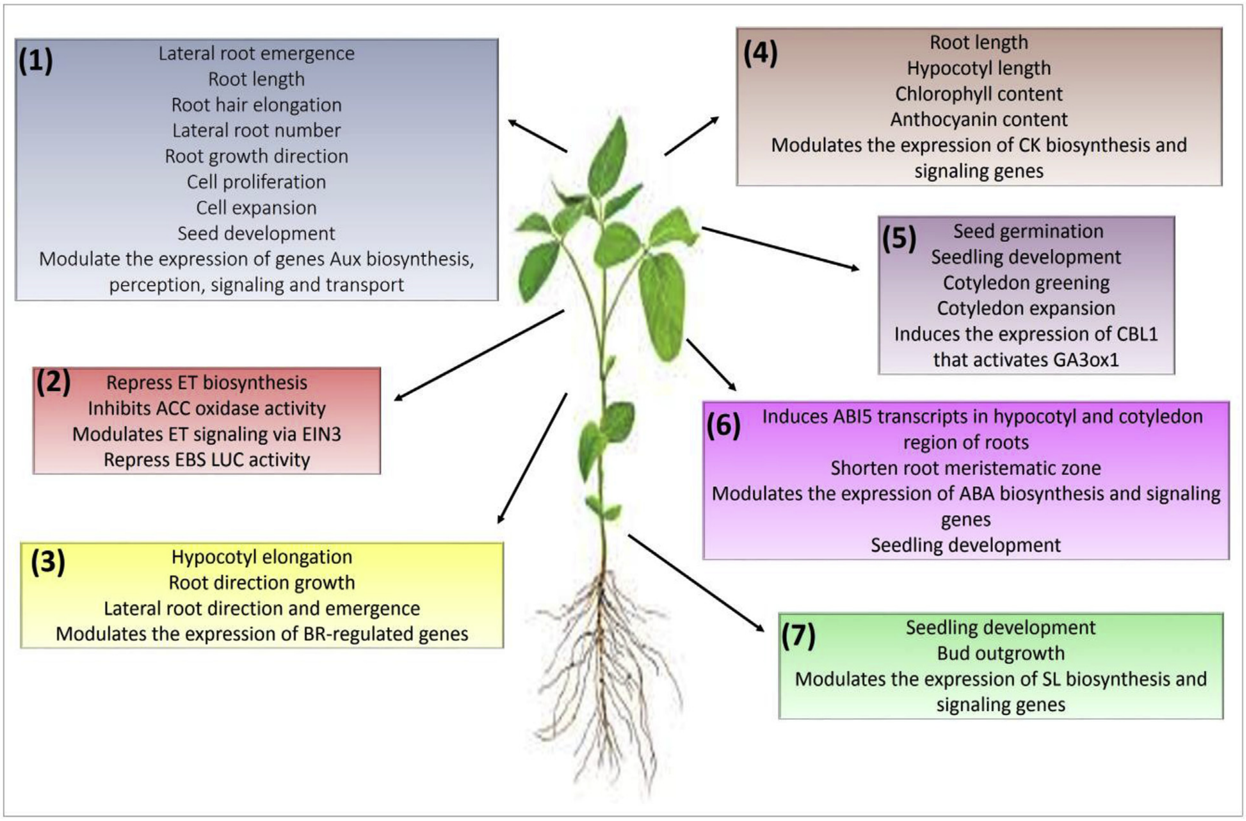

Fig. 2. Interaction of Glc with phytohormones in mediating the physiology of the plants. (1) Glc crosstalk with Aux, (2) Glc crosstalk with ET, (3) Glc crosstalk with BR, (4) Glc crosstalk with CK, (5) Glc crosstalk with GA, (6) Glc crosstalk with ABA, (7) Glc crosstalk with SL.

decline in root length defending the view that high Glc (5%) concentration counteract CK-mediated inhibition in root length (Table 1, Fig. 2). In Arabidopsis, 0–3% Glc enhance hypocotyl length whereas 5% Glc leads to decline in hypocotyl length. However, a significant decline in hypocotyl length was observed at all BAP concentrations (0, 10^{-7}, 5×10^{-7}, 10^{-6} M) (Kushwah and Laxmi, 2014) (Table 1). Furthermore, *gin2-1* mutants were very less sensitive towards CK for hypocotyl length as compared to their respective WT plants. It validates the fact that Glc and CK crosstalk via HXK1-dependent pathway mediate the hypocotyl length (Kushwah and Laxmi, 2014). Different concentrations of Glc (0, 1%, 3% and 5%) significantly increase chlorophyll content and a significant decline in chlorophyll content was observed at all BAP concentrations (0, 10^{-7}, 5×10^{-7}, 10^{-6} M) (Kushwah and Laxmi, 2014) (Table 1, Fig. 2). Exogenous application of Glc (0, 1%, 3% and 5%) leads to a significant enhancement in anthocyanin production. Combination of Glc and BAP further enhances anthocyanin production (Kushwah and Laxmi, 2014) (Table 1, Fig. 2). Exogenous application of different doses of Glc increase root hair initiation as well as elongation in Arabidopsis. Moreover, extending study on CK signaling mutants (*ahk4, arr1, 10, 11* and *arr3, 4, 5, 6, 8, 9*) displays no visible enhancement in root hair initiation at 3% Glc. Even when Glc concentration rose to 5%, very small numbers of root hair were seen in these mutants as compared to WT (Kushwah and Laxmi, 2017). These findings further support the view that CK signaling en route Glc signaling in mediating root hair initiation in Arabidopsis. Uncovering researches provides an evidence that Glc interacts with CK via HXK1-dependent pathway as *gin2* mutants are very less effective or even resistant at all concentration of Glc whereas *gpa1* and *thylakoid formation 1 (thf1)* (defective in HXK1-independent pathway) shows almost alike Glc sensitivity as compared to WT plants. This view validates the fact that Glc crosstalk with CK via HXK1-dependent pathway to control root hair initiation (Kushwah and Laxmi, 2017).

2.3. Glucose and gibberellins

In larger context, GA is known to mediate incalculable physiological processes, including seed germination, seedling development, greening as well as expansion of cotyledon (Leon and Sheen, 2003; Dekkers et al., 2004) (Fig. 2). Intriguing studies reveals that Ca^{2+} acts as secondary messenger in signal transduction via distinct calcium sensors where calcineurin B-like (CBL) protein works as very elusive calcium sensor in plants that gets activated under abiotic stress responses (Li et al., 2013). Exogenous application of sugars induced Ca^{2+} accumulation in cytosol affecting Ca^{2+} signaling that alters the expression of sugar response genes (Furuichi et al., 2001). In Arabidopsis, Glc leads to the induction of CBL1 and *cbl1* mutants are hypersensitive to Glc and paclobutrazol (PAC) (GA inhibitor) (Li et al., 2013) (Table 1). Exogenous application of 3% Glc induces the expression of *CaBP-22* and *annexin* (associated with Ca^{2+} regulation) genes and CBL (calcium ion binding protein) (Price et al., 2004). However, 3% sucrose (Suc) and 3% fructose (Fru) do not significantly enhanced expression of *CBL1 mRNA*. This view provides us the fact that amongst above-mentioned sugars, Glc acts as sole guardian to induce the expression of CBL1 (Li et al., 2013). Exogenous supply of 3% Glc do not shows any effect on the expansion and greening of cotyledons in WT plants whereas cotyledon expansion and greening is highly repressed in *cbl1* mutants (Li et al., 2013) (Fig. 1). In WT seedlings, the germination rate was 83% with only 17% reduction while in *cbl1* mutants the germination rate was 30% with 70% reduction by the application of 3% Glc suggesting that CBL1 intrusion enhances Glc sensitivity during seed germination in Arabidopsis (Li et al., 2013). Apart from this, pretreatment of WT seedlings with 3% Glc for 5 days does not shows any effect on root elongation whereas root growth was clearly inhibited in *cbl1* mutant plants (Li et al., 2013). Exogenous application of 3% Glc cause a slight repression of chlorophyll a/b-binding protein (CAB1), asparagine synthetase 1 (ASN1), plastocyanin

(PC) and ribulose-1, 5-bisphosphate carboxylase (RBCS) in WT seedlings but strongly repressed in *cbl1* mutant. Moreover, promotes the expression of ADP-glucose pyrophosphrylase (APL3) and chalcone synthase (CHS) to several-folds in WT seedlings as compared to *cbl1* mutants (Li et al., 2013) suggesting that *cbl1* mutants shows Glc hypersensitivity. Reports were also in favour that CBL1 suppression affects GA-mediated plant response. Exogenous application of 0.5 μM PAC shows 20% germination in *cbl1* mutants and it was about 78% in WT seedlings (Li et al., 2013). Consistent with the study, combination of 0.5 μM PAC and 1 μM GA attenuates the negative effect on germination in *cbl1* mutants (Li et al., 2013) (Table 1) validating the indirect intimacy between Glc and GA signaling. Indirect hidden interconnectivity between Glc and GA where the expression of *GA3ox1* gene is much reduced in *cbl1* mutants as compared to WT seedlings was noted (Li et al., 2013). Moreover, Glc acts as leading actor in GA signaling via up-regulation of *RGL2* (negative regulator of GA signaling) gene (Lee et al., 2002; Yuan and Wysocka-Dillerb, 2006) (Fig. 1). The remaining link proven here is that Glc induces the expression of CBL1 which further activates *GA3ox1* gene and its crucial involvement in seed germination and seedling development (Fig. 2).

Exogenous application of different concentration of GA3 (30, 50, 80 and 100 μM) stimulates Glc, Suc and Fru accumulation in *Vitis vinifera* suspension cells (Zhang et al., 2014). These above-mentioned GA3 concentrations down-regulate the expression of HXK1, HXK2 and sucrose synthase (SUS) whereas the expression pattern of cell wall invertases (CWINV) was seems to be up-regulated. On the contrary, exogenous application of different concentration of Glc (0, 30, 60, 90, and 120 mM) upregulates the expression of HXK1, HXK2 and SUS whereas down-regulate the expression of CWINV (Zhang et al., 2014). In addition, combination of Glc and GA3 down-regulate the expression of HXK1 and HXK2 to a much larger extent as compared to the sole application of either Glc or GA3 supporting the view that GA-mediated repression antagonize Glc up-regulation of HXK1 and HXK2 (Zhang et al., 2014). Further extending researches favours that Glc analogs, such as 2-deoxy-glucose (2dGlc) (phosphorylated by HXK) down-regulates the expression of CWINV and 6-deoxy-Glc (6dGlc) (not good HXK substrate) have no effect on CWINV validating the fact that Glc-mediated inhibition on CWINV is dependent on HXK phosphorylation (Zhang et al., 2014). Evidences also provide the view that Glc and 2-dGlc down-regulate the expression of SUS whereas 6-dGlc and GlcN have no effect on the expression of SUS suggesting that SUS expression is dependent on HXK phosphorylation (Zhang et al., 2014). Compiling evidences suggests that GA antagonizes Glc-mediated effect via HXK1 phosphorylation in *V. vinifera* plants.

2.4. Glucose and ethylene

Several researches focused on Glc-ET crosstalk to extend its abbreviated knowledge in plants. In Arabidopsis, Glc is antagonistically related ET where it leads to the degradation of ethylene insensitive 3 (EIN3) which is involve in ET signaling (Yanagisawa et al., 2003, Fig. 1). In *Zea mays* protoplasts, 2 mM and 10 mM Glc showed a significantly repress *EIN3-binding sequence-luciferase* gene *(EBS-LUC)* expression (Table 1, Fig. 2). However, 3-O-methyl-D-glucose (3-OMG) does not has any effect on EIN3 (Yanagisawa et al., 2003) providing a direct evidence that Glc-mediated degradation of EIN3 is HXK-dependent (Yanagisawa et al., 2003). Addition of ET precursor, 1-aminocyclopropane-1-carboxylic acid (ACC) to the plates containing 6% Glc overcomes Glc-induced developmental arrest in WT plants of Arabidopsis. Moreover, *ethylene overproduction (eto1-1)* mutant and *constitutive ethylene triple response (ctr1-1)* mutant overcome Glc-induced developmental arrest without ACC application (Zhou et al., 1998) ascertaining that Glc sensitivity is very closely related to ET signaling. In tomato fruits, Glc application inhibits the activity of ACC oxidase (a key enzyme in ET biosynthesis) indicates that Glc suppress ET-mediated fruit ripening (Hong et al., 2004) (Fig. 2).

2.5. Glucose and abscisic acid

An extensive body of research demonstrate that Glc inhibits root meristem growth via *ABA INSENSITIVE 5 (ABI5),* which further represses PIN1 accumulation and Aux activity in Arabidopsis (Yuan et al., 2014) (Fig. 1). Exogenous application of different concentrations of Glc (1%, 3% and 5%) to 7-day-old Arabidopsis seedlings for 3 days represses primary root growth by shortening the root meristematic zone (Yuan et al., 2014) (Table 1, Fig. 2). Further intricacies demonstrate that 1%, 3% and 5% Glc manifested significant decrease of 0.47, 0.41 and 0.29, respectively in root meristematic zone. Intriguingly, the above-mentioned Glc concentrations also significantly induced *ABI5* (Glc hypersensitivity) in hypocotyl and cotyledon region in the roots of 5 day old Arabidopsis seedlings for 3 days (Yuan et al., 2014) (Fig. 2). Here, 3% Glc (2.4 fold) and 5% Glc (4 fold) displays maximum elevation in *ABI5* transcript level as compared to 1% Glc. An indecipherable confirmation also uncovered where *ABI5* induction is associated with the reduction of PIN1 protein accumulation which further reduces Aux activity and ultimately results in shortening of root meristematic zone in Arabidopsis (Yuan et al., 2014) (Table 1). In other study Glc interacts with ABA where Glc antagonizes ET signaling by inducing the expression of *ABA2/GIN1* and other genes associated with ABA biosynthesis and signaling (Cheng et al., 2002) (Fig. 2). Exogenous application of 4% Glc and 100 nM ABA restores Glc sensitivity in *gin1* and *gin5* (ABA-deficient) mutants but not in *abi4* (ABA-insensitive) mutants (Cheng et al., 2002). Exogenous application of 2 and 6% Glc repress the expression of *plant defensin family (PDF1.2)* that require endogenous ET for its expression whereas no suppression was observed in *aba2/gin1* mutants provides a portrayal that Glc and ET signaling acts antagonistically and *ABA2/GIN1* genes are associated with ABA biosynthesis in this pathway (Cheng et al., 2002). Exogenous application of 2 and 6% Glc also up-regulate the expression of several ABA biosynthetic genes, such as *ABA1* gene that encodes zeaxanthin epoxidase, *AAO3* gene that encodes abscisic aldehyde oxidase 3 and *ABA3* gene encoding molybdenum sulfurase cofactor in Arabidopsis (Table 1, Fig. 1). Moreover, Glc-mediated induction was obliterated in *gin1-3* null mutant enough to encapsulate the fact that endogenous ABA plays a key role in Glc-mediated induction of ABA biosynthetic genes (Cheng et al., 2002). This research fills the dark hole where ABA and Glc reveals very uncanny similarity in inducing seedling development in Arabidopsis and ET signaling occupies an entirely different tangent where ET acts antagonistically to both these actors (Fig. 2).

2.6. Glucose and brassinosteroids

In general, Glc and brassinosteroids (BRs) works synergistically as well as antagonistically to mediate plant functions. In particular, BR mediates the up-and down-regulation of 190 and 113 genes, respectively (Gupta et al., 2015). Out of 190 BR up-regulated genes, Glc alone up-regulates and down-regulates the expression of 83 and 55 genes, respectively. Out of 113 BR down-regulated genes 37 and 42 genes are up- and down-regulated, respectively by Glc alone. In total, Glc mediates the expression of 63% (217) BR-regulated genes where 125 (58%) are synergistically regulated whereas 92 (42%) genes are antagonistically regulated by Glc (Gupta et al., 2015). A fistful of studies on Arabidopsis ascertained that BR facilitate Glc-mediated hypocotyl length in dark (Zhang and He, 2015). Exogenous application of 90 mM Suc, Glc and mannitol (Man) to WT (7-day old) seedlings kept in shade successively for the next 7 days results in enhancement of hypocotyl elongation where Glc results in impeccably maximum increment in hypocotyl length followed by Suc and Man. Specifically, in both light and dark grown WT seedlings 1% Glc stimulates hypocotyl elongation whereas 5% Glc inhibits the same (Gupta et al., 2015) (Table 1). Moreover, combined application of different Glc concentrations (1%, 3% and 5%) and BR (10 nM, 100 nM and 1 μM) leads to significant decline in hypocotyl elongation underlining Glc and BR crosstalk in

Arabidopsis (Gupta et al., 2015) (Table 1, Fig. 2). Consistently, *gin2-1* displays defect in hypocotyl elongation uncovering the fact that HXK1 plays a significant role in hypocotyl elongation in dark (Zhang and He, 2015). The study also throws up overlaps where exogenous sugars enhance *BRASSINAZOLE RESISTANT1 (BZR1)*, a gene encoding BR-activated transcription factor in dark (Fig. 1). In Arabidopsis, *del2-1* (BR biosynthetic) mutant and brazzinazole (BRZ), BR biosynthetic inhibitor impaired sugar-induced hypocotyl elongation in dark. Moreover, *gin2-1* mutants of Arabidopsis shows very less sensitivity towards BRZ accumulating more concrete evidence that BR is crucial for sugar-induced hypocotyl elongation (Zhang and He, 2015). Consistently, in the same study exogenous application of brassinolide (BL) leads to enhancement in hypocotyl ratio demonstrating that Glc-induced hypocotyl elongation is HXK1-dependent where BR acts downstream in the same pathway.

Another study comes as a milestone where Glc and BR crosstalk was reported in the control of root growth direction in Arabidopsis (Singh et al., 2014) (Fig. 2). Here, roots grow vertically in Glc-free medium whereas Glc concentration (1%, 3% and 5%) portrays a marked deviation in roots from vertical in dark. Also, 5% Glc (50°) shows maximum degree of deviation as compared to untreated control (20°) (Table 1). Not surprisingly, the same concentration of Man and sorbitol (Sor) shows very little influence on root growth deviation. In contrast, 3-OMG does not encroach root growth deviation to any extent and *gin2* mutants impeccably respond towards Glc-induced root growth deviation (Singh et al., 2014) (Table 1) certainly reflects that Glc-mediated root growth deviation involves HXK1-dependent as well as HXK1-independent signaling. Intriguingly, Glc and BR acts in a synergistic manner to induce root growth deviation from vertical and application of BRZ inhibits Glc-induced root growth deviation. *brassinosteroid insensitive1-6 (bril1-6)* that shows no receptivity towards BR) exhibits no response towards Glc-induced root growth deviation and *brassinazole resistant1-1D (bzr1-1D)* showcase an overstated Glc-induced root growth deviation unpacks the fact that BR signaling enhances the existing momentum Glc-mediated root growth deviation (Singh et al., 2014) (Table 1). This study also suggests that protein phosphatase limits root deviation from vertical. To reveal the hidden interconnectivity between brassinosteroid insensitive1 (BRI1) and protein phosphatase 2A (PP2A) activity, *roots curl in naphthyl phthalamic acid1 (rcn1)* mutants were used that shows least PP2A activity. Here, both Glc and BR treatment leads to enhanced root growth deviation from vertical as compared to WT plants. However, maximum effect on root growth deviation was observed at 3% Glc and 10 nM BR whereas normal root growth deviation was recovered by BRZ application reveals that Glc enhance BRI1 internalization by limiting protein phosphatase activity in Arabidopsis (Singh et al., 2014).

Evidently, BR also acts downstream in Glc-induced lateral root development in Arabidopsis (Gupta et al., 2014) (Fig. 2). Exogenous application of different concentrations of Glc (0.5%, 1%, 3%, 4% and 5%) to for 3–5 day WT seedlings grown in ½ MS medium prompted lateral root development significantly in a concentration-dependent manner when compared to their untreated controls. In addition, similar doses of Man do not promote lateral root primordium and 3-OMG does not induce lateral root primordium to any extent. Also, *rgs1-1, rgs1-2, gpa1-1, gpa1-2* and *thf1-1* were almost insensitive in terms of lateral root formation as compared to their WT seedlings ascertaining that Glc-induced lateral root formation is HXK1-dependent (Gupta et al., 2014) (Table 1). Further intricacies displays that exogenous application of 10 nM BR and 1 and 3% Glc significantly prompted lateral root development whereas 100 nM and 1 μM BR seems inhibitory at all the doses of Glc. Moreover BRZ application further inhibits Glc-induced lateral root development. In *gin2-1* mutants, BR shows a very meagre response towards Glc-induced lateral root development pointing out the fact that BR mediates Glc-induced lateral root development via HXK1-dependent pathway (Gupta et al., 2014) (Table 1). The results of the research also resurfaced that BRI1 is epistatic to HXK1 to mediate lateral root development where *gin2-1bri1-6* double mutants shows analogous effects as *bri1-6* mutant plants marked the culmination that BR holds an upper hand in Glc-induced lateral root development in Arabidopsis (Gupta et al., 2014).

2.7. Glucose and strigolactones

A new dimension has been added in Glc research from past few years pointing out Glc and SL crosstalk in plants. In Arabidopsis, SLs are involved in sugar signaling to modulate early seedling development (Li et al., 2016). Exogenous application of 2 μM (3aR*,8bS*,E)-3-(((R*)-4-methyl-5-oxo-2,5-dihydrofuran-2-yloxy)methylene)-3, 3a, 4, 8b tetrahydro-2H-indeno [1,2-b] furan-2-one (GR24) to *max1* (SL-deficient) mutant incisively inhibits seedling development as compared to WT seedlings whereas no inhibition was reported in *max2* (SL-insensitive) mutant. Moreover, SL diligently pronounced inhibition in seedling development even at 1% Glc ascertaining that SL intensify Glc-induced repression during seedling development (Li et al., 2016) (Table 1). A comparative transcriptomic analysis surfaced that application of 2% Glc for 3 days up-regulate and down-regulate 39 and 236 genes, respectively in WT seedlings. However, *max2* mutants displays 219 and 334 up-and down-regulation of genes, respectively whereas *hxk1* mutants imprint 202 and 347 up-and down-regulated genes. However, the expression of SL biosynthesis *(D27, MAX1, MAX3* and *MAX4)* and SL signaling *(STH7, KUF1* and *IAA1)* genes do not trigger a remarkable change providing the hard evidence that 2% Glc is insufficient to induce SL biosynthesis as well as signaling (Price et al., 2004). In spite of phenotypic similarity between *max2* and *hxk1* mutants, these mutants differs in Glc hyposensitivity as 1/2 up-regulated genes and 2/3 down-regulated genes in *max2* differ from *hxk1* mutants (Li et al., 2016). Specifically, exogenous application of Glc significantly down-regulate the expression of *root hair specific (RHS15, RHS17 and RHS19)* genes in *hxk1* mutants. However, *max2* mutants do not trigger much change in these genes as compared to their respective WT plants with no Glc treatment (Li et al., 2016) manifested that Glc-mediated negative regulation is independent of HXK1 signaling in contrast to SL signaling. Several stress related genes were also induced in *hxk1* mutants irrespective of their WT and *max* mutant seedlings (Li et al., 2016). As the rate of gene overlap between *hxk1* and *max1* mutants is relatively very low further supporting the fact that SL signaling mediates seedling development via HXK1-independent pathway.

A study provides a glimpse that sugars over-ride the inhibitory effect of Aux in Arabidopsis (Barbier et al., 2015a,b). Intriguingly, growing shoot apex having high sink strength deprives axillary buds of sugars, maintaining their dormancy. However, after decapitation, apical sink is released enabling bud uptake of sugars leading to outgrowth (Barbier et al., 2015a,b). This study also manifested that under low photosynthetic rate (due to low light) displays low sugar level in buds as well as whole plant causing bud suppression and outgrowth and hence, little branching. In contrast, high photosynthetic rate enhance the expression and activity of sucrose transporters and invertases (factors involve in determining sugar sink strength) that enhance the competitiveness of buds for sugars which further enhance bud outgrowth (Barbier et al., 2015a,b). This research was a gamble but proved a masterstroke where sugars act as a first signal for bud outgrowth. Another study set ablaze where exogenous application of sucrose down-regulated the expression of *MAX2* (SL biosynthesis gene) and *BRANCHED 1* (*RhBRC1*) (inhibits axillary bud outgrowth) in *Rosa hybrida* (Barbier et al., 2015a,b) (Fig. 1). Here, the relative expression of *RwMAX3* and *RwMAX4* in stems grown for 96 h with 100 mM Suc or Man was dropped significantly in stems excision. However, no such down-regulation was observed in nodes solving complex quagmire that *RwMAX3* and *RwMAX4* expression is related to Aux depletion and not to Suc (Barbier et al., 2015a,b). In contrast, *RwMAX2* expression displays much early repression when treated with different concentration of Suc (10, 50, 100 and 250 mM) as compared to 100 mM Man, solved an unresolved puzzle where Suc repressed the *RwMAX2* (chief regulatory gene in SL signal transduction) in a concentration-dependent manner (Barbier et al., 2015a,b). Also, the relative expression of *RhBRC1* is down-regulated by Suc (10, 50, 100 and 250 mM) more significantly as compared to 100 mM Man application for 24 h. Considering above researches, Aux and SL came together in positive collaborative framework and sugars acts antagonistically to both Aux and SL to effortlessly promote bud outgrowth (Table 1).

3. Conclusions

Sugars are ubiquitously distributed in plants to maintain overall metabolism. In plant cells, sugars are primarily produced from photosynthesis that functions in building large organic compounds and energy storage to facilitate chemical reactions. Intriguingly, sugars functions as nutrient as well as signaling molecule in plants. The chief function of sugar signals is to facilitate plant growth and development by interacting with other signal transduction pathways. Phytohormones, such as Aux, CK, GA, ET, ABA, BR and SL modulate cell division and differentiation in the presence of sugars. More recently, a direct and indirect interaction has been observed between sugar and hormone signaling pathways where HXK acts as a conserved Glc sensor. In this review, we are focusing on the role of Glc in modulating plant physiological processes via HXK-dependent and independent signaling. This review article also provides very valuable insights of the effects of exogenous application of Glc and different phytohormones on cell proliferation and expansion, seed germination, cotyledon greening and expansion, root development as well as root growth direction and bud outgrowth. However, research is very inadequate till date and needs an extensive research where Glc and phytohormones interact to enhance photosynthesis which further enhances plant productivity. Diverse research via use of intricate techniques is still needed concentrating on Glc sensors and genes wherein they acts upstream or downstream in Glc and phytohormone signaling pathways. Further investigations on Glc and TOR signaling is still needed where Glc activates TOR kinase that functions as chief transcription regulator of genes associated with Krebs cycle, glycolysis, biosynthesis of proteins, amino acids, lipids, nucleotides and ribosome biogenesis.

Contribution

All the authors are equally contributed.

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