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Review Article

Hormonal interactions underlying parthenocarpic fruit formation in horticultural crops

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Abstract

In some horticultural crops, such as Cucurbitaceae, Solanaceae, and Rosaceae species, fruit set and development can occur without the fertilization of ovules, a process known as parthenocarpy. Parthenocarpy is an important agricultural trait that can not only mitigate fruit yield losses caused by environmental stresses but can also induce the development of seedless fruit, which is a desirable trait for consumers. In the present review, the induction of parthenocarpic fruit by the application of hormones such as auxins (2,4 dichlorophenoxyacetic acid; naphthaleneacetic acid), cytokinins (forchlorfenuron; 6-benzylaminopurine), gibberellic acids, and brassinosteroids is first presented. Then, the molecular mechanisms of parthenocarpic fruit formation, mainly related to plant hormones, are presented. Auxins, gibberellic acids, and cytokinins are categorized as primary players in initiating fruit set. Other hormones, such as ethylene, brassinosteroids, and melatonin, also participate in parthenocarpic fruit formation. Additionally, synergistic and antagonistic crosstalk between these hormones is crucial for deciding the fate of fruit set. Finally, we highlight knowledge gaps and suggest future directions of research on parthenocarpic fruit formation in horticultural crops.

Introduction

Flowering plants must go through the process of fertilization to achieve successful fruit setting. However, some plants can produce fruits without fertilization by adopting the parthenocarpy mechanism [1, 2]. Plant hormones are closely associated with parthenocarpy because ovaries that generate parthenocarpic fruits show higher endogenous hormonal contents [3, 4]. The first report on parthenocarpy can be traced back to the late 19th century (Sturtevant in the 1890s), after which Hawthorn observed a tomato (*Solanum lycopersicum*) plant bearing seedless fruits [5]. Since then, parthenocarpic fruit production has received increasing attention from farmers, breeders, and scientists.

The interest in parthenocarpic traits in horticultural crops is increasing because of their importance in improving fruit quality and plant resistance and alleviating preharvest drop. First, fruit seedlessness is a desirable trait for consumers (Fig. 1). In addition, parthenocarpic fruits have a greater flesh content because edible pulp or expended mesocarp replaces the seed and seed cavities [6, 7]. The above features make such fruits ideal for making jelly and other products [7]. Another remarkable aspect of parthenocarpic fruits is the improvement of fruit quality. For example, the browning and bitterness caused by seeds in some horticultural crops, such as avocado (*Persea americana*) and eggplant (*Solanum melongena*), can be avoided by producing parthenocarpic fruits [8–10]. Acidity was shown to be alleviated in gibberellic acid (GA)-treated parthenocarpic apple (*Malus domestica*) fruits. In tomato, the *high fruit set under stress (hfs)* mutant showed better fruit acidity and higher contents of citric acid, proline, glutamate, fructose, glucose, and dry matter than the corresponding wild type [8]. Similarly, *AGAMOUS-LIKE 6 (SlAGL6)* transgenic parthenocarpic plants showed higher red fruit weights and brix levels than wild type plants [9]. N-(2-Chloro-4-pyridyl)-N′-phenylurea (CPPU) induced the production of parthenocarpic cucumber fruit, which showed higher fruit hardness, a crucial trait for prolonging shelf life [10]. The application of 2,4-dichlorophenoxyacetic acid (2,4-D) resulted in parthenocarpic sweet chili pepper (*Capsicum annum*) with greater pungency than pollinated fruits [11].

Preharvest fruit drop is a major problem in the production of soft-fleshed fruits such as tomato and persimmon [12]. Fruit drop can be commonly observed in unpollinated/parthenocarpic fruits. The application of hormones and other growth-promoting compounds to induce parthenocarpic fruits also inhibits fruit drop by increasing the size and strength of peduncles, as observed in cashew (*Anacardium occidentale*) [13]. In line with these findings, the transient overexpression of the *GA20ox* (gibberellin biosynthetic) gene induced

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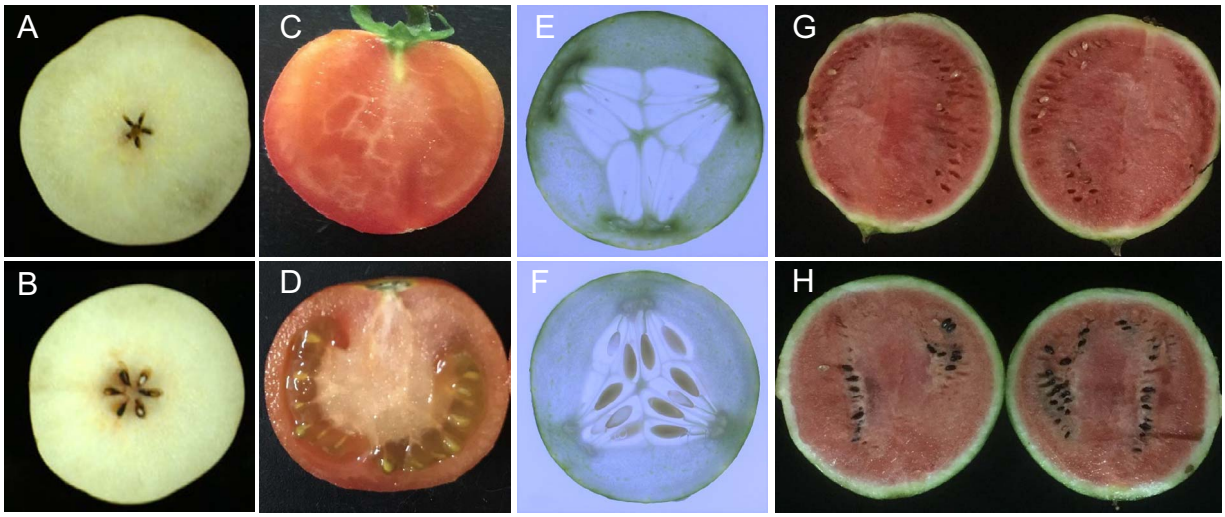

Figure 1. Formation of seedless fruit in horticultural crops by generating parthenocarpic line. (A) and (B) CPPU-induced and pollinated pear fruits. (C) and (D) CPPU-induced and pollinated tomato fruits. (E) and (F) CPPU-induced and pollinated cucumber fruits. (G) and (H) Soft X-ray-induced and pollinated watermelon fruits. (A) and (B) were cited from Niu et al. (2015) [20], and (G) and (H) were cited from Hu et al. (2019) [21] with the authors' permission.

parthenocarpy in pear (*Pyrus communis*) fruit and significantly reduced preharvest fruit drop [14].

Numerous studies have indicated that plants with parthenocarpic fruit may perform better under abiotic and biotic stresses than plants that require fertilization. For instance, parthenocarpic eggplant lines showed high resistance to *Fusarium* wilt disease caused by *Fusarium oxysporum* f. sp. [15, 16]. The parthenocarpic tomatoes of the *SlAGL6* knockout mutant showed enhanced resistance to heat stress [9]. Additionally, *Slagl6* plants bore more fruits than plants of their parental line, which displayed an 83% reduction in overall yield under heat stress [9]. Similarly, the yield of the tomato *hfs* mutant, which produces seedless fruits, was shown to be higher than that of the wild type under high temperature stress [8]. The *pf1* mutant in tomato which lacking a single locus in the *SlHB15A* gene (encoding a classIII homeodomain leucine zipper) produced parthenocarpic fruits under heat stress [17]. A gain-of-function mutation in the *Alq-TAGL1* gene promoted parthenocarpic fruit set in tomato plants, which produced more fruits than the wild type [18]. The mutant plants displayed enhanced salinity tolerance by producing more fruits than the wild type when grown in saline conditions [18]. In addition, some plants like banana showed natural parthenocarpy ability. Significant difference between the expression level of hormone related genes were observed in the unfertilized ovary of seeded and seedless banana cultivar [19]. Therefore, it can be suggested that hormones play major roles in regulating parthenocarpy.

The purpose of this review is to present updated information related to hormone-induced parthenocarpic fruit setting in different horticultural plants. Furthermore, the molecular understanding of hormone-mediated parthenocarpy is extensively discussed. Finally, we highlight knowledge gaps and suggest future directions in the field of parthenocarpic fruit formation research.

The induction of parthenocarpic fruit by hormone application

The application of hormones for inducing parthenocarpy has been in practice since the mid-to-late 20th century [22, 23]. Parthenocarpic fruits are usually influenced by the exogenous application of plant growth regulators, such as auxins (2,4-dichlorophenoxyacetic acid, 2,4-D; naphthaleneacetic acid, NAA), cytokinins (CKs) (forchlorfenuron, CPPU; 6-benzylaminopurine), gibberellic acids (GAs), and brassinosteroids (BR) [24, 25]. Other hormones, such as ethylene and melatonin, have also been reported to be involved in parthenocarpy. In the subsequent sections, we summarize the recent findings related to hormone-mediated parthenocarpic fruit production (Table 1).

Auxin

The treatment of unpollinated ovaries with auxin and its analogs can bypass fertilization and generate seedless (parthenocarpic) fruits in crops plants, such as tomato, cucumber, pear, and watermelon [11, 26]. The synthetic auxin 2,4-D was shown to successfully induce parthenocarpic fruits in tomato and pear [27, 28]. Another synthetic auxin (NAA) was found to be effective in parthenocarpic fruit formation in cucumber (*Cucumis sativus*) [11] and strawberry (*Fragaria vesca*) by prompting the cell division process [29]. In citrus (*Citrus* × *latifolia*) plants, indole-3-acetic acid (IAA) was efficient in inducing fruit setting [30]. More recently, an ovary injection method was used to produce seedless okra (*Abelmoschus esculentus*) [31]. The injection of IAA (100 mg L^{-1}) solution into ovaries at the anthesis stage resulted in 100% pod setting rate and produced seedless okra with better quality [31]. In grapes (*Vitis vinefera*), the application of 4-chlorophenoxyacetic acid (4-CPA), also effectively induced parthenocarpic grape fruits [32]. The efficient induction of parthenocarpic fruits by auxin

Table 1. The application of hormones to induce parthenocarpic fruits in horticultural crops

Hormones	Types	Crop Species	References
Auxin	2,4-D	Tomato, Pear, sweet chili pepper	[12, 28, 56]
	NPA	Tomato	[57]
	NAA	Cucumber, Strawberry, African palm	[4, 11, 29, 58]
	IAA	Okra	[31]
	β-naphthoxyacetic acid	Eggplant	[59]
Brassinosteroids	EBR	Cucumber	[47]
	BZR	Sugar apple	[48]
Cytokinin	BAP	Grapes	[32]
	CPPU	Cucumber, Fig, Pears, Kiwi, Pointed gourd	[11, 36, 37, 60, 61]
Gibberellic acid	GA3	Citrus, Grapes, Loquat, Persimmon, Tomato tree fruit	[44,46,62–65]
	GA4	Pear	[66]
	GA4 + 7	Pear	[45]
	PAC	Pear	[28]
Ethylene	ACC	Tomato	[53]
	1-MCP	Tomato	[51]
	AVG	Zucchini squash	[52]
Melatonin	melatonin	Pear	[6]

suggests the vital role of auxin in fruit setting of various horticultural crops.

Cytokinin

CK was derived from "cytokinesis" due to the specific cytokinesis-promoting ability of this hormone [33]. CK has long been known to play a crucial role in organ development by inducing cell division [33]. The participation of CK in influencing parthenocarpic fruit setting has been reported in many economically important horticultural crops [34]. For instance, the application of *t*-zeatin (ZT), a synthetic CK to the unpollinated ovaries of tomato plants produced parthenocarpic tomato fruits with a fruit setting percentage of 80% [35]. In contrast, unpollinated ovaries treated with water were unable to produce fruits [35]. CPPU has been sprayed over the pear cultivar "Dangshansu" [36]. CPPU induced the plants to produce parthenocarpic pears by increasing the IAA content while suppressing the abscisic acid (ABA) content [36]. Interestingly, the CPPU treatment of unpollinated ovaries resulted in a 10 fold increase in the fruit yield compared with the fruit yield of pollinated ovaries. However, unpollinated ovaries without CPPU treatment failed to generate fruits [36]. CK-induced parthenocarpic fruit production has also been described in cucumber [4, 11], fig (*Ficus carica L.*) [37], and grapes [32].

Gibberellic acid

GA is a key hormone regulating the vegetative and reproductive stages of plants [38–40]. GA is involved in the positive modulation of many fruit-related traits and is vital for the successful production of fruits [41, 42]. Numerous studies related to the participation of GA in parthenocarpy have been reported previously. For example, custard apple production has been shown to be severely hampered by environmental stresses, particularly in pollination stages [43]. To avoid this problem and produce parthenocarpic custard apples, the spraying of GA3 (1500 ppm) has successfully induced seedless parthenocarpic fruit production [43]. GA3 treatment of the "Honeycrisp" apple cultivar also resulted in parthenocarpic fruit production [8]. In the "Early sweet" grape cultivar, the application of GA3 induced parthenocarpic fruit with normal size [44]. In some crops, such as cucumber, treatment with GA3 alone was unable to induce parthenocarpy [11]. However, the GA4 + 7 combinations successfully induced parthenocarpy in cucumber [11]. Similarly, the application of GA4 + 7 to the pear cultivar "Cuiguan" led to higher setting (91.88%) of parthenocarpic pear fruits with a higher sucrose content than the pollinated fruits [20]. In pear, the application of GA3 induced fruit setting; however, all the fruits were lost before harvesting. Interestingly, no fruit abscission was observed in GA4 + 7-treated pear plants [45]. Thus, GA4 + 7, instead of GA3, may play an important role during the pear and cucumber fruit setting. In contrast, exogenous GA3 applications induced fruit setting in the "Rojo Brilliante" persimmon (*Diospyros spp*) cultivar by increasing the inner content of GA1 and GA4 [46].

Brassinosteroid

BRs are a group of steroid hormones that play an essential role in the growth and development of plants. Compared with auxin, GA, and CK, fewer reports are related to BR-induced parthenocarpic fruit setting. In cucumber, the BR analog 24-epibrassinolide (EBR) successfully induced parthenocarpic fruit production when applied at a rate of 0.2 μM [47]. In contrast, the application of the BR biosynthesis inhibitor brassinazole (BRZ) at 0.4 μM caused a significant reduction in ovaries setting fruits, but this could be rescued by treatment with 0.2 μM EBR; however, the treatment with a high concentration of BRZ (4 or 40 μM) completely abolished the fruit setting capacity [47]. More recently, the application of another BR analog, brassinolide, to sugar apple (*Annona Squamosa L.*) trees produced high-quality parthenocarpic fruits [48]. These reports indicate the potential of BRs' in producing

parthenocarpic fruit and provide grounds for considering the role of these vital biomolecules in inducing early fruit setting in different horticultural crops.

Ethylene

Ethylene plays well-documented role in postharvest biology and plant sexual determination [49, 50]. The negative role of ethylene in fruit set has been reported previously. For instance, the application of 1–methylcyclopropene (1-MCP), an ethylene inhibitor, to unpollinated tomato ovaries significantly reduced the ethylene content and facilitated the parthenocarpic fruit setting [51]. In zucchini (*Cucurbita pepo*), the parthenocarpic ability of different cultivars is dependent on the internal ethylene level [52]. The parthenocarpic line "Cavili" showed lower ethylene content, while the nonparthenocarpic line "Tosca" showed a higher level of ethylene in the fruits. Aminoethoxyvinylglycine (AVG), the ethylene biosynthesis inhibitor, also increased parthenocarpic fruit production by suppressing ethylene production in unpollinated ovaries [52]. The application of 1-aminocyclopropane-1-carboxylic acid (ACC) (precursor of ethylene biosynthesis) to tomato ovaries suppressed fruit setting and highlighted the negative role of ethylene [53].

Melatonin

Melatonin (*N*-acetyl-5-methoxytryptamine) was first identified as an animal hormone in frogs [54]. Melatonin was first reported in plants in 1955, and since then, extensive research has been carried out to investigate its role in Plantae [54, 55]. The function of melatonin in parthenocarpic fruit formation had been reported only in pear [6]. Spraying exogenous melatonin (100 μM) on the unpollinated flowers of the pear cultivar "Starkrimson" induced parthenocarpic fruit of a similar size to pollinated fruits. Additionally, the melatonin-induced fruit displayed better nutritional values than the pollinated fruits [6].

Hormonal regulation of parthenocarpic fruit formation

The role of auxin in parthenocarpic fruit formation

Auxin, the hormone which is mobile in nature, regulates plant development mainly via its biosynthesis, transportation, and signaling/perception [67, 68]. The specific roles of auxin in parthenocarpic fruit setting are discussed below. The involvement of auxin biosynthesis, transport, and signaling genes in regulating parthenocarpic fruit formation is shown in Table 2.

Auxin biosynthesis

Thus far, several auxin biosynthesis pathways such as IAOx (indole-3- acetaldoxime), IAM (indole-3-acetamide), and Trp-IPyA (tryptophan-indole-3-pyruvic acid), have been documented. Accordingly, most of the available literature has only reported the role of the Trp-IPyA pathway in parthenocarpic fruit setting. *TRYPTOPHAN AMINOTRANSFERASE OF ARABIDOPSIS* (*TAA1*) genes initiate the deamination of Trp and convert it into IPyA. Following that, the irreversible and rate-limiting reaction catalyzed by YUCCA genes (containing flavin-containing monooxygenases) ensures the decarboxylation of IPyA into IAA [69–72].

In loquat (*Eriobotrya japonica*), *YUCCA10* was significantly upregulated in GA3-treated ovaries but suppressed in untreated ovaries [65]. Similarly, in cherry, *PavYUCCA10* was induced in GA3-treated parthenocarpic fruits [73]. The auxin biosynthesis genes *SlTAR1*, *ToFZY2*, and *ToFZY3 (YUCCA* homologs *FLOOZY)* were substantially upregulated in CRISPR-mediated knockout lines of tomato *SlAGL6*, which showed a parthenocarpic phenotype [74]. The mRNA levels of *SlTAR2, ToFZY1*, *ToFZY2*, and *ToFZY5* were amplified many fold in comparison to control (unpollinated) tomato ovaries [75]. The *PARENTAL ADVICE-1* (*PAD-1*) gene in eggplant shares similarities with the *Arabidopsis VAS1* gene, which coordinates the reverse reaction of Trp-IPyA in the IAA biosynthesis pathway. A loss-of-function mutation in *PAD-1* increased IAA accumulation in unpollinated ovaries, thus generating parthenocarpic eggplant fruit [76]. A significant difference in IPyA contents was observed in wild type and *pad-1* mutant plant ovaries. The function of the *PAD-1* gene was also verified in tomato and pepper plants. *PAD-1* antisense plants showed higher IAA contents in the ovaries at the anthesis stage and yielded normal sized parthenocarpic tomato and pepper fruits [76]. Interestingly, it has been suggested that the higher generation of auxin in the anthesis stage serves as an early signaling element that facilitates the production of parthenocarpic fruit by unfertilized ovaries. For instance, in normal pollinated ovaries, the *PAD-1* gene may be involved in the homeostasis of IAA and thus does not affect the normal transition of the ovary into fruit. Additionally, the pollination-mediated suppression of the *PAD-1* gene could be the reason for normal fruit setting [76]. On the other hand, the *PAD-1* gene in unpollinated ovaries hampers the biosynthesis of IAA by reversing the reaction of Trp-IPyA. Knockout of the *PAD-1* gene nullifies its adverse effects on IAA biosynthesis in unpollinated ovaries, resulting in normal-sized parthenocarpic fruit (Fig. 2). The *ToFZY2* and *ToFZY3* genes were significantly upregulated in fertilized ovaries of wild type and the unfertilized ovaries of *pf1* tomato mutant [17]. All of the above evidence supports the notion that the generation of parthenocarpic fruits by unfertilized ovaries largely depends on higher endogenous IAA content.

Auxin transportation

Auxin is a polar transport molecule and requires carriers to reach its target tissue [77]. Three prominent *PIN-FORMED* (*PIN*), *AUX1/LAX* (auxin influx carriers), and the *B subfamily of ATP-binding cassette* (*ABCB*) transporters gene families carry auxin in plants, passing through different hubs and phases. Among these three families,

Table 2. Involvement of auxin biosynthesis, transport, and signaling genes in regulating parthenocarpic fruit formation

Auxin	Crops	Plant materials	Genes	References
Biosynthesis genes	Cherry	GA3 application	*PavYUCCA10* ↑	[73]
	Tomato	CRISPR/Cas9 knockout of *SlAGL6* gene	*SlTAR1*, *toFZY2*, and *toFZY3* ↑	[74]
	Eggplant	Identification of mutant by a forward genetic screen	*pad-1* ↓	[76]
	Tomato	RNAi-generated antisense plants	*PAD-1* ↓	[76]
	Eggplant	RNAi-mediated silencing	*PAD-1* ↓	[76]
	Tomato	hydra mutant (*SPL/NZZ*)	*ToFZY3* ↑	[82]
Transport/Carriers genes	Tomato	RNAi-mediated suppression	*Aucsia* ↓	[85]
	Tomato	*hydra* mutant (*SPL/NZZ*)	*SlPIN1*, *SlPIN4* ↓	[82]
	Tomato	RNAi system	*SlPIN8* ↓	[84]
Signaling transduction genes	Strawberry	Loss-of-function mutation in *fverga1–1* gene	*FveARF8* ↓	[97]
	Tomato	*Pf1* mutant	*SlARF7* ↓	[17]
	Tomato	RNAi silencing of *SlARF7*	*SlARF5*, *SlARF7*, *SlARF8b* ↓	[56]
	Tomato	Heterologous overexpression	*PpIAA19*, *CsTIR1* and *CsAFB2* ↑	[100, 103]
	Tomato	*tap-3 (Tomato APETALA3)* loss of function mutant	*SlARF7*, *SlARF8* ↓	[104]
	Cucumber	Induced transcription in a parthenocarpic line	*AUX 22A-like-1*, *AUX22B-like-2* and *AUX 28-like* ↑	[4]
	Tomato	RNAi silencing of *SlARF5*	*SlARF9*, *SlIAA1*, *SlIAA2* and *SlIAA14* ↓	[102]
	Zucchini	Auxin treatment	*ARF5* and *ARF18* ↓	[105]

↑ = Upregulated, ↓ = Downregulated.

PIN genes are major auxin efflux transporters and instrumental in homeostasis and tightly regulate the auxin-related phenotype in plants [78, 79]. The *AUX1/LAX* genes are key auxin influx carriers, mainly responsible for regulating the intercellular transport of auxin [80]. Plant *ABC* transporters are divided into eight subfamilies (A-I) based on the presence of TMDs, amino acid sequence and function [81].

In the parthenocarpic tomato *hydra SPOROCYTELESS/NOZZLE (SPL/NZZ)* mutant, *SlPIN1*, *SlPIN2*, and *SlPIN4* gene expression was enhanced in comparison to that in the wild type, which indicated the positive role of *PIN* family genes in parthenocarpic fruit formation [82]. However, the silencing of *SlPIN4* also resulted in successful fruit setting and the production of parthenocarpic tomato fruits in the absence of pollination [83].

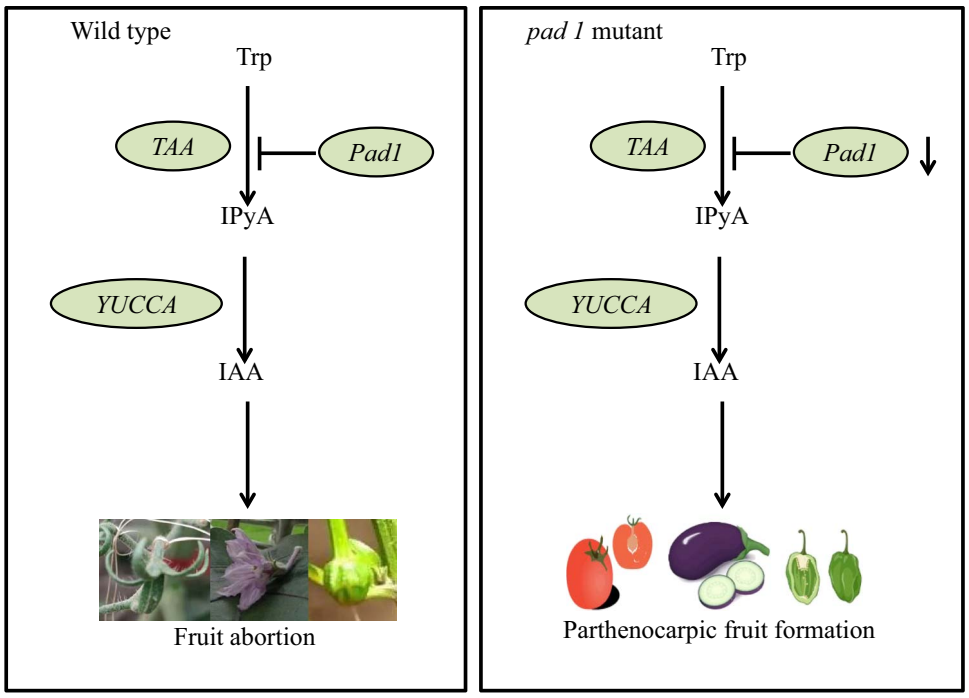

Figure 2. The regulatory role of the auxin biosynthesis pathway in parthenocarpic fruit formation in Solanaceae crops. The PAD-1 gene in unpollinated ovaries reverses the catalytic reaction transforming Trp to IPyA, which further hampers the biosynthesis of IAA. This ultimately results in very small fruit or a complete absence of the ovary (A). The unpollinated ovary of the pad-1 loss-of-function mutant maintains the normal production of IAA via the Trp-IPyA pathway governed by the TAA and YUCCA genes. Enhanced accumulation of IAA in unpollinated ovaries produces regular sized parthenocarpic fruits (B).

The abnormal male gametophytes of *SlPIN8* antisense lines also achieved in parthenocarpic fruit setting. The expression of genes (*TomA108, Ms10* [35], and *5B-CRP*) regulating anther and tapetum development was suppressed in *SlPIN8* RNAi lines [84]. Notably, similar IAA contents were observed in wild type and *SlPIN8*-silenced plants [84]. This research suggests the complex roles of *PIN* transporter genes in regulating parthenocarpic fruit sets.

ABCB family genes also serves as auxin transporters, and their role in fruit set has been highlighted recently [81]. The *SlABCB4* gene was characterized in tomato based on its higher expression during early fruit developmental stages [81]. The transient expression of the *SlABCB4* gene in tomato plants increased endogenous IAA contents many fold relative to the wild type. Therefore, it can be proposed that the *SlABCB4* gene could facilitate fruit development via auxin distribution. However, the study did not conduct a parthenocarpic assay to analyze how this gene functions in the absence of fertilization [81]. From the above observations, the *SlABCB4* gene could be categorized as a positive regulator of fruit set and may function differently than the other reported auxin transporters, such as *PIN4* and *PIN8*. More research is required to functionally characterize and further study the involvement of this gene and other genes of the *ABCB* family in parthenocarpic fruit setting. The *AUX1/LAX* family genes encode the primary auxin influx carriers in plant cells; however, the direct involvement of *AUX1/LAX* in parthenocarpic fruit formation has yet to be revealed.

Aucsia (auxin cum silencing action), which does not belong to any of the three auxin transporter families, was also shown to be involved in parthenocarpic fruit formation [85]. The silencing of the *Aucsia* gene in tomato plants led to higher IAA contents and parthenocarpic fruit production. Interestingly, the *Aucsia* gene showed increased sensitivity to exogenous auxin transport inhibitor N-1-naphthylphthalamic (NPA), and its silencing arrested the transport of auxin from unpollinated ovaries many fold. Therefore, it can be suggested that the reduction of auxin transport could be attributed to *Aucsia* gene loss-of-function in the tomato plant, which ultimately ensured parthenocarpic fruit setting [85].

Auxin signaling transduction

The dynamic ability of auxin to tune growth activities largely depends on auxin signaling genes. Relative to auxin biosynthesis and transportation, the roles of auxin signal transduction genes in parthenocarpic fruit formation have been intensively studied in parthenocarpic fruit formation. There are three major auxin signaling gene families, namely the *auxin/Indole-3-Acetic Acid* (*AUX/IAA*), transport inhibitor response 1/auxin signaling f-box proteins (*TIR1/AFB*), and auxin-responsive factor (*ARF*) families [86–88]. Among these three gene families, *AUX/IAA* genes are categorized as early auxin-responsive genes and involved in the fine tuning of auxin levels [89]. These *AUX/IAA* genes are responsible for regulating various important traits such as fruit development and postharvest biology [90]. The *TIR1/AFB* auxin co-receptors mediate diverse responses to auxin, and are mainly involved in the seed abortion, embryo development and fruit setting [87]. *ARF* gene family generally function as transcriptional activator or repressor following their binding with the promoter region of auxin-responsive genes to regulate various plant developmental processes [91, 92].

Recently, the influence of *AUX/IAA* genes on fruit set has been highlighted in several reports. For example, in tomato, the knockdown of the *SlIAA9* gene resulted in parthenocarpic fruit formation [93–95]. The transcriptional inhibition of the *SlIAA9* gene rescued the growth of unpollinated ovaries. Additionally, the induction of the expression of *SlTAR1, ToFZY,* and *ToFZY5* and the suppression of *SlAGL6* (a key negative regulator of fruit set) in *SlIAA9*-silenced tomato plants could be possible cause of parthenocarpic fruit formation [93]. In contrast, Mignolli et al. revealed that *SlIAA2* and *SlIAA14* displayed upregulated expression patterns in the tomato *pro* (DELLA gene loss of function) mutant under 4-CPA treatment and in pollinated ovaries [96]. The induction of *SlIAA2* and *SlIAA14* transcription in the *pro* mutant yielded seedless tomato fruits, indicating the positive involvement of these genes in parthenocarpic fruit set [96]. In cucumber, the expression levels of several auxin signal transduction genes (*AUX 22A-like-1, AUX22B-like-2,* and *AUX 28-like*) were higher in the parthenocarpic DDX line than in the nonparthenocarpic ZK line [4]. In strawberry, suppressed expression of the *FveIAA4* gene was observed in the receptacles of wild type and *srl-1* natural parthenocarpic mutant plants [97]. Considering all of these findings together, it can be inferred that although *AUX/IAA* genes belong to same gene family, they show functional variation, particularly at the fruit setting stage. However, research on this topic is still scarce and therefore requires further experimental work to illuminate the role of these genes in parthenocarpic fruit settings.

The *TIR1/AFB* genes play central roles in the complex auxin signaling pathway [98], and their function in parthenocarpic fruit setting has been well studied in some horticultural crops. In tomato, the overexpression of the *SlTIR1* gene generated parthenocarpic fruit. Simultaneous flower and fruit development were also observed; because of this, the gap between the stigma and stamen became wider, which caused the failure of normal self-pollination [99]. The loss of pollination and lack of endogenous hormone quantification left the open question of how the *SlTIR1* gene induces early fruit set. The roles of *TIR1* along with the *AFB2* gene in orchestrating parthenocarpic fruit formation before pollination have been well studied in cucumber by Xu et al. [100]. In this study, the heterologous overexpression of two auxin receptor genes (*CsTIR1* and *CsAFB2*) in tomatoes resulted in an early fruit set phenotype before anthesis. The *SEEDSTICK* gene, regulating fertilization and seed

development, was suppressed in *CsTIR1* and *CsAFB2* transgenic lines. Although the researchers did not quantify endogenous hormone contents, the apparent increase in the sensitivity of *CsTIR1* and *CsAFB2* genes to exogenous GA3 and BR provided clues about their involvement in GA3- and BR-mediated parthenocarpy in cucumber.

The roles of *ARF* in parthenocarpy have been discussed previously in different horticultural crops. In eggplant, lower expression of the *SmARF8* gene was detected in the unfertilized ovaries of the *13–3* mutant line, which yielded parthenocarpic fruit [101]. Furthermore, in *SmARF8* antisense plants, parthenocarpic fruit was generated by inhibiting conjugation with *AUX/IAA* transcriptional repressors. Hence, it can be suggested that *SmARF8* could be associated with the negative regulation of fruit set in the absence of fertilization. However, the overexpression of the *SmARF8* gene also induced parthenocarpy. Likewise, the exogenous application of auxin induced the expression of the *SmARF8* gene in unfertilized ovaries and led to the formation of parthenocarpic fruit in eggplant and tomato [96, 101]. The parthenocarpic fruit phenotype observed in the *SmARF8* overexpressing plants might have resulted from the autoregulation of transcription via a negative feedback loop. In strawberry, the *fvearf8–1* mutant failed to produce parthenocarpic fruit [97], which indicated the complex mechanism of the *ARF8* gene. In tomato, another *ARF* gene (*SlARF5*) was found to be responsible for regulating parthenocarpy. Higher transcriptional activity of *SlARF5* was recorded in emasculated ovaries of tomato plants, which failed to produce fruit [102]. The suppressed expression of *SlARF5* in the pollinated ovaries of the wild type suggested that *SlARF5* gene suppression is required for normal fruit setting. *SlARF5* RNAi plants yielded parthenocarpic fruits by suppressing the transcription of auxin signaling genes such as *SlARF9, SlIAA1, SlIAA2,* and *SlIAA14* [102]. However, the exact role of the auxin signaling pathway in parthenocarpic fruit formation needs to be explained by future research.

The role of gibberellic acid in parthenocarpic fruit formation

The roles of GA are instrumental in plants, from germination to fruit development and ripening. The activity of GA largely depends on its biosynthesis, catabolism, and signaling genes [106]. The involvement of GA in the parthenocarpic fruit setting has been reported in various horticultural crops, such as cucumber, tomato, and pear.

Gibberellic acid biosynthesis

The GA biosynthesis process begins with the conversion of geranylgeranyl diphosphate into *ent*-kaurene. This step is catalyzed by two enzymes: ent-copalyl diphosphate synthase (CPS) and *ent*-kaurene synthase (KS). Next, two other enzymes (*ent*-kaurene oxidase (KO) and *ent*-kaurenoic acid oxidase (KAO)) convert *ent*-kaurene into GA12, which is the first active GA in the GA biosynthesis pathway. Furthermore, two divergent pathways leading to the biosynthesis of GA1 and GA4 are driven by the GA13-oxidase (GA13ox), GA 20-oxidases (GA20ox), and GA 3-oxidases (GA3ox) enzymes [106]. The concentrations of these active GAs depend on the primary GA deactivation enzyme GA2-oxidase [106]. *GA2ox* (a major GA degradation gene) encodes GA2ox, which catalyzes the degradation of GA1 + 4 (active GA) and is crucial for GA homeostasis in plants [107]. Here, we precisely discuss the role of GA biosynthesis and degradation genes in inducing parthenocarpic fruit formation.

Exogenous application of GA to unpollinated ovaries produced parthenocarpic fruits indicated that GA plays a vital role in this process. In pear, GA biosynthesis gene *GA20ox* was dominantly expressed in pollinated fruits [14]. The overexpression of the *SlGA20ox* and *PbGA20ox* genes in tomato and pear, respectively, increased GA4 levels and resulted in the production of parthenocarpic fruits [14]. The tomato *APETALA3* loss-of-function mutant displayed intensive cell division and expansion activity and ultimately produced parthenocarpic fruit [104]. Fruit set was accompanied by the upregulation of GA biosynthesis genes (*SlGA20ox1, SlGA20ox2, and SlGA20ox3*) and the downregulation of GA deactivation gene *SlGA2ox1* [104]. In addition, *SlGA2ox* RNAi plants displayed enhanced levels of active GA1 and GA4 in the stem and ovaries which led to the production of parthenocarpic fruits in tomato [107]. Together, these findings demonstrate the participation of GA biosynthesis and degradation in regulating parthenocarpic fruit set. However, in some species, such as pear, the GA level was not observed to increase in the unpollinated ovaries that produced parthenocarpic fruit [36]. Therefore, it can be suggested that other unknown players can replace the role of GA biosynthesis in inducing parthenocarpic fruit set laying a foundation for further research.

Gibberellic acid signaling transduction

The regulation of GA metabolism via GA signaling pathway is vital for GA homeostasis. *DELLA* and *GID1* (*GA INSENSITIVE DWARF1*) are two primary components of the GA signaling pathway. *DELLA* is considered to be a key negative regulator of GA because of its involvement in the induction of *GA2ox* genes (GA inactivation). *GID1*, on the other hand, is an important GA perception gene and an activator of the GA biosynthesis gene family (*GA20ox and GA3ox)* [106]. The plant developmental processes governed by the *DELLA-GID1* module has been explained previously [108]. In addition, a series of studies have elucidated the role of the GA signaling pathway in parthenocarpic fruit setting.

In tomato, the RNAi-mediated silencing of the *SlDELLA* gene enhanced GA biosynthesis gene expression and generated parthenocarpic fruits [109]. In contrast, blocking pollination in the wild type plants enhanced *SlDELLA* expression, resulting in the death of ovaries [109]. In another study, the mutation in $pro^{\Delta GRAS}$, a DELLA *pro* mutant with a unique recessive allele was identified

[110]. The mutation in $pro^{\Delta GRAS}$ was caused by a missing transposon in the VHIID domain of the GRAS DELLA protein. The $pro^{\Delta GRAS}$ mutant displayed a defective fertilization phenotype mainly because of the development of a long style and produced parthenocarpic tomato fruit. The pollen tubes of $pro^{\Delta GRAS}$ plants stopped growing immediately post-germination, and the constitutive production of GA could be the reason for the parthenocarpic fruit setting phenotype [110]. A more comprehensive description of DELLA-mediated parthenocarpic fruit setting was presented by Shinozaki et al. [111]. A multiomics approach (transcriptome, proteome, metabolome) was employed to study the detailed mechanism underlying *pro*-mediated parthenocarpy in tomatoes. The research revealed intensive metabolic activity in the ovaries of the *pro* mutant. Specifically, metabolites such as hexose, hexose phosphate, and organic acids were triggered. A carrier of tonoplast sugar boosted the influx of sugar into the vacuole of ovaries undergoing fruit setting. Furthermore, in the absence of fertilization, the fructokinase enzyme assists in the pulling out of fructose from the vacuole to facilitate the biosynthesis of the cell wall and provide energy prompting ovary growth, thus producing parthenocarpic tomato fruit. The GA content and the gene expression of *SlG20ox* were downregulated in the unpollinated ovaries of the *pro* mutant. This finding indicated that parthenocarpic fruit setting in the *pro* mutant was brought about by the modulation of GA biosynthesis genes and the accumulation of energy metabolites for rapid ovary growth [111]. However, the questions of how the GA cascade positively influences the sugar sink in unpollinated ovaries remains unclear. There may be an element that functions as an energy on/off switch upstream of the GA signaling pathway during the fruit setting stage.

The role of cytokinin in parthenocarpic fruit formation

CK are a group of hormones derived from adenine that actively participate in various signaling pathways and play a central role in many developmental processes [112, 113]. The involvement of CK in fruit set has been investigated and has quickly become a subject of major interest because of the excellent results obtained [4]. The participation of CK biosynthesis- and signaling-related genes in parthenocarpic fruit setting is reviewed below.

Cytokinin biosynthesis

The spatial and temporal biosynthesis of CK largely depends on the homeostasis between synthesis and catabolism [114]. The first step of CK biosynthesis is the production of isopentenyladenine nucleotides, which is catalyzed by adenosine phosphate-isopentenyltransferase (IPT) [115, 116]. A cytochrome P450 monooxygenase (CYP735A) hydroxylates the prenyl side chain of isopentenyl adenosine phosphates to produce *trans*-zeatin-type species. The LONELY GUY (LOG) enzyme converts the nucleotide precursors to their active forms, while CK oxidases (*CKXs*) catalyze the degradation of CK. Plants exhibit four active types of CKs: isopentenyladenine (iP), *trans*-zeatin (tZ), cis-zeatin (cZ) and dihydrozeatin (DZ), along with other inactive precursors such as, *trans*-zeatin riboside (tZR), isopentenyladenosine (iPR), dihydrozeatin riboside (DZR) [115–117]. The involvement of these CKs in parthenocarpic fruit formation has been highlighted in different horticultural crops. In tomato, tZR, IP, DZR, and iPR contents and the expression of CK biosynthesis genes (*lIPT3, SlIPT4, SlLOG6*, and *SlLOG8*) were shown to be sharply induced in CPPU-treated ovaries in the anthesis stage. Conversely, unfertilized tomato ovaries treated with water were found to exhibit low endogenous CK levels and reduced expression of CK biosynthesis genes and consequently failed to produce any fruits [118]. In cucumber, four types of CKs (iP, tZ, cZ, and DZ) showed abundant accumulation in the parthenocarpic line DDX relative to the nonparthenocarpic line ZK. The enhanced expression of CK biosynthesis genes such as *CYP735A1, CYP735A2*, and *LOG1* and decreased expression of the CK dehydrogenase genes *CKX1* and *CKX3* in DDX could be the reason for the high parthenocarpic fruit set ratio in DDX [4]. Enhanced level of CK (DZ and iP) were recorded in RNAi-generated lines of *TOPLESS1 (SlTPL1)* gene, produced parthenocarpic tomato [119].

Cytokinin signaling transduction

CK is a low-molecular-weight hormone that interacts with an array of other hormones via the multistep phosphorelay system (MSP) consisting of catalytic receptors-sensor histidine kinases (HKs), phosphotransmitters (HPts), and transcription factors-response regulators (RRs) [120]. The CK signaling pathway involves the His-Asp phosphorelay, which is similar to the His-Asp phosphorelay identified in the bacterial two-component signaling system [121]. The His-Asp phosphorelay helps bacteria sense and respond to various environmental stimuli. In plants, the two-component signaling system involves four phosphorylation events in which histidine and aspartate residues are interchanged [122]. There are two types of RR genes: type-B RRs and type-A RRs, which regulate CK signaling in the plant during multiple developmental processes [123–125]. Typically, type-A RR genes are categorized as negative feedback regulators of CK signaling. The type-B RRs genes activate the transcription of type-A RR genes following CK application [122, 125]. The multistep histidine kinase (*AHK*) genes are primary CK receptors composed of three conserved domains: the CHASE, histidine kinase, and receiver domains [125]. Here, we discuss the participation of these CK signaling genes in prompting parthenocarpic fruit formation.

In cucumber, enhanced transcription of the CK signaling gene *CsRR8/9b* was recorded in both CPPU-induced and natural parthenocarpic fruits [4]. Without CPPU treatment, the expression of *CsRR8/9b* genes decreased greatly in the non-parthenocarpic line ZK, whereas other CK signaling genes, such as *CsRR3/4a, CsRR3/4b,*

CsRR8/9a, and *CsRR8/9c*, were strongly induced [4]. This suggested negative roles of the *CsRR3/4a*, *CsRR3/4b*, *CsRR8/9a*, and *CsRR8/9c* genes in regulating cucumber fruit set in the absence of fertilization. Similarly, in *F. carica* L. plants, three CK signaling genes, *comp25194_c0*, *comp22053_c0*, and *comp16589_c0*, displayed persistently upregulated expression in CPPU-treated unfertilized ovaries that later produced parthenocarpic fruits [37]. Alternatively, the ABA biosynthesis gene *NCED* (*comp26438_c0*) and the ABA signaling gene *AFB* (*comp15261_c1 and comp30505*) exhibited reduced expression in CPPU-treated flowers and receptacle tissue [37]. In pear, genes modulating CK signaling, including *PbAHK4*, *PbAHK5-like*, *PbAHP5-like*, *PbRR9-like*, and *PbRR10-like*, were triggered in response to exogenous CPPU [36]. It was revealed that the *PbRR9-like* gene bound to the promoters of *PBNCED6* and *PbYUCCA4* to suppress the activity of *PbNCED6* and stimulate that of *PbYUCCA4* [36]. Under CK application, curtailed ABA biosynthesis and enhanced auxin biosynthesis could be responsible for the unfertilized ovary growth that later yielded parthenocarpic pear fruits [36]. Altogether, the above studies confirm the involvement of CK signaling genes in parthenocarpic fruit formation. However, these genes have yet to be functionally characterized.

The role of ethylene in parthenocarpic fruit formation

Ethylene is a gaseous molecule and can diffuse quickly from its site of synthesis. As discussed above, the application of exogenous ethylene negatively regulates fruit set. Below, we summarize how ethylene biosynthesis and signaling regulate parthenocarpy in different horticultural plants.

Ethylene biosynthesis

In ethylene biosynthesis pathway, ACC synthase (ACS) enzyme initiates S-adenosyl-L-methionine (SAM) conversion into ACC. Then, ACC oxidase (ACO) catalyzes the transformation of ACC into ethylene [126, 127]. The genes regulating these enzymes have become a subject of intensive research, as they play crucial roles in regulating parthenocarpic fruit settings. For example, the expression of ethylene biosynthesis genes (*CpACS4*, *CpACS6*, and *CpACS7*) was shown to be high in unpollinated zucchini ovaries [52]. In contrast, suppressed transcriptional activities of these genes were recorded in pollinated ovaries. The exogenous application of the ethylene biosynthesis inhibitor AVG to unpollinated zucchini ovaries yielded parthenocarpic fruits [52, 128]. In tomato, the enhanced production of endogenous ethylene in unpollinated ovaries was associated with higher expression of the ethylene biosynthesis genes *LeACS6*, *LeACO2*, *and LeACO4* [53]. On the other hand, lower transcription of the *LeACS6*, *LeACO2*, and *LeACO4* genes was observed in the unpollinated ovaries of the parthenocarpic *iaa9* mutant [53]. Similarly, decreased expression of *ACO4* gene was recorded in the tomato parthenocarpic mutant *pf1* [17]. The above results suggest a negative role of ethylene biosynthesis in regulating fruit sets. However, the study from Matsuo et al. reported that no significant difference in ethylene contents between wild type and *pad-1* eggplant mutant plants [76]. As explained above (Auxin biosynthesis section), the *pad-1* mutant generated normal-sized parthenocarpic fruit, whereas blocking ethylene production with ethylene inhibitors or by generating loss-of-function mutants of ethylene biosynthesis genes resulted in the production of small parthenocarpic fruits [53, 76]. To determine how ethylene participates in modulating fruit size, Xin et al. demonstrated that the complete inhibition of ethylene biosynthesis negatively affected cell division and thus resulted in the production of miniature fruit even when fertilization occurred [129]. This can also be explained by a study of Martínez et al. [52], who observed basal synthesized ethylene level at the anthesis stage in fertilized ovaries. Therefore, it can be suggested that ethylene functions in a dose-dependent manner during the anthesis stage to regulate fruit setting and the size of fruit.

Ethylene signaling transduction

Ethylene signaling mainly include the ethylene insensitive 1, 2, and 3 (EIN1, 2, 3), EIN3-like (EIL), constitutive triple response 1 (CTR1), and ethylene response factors (ERFs) [130]. In zucchini, an increase in the transcription of ethylene signaling and perception genes, such as *CpETR1*, *CpERS1*, *CpCTR1*, *CpCTR2*, *CpEIN3.1*, and *CpEIN3.2* triggered the abscission of ovaries and caused fruit abortion [52]. The tomato ethylene-insensitive mutant *Sletr1* produced parthenocarpic fruits, and early fruit setting was associated with the blockage of ethylene perception in unfertilized flowers [53]. The expression of ethylene signaling genes also decreased greatly in ovaries of the *Sletr1* mutant [53]. In cucumber, a major QTL designated Parthenocarpy 2.1 (Parth 2.1) was identified in 145 F2:3 families derived from a cross of EC1 (a parthenocarpic inbred line) and 8419 s-1 (a nonparthenocarpic inbred line). The Parth 2.1 comprised 57 candidate genes. Among these 57 genes, *CsEIN1*, an ethylene signaling gene, was found to be upregulated in unfertilized ovaries [26]. The transcription of *SlEIL2* and *SlERF1* substantially decreased in the *pf1* parthenocarpic tomato mutant [17]. A better understanding of how ethylene signaling genes participate in parthenocarpy was provided by Wang et al. [131]. It was shown that the ethylene signaling gene *PbEIL1* could bind to *SENESCENCE-ASSOCIATED CYSTEINE PROTEINASE 1* (*PbCysp1*) in the parthenocarpic pear cultivar "1913" and caused ovule senescence. The overexpression of *PbEIL1* in tomato increased the senescence of transgenic seeds by inducing the expression of *PbCysp1*. This indicated that *PbEIL1* acts upstream of *PbCysp1* and is a key player in the production of seedless pear fruit [131]. Despite the number of reported-lines of evidence, the complex roles of ethylene signaling genes are far from clear and need to be elucidated in different horticultural species.

Brassinosteroid

The genes involved in BR biosynthesis and signaling have mainly been identified in *Arabidopsis* and tomato [132]. BR biosynthesis pathway genes such as BR-6-oxidase (*BR6ox1)* and sterol methyltransferase (*SMT*) have been shown to regulate parthenocarpic fruit set, as described below. In BR signaling pathway, BRs are perceived by membrane-localized leucine-rich-repeat-receptor kinase BRI1 or by the BRI1-like homologs, BRL1 and BRL3 [133]. After binding to BRs, BRI1 and its co-receptor BRI1-Associated Receptor Kinase 1 (BIRK1) phosphorylate each other. This results in triggering a cytoplasmic phosphorylation/dephosphorylation signaling cascade which deactivates the GSK3-like kinase BRASSINOSTEROID INSENSITIVE 2 (BIN2) through dephosphorylating [133]. Additionally, the role of BR signaling genes in parthenocarpic fruit formation is briefly highlighted.

In cucumber, the exogenous application of EBR to the cucumber Jinchun No. 4 cultivar successfully induced parthenocarpic fruit by suppressing the expression of *BR6ox1* [47]. In contrast, the application of brassinazole upregulated the expression of *Br6ox1,* leading to the abortion of unpollinated ovaries. In addition, the application of EBR to unfertilized ovaries boosted the transcription of *SMT* and cycling-related genes (*CycA* and *CycB*), which are regulators of cell division. A similar gene expression profile was observed in fertilized ovaries [47]. These findings imply that BR biosynthesis positively affects parthenocarpic fruit set in cucumber. The "EC1" natural parthenocarpic line of cucumber was investigated to identify hormone-related genes regulating its fruit set [3]. The study revealed that most of the genes differentially expressed during the fruit setting stage of the EC1 line were BR genes. For example, BR signaling genes such as *BIN1-associated receptor kinase 1* (*BIRK1a*), *BIRK1b,* and *BIRK1c* were highly expressed and could be vital for successful cucumber fruit set [3]. However, in tomato, the application of BR failed to induce parthenocarpic fruits [24, 109], which led us to infer that BR efficiency varies among crops. Regarding to these positive roles of BR biosynthesis and signaling genes, research is relatively scarce, and more attention will be required to study these molecules in detail.

Melatonin

In contrast to the general roles of auxin and GA in inducing parthenocarpy in different horticultural crops, a positive role of melatonin has been reported only in pears. The transcription levels of *cyclin* and *expansin* genes were shown to be enhanced after the melatonin treatment. Fruit setting is an energy-consuming process in plants and requires essential nutrients at higher levels. Studies have suggested that genes involved in photosynthesis and carbohydrate metabolism facilitate the influx of necessary nutrients into unfertilized ovaries of apple, cherry, and fig to produce fruits [134–139]. Accordingly, the application of melatonin in pear promoted photosynthetic activities, which resulted in the increased movement of sugar from "source" to "sink" sites. The transcription of genes involved in sucrose synthesis was promoted by melatonin treatment [6]. However, the researcher did not quantify endogenous melatonin contents or analyze the expression of melatonin biosynthesis genes. Further research related to melatonin biosynthesis or signal transduction will contribute to our understanding of melatonin-mediated parthenocarpic fruit setting.

Other factors influencing parthenocarpy via hormonal regulation

In addition to the direct participation of hormones, other factors, such as sugars and flavonoids, have been found to regulate parthenocarpic fruit formation by affecting the balance of plant hormones.

Sugars

Sugars provide energy inputs to plants under adverse and customary conditions to regulate vital developmental processes, including fruit set [137, 138]. The cell wall invertase (CWIN) gene *LIN5* plays a central role in hydrolyzing sucrose to produce glucose, while the invertase inhibitor (*INH1)* gene is a negative modulator of *LIN5* in tomato plants [139]. The breakdown of sucrose into glucose by *LIN5* induces metabolic activities and is crucial in the transformation of the ovary into a fruit; however, *INH1* negatively regulates fruit set because it compromises *LIN5* activity [139]. RNAi-mediated silencing of the *INH1* gene significantly increased the fruit setting percentage by eliciting an influx of key sugar metabolites into the ovary [140]. In *INH1*-silenced plants, the *LIN5* gene and two auxin biosynthesis genes, *ToFZY1* and *ToFZY6,* were upregulated. On the other hand, the *SlIAA9* and *SlARF7* genes, which are negative regulators of fruit set, displayed suppressed expression in *INH1*-silenced plants [140]. More recently, the positive role of sugars (sucrose and fructose) in parthenocarpic fruit formation was also proven in cucumber [141]. Parthenocarpic fruit formation was inhibited by limiting the photosynthetic activity of leaves but was recovered by the exogenous application of sucrose and fructose. Under sucrose and fructose treatment, the auxin signaling gene *IAA14* and the CK signaling gene *RR17* were upregulated. Additionally, an obvious increase in endogenous sugar contents after sucrose and fructose supplementation was observed [141]. The above results clearly demonstrated the positive functions of sugars in fruit setting and showed that they could be used to increase the parthenocarpic fruit yield in different horticultural crops. A model depicting parthenocarpic fruit production following exogenous sugar treatment and *INH1* and *CWIN* gene-mediated sugar influx is shown in Fig. 3. Sugar functions in coordination with auxin and CK to intensify the metabolic activities (cell division and expansion) of unfertilized ovaries, consequently ensuring parthenocarpic fruit formation.

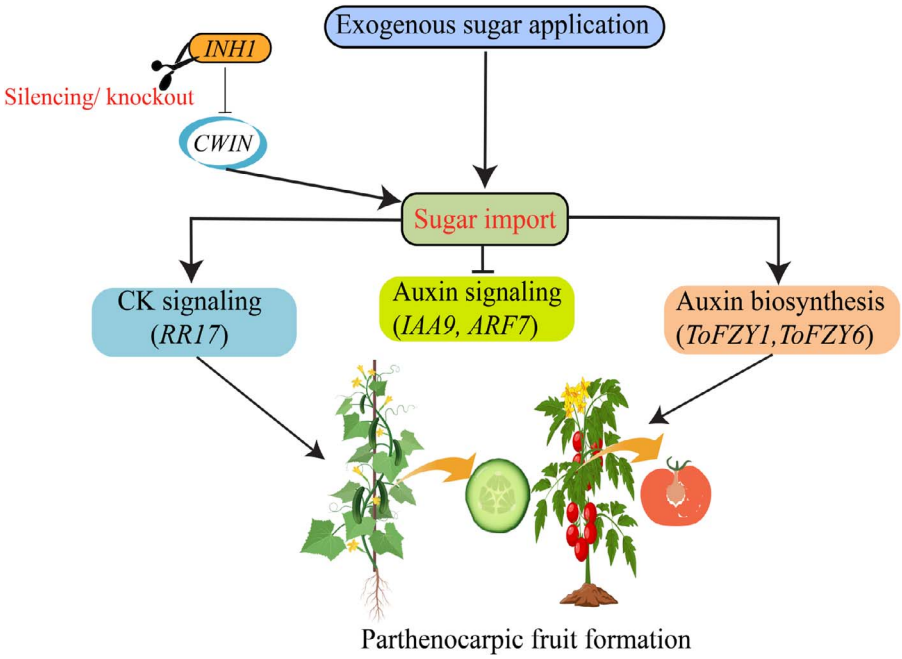

Figure 3. Illustration of the crucial regulatory role of sugar in parthenocarpic fruit formation. The INHI gene is an invertase inhibitor that alters sugar influx from "sources" to "sinks". Inhibiting the transcription of the INH1 gene by silencing it via RNAi or CRISPR knockout induces CWIN gene expression. The upregulated expression of the CWIN gene promotes sugar import into ovaries. The high sugar level facilitates metabolic activity, increases the expression of auxin biosynthesis genes (ToFZY1 and ToFZY6), and suppresses the expression of auxin signaling genes (IAA9 and ARF7). The enhancement of auxin biosynthesis in the unpollinated ovaries stimulates CK-mediated cell division and expansion, thus producing parthenocarpic fruit.

Flavonoids

Flavonoids are considered essential plant metabolites and function in many developmental processes [142, 143]. The role of flavonoids in parthenocarpic fruit setting has been proven in tomatoes. For instance, the silencing of the *CHALCONE SYNTHASE* (*CHS*) gene, which encodes the first enzyme in the flavonoid pathway, produces seedless tomato fruits [144, 145]. *Chs* antisense lines displayed a similar phenotype to RNAi-*SlPIN8* tomato plants (section 4.1.2). The silencing of *Chs* and *SlPIN8* both hindered pollens' viability and produced fertilization-dependent parthenocarpic fruits. Studies also reported that silencing flavonoid biosynthesis genes improved cell-to-cell auxin transport by increasing the transcription of *PIN* genes [146]. *PIN* genes such as *SlPIN4* and *SlPIN8* have been reported to negatively regulate the fruit set. If the absence of flavonoids facilitates the transcription of auxin transport carriers, then questions such as how *Chs* antisense plants produce parthenocarpic fruits arise. There may be an unknown signaling cascade that regulates parthenocarpic fruit setting in loss-of-function *Chs* plants. Additionally, the interactions of flavonoids with hormones need to be addressed in detail.

Hormonal interactions underlying parthenocarpy

Fruit setting is a complex multigenic trait that always depends on the interaction and crosstalk among different hormones. Below, we discuss recent developments regarding the regulation of parthenocarpic fruit formation by hormonal crosstalk.

It is clear that auxin plays a central role in parthenocarpic fruit formation. The crosstalk of auxin with GA, CK, and ethylene is involved in parthenocarpic fruit formation in tomato, cucumber, pear, grape, loquat, and fig. In pear, the exogenous application of 2,4-D increased the expression of the GA biosynthesis genes *GA20ox and GA3ox* in unfertilized ovaries, which produced parthenocarpic pear fruits, indicating the importance of auxin-GA crosstalk in the fruit setting stage [28]. ARF and AUX/IAA facilitate the conjugation between auxin and GA. Simultaneously, *GH3 (Gretchen Hagen 3)* family genes are responsible for maintaining auxin homeostasis by fusing with free auxin molecules [86, 92]. ARF, which possesses both overlapping and distinct functions, has been well studied in multiple crops during fruit setting (Section 4.1.3). In tomato, the *SlARF7* gene was shown to dimerize with *SlIAA9* and *SlDELLA* via two protein binding regions. These interactions significantly inhibited the transcription of *GH3.2* and *GA20ox1/GA3ox1*, hence negatively affecting the fruit set. Upon regular fertilization, the ovule released auxin and GA exclusively by degrading *SlIAA9* and *SlDELLA* and, as a result, allowed *SlARF7* to stimulate the auxin- and GA-mediated initiation of fruit set [56]. In strawberry, *Fverga1* CRISPR knockout mutants produced parthenocarpic strawberry fruits. *FveRGA1*, a GA signaling gene, bound *FveARF8* and suppressed its expression, thus increasing sensitivity to auxin [97]. The increase in auxin sensitivity obtained by inhibiting *FveARF8* indirectly triggered the transcription of the *FveGID1* gene. The induction of *FveGID1* mRNA accumulation enhanced GA sensitivity and, repressed

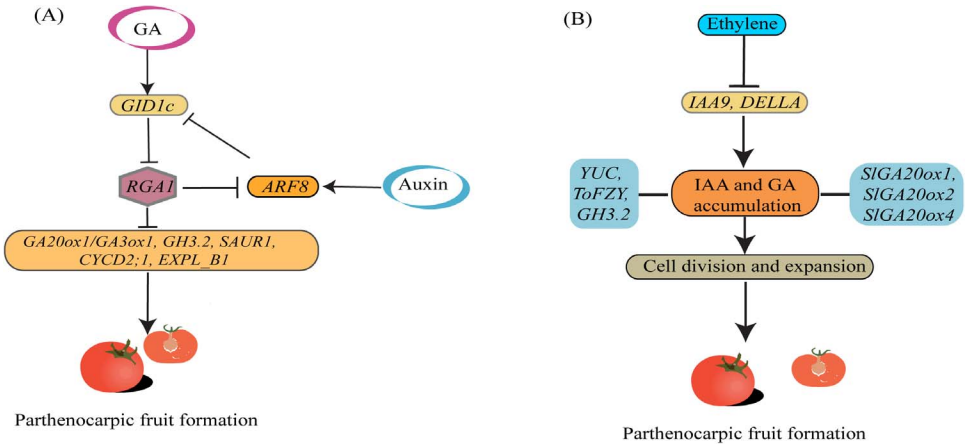

Figure 4. The role of auxin-GA and CK-auxin-GA crosstalk in parthenocarpic fruit formation in horticultural crops. (A) The suppression of ARF8 transcription after binding with RGA1 increases auxin sensitivity, further stimulating the expression of GID1. The enhanced expression of GID increases GA sensitivity, and this enhanced GA sensitivity represses RGA1 via a negative feedback loop and frees auxin and GA to initiate fruit set. (B) Ethylene negatively regulates the gene expression of IAA9 and DELLA, which blocks auxin and GA degradation. The induced auxin and GA biosynthesis genes trigger the accumulation of IAA and GA, further stimulating cell division and expansion. The improved cell division and expansion activity in unfertilized ovaries causes them to grow, hence producing parthenocarpic fruit.

FveRGA1 via a feedback loop. The increase in auxin-GA sensitivity upregulated the expression of cell cycle and expansion genes such as *FveCYCD2;1, FveSAUR1, and FveEXPL_B1*. A model of the auxin-GA crosstalk that regulate the fruit setting is depicted in Fig. 4A.

Ethylene has been shown to influence fruit sets mainly in a negative way by engaging in antagonistic crosstalk with auxin and GA. In tomato plants, the brief induction of *ERF* genes upon fertilization suppressed ethylene generation via pollination mediated auxin and GA production [147]. However, ethylene signaling could not be repressed in unpollinated ovaries with compromised auxin and GA biosynthesis/accumulation, and fruit set was therefore inhibited [147]. In watermelon, a similar model was reported [21]. Ethylene biosynthesis genes were expressed dominantly in the unfertilized ovaries of watermelon. These ethylene biosynthesis genes antagonistically regulated auxin (*YUCCAs*, *ToFZY,* and *GH3.2*) and GA (*GA20ox*) related genes by engaging in a synergistic relationship with *IAA9* and *DELLA* and, as a result, prevented the ovaries from initiating fruit set [21]. In tomato, a study conducted by Shinozaki et al. demonstrated that higher ethylene accumulation in unpollinated ovaries stabilized *DELLA* and GA inactivation genes (*SlGA2ox4, SlGA2ox5*) [51, 53]. The enhanced transcription of *DELLA* antagonized the biosynthesis of GA by suppressing the *SlGA20ox3* gene. The inhibition of GA biosynthesis further caused the failure of fruit set. Conversely, the inhibition of ethylene perception in *Slter-1-1* (loss-of-function mutant of ethylene reception) produced a higher parthenocarpic fruit set by increasing GA accumulation levels in unfertilized ovaries by increasing the transcription of *SlGA20ox1, SlGA20ox2,* and *SlGA20ox4* [53]. The accumulation of IAA and GA in the unfertilized ovaries stimulated the cell division and expansion processes necessary for parthenocarpic fruit set. A graphical representation of the auxin-GA-ethylene interaction is illustrated in Fig. 4B.

The plant hormone CK was also found to regulate parthenocarpic fruit formation by interacting with the auxin or GA pathway. For example, the application of CPPU caused parthenocarpic fruit set in pear by interacting with auxin [36]. The CK signaling gene *PbRR9* bound to the promoter region of *PbYUCCA4* to induce auxin biosynthesis. The transient overexpression of *PbRR9* in pear fruits increased the expression of *PbYUCCA4* [36]. 6-benzyladenine application either alone or combined with 4-CPA significantly increased GA1 + 3 and GA4 + 7 levels and enhanced the mRNA accumulation of *VvGA20ox1*, *VvGA20ox2*, and *VvGA20ox3* in unfertilized ovaries, thus producing parthenocarpic grapes [32].

In pear, the application of melatonin to unpollinated ovaries significantly enhanced the endogenous levels of GA3 and GA4 [6]. The upregulation of a GA biosynthesis gene (*PbGA20ox*) and the downregulation of a GA degradation gene (*PbGA2ox*) were also observed. Following paclobutrazol (PAC) treatment, the majority of the ovaries failed to produce fruits [6]. This result suggested that melatonin-mediated parthenocarpy was dependent on GA. On the other hand, melatonin-induced pear parthenocarpy was shown to be independent of auxin, as no significant difference in IAA was observed between melatonin-treated and wild type ovaries [6].

Conclusions and future directions

Parthenocarpy overcomes the risk of a low yield due to a disrupted fertilization process and produces seedless fruits, which is a highly preferred agronomic trait in horticultural crops. The application of hormones for inducing parthenocarpic fruit production is well established in a variety of horticultural crops [4, 11, 111]. Auxin, GA, and CK are categorized as primary players in initiating

fruit set. Other hormones, such as ethylene, BR, and melatonin also participate in parthenocarpic fruit formation. Additionally, synergistic and antagonistic crosstalk between these hormones is crucial in defining the fate of fruit set. The synergy between auxin, CK, and GA suppresses ethylene signaling. Moreover, the inhibition of DELLA increases sugar influx into unfertilized ovaries and, as a result, enhances cell division and expansion by promoting auxin and GA biosynthesis. Despite the plethora of literature available, the below issues remain to be further clarified.

- The silencing of auxin efflux transporter genes such as *PIN4* and *PIN8* induces parthenocarpy by blocking the transport of auxin from unfertilized ovaries. However, in the *hydra* mutant, *SlPIN1*, *SlPIN2,* and *SlPIN4* showed upregulated expression during the fruit setting stage.
- The positive role of auxin has been confirmed in various horticultural crops. However, contrasting functions of some auxin signaling genes from the IAA family has been observed. It is important to elucidate the regulatory mechanism of different IAA genes.
- Exogenous CK and CK biosynthesis and signaling genes are positive regulators of parthenocarpy. However, functional studies to clarify the detailed mechanism of CK-induced parthenocarpy are lacking.
- Sugars, serving as energy resources or signaling molecules, are drivers of parthenocarpic fruit formation. The interplay among sugars and the plant hormones auxin, GA, and CK needs to be further explored to understand the physiological and molecular mechanisms of parthenocarpy.
- Despite the positive role of BR and melatonin, the involvement of their biosynthesis and signaling genes in parthenocarpic fruit setting has yet to be studied.

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Author Contribution

Rahat Sharif: Compiled the contents and drafted the manuscript. Li Su: Collected the literature and contributed to manuscript writing. Xuehao Chen: Acquired funding and participated in writing (review & editing). Xiaohua Qi: Conceived the idea, acquired funding and participated in writing (review & editing). All authors have read and approved the final version of the manuscript.

Conflict Interests statements

The authors declare that they have no known competing financial interests or personal relationships that could have influenced the work reported in this paper.

Supplementary data

Supplementary data is available at *Horticulture Research* online.

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