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REVIEW

The dual function of elicitors and effectors from insects: reviewing the 'arms race' against plant defenses

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Abstract

Key Message **This review provides an overview, analysis, and reflection on insect elicitors and effectors (particularly from oral secretions) in the context of the 'arms race' with host plants.**

Abstract Following injury by an insect herbivore, plants rapidly activate induced defenses that may directly or indirectly affect the insect. Such defense pathways are influenced by a multitude of factors; however, cues from the insect's oral secretions are perhaps the most well studied mediators of such plant responses. The relationship between plants and their insect herbivores is often termed an 'evolutionary arms race' of strategies for each organism to either overcome defenses or to avoid attack. However, these compounds that can elicit a plant defense response that is detrimental to the insect may also benefit the physiology or metabolism of an insect species. Indeed, several insect elicitors of plant defenses (such as the fatty acid-amino acid conjugate, volicitin) are known to enhance an insect's ability to obtain nutritionally important compounds from plant tissue. Here we re-examine the well-known elicitors and effectors from chewing insects to demonstrate not only our incomplete understanding of the specific biochemical and molecular cascades involved in these interactions but also to consider the role of these compounds for the insect species itself. Finally, this overview discusses opportunities for research in the field of plant-insect interactions by utilizing tools such as genomics and proteomics to integrate the future study of these interactions through ecological, physiological, and evolutionary disciplines.

Keywords Elicitors · Effectors · Plant-insect interactions · 'Arms race'

Introduction

Following injury by an insect herbivore, plant species rapidly activate induced defenses through which an insect species may be *directly* affected through toxic or anti-nutritive properties or *indirectly* affected through volatile cues to predators or parasitoids of the insect species (Karban and Baldwin 1997; Chen 2008; Felton and Tumlinson 2008; Melotto et al. 2008; Louis et al. 2013). Such defense pathways are influenced by a multitude of factors, particularly insect-produced cues, (known as elicitors and effectors) many of which occur in the oral secretions of an insect species (Turlings et al. 1993; Delphia et al. 2007; Diezel et al. 2009; Tian et al. 2012a; Louis et al. 2013; Chuang et al. 2014).

Insect-derived compounds that influence plant defenses through activating such responses are termed *elicitors*, whereas those molecules that disrupt plant defense pathways are referred to as *effectors* (Felton and Tumlinson 2008; Chen and Mao 2020; Malik et al. 2021). It is worth noting that the term Herbivore-Associated Molecular Pattern (HAMP) is based on the vocabulary used to described elicitors produced by microbes or by the host plant that activates the host's plant defense responses (Microbial-Associated Molecular Pattern or MAMP) (Felton and Tumlinson 2008; Mithofer and Boland 2008). Therefore, HAMPs refer to insect-derived compounds that activate defense responses in a host plant species and are synonymous with compounds called elicitors. For simplicity, HAMPs will be referred to as elicitors throughout this review. However, a particular compound can activate one plant's defense pathways and disrupt that of another species (Musser et al. 2005a; Tian

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et al. 2012a, b). It is, therefore, essential to consider the ecological context in which specific interactions exist.

Insect-derived compounds are frequently located in the oral secretions of an insect and therefore, in direct contact with host plant tissue. In caterpillars, 'oral secretions' refers broadly to the combination of the saliva and regurgitant (Musser et al. 2006). Caterpillar saliva is secreted from labial glands through the spinneret and from the mandibular glands through pores in the mandibles. In some species, salivary glands are modified to produce and secrete silk for 'ballooning' or pupation (Takai et al. 2018; Mikó et al. 2019). Regurgitant, though, is comprised primarily of gut contents and some saliva (Liu et al. 2004; Tian et al. 2012a; Chuang et al. 2014). Some caterpillar species defensively regurgitate, dispelling gut contents when disturbed (Grant 2006). The compounds of these oral secretions often profoundly influence host plant defense responses. However, bacteria in caterpillar frass or in beetle regurgitant, the oviposition fluid from weevils or sawflies, and some insect pheromone compounds can also either disrupt or elicit plant defenses.

Here we will discuss many of the insect-derived compounds that act as elicitors and/or effectors in altering the defense responses of a host plant species. Due to the variety of insect species, host plants, and types of host plant defense responses, our understanding of these interactions serves as a cross section of the complex 'arms race' between insect species and their host plant species. This overview demonstrates our incomplete understanding of the specific biochemical and molecular cascades involved in these interactions. It also encourages us to consider the role of these compounds for the insect species itself. Some elicitors are known to have a beneficial role in the insect's physiology or metabolism (Yu 1989; Mori and Yoshinaga 2011). For instance, it is possible that the benefit a caterpillar species derives from elicitors such as volicitin and other fatty-acid amino-acid conjugates (FACs) through nitrogen metabolism, outweighs the occasional cost of being parasitized by wasps orienting to plant volatiles produced in response to these compounds. Finally, this overview discusses the exciting research opportunities present in this field which should utilize tools such as genomics and proteomics to integrate the continued study of these interactions through ecological, physiological, and evolutionary disciplines.

Elicitors

Insect-derived compounds that activate plant defense pathways are referred to as elicitors (Felton and Tumlinson 2008). The compounds are frequently found in insect oral secretions but have also been identified from oviposition fluid and pheromones involved in aggregating and mating, and may upregulate defense genes and phytohormones, induce specific plant volatiles and secondary metabolites, and/or callus formation (Helms et al. 2013, 2014, 2017; Bittner et al. 2019; Magalhães et al. 2019). However, insect elicitor compounds can have a beneficial role for the insect itself. For instance, mating pheromones facilitate reproductive success, and FACs enhance nitrogen metabolism for many caterpillar species (Mori and Yoshinaga 2011; Helms et al. 2013, 2014, 2017). The benefits to the physiology or reproductive success of an insect species may outweigh possible parasitoid attraction or other deleterious effects. These compounds and the interactions and responses they facilitate may provide a 'snapshot' of the arms race between certain plant and insect species.

The β-glucosidase oral elicitor

β-Glucosidase is a hydrolytic enzyme that catalyzes the hydrolysis of glycosidic linkages in glycosides and is found in a wide diversity of insect species, including locusts, cockroaches, aphids, and caterpillars (Lindroth 1988; Yu 1989; Mattiacci et al. 1995). For example, the eastern tiger swallowtail (*Papilio glaucus*) feeds on plant species in the Salicaceae, many of which contain phenolic glycosides. A subspecies, *P. g. canadensis*, is adapted to these compounds and exhibited a lower β-glucosidase activity when forced to feed on them. However, *P. g. glaucus* does not have an adaptation to phenolic glycosides and exhibited a higher activity of this elicitor when feeding on these compounds (Lindroth 1988). Presumably, the β-glucosidase benefits an insect species by detoxifying host plant allelochemicals to which it is not adapted (Lindroth 1988; Yu 1989). This elicitor appears to have a quantitative difference in activity among various caterpillar species that have been tested (Yu 1989). Within a species, elicitor activity may also vary by host plant species and seasonality (Lindroth 1988; Yu 1989).

β-Glucosidase functions as an elicitor of plant defense by hydrolyzing a variety of glucosides during caterpillar herbivory, cleaving plant volatile compounds conjugated to them (Lindroth 1988; Yu 1989; Mattiacci et al. 1995; Felton and Tumlinson 2008). In maize (*Zea mays*) and lima bean (*Phaseolus lunatus*), β-glucosidase will activate, among other things, of the biosynthesis of various terpenes (Hopke et al. 1994). However, jasmonic acid (JA) treatment alone elicited the emission of most, but not all, the volatiles emitted by β-glucosidase treatment (Hopke et al. 1994) (Table 1). Furthermore, the induction of a volatile profile from cabbage during herbivory of the β-glucosidase containing cabbage white butterfly, *Pieris brassicae* (Linnaeus), is attractive to parasitic wasps of the caterpillar (Mattiacci et al. 1995).

That some volatile compounds are triggered by both or one or the other of these externally applied compounds indicates that different plant signals and transducers may be responsible for various pathways leading to volatile emission

Table 1 Most insect-derived compounds and the response of host plant species to these compounds. A compound may not always act as an elicitor (activating plant defense responses) or an effector (disrupting plant defense responses)

Compound	Insect	Role in Insect	Plant	Plant Response	Compound Classification*	Reference(s)
β-glucosidase	*P. brassicase*	Detoxifying host plant chemicals	*Brassica oleracea*	Increased VOC emission	Elicitor	Mattiacci et al. (1995)
FACs	*S. exigua*	Nitrogen assimilation	*Zea mays*	Increased VOC emission	Elicitor	Turlings et al. (1995) Alborn et al. (1997) Yoshinaga et al. (2008)
			Nicotiana tabacum	Reduced nicotine	Effector	Diezel et al. (2009); Halitschke et al. (2001)
	S. frugiperda		*Vigna unguiculata*	None		
Inceptin	*S. frugiperda*	?	*Vigna unguiculata*	Induced ethylene	Effector	Schmelz et al. (2006, 2007, 2009)
				Induced SA		
				Induced JA	Elicitor	
				Induced VOC emission		
				Induced cinnamic acid		
				Induced cystatin transcripts		
			Zea mays	None		
Caeliferins	*S. americana*	Defensive regurgitant (?)	*Zea mays*	Increased VOC emission	Elicitor	Alborn et al. (2007a, b)
Bruchins	*Bruchus* spp	Egg pathogen resistance	*Pisum sativum*	Callus formation	Elicitor	Doss (2005)
				Induce isoflavone synthase gene (JA)		
				Induce pisatin	Effector	Cruickshank and Perrin (1962) Hammerschmidt and Nicholson (1999) Cooper et al. (2005)
Sawfly oviposition fluid	*D. pini*	?	*Pinus sylvestris*	Induces VOC emission	Elicitor	Mumm et al. (2003)
				Increased terpene synthase rates		Köpke et al. (2008)
				Decreased ethylene		Schröder et al. (2007)
				Accumulated ROS		Bittner et al. (2017)
E, *S*, - conophthorin	*E. solidaginis*	Mating	*Solidago altissima*	Induced JA Increased VOC emission	Elicitor	Helms et al. (2013; 2014; 2017)

Table 1 (continued)

Compound		Insect	Role in Insect	Plant	Plant Response	Compound Classification*	Reference(s)
Male sawfly pheromone		*D. pini*	Mating	*Pinus sylvestris*	Increased H_2O_2 Increased defense gene expression	Elicitor	Bittner et al. (2019)
Frass proteins	Unknown	*O. nubilalis*	?	*Zea mays*	Sustained defense gene expression (*lox3* and *mpi*) Suppressed pathogen induced gene expression (*pr5*)	Elicitor	Ray et al. (2016a, b, c) lessons from far end
		T. ni	?	*Brassica oleracea*	Increased defense gene transcripts (*lox3* and *tpi*) Decreased pathogen induced gene transcripts (*Pr1*)	Elicitor (?)	
		S. litura	?	*Oryza sativa*	Increased *RCI-1* transcripts Increased rice proteinase inhibitor transcript (*RPI*) Suppressed *NPR1* transcripts	Elicitor	
		H. zea	?	*Solanum lycopersicon* leaves	Increased herbivore defense gene transcripts (*Lox D, Pin2, TPI*)	Elicitor	
			?	*Solanum lycopersicon* fruit	Increased *Lox D* and *Pin2* transcripts Suppressed TPI activity	Elicitor (?)	
	Pr4 Endochitinase A	*S. frugiperda*	?	*Zea mays*	Suppressed herbivore induced defense gene expression (*mpi*) Induced pathogen defense gene expression (*pr5*)	Effector	Ray et al. (2015, 2016a, b, c, 2020)

Table 1 (continued)

Compound		Insect	Role in Insect	Plant	Plant Response	Compound Classification*	Reference(s)
Glucose oxidase (GOX)		*H. zea* *H. virescens* *S. exigua*	Antimicrobial properties	*Solanum lycopersicon*	Increased trichome density and JA Induced PI Pin2 and TPIs	Elicitor	Tian et al. (2012a, b)
					Closured stomata (VOC inhibition)	Effector (?)	Lin et al. (2021)
		T. ni *M. sexta* *S. frugiperda*		*Solanum lycopersicon*	no detected response		Tian et al. (2012a, b) Louis et al. (2013)
		H. zea *H. virescens* *Heliothis virescens*	Enhance host plant nutritive quality	*Nicotiana tabacum*	Reduced nicotine production Reduced volatile nicotine	Effector	Eichenseer et al. (1999) Musser et al. (2002;) Delphia et al. (2006)
GLV-modifying compounds	HALT	*S. exigua* *S. frugiperda* *T. ni* *M. sexta*	?	*Zea mays*	Prevented biosynthesis and emission of GLVs	Effector	Jones et al. (2019)
	Isomerase	*M. sexta*	?	*Nicotiana tabacum*	Isomerized (*Z*)-3-hexenal to (*E*)-2-hexenl	Elicitor (?)	Allman and Baldwin (2010)
	FHD	*B. mori*	?	*Morus* sp.	Prevented biosynthesis and emission of GLVs	Effector	Takai et al. (2018)
Phospholipase C (PLC)		*S. frugiperda*	?	*Zea mays*	Induced PIs	Elicitor	Acevedo et al. (2017)
				Cynodon dactylon	Suppressed trypsin inhibitors	Effector	
HARP		*H. armigera*	?	*Gossypium* sp.	Blocked JA signal transduction	Effector	Chen et al. (2019)
ATP hydrolyzing enzymes		*H. zea*	Involved in signaling pathways for physiological processes	*Solanum lycopersicon*	Suppressed genes regulated by JA and ethylene and trichome production	Effector	Wu et al. (2012) Felton et al. (2018)
Protein tyrosine phosphatase (PTP)		*H. zea*	Involved in signaling pathway for physiological processes	*Solanum lycopersicon*	Suppressed JA-regulated protein accumulation	Effector	Ward et al. (1994) Felton et al. (2018)
Bacteria lysing enzyme		*H. zea* *M. sexta* *H. virescens*	Antibacterial factor?		Lysed plant surface bacteria	Effector?	Morishima et al. (1988) Liu et al. (2004)

Table 1 (continued)

Compound		Insect	Role in Insect	Plant	Plant Response	Compound Classification*	Reference(s)
	Pantoea ananatis	*S. frugiperda*	?	*Solanum lycopersicon*	Downregulated plant defense proteins PPO and trypsin PI	Effector	Acevedo et al. (2017)
				Zea mays	Upregulated herbivore- induced PI expression	Elicitor	
Oral secretion bacteria	*Enterobacteriaceae 1*			*Solanum lycopersicon*	Downregulated plant defense proteins PPO and trypsin PI	Effector	
				Zea mays	Upregulated herbivore- induced PI expression	Elicitor	
	Raoultella spp.			*Solanum lycopersicon*	Downregulated peroxidase activity Upregulated trypsin PI	Elicitor	
				Zea mays	Upregulated expression of herbivore induced PI	Elicitor	
	Stenotrophomonas sp. *Pseudomonas* sp. *Enterobacter* sp.	*L. decemlineata*		*Solanum lycopersicon*	Reduced PPO activity Increases SA and decreases JA responsive gene expression	Effector	Chung et al. (2013)

Traditionally induced VOC (including GLV) emission is considered a plant defense response which can act as a signal to insect predators and parasitoids of an insect herbivore (Turlings et al. 1995; Scala et al. 2013). Additionally, the salicylic acid (SA) pathway is usually upregulated through pathogen infestation, often inhibiting the insect wound-induced jasmonic acid (JA) pathway and vice versa (Chung et al. 2013)

(?) indicates uncertainty about the function or classification of a compound.

(Hopke et al. 1994). It appears, in cabbage at least, that mechanical damage in conjunction with β-glucosidase application must occur to elicit herbivore-induced plant volatiles (HIPVs) (Matticci et al. 1995). Since this observation has not been reported in maize and lima bean, this requirement bears further investigation as it could provide clues as to the transportation and perception of this elicitor by the plant. Further work to conclusively demonstrate the cleavage of the volatile-sugar conjugate by the β-glucosidase and the impact of this elicitor on other plant defense responses, such as phytohormone accumulation, would be beneficial. Additionally, it has not been definitively shown that the benefit of caterpillar β-glucosidase for host detoxification outweighs potential parasitizing indirectly brought about by the emission of volatile compounds in response to this elicitor.

The fatty-acid amino-acid conjugate (FACs) oral elicitors

The FACs are unsaturated 18-carbon fatty acids coupled to glutamine or glutamate (Pohnert et al. 1999). A comprehensive review of FAC elicitor biosynthesis was published by Tumlinson and Lait (2005). Essentially, membrane-bound fatty acids of the plant are released during leaf damage and modified by the feeding caterpillar through the addition of an amino acid (Truitt et al. 2004). This contribution of the amino acid from the insect species and the fatty acid from the plant species allows for a diversity of FACs influenced by caterpillar diet (Felton and Tumlinson 2008). In fact, the significant differences in the quantities of the N-acylamino acid conjugates in the oral secretions of three noctuid species, suggest that the various proportions of these compounds are species-specific (Mori et al. 2003). Indeed, the patterns by which FACs occur in caterpillar species regurgitant are classified into four types: (a) glutamine conjugates only, (b) glutamine and glutamic acid conjugates, (c) glutamine conjugates and those with hydroxylated fatty acids, and (d) all of them (Mori and Yoshinaga 2011).

FACs facilitate nitrogen assimilation in those insects with glutamine-type FACs; however, the physiological roles and details of the biosynthetic pathways of glutamic-acid FACs are not known (Yoshinaga et al. 2008; Mori and Yoshinaga 2011). Glutamine is one of the key compounds for nitrogen metabolism in insect species, and glutamine synthesis in the caterpillar gut was enhanced when an artificial diet was enriched with linolenic acid, resulting in an over 20% increase in nitrogen assimilation efficiency (Yoshinaga et al. 2008). The positive effect of nitrogen assimilation for larvae growth may offset the induced plant defenses and attraction of natural enemies by FACs (Yoshinaga et al. 2008). However, such a tradeoff still needs to be shown conclusively.

During herbivory on maize, the beet armyworm, *Spodoptera exigua*, triggers the release of a specific suite of HIPVs, different from those emitted during mechanical damage, which serves as a chemical cue for parasitic wasps (Turlings et al. 1993, 1995). A FAC, *N*-(17-hydroxylinolenoyl)-L-glutamine (volicitin) was identified from the caterpillar regurgitant as the compound responsible for eliciting the induced volatile response (Fig. 1A) (Alborn et al. 1997). In addition to volicitin, there is extensive diversification of the FACs across the Lepidopteran caterpillars; they have also been identified in *Teleogryllus taiwanemma* (crickets; Orthoptera) and *Drosophila melanogaster* (fruit flies; Diptera) (Yoshinaga et al. 2010, 2014; Mori and Yoshinaga 2011).

The addition of FACs to lima bean triggered a strong membrane potential depolarization at the damage site which then spread throughout the leaf (Maffei et al. 2004). Since Ca^{2+} acts as an intracellular secondary messenger in plant cells, the depolarization of the cell membrane potential and Ca^{2+} influx is likely at least a part of the signaling cascade from the plant species detection of FACs to induced defense responses (Lecourieux et al. 2006). This elicitor is perceived through the binding of a protein-ligand interaction, although the relationship of this step to induced defense responses in the plant species is unclear (Truitt and Paré 2004; Truitt et al. 2004). Either through increased Ca^{2+} influx or directly, FACs induce the expression and activity of specific genes involved in terpenoid biosynthesis, specifically those for terpene synthases (Paré and Tumlinson 1997; Bouwmeester et al. 1999; Arimura et al. 2004; Gomez et al. 2005). Volatiles elicited from volicitin application, including a set of acyclic terpenes and indole (via the shikimate pathway), may be biosynthesized *de novo* following insect damage; on the other hand, in some plant species, such as *Gossypium hirsutum* (Linnaeus), cyclic terpenes, butyrates, and green leaf volatiles (GLVs) may be released from storage or synthesized from intermediates (Paré and Tumlinson 1997).

In addition to eliciting volatiles, FAC application to plant species elicits several herbivore-associated defense responses such as bursts in plant phytohormones (Table 1) (Schmelz et al. 2009). Interestingly, FAC application can also lead to the suppression of plant direct defenses, such as nicotine, which is an attribute of an insect effector (Diezel et al. 2009; Halitschke et al. 2001). Insect compounds that decrease or suppress plant defenses are typically considered to be effectors (see next section on Effectors). It may be that these compounds can act to both prevent (nicotine reduction) and elicit (volatile emission and JA induction) plant defense responses, dependent on additional factors such as host plant species (Fig. 2). The evident functional duality of FACs deserves further examination. Such work will provide valuable tools for the further characterization of plant responses to chewing insect species. Specifically, the identification and characterization of the volicitin binding protein, the enzymes encoded by terpene synthase genes, and the genomic sequences that regulate these processes

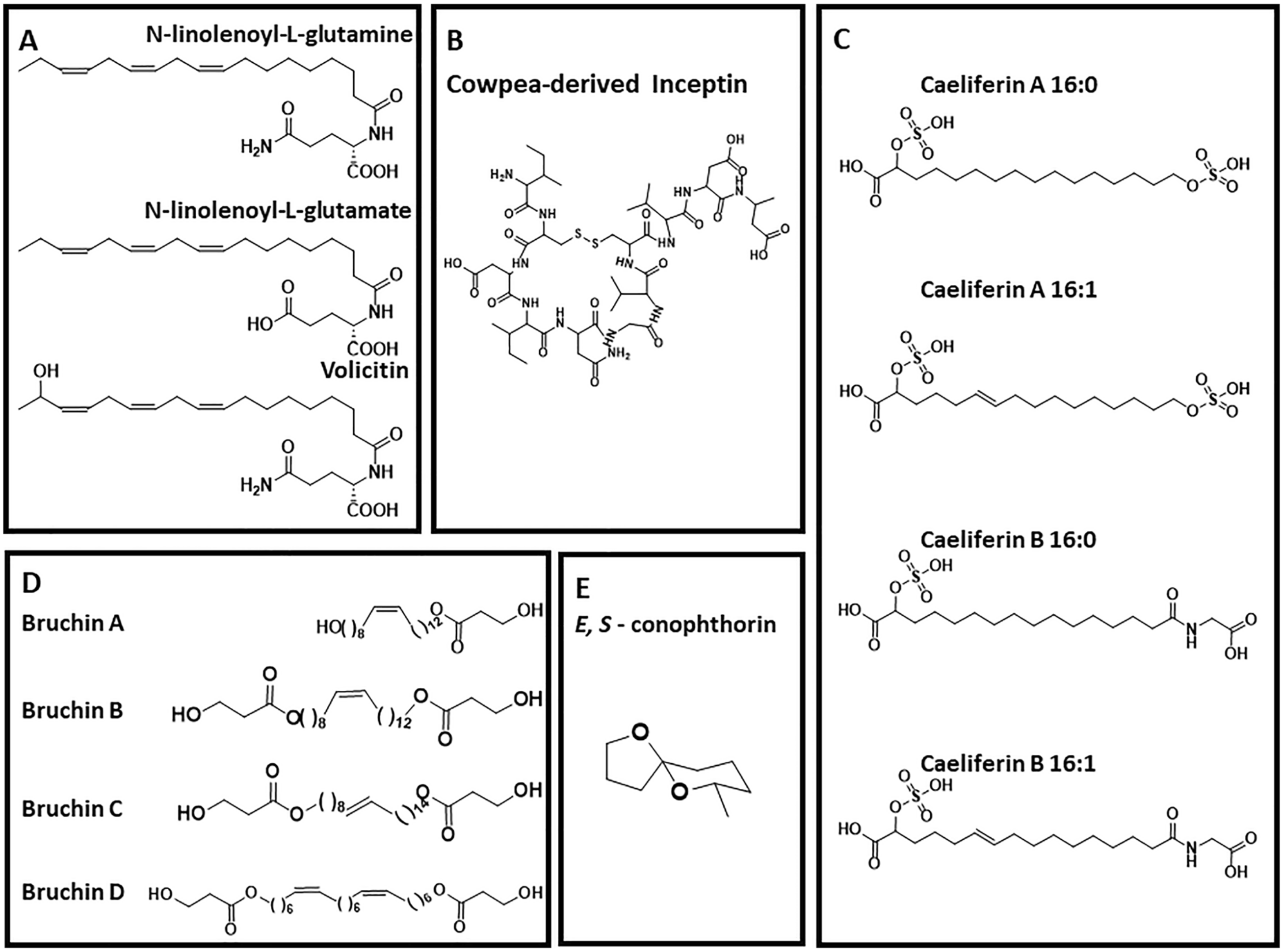

Fig. 1 Insect elicitor structures. Those from insect oral secretions include: **A** Fatty-acid amino-acid conjugates, **B** Cowpea-derived inceptin, and **C** Caeliferins. **D** Bruchins compose a portion of weevil (*Bruchus* spp.) oviposition fluid, while **E** *E, S*—conophthorin is part of the male gall fly (*Eurosta solidaginis*) pheromone (Alborn et al. 1997, 2007a, b; Doss et al. 2000; Oliver et al. 2000; Schmelz et al. 2006; Helms et al. 2013). Figure created with ChemDraw Prime 17.1 in Microsoft Office 365 PowerPoint

will advance in the decoding of the plant signaling cascade (Truitt et al. 2004; Gomez et al. 2005).

The inceptin oral elicitors

Inceptins, from the fall armyworm, *Spodoptera frugiperda*, are disulfide-bridged peptides derived from cowpea (*Vigna unguiculata*), chloroplastic ATP synthase γ-subunits (cATPCs) (Fig. 1B) (Schmelz et al. 2006). cATPCs are essential components of chloroplastic ATP synthase, necessary for a plant species to catalyze the synthesis of ATP from ADP and phosphate (Schmelz et al. 2006). When ingested by *S. frugiperda*, cATPCs are proteolyzed in the gut; some of the resulting peptide fragments, termed inceptins, induce cowpea defense responses (Table 1) (Schmelz et al. 2006; Schmelz et al. 2007). Several caterpillar species produce active inceptins (Schmelz et al. 2012). Although lepidopteran larvae generate inceptins through both N- and C-terminal proteolysis, the velvetbean caterpillar (*Anticarsia gemmatalis*) proteolyzes cATPC by removing the C-terminal alanine. This shorter inceptin disrupts cowpea defense responses, acting as an *A. gemmatialis* effector (Schmelz et al. 2012).

Synthetic inceptins induce ethylene, JA, salicylic acid (SA), volatile emission, cinnamic acid, and transcripts of cystatin, a protease inhibitor, in cowpea plants, indicating that inceptins induce direct and indirect cowpea defenses (Fig. 2) (Schmelz et al. 2006, 2009). These enhanced defenses led to a direct effect on *S. frugiperda*; larvae fed on plants previously treated with inceptins exhibited reduced biomass compared to larvae fed on untreated plants (Schmelz et al. 2006). Inceptins, then, are essential in inducing direct and indirect defenses, with major ramifications for the plant species, herbivore species, and potentially the surrounding environment (i.e., predators and parasitoids). Particularly, the induced phytohormones during this process form part of a complex defense signaling cascade for

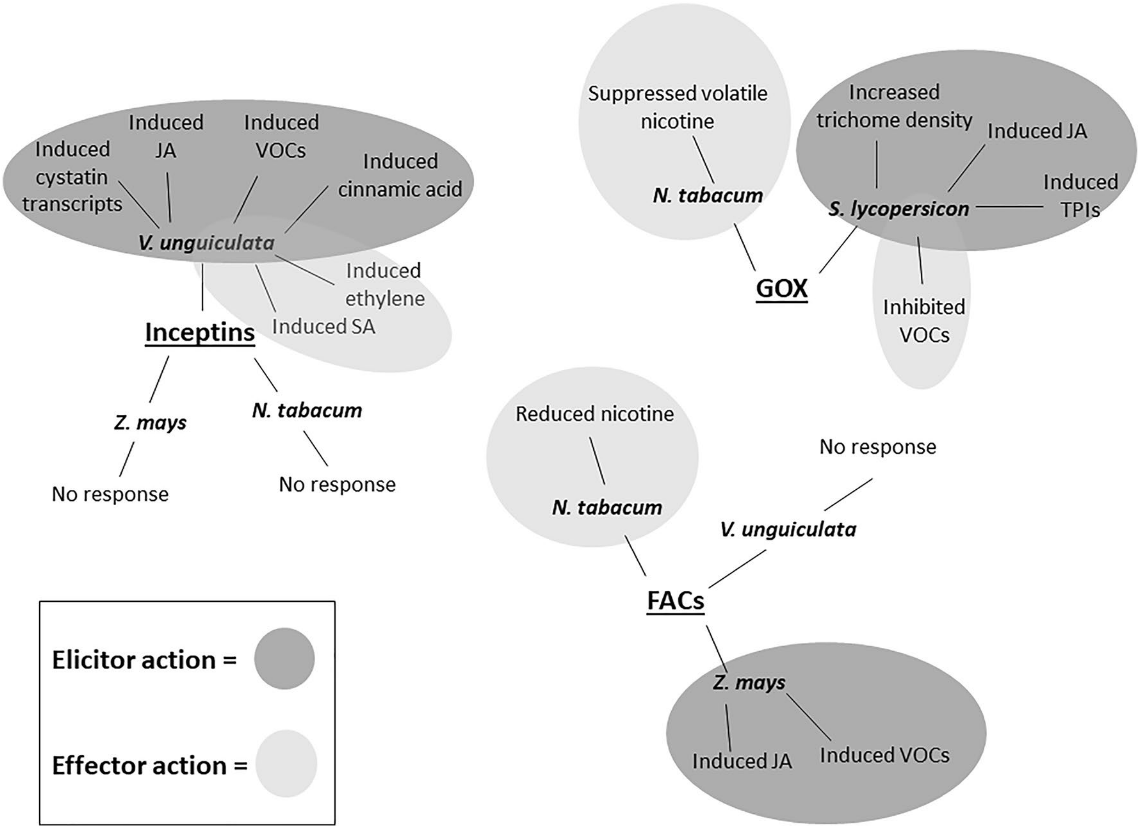

Fig. 2 The classification of plant defense responses from selected insect-derived compounds—inceptins, fatty acid-amino acid conjugates (FACs), and glucose oxidase (GOX) based which plant defense responses are activated (elicitors; dark grey) or disrupted (effectors; light grey). Figure created in Microsoft Office 365 PowerPoint

the plant species (Schmelz et al. 2006, 2009). Undoubtedly, inceptins act early in these signaling pathways to trigger a variety of responses from cowpea, leading to the reduced biomass of *S. frugiperda* fed on induced cowpea plants (Schmelz et al. 2006).

Since inceptin production is dependent on proteolysis in the caterpillar gut, only caterpillar larvae that have previously ingested cATPCs and proteolyzed them 'correctly' can induce cowpea defenses during herbivory (Schmelz et al. 2006). The cATPC sequence is conserved throughout most photosynthesizing plant species, perhaps because of its association with chloroplasts (Schmelz et al. 2006, 2009). Fall armyworm proteolyzes inceptins from cATPCs obtained through herbivory on maize or cowpea (and presumably many other plants); however, the inceptin receptor (INR) appears to be only functional in a group of plants within the Fabaceae (Steinbrenner et al. 2020). For example, maize-derived inceptin triggers defense responses in cowpea, but does not induce such defense responses in maize (Fig. 2) (Schmelz et al. 2006). It is unknown if cATPC is cleaved in other herbivorous caterpillar guts to produce inceptin peptides. Inceptins do not appear to induce maize or tobacco defense responses. (Schmelz et al. 2006, 2009).

Inceptins are not permanent elicitors in the caterpillar oral secretions. Due to exo- and endopeptidases in the insect gut, inceptins are proteolytically cleaved over time and become inactive, no longer able to induce plant defense responses (Schmelz et al. 2006). Some variation in the active inceptin peptide can occur, perhaps reflecting different cleavage sites and/or plant species variation of cATPC. However, the C terminal alanine is necessary for activity (Schmelz et al. 2007). For example, the presence of a lysine in the spinach inceptin peptide, resulted in its cleavage and the loss of its inducing defense response activity (Schmelz et al. 2007). Since the inceptin sequence in cowpea and several other plant species is established, this area of peptide elicitors is wide open for a variety of studies to further understand the source, synthesis, role, activities, and receptors involved in these interactions (Schmelz et al. 2006).

The *S. frugiperda*-cowpea-inceptin system is unique in that (1) very few caterpillars have been examined for proteolyzing inceptins from plant cATPC, (2) cowpea is the only tested plant in which defense responses were elicited, and (3) inceptin can be proteolyzed from the cATPCs of several plant species but, to date, is perceived only by select species within the Fabaceae. This system, while studied in detail similar to the FAC elicitors, represents a curious deviation from those compounds. While *S. frugiperda* regurgitant contains FAC elicitors, these elicitors do not induce cowpea defense responses (Spiteller et al. 2001; Schmelz et al. 2006). It is evident that plant species both specifically influence and respond to the composition of caterpillar oral secretions. The thorough approach to the discovery and activity of inceptins should serve as a model on which to research other elicitors and effectors. Through such work, the specifics of the elicitor, its role and mechanism, and the discovery of a unique receptor for it have been elucidated.

The caeliferin oral elicitors

Grasshopper (*Schistocerca americana*) regurgitant elicits HIPVs from maize seedlings (Table 1) (Alborn et al. 2007a, b). The eliciting compounds are sulphur-containing fatty-acid elicitors of plant volatiles, termed caeliferins (Fig. 1C). Interestingly, the composition of caeliferins will change in wild grasshopper populations when confined in the laboratory, independent of diet. The factors that cause this change are unknown (Alborn et al. 2007a, b). Though the precursors for caeliferins have not been determined, it follows that fatty acids—possibly derived from maize—are an important part of this elicitor. Caeliferins may interact with a sulfotransferase to transform 12-hydroxy-jasmonate into its corresponding sulfate (as shown in *Arabidopsis thaliana*) (Schmelz et al. 2009). If this interaction occurs, potentially caeliferins are partly involved in deactivating part of the plant response to herbivory through the JA pathway.

Considering the variation in the response, or lack of response, of other elicitors, particularly volicitin, among plant species, it is surprising that the full activity range of caelferins on plant defense responses has not been accomplished (Schmelz et al. 2009). These elicitors may serve as part of the insect's chemical defense, since *S. americana* will readily regurgitate when attacked; however, this deterrent effect has yet to be tested. The advantage of caeliferin is unclear for *S. americana* and the advantage of caeliferin-induced maize volatiles is unknown for the plant species Alborn et al. (2007a, b) suggested that these VOCs may deter further feeding by *S. americana* or aid in aggregation. The little-known caeliferin elicitors represent a research area replete with possibilities to determine the activity range, deterrent effect, parasitoid attraction, the solitary vs. gregarious nature of *S. americana*, and maize signaling.

The bruchin elicitors

Bruchins are mono- and bis-(3-hydroxypropanoate) esters of long-chain α, ω-diols deposited on pea pods (*Pisum sativum* L.) by ovipositing pea and cowpea weevils (*Bruchus* spp.) (Fig. 1D) (Doss et al. 2000; Oliver et al. 2000). Bruchins form calluses in the pod tissue beneath the weevil egg, impeding larval entry into the pod (Doss et al. 2000). Some bruchins are intensely active; callus formation can be initiated by applications of these elicitors at concentrations as low as 0.5–1.0 fmol (Oliver et al. 2000; Doss et al. 2000).

In addition to forming a physical structure to impede weevil larvae, bruchins induce the upregulation of an isoflavone synthase gene, an enzyme involved in JA synthesis (12-oxo-phytodienoic acid 10,11-reductase; OPDAR), and the isoflavone, pisatin (Cooper et al. 2005; Doss 2005). Pea pisatin levels were increased after bruchin treatment and remained detectible for more than 64 h (Cooper et al. 2005). Since this isoflavone is induced by pathogen infection to the plant, its induction after treatment with an insect oviposition elicitor is curious (Cruickshank and Perrin 1962, Hammerschmidt and Nicholson 1999, Cooper et al. 2005). Bruchins induce several types of pea defense responses—the callus formation as a physical barrier, synthesis of the antibiotic compound, pisatin, and enzymes involved in phytohormone signaling (Table 1) (Doss 2005).

The structural requirements for bruchin activity are unknown; possibly they are offshoots of fatty acid synthesis or metabolism, potentially placing them in a similar level of functionality as FACs (Doss et al. 2000). Certainly, both FACs and bruchins initiate a complex plant-signaling sequence that ultimately has a negative effect on the insect species that produced the compound, although the full mechanism of this is unknown (Doss et al. 2000; Cooper et al. 2005). Bruchins likely have a beneficial role for the weevil to balance possible offspring mortality due to callus formation (Cooper et al. 2005). Perhaps the production of bruchins is related to egg pathogen resistance; however, it has not been definitively demonstrated that pisatin promotes disease resistance to benefit the weevil. (Doss et al. 2000).

The sawfly oviposition fluid elicitor

The oviduct secretions of the pine sawfly, *Diprion pini* appears to contain an elicitor that induces local and systemic terpenoid volatile production in *Pinus sylvestris* (Scots pine). This volatile signal attracts an egg parasitoid (*Chrysonotomyia ruforum*) which kills the egg, thereby preventing damage to the plant from feeding sawfly larvae (Mumm et al. 2003). This elicitor is applied to the eggs of the female sawfly when they are inserted into a slit in the pine needle; it may be a peptide or protein, or a component bound to these (Hilker et al. 2005). The elicitor in the sawfly oviduct secretion has not been characterized, although *P. sylvestris* defense responses to it are well described.

The elicitor enhanced transcription rates of the terpene synthases *PsTPS* 1 and *PsTPS* 2 at 72 h after egg deposition, matching the timing of particular odor attractiveness to the parasitoid (Table 1) (Köpke et al. 2008). Egg deposition also decreased pine ethylene emission compared to controls (Schröder et al. 2007). *P. sylvestris* responded to egg deposition by accumulating ROS (reactive oxygen species) and reducing ROS scavenger catalase activity (Bittner et al. 2017). Since ROS play an important role in plant defense against a myriad of biotic stressors, this response could lead to egg mortality and/or deterrence against future larval herbivory (Bittner et al. 2017). Indeed, sawfly larvae that began development on twigs from which they hatched gained less weight and suffered higher mortality than those fed on egg-free twigs (Beyaert et al. 2012). However, other than the likely induction of terpenoid volatiles and ROS accumulation, the elicitor from sawfly oviduct secretions does not appear to affect the plant's defensive potential against sawfly larvae (Beyaert et al. 2012).

There are numerous research opportunities in the sawfly, pine, parasitoid system. Future research must include the identification of the elicitor in the oviduct secretion (Hilker et al. 2005). An understanding of the elicitor compound and its mechanism of action will provide insights into its role for the sawfly itself. Finally, studies on the upregulation of *P. sylvestris* genes and phytohormones will provide clarity on the effect of plant defenses on sawfly eggs.

Other compounds that act like elicitors

Although oral secretions are the primary means through which plants perceive insect herbivores, insect pheromones, oviposition, and frass deposition are also capable of inducing plant defense responses (Helms et al. 2013; Ray et al. 2015, 2016a, b, c; Bittner et al. 2019). Goldenrod (*Solidago altissima*) exposed to *E, S*, - conophthorin, the major component of the male gall fly (*Eurosta solidaginis*) sex pheromone, exhibit induced JA accumulation, HIPV emission, and reduced susceptibility to damage by the specialist herbivore *Trirhabda virgata* (Fig. 1E) (Helms et al. 2013, 2014, 2017). The male sawfly (*D pini*) sex pheromone can increase hydrogen peroxide concentrations and defense-related gene expression after egg deposition in the pine needles of *Pinus sylvestris* (Bittner et al. 2019). The aggregation pheromone of *Anthonomus grandis* (boll weevil; Boheman) increased the VOC emission from the host plant *G. hirsutum* subsequently becoming more attractive to a parasitic wasp *Bracon vulgaris* (Magalhães et al. 2019). The elicitors of *Tetranychus urticae* (the two-spotted spider mite), tetranin1 and tetranin2, increased transcript abundances of defense genes and induced phytohormone biosynthesis of the host leaf which resulted in reduced survivability of the mite (Iida et al. 2019). Lastly, caterpillar frass (or molecules derived from it) induce plant defenses specific to each host-herbivore system, depending on the frass composition, the plant organ on which it is deposited, and the insect species Ray et al. 2015, 2016a-b; 2020). These non-oral cues represent a novel class of compounds able to elicit plant defense responses (Table 1).

Summary of elicitors

To summarize, plant defense responses to insect elicitors can include volatile emission, callus formation, and/or phytohormone induction. However, signal transduction from elicitor application to the defense response is often unclear or unknown (Truitt and Paré 2004; Bonaventure et al. 2011). Furthermore, the complexity of the elicited defense response—tritrophic interactions with predators or parasitoids of the herbivorous insect species—has been reported for some elicitors (β-glucosidase, FACs, inceptins) but not others (caeliferins, bruchins, and the sawfly oviposition fluid). Finally, some elicitors can benefit the insect species that produce them, detoxifying host plant chemicals (β-glucosidase) or aiding in the insect's nitrogen metabolism (FACs) (Lindroth 1988, 1989; Yoshinaga et al. 2008). The apparent 'dual-purpose' of several effectors—their benefit to the insect's physiological processes and yet their perception by the plant species to initiate defense responses—will be discussed later in this review.

Effectors

Compounds found in insect oral secretions that disrupt plant defense pathways are termed effectors. While insect saliva can have numerous functions; the most obvious is its role in facilitating food ingestion and digestion of an insect species (Ribeiro 1987; Ribeiro et al. 1995; Eichenseer et al. 1999). Secreted salivary proteins can modify host plant tissues to increase their nutritional suitability and/or manipulate host plant defensive responses. Insect species are generally benefited from these compounds through their ability to manipulate host plant defense responses. Much like elicitor compounds, effectors can be identified through a response of the host plant species. However, it is imperative to confirm that their role and mode of action for beneficially manipulating host plant defenses (Eichenseer et al. 1999).

The glucose oxidase (GOX) effector

As an effector, glucose oxidase (GOX) represents an insect compound with the capacity to decrease host plant defense responses (Felton and Tumlinson 2008). This enzyme, present in the saliva of many caterpillars, catalyzes the oxidation of glucose to produce gluconic acid and H_2O_2 (Eichenseer et al. 1999, 2010). These enzymes are about 70 kDa and are part of the GMC-oxidoreductases (Tang et al. 2012). These effectors may serve as part of an antioxidant enzyme system in the insect midgut by mitigating the oxidation of ingested food during herbivory (Eichenseer et al. 1999, 2010).

The GOX reaction also has antimicrobial properties. Gluconic acid, the product of this reaction, regulates plant gene expression and plays a key role in plant defense signaling against pathogens (Musser et al. 2005a, b). Indeed, the GOX reaction, enhanced with supplemental glucose, reduced the growth of the bacteria *Serratia marcescens* and *Pseudomonas aeruginosa* (Musser et al. 2005b). The acidic nature of gluconic acid may account for the observed antimicrobial properties. The formation of this antimicrobial agent by the GOX reaction may function to prevent the ingestion of plant-based bacteria by the caterpillar and may also protect the plant's wound site from general infection during herbivory.

The subsequent bursts of H_2O_2 from the GOX reaction may serve as an inter-plant signal since H_2O_2 is believed to be an upstream plant signal that can lead to phytohormone biosynthesis which interferes with JA-dependent responses (Merkx-Jaques and Bede 2005; Peiffer and Felton 2005). A caterpillar species may use H_2O_2 to enhance the nutritive quality of the host by denaturing ingested plant oxidative enzymes in addition to suppressing the wound-inducible defenses in some host plants species (Table 1) (Eichenseer et al. 1999).

A sugar substrate is necessary for the GOX reaction. Glucose, in particular, is an optimal substrate for caterpillar GOXs (Eichenseer et al. 1999). Since sugars such as glucose are required for GOX to produce gluconic acid and H_2O_2, it follows that glucose availability in host plant tissues may function as a rate-limiting factor in eliciting plant responses. Eastern corn borer (*Ostrinia nubilalis*) GOX-containing saliva induces tomato but not maize defenses, likely due to higher levels of glucose in tomato (Fig. 2) (Louis et al. 2013). Additionally, tobacco leaves or an artificial diet supplemented with glucose increased GOX activity in *Helicoverpa armigera* salivary glands (Hu et al. 2008). Salivary GOX from *H. zea* induced a large variation of defense protein induction among tested solanaceous plants (Lin et al. 2020). For instance, while GOX reduced tobacco defenses, this effector increased tomato defenses (Musser et al. 2002, 2005a, b; Tian et al. 2012a, b; Lin et al. 2020). As the rate-limiting step in this reaction, glucose may (1) affect translational or posttranslational regulation of GOX, increasing the transcriptional expression of this enzyme, (2) serve as the rate-limiting substrate for GOX, or (3) influence this reaction in a combination of these methods (Tang et al. 2012; Louis et al. 2013).

GOX activity can be dependent not only on a host plant species but also on the caterpillar species (Table 1) (Merkx-Jacques and Bede 2005; Hu et al. 2008; Eichenseer et al. 2010; Tang et al. 2012; Louis et al. 2013). The saliva from different caterpillar species can influence plant defense responses in different ways. *H. zea* herbivory or synthetic GOX application to tomato leaves induced transcript levels of the proteinase inhibitor Pin2. Salivary gland homogenates from species that do not produce high levels of GOX (*Trichoplusia ni*, *Manduca sexta*, and *S. frugiperda*) did not increase tomato Pin2 transcripts; however, gland homogenates from species with high levels of GOX (*Heliothis virescens* and *S. exigua*) did increase those transcripts (Table 1) (Tian et al. 2012a, b). This variation may play an adaptive role in fitness to host plant species or it may merely be a consequence of dietary factors and insect development stage (Merkx-Jacques and Bede 2005; Hu et al. 2008; Eichenseer et al. 2010).

Overall, GOX activity is statistically higher in the saliva of generalist caterpillar species than those with a more specialized host range (Eichenseer et al. 2010). Such higher GOX activity is likely not from a greater transcription rate of the enzyme but by greater transcription stability or a combination of rate and stability (Yang 2017). High GOX activity in phytophagous caterpillar species may contribute to host-range expansion (Eichenseer et al. 2010). If GOX activity is dependent on both the herbivore and plant species, then it stands to reason that there are decidedly different plant responses to GOX. This has been observed in a comparison of the effects of this effector on tobacco and tomato.

Tobacco

GOX strongly mitigated induced defenses in tobacco (Fig. 2) (Peiffer and Felton 2005). *H. zea* GOX reduced nicotine production induced by herbivory by more than 26% (Musser et al. 2002). *Heliothis virescens* saliva, also containing GOX, suppressed volatile nicotine (Delphia et al. 2006). In turn, nicotine reduction enhanced caterpillar fitness; *H. zea* neonates reared on tobacco with reduced nicotine (from prior GOX application) experienced increased survival and body weights (Musser et al. 2002). Since GOX activity is higher in *H. zea* glands after tobacco herbivory, this effector may be necessary to contend with nicotine production (Peiffer and Felton 2005). Since nicotine is synthesized in the roots and transported through the xylem, suppression of foliar nicotine may be due to stomata closure caused by GOX (Lin et al. 2021). Further research is necessary to elucidate the particular relationships and pathways involved in this effector system.

Tomato

GOX elicits an opposite response in the closely related solanaceous plant tomato, *Solanum lycopersicum*. GOX induced anti-nutritive trypsin protease inhibitors (TPIs) in tomato, inhibiting digestive serine proteases in the caterpillar gut (Musser et al. 2005a; Lin et al. 2020). It must be noted though, that damage to tomato leaves, whether treated with GOX or not, will induce TPIs (Musser et al. 2005a, b). Transcripts of another protease inhibitor, Pin2, were induced by *S. exigua*, *H. virescens*, and *H. zea* salivary gland homogenates, but were not by those of *T. ni*, *M. sexta*, and *S. frugiperda* (Tian et al. 2012a, b; Louis et al. 2013). This disparity in response may represent differing GOX activities among the examined caterpillar species. The saliva of some caterpillar species (which contains GOX) also increased JA levels in tomato (Fig. 2; Table 1) (Tian et al. 2012a, b). Caterpillars fed on Pin2-induced plants experienced reduced larval growth (Louis et al. 2013). GOX treatment reduced *H. zea* growth on tomato (Lin et al. 2020). Furthermore, GOX-producing *H. zea* herbivory inhibited tomato volatile emission (compared to the increased volatile emission during feeding by caterpillars unable to produce this effector through CRISPR-CAS9 gene editing), at least partially due to stomatal closure in response to GOX application (Lin et al. 2021).

Additionally, GOX induced tomato physical defenses. GOX-producing *H. zea* herbivory triggered a higher density of type VI glandular trichomes on tomato leaves than herbivory by caterpillars unable to produce GOX (Fig. 2; Table 1) (Tian et al. 2012a, b). It is evident that tomatoes treated with GOX are deleterious to the fitness of caterpillar species, and that GOX triggered an elicitor-type responses in tomato. Thus, it remains to be seen whether this is due to GOX-induced proteases, physical defenses, responses due to JA induction or a combination of these mechanisms.

Surveys across plant species are important in understanding the role of GOX in specialist and generalist herbivore species (Eichenseer et al. 2010). Studies to better understand the rate-dependent factors in these interactions are also essential (Hu et al. 2008; Tang et al. 2012). Each insect/plant system has specific factors that determine the activity of GOX. The glucose content of the plant species, specific types of plant defenses, and particular insect herbivore species demonstrate the diversity and complexity within each system Bede et al. 2006; Merkx-Jacques and Bede 2005; Yang 2017). Therefore, it is necessary to consider both plant and insect factors, as well as to consider the breadth of plant defense responses to GOX—gene transcripts, phytohormones, constitutive defenses, and volatile emission.

The effectors modifying GLVs

Plant green leaf volatiles (GLVs) are modified during insect herbivory by several effectors that alter the emission of these volatiles (Matsui and Koekuka 2016; Jones et al. 2019). GLVs are small aldehydes, alcohols, and esters believed to be degradation products of the plant lipoxygenase (LOX) pathway. These compounds are emitted from all green plant species in response to biotic and abiotic stress and play an important role in signaling host plant attraction and deterrence of herbivores, attracting parasitoids to deleterious herbivores, influencing pathogen infection, and inter- and intra-plant signaling (Scala et al. 2013; Matsui and Koeduka 2016; Ameye et al. 2018). Many of the aforementioned interactions are indirect plant defense responses (such as the emission of HIPVs, which parasitoids learn is indicative of prey—the feeding herbivore) (Matsui and Koeduka 2016). In this sense, effectors that modify GLV emission are altering a common plant stress response that is part of the plant's defensive signaling.

A *Bombyx mori* fatty acid hydroperoxide dehydratase (BmFHD) effector suppresses GLV production (Table 1) (Takai et al. 2018). This enzyme converts 13(*S*)-hydroperoxyl (9*Z*, 11*E*, 15*Z*)—oxadecatrienoic acid (13-HPOT), the immediate precursor of GLVs, into its keto-derivative, thereby removing it from the GLV biosynthetic pathway (Matsui and Koeduka 2016; Takai et al. 2018). A tachinid parasitoid fly of *B. mori* (*Zenillia dolosa*) laid fewer eggs when exposed to mulberry leaves infested with *B. mori* producing BmFHD than when exposed to leaves beset with caterpillars unable to secret this enzyme (Takai et al. 2018). This clear response activity demonstrates the importance of GLVs in the mulberry volatile signal for *Z. dolosa*. Homologs of this enzymatic effector are present in other caterpillar species (Takai et al. 2018; Jones et al. 2019).

In addition to the FHD effector, a heat-stable small molecule is present in the gut contents (regurgitant) of *M. sexta*, *Trichoplusia ni*, *S. frugiperda*, and *S. exigua*. This **H**exen**AL** **T**rapping (HALT) effector directly reacts with (*Z*)-3-hexenal, the first GLV biosynthesized (Table 1) (Jones et al. 2019). Efforts are ongoing to characterize this effector, its mode of action, and its distribution throughout the herbivorous Lepidoptera.

An isomerase in *M. sexta* oral secretions converts the (*Z*)-3-hexenal GLV to its (*E*)-2-isomer, changing the ratio of released GLVs into the environment (Table 1) (Allmann and Baldwin 2010). Tobacco plants emitting the (*E*)-isomer GLV are attractive to predatory *Geocoris* spp. beetles, indicating a likely meal (Allmann and Baldwin 2010). This isomerase has been partially characterized (Allmann dissertation). Similar isomerizing activity has been detected in the oral secretions (specifically in homogenates of the salivary glands) of several noctuid species (Allmann and Baldwin 2010; Jones et al. 2019). Since the shift of the volatile ratio from (*Z*)-3-hexenal to (*E*)-2-hexenal emission is attractive to predatory beetles, the isomerase triggering it technically fits the definition of an elicitor (similar to the emission of maize HIPVs which are attractive to herbivore parasitoids when treated with the FAC elicitors).

While the FHD, HALT, and isomerase compounds alter GLV emission from host plants, thus far the isomerase is the only compound that has been shown to directly influence an insect response. Naturally, the classification of these compounds as effectors assumes that GLVs can act as an early defense response to stressors of plant species (Scala et al. 2013; Matsui and Koeduka 2016). The variety of mechanisms through which caterpillar species suppress or modify GLV emission from their host plant species, suggests a need for the insect to counteract indirect volatile defense responses (Jones et al. 2019).

The other effector compounds

Several other effectors from caterpillar oral secretions decrease the host plant's defense responses. The saliva of either the rice or maize *S. frugiperda* strains feeding on non-preferred host plants contains higher phospholipase C (PLC) activity (Acevedo et al. 2017). Increased activity of this effector induced greater accumulation of protease inhibitors or suppressed the induction of trypsin inhibitor activity, in maize and Bermuda grass, respectively (Acevedo et al. 2017). The fact that saliva composition is adjustable to influence host plant defenses, is indicative that saliva components can be adaptable to host plant species. *S. frugiperda* saliva also contains benzoic acid and the phytohormones JA, SA, and abscisic acid, which when applied to plant species at equivalent concentrations, upregulated a proteinase inhibitor gene expression in maize and down-regulated several herbivore-induced defenses in tomato (Acevedo et al. 2019). The *Helicoverpa armigera* R-like protein 1 (HARP) interacts directly with plant JA2 receptors, blocking JA signal transduction, and rendering the host plant species susceptible to herbivory (Chen et al. 2019). Interestingly, the host plant species may modulate this effector since HARP is induced during insect herbivory on gossypol, a major defense compound in cotton plants (*Gossypium* sp.) (Chen et al. 2019). ATP hydrolyzing enzymes from *H. zea* salivary glands suppress the defense genes regulated by the JA and ethylene pathways as well as the production of glandular trichomes of tomato (Wu et al. 2012; Felton et al. 2018). Extracellular ATP (eATP) is a damage-associated molecular pattern (DAMP) that is released in plant tissues following wounding, and acts on JA defense signaling to amplify plant defenses; thus, salivary ATPases may be directly hydrolyzing this DAMP to attenuate JA responses (Choi et al. 2014; Tripathi et al. 2018). The salivary protein tyrosine phosphatase (PTP) suppressed the wound-induced accumulation of JA-regulated proteins (Ward et al. 1994; Felton et al. 2018). Finally, sundry caterpillar species utilize a salivary enzyme that lyses bacteria on the surface of a plant species, possibly providing the herbivore with an immediate antibacterial factor (Liu et al. 2004). The release of peptidoglycan and other cell fragments from this lysis may also trigger complex signaling among the phytohormone signaling pathways of the plant species (Table 1) (Morishima et al. 1988; Liu et al. 2004).

Additionally, other insect-derived compounds from aphid feeding, oviposition fluid, and the bacteria present in oral secretions can disrupt the defenses of a plant to specific herbivores. The aphid (*Myzus persicae*; green peach aphid) salivary protein Mp55, released into the host plant during phloem feeding, resulted in increased aphid reproduction (Elzinga et al. 2014). The small brown planhopper (*Laodelphax striatellus*) had an effector that attenuated host rice plant defenses by preventing hydrogen peroxide (H_2O_2) accumulation and promoting insect performance. This C-terminal polypeptide of vitellogenin (VgC) interacted directly with the rice transcription factor OsWRKY71 (Ji et al. 2021). Similarly, *P. brassicae* and *S. littoralis* egg extract reduced the induction of insect responsive genes and induced SA accumulation which negatively interfered with JA pathways of the host plant species (Bruessow et al. 2010). Egg-derived effectors suppress plant defenses and by doing so, confer an advantage to an insect species offspring (Bruessow et al. 2010). Microbes in oral secretions are capable of modifying defense protein expression, depending on the host plant species and the suite of bacteria present, which can subsequently affect an insect's growth or reproductive success (Chung et al. 2013; Acevedo et al. 2017). Bacteria (Stenotrophomonas, Pseudomonas, and Enterobacter sp.) in the oral secretions of *Leptinotarsa decemlineata* (Colorado potato beetle) larvae decreased JA and JA-responsive antiherbivore defenses, and increased SA and SA-responsive gene expression in tomato (*Solanum lycopersicum*) (Chung et al. 2013). Diverse insect-derived compounds and bacterial symbionts can be perceived by host plant species in such a way as to disrupt plant defense responses (Table 1).

Summary of effectors

By disrupting plant defenses as opposed to eliciting them, insect effectors act in contrast to insect elicitors (Felton and Tumlinson 2008) However, plant species may respond to effectors in an elicitor-like fashion (GOX treated tomato plants increase their defenses) while other plant species may respond to these compounds by a reduction in defense responses (GOX-treated tobacco plants decrease their defenses) (Musser et al. 2005a; Peiffer and Felton 2005; Lin et al. 2020). Additionally, plant species may respond differently to GLV effectors, perhaps in part because plant species often biosynthesize different quantities of these volatiles (Engelberth and Engelberth 2020) As with elicitors, these insect-derived compounds appear to benefit the insect species; however, some plant species may respond defensively to them.

Conclusions

The coevolution of plants and insect herbivores resulted in a profusion of defense molecules and strategies for both sides of this relationship (Acevedo et al. 2015; Malik et al. 2021; Zunjarrao et al. 2020). The 'arms race' perspective of these interactions represents a specific cross-section of interactions within evolutionary time, rather than charting the relationship of an insect and host plant over its evolutionary history. The compounds involved in these defense strategies are often derived from conserved structural features of herbivores (for instance many elicitors—volicitin, caeliferins, bruchins—are derived from fatty acid biosynthesis or metabolism), and therefore, have a role in the physiology or metabolism of the herbivorous insect species. For example, the particular glutamate and linolenic acid-based FACs that elicit HIPVs which subsequently attract parasitoids play a critical role in assimilating nitrogen for the caterpillar (Tumlinson and Engelberth 2008; Yoshinaga et al. 2008; Mori and Yoshinaga 2011). Interestingly, the interactions between plant species and their insect herbivores bear parallels to those between plant species and pathogens. (Tumlinson and Felton 2008). Studies detailing the role of insect-derived bacteria in manipulating plant-insect interactions provide a place for the fields of plant pathology and plant-herbivory to intersect via shared concepts (Jones and Dangl 2006; Chung et al. 2013; Acevedo et al. 2017).

Continued research is necessary to determine the ecological and evolutionary significance of elicitors and effectors for both the plant and insect species in these interactions (Felton and Tumlinson 2008). Undoubtedly there are elicitors and effectors as yet undescribed, in addition to those that deserve further study. A significant challenge that has not yet been undertaken is the assessment of the known range of these compounds for a particular insect species, and the resulting defense responses and signaling cascades of a particular host plant species. A second challenge in this area is determining the host plant range for generalist and specialist insects and the responses of the plants to such an insect's particular cocktail of elicitors and effectors. These questions are dependent on a detectible defense response from the host plant species. Through utilizing the wealth of genomic, proteomic, and metabolomic tools, the available data from model plant systems, and insect feeding assays we can refine our ability to detect plant defense responses to herbivory. Furthermore, the literature from plant-pathogen interactions should provide a strong framework for approaching these interactions and should be further utilized to provide the context, structure, and direction to this challenge (Jones and Dangl 2006; Felton and Tumlinson 2008).

A holistic understanding of plant-insect interactions must account for the ecological and physiological context in which a plant species perceives and responds to herbivore-associated signals (Felton and Tumlinson 2008; Acevedo et al. 2015). Such an approach would consider the specific molecular steps at which an insect-derived compounds will influence plant signaling pathways. Plant molecular components involved in perception, recognition, and signal transduction of insect elicitors and effectors have recently been the subject of increased interest and review Chen and Mao 2020; Erb and Reymond 2019; Malik et al. 2021). Recent reviews have also emphasized the machinery of herbivory sensing and the cellular and systemic signaling in plants responding to insect-derived compounds (Arimura 2020), the role of jasmonate as the main regulator in plant signaling against insect species (Chen and Mao 2020), the molecular events involved in these interactions, plant defense mechanisms, and insect strategies used to combat plant defense (Zunjarrao et al. 2020). Although such work presents a considerable challenge, it offers exciting opportunities to discover new interactions in the field of chemical ecology. Recent insights into the cellular pathways by which plant species sense elicitors and elicit defense responses against herbivore species will increase applications of this research for agriculture (Acevedo et al. 2015; Arimura 2020). In light of the increased focus towards improved crop production through the reduction of pesticides, it is essential to recognize both the challenges and the opportunities in the areas of plant signaling, plant defense responses to herbivores, and herbivore strategies for challenging those defense responses.

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References

Acevedo FE, Rivera-Vega LJ, Chung SH, Ray S, Felton GW (2015) Cues from chewing insects — the intersection of DAMPs, HAMPs, MAMPs and effectors. Curr Opin Plant Biol 26:80–86. https://doi.org/10.1016/j.pbi.2015.05.029

Acevedo FE, Peiffer M, Tan CW, Stanley BA, Stanley A, Wang J, Jones AG, Hoover K, Rosa C, Luthe D, Felton G (2017) Fall armyworm-associated gut bacteria modulate plant defense responses. Mol Plant-Microbe Interact 30(2):127–137

Acevedo FE, Smith P, Peiffer M, Helms A, Tooker J, Felton GW (2019) Phytohormones in fall armyworm saliva modulate defense responses in plants. J Chem Ecol 45(7):598–609

Alborn HT, Turlings TCJ, Jones T, Stenhagen G, Loughrin JH, Tumlinson JH (1997) An elicitor of plant volatiles from beet armyworm oral secretion. Science 276(5314):945–949

Alborn HT, Hansen TV, Jones TH, Bennett DC, Tumlinson JH, Schmelz EA, Teal PE (2007a) Disulfooxy fatty acids from the American bird grasshopper Schistocerca americana, elicitors of plant volatiles. Proc Natl Acad Sci 104(32):12976–12981

Alborn HT, Hansen TV, Jones TH, Bennett DC, Tumlinson JH, Schmelz EA, Teal PE (2007b) Disulfooxy fatty acids from the American bird grasshopper Schistocerca americana, elicitors of plant volatiles. Proc Nat Acad Sci Aug 104(32):12976–12981

Allmann S, Baldwin IT (2010) Insects betray themselves in nature to predators by rapid isomerization of green leaf volatiles. Science 329(5995):1075–1078

Allmann S, Späthe A, Bisch-Knaden S, Kallenbach M, Schuurink RC, Reinecke A, Sachse S, Baldwin IT, Hansson B (2012) Isomerization of green leaf volatiles alters the behavioral responses of female *Manduca* moths. Dissertation, University of Amsterdam

Ameye M, Allmann S, Verwaeren J, Smagghe G, Haesaert G, Schuurink RC, Audenaert K (2018) Green leaf volatile production by plants: a meta-analysis. New Phytol 220(3):666–683

Arimura GI (2020) Making sense of the way plants sense herbivores. Trends in Plant Sci 26(3):288–298

Arimura GI, Ozawa R, Kugimiya S, Takabayashi J, Bohlmann J (2004) Herbivore-induced defense response in a model legume. Two-spotted spider mites induce emission of (*E*)-β-ocimene and transcript accumulation of (*E*)-β-ocimene synthase in *Lotus japonicus*. Plant Phys 135(4):1976–1983

Bede JC, Musser RO, Felton GW, Korth KL (2006) Caterpillar herbivory and salivary enzymes decrease transcript levels of *Medicago truncatula* genes encoding early enzymes in terpenoid biosynthesis. Plant Mol Biol 60(4):519–531

Beyaert I, Köpke D, Stiller J, Hammerbacher A, Yoneya K, Schmidt A, Gershenzon J, Hilker M (2012) Can insect egg deposition 'warn'a plant of future feeding damage by herbivorous larvae? Proc R Soc B Biol Sci 279(1726):101–108

Bittner N, Trauer-Kizilelma U, Hilker M (2017) Early plant defence against insect attack: involvement of reactive oxygen species in plant responses to insect egg deposition. Planta 245(5):993–1007

Bittner N, Hundacker J, Achotegui-Castells A, Anderbrant O, Hilker M (2019) Defense of Scots pine against sawfly eggs (*Diprion pini*) is primed by exposure to sawfly sex pheromones. Proc Natl Acad Sci 116(49):24668–24675

Bonaventure G, VanDoorn A, Baldwin IT (2011) Herbivore-associated elicitors: FAC signaling and metabolism. Trends Plant Sci 16(6):294–299

Bouwmeester HJ, Verstappen FW, Posthumus MA, Dicke M (1999) Spider mite-induced (3*S*)-(*E*)-nerolidol synthase activity in cucumber and lima bean. The first dedicated step in acyclic C11-homoterpene biosynthesis. Plant Phys 121(1):173–180

Bruessow F, Gouhier-Darimont C, Buchala A, Metraux JP, Reymond P (2010) Insect eggs suppress plant defence against chewing herbivores. Plant J 62(5):876–885

Chen MS (2008) Inducible direct plant defense against insect herbivores: a review. Insect Sci 15(2):101–114

Chen CY, Mao YB (2020) Research advances in plant–insect molecular interaction. F1000Research. https://doi.org/10.12688/f1000research.21502.1

Chen CY, Liu YQ, Song WM, Chen DY, Chen FY, Chen XY, Chen ZW, Ge SX, Wang CZ, Zhan S, Chen XY (2019) An effector from cotton bollworm oral secretion impairs host plant defense signaling. Proc Natl Acad Sci 116(28):14331–14338

Choi J, Tanaka K, Cao Y, Qi Y, Qiu J, Liang Y, Lee SY, Stacy G (2014) Identification of a plant receptor of extracelluar ATP. Science 343(6168):290–294

Chuang WP, Ray S, Acevedo FE, Peiffer M, Felton GW, Luthe DS (2014) Herbivore cues from the fall armyworm (*Spodoptera frugiperda*) larvae trigger direct defenses in maize. Mol Plant-Microbe Interac 27(5):461–470

Chung SH, Rosa C, Scully ED, Peiffer M, Tooker JF, Hoover K, Luthe DS, Felton GW (2013) Herbivore exploits orally secreted bacteria to suppress plant defenses. PNAS 110(39):15728–15733

Cooper LD, Doss RP, Price R, Peterson K, Oliver JE (2005) Application of Bruchin B to pea pods results in the up-regulation of CYP93C18, a putative isoflavone synthase gene, and an increase in the level of pisatin, an isoflavone phytoalexin. J Exp Bot 56(414):1229–1237

Cruickshank IAM (1962) Studies on phytoalexins IV. The antimicrobial spectrum of pisatin. Aust J Biol Sci 15(1):147–159

Delphia CM, Mescher MC, Felton G, Moraes CMD (2006) The role of insect-derived cues in eliciting indirect plant defenses in tobacco, *Nicotiana tabacum*. Plant Signal Behav 1(5):243–250

Delphia CM, Mescher MC, De Moraes CM (2007) Induction of plant volatiles by herbivores with different feeding habits and the effects of induced defenses on host-plant selection by thrips. J Chem Ecol 33(5):997–1012

Diezel C, von Dahl CC, Gaquerel E, Baldwin IT (2009) Different lepidopteran elicitors account for cross-talk in herbivory-induced phytohormone signaling. Plant Phys 150(3):1576–1586

Doss RP (2005) Treatment of pea pods with Bruchin B results in up-regulation of a gene similar to MtN19. Plant Phys Biochem 43(3):225–231

Doss RP, Oliver JE, Proebsting WM, Potter SW, Kuy S, Clement SL, Williamson RT, Carney JR, DeVilbiss ED (2000) Bruchins: insect-derived plant regulators that stimulate neoplasm formation. Proc Nat Acad Sci 97(11):6218–6223

Eichenseer H, Mathews MC, Bi JL, Murphy JB, Felton GW (1999) Salivary glucose oxidase: multifunctional roles for *Helicoverpa zea*? Arch Insect Biochem Phys Publ Collab Entomol Soc Am 42(1):99–109

Eichenseer H, Mathews MC, Powell JS, Felton GW (2010) Survey of a salivary effector in caterpillars: glucose oxidase variation and correlation with host range. J Chem Ecol 36(8):885–897

Elzinga DA, De Vos M, Jander G (2014) Suppression of plant defenses by a *Myzus persicae* (green peach aphid) salivary effector protein. Mol Plant Microbe Interact 27(7):747–756

Engelberth J, Engelberth M (2020) Variability in the capacity to produce damage-induced aldehyde green leaf volatiles among different plant species provides novel insights into biosynthetic diversity. Plants 9(2):213

Erb M, Reymond P (2019) Molecular interactions between plants and insect herbivores. Annu Rev Plant Bio 70:527–557

Felton GW (2008) Caterpillar secretions and induced plant responses. In: Schaller A (ed) Induced plant resistance to herbivory. Springer, Dordrecht, pp 369–387

Felton GW, Tumlinson JH (2008) Plant–insect dialogs: complex interactions at the plant–insect interface. Curr Op Plant Bio 11(4):457–463

Felton GW, Chung SH, Hernandez MGE, Louis J, Peiffer M, Tian D (2018) Herbivore oral secretions are the first line of protection against plant-induced defenses. Annu Plant Rev 47:37–76

Gomez SK, Cox MM, Bede JC, Inoue K, Alborn HT, Tumlinson JH, Korth KL (2005) Lepidopteran herbivory and oral factors induce transcripts encoding novel terpene synthases in *Medicago truncatula*. Arch Insect Biochem Phys Publ Collab Entomol Soc Am 58(2):114–127

Grant JB (2006) Diversification of gut morphology in caterpillars is associated with defensive behavior. J Exp Bio 209(15):3018–3024

Halitschke R, Schittko U, Pohnert G, Boland W, Baldwin IT (2001) Molecular interactions between the specialist herbivore *Manduca sexta* (Lepidoptera, Sphingidae) and its natural host *Nicotiana attenuata*. III. Fatty acid-amino acid conjugates in herbivore oral secretions are necessary and sufficient for herbivore-specific plant responses. Plant Phys 125(2):711–717

Hammerschmidt R, Nicholson RL (1999) A survey of plant defense responses to pathogens. In: Agrawal AA, Tuzun S, Bent E (eds) Induced plant defenses against pathogens and herbivores: biochemistry, ecology, and agriculture. APS Press, St. Paul, pp 55–71

Helms AM, De Moraes CM, Tooker JF, Mescher MC (2013) Exposure of *Solidago altissima* plants to volatile emissions of an insect antagonist (*Eurosta solidaginis*) deters subsequent herbivory. Proc Nat Acad Sci 110(1):199–204

Helms AM, De Moraes CM, Mescher MC, Tooker JF (2014) The volatile emission of *Eurosta solidaginis* primes herbivore-induced volatile production in *Solidago altissima* and does not directly deter insect feeding. BMC Plant Biol 14(1):1–10

Helms AM, De Moraes CM, Tröger A, Alborn HT, Francke W, Tooker JF, Mescher MC (2017) Identification of an insect-produced olfactory cue that primes plant defenses. Nat Commun 8(1):1–9

Hilker M, Stein C, Schröder R, Varama M, Mumm R (2005) Insect egg deposition induces defense responses in *Pinus sylvestris*: characterization of the elicitor. J Exp Biol 208(10):1849–1854

Hopke J, Donath J, Blechert S, Boland W (1994) Herbivore-induced volatiles: the emission of acyclic homoterpenes from leaves of *Phaseolus lunatus* and *Zea mays* can be triggered by a β-glucosidase and jasmonic acid. Febs Lett 352(2):146–150

Hu YH, Leung DW, Kang L, Wang CZ (2008) Diet factors responsible for the change of the glucose oxidase activity in labial salivary glands of *Helicoverpa armigera*. Arch Insect Biochem Phys Publ Collab Entomol Soc Am 68(2):113–121

Iida J, Desaki Y, Hata K, Uemura T, Yasuno A, Islam M, Maffei ME, Ozawa R, Nakajima T, Galis I, Arimura GI (2019) Tetranins: new putative spider mite elicitors of host plant defense. New Phytol 224(2):875–885

Ji R, Fu J, Shi Y, Li J, Jing M, Wang L, Yang S, Tian T, Wang L, Ju J, Guo H (2021) Vitellogenin from planthopper oral secretion acts as a novel effector to impair plant defenses. New Phys. https://doi.org/10.1111/nph.17620

Jones JD, Dangl JL (2006) The plant immune system. Nature 444(7117):323–329

Jones AC, Seidl-Adams I, Engelberth J, Hunter CT, Alborn H, Tumlinson JH (2019) Herbivorous caterpillars can utilize three mechanisms to alter green leaf volatile emission. Environ Entomol 48(2):419–425

Karban R, Baldwin IT (1997) Induced responses to herbivory. University of Chicago Press, Chicago

Köpke D, Schröder R, Fischer HM, Gershenzon J, Hilker M, Schmidt A (2008) Does egg deposition by herbivorous pine sawflies affect transcription of sesquiterpene synthases in pine? Planta 228(3):427–438

Lecourieux D, Ranjeva R, Pugin A (2006) Calcium in plant defence-signalling pathways. New Phytol 171(2):249–269

Lin PA, Peiffer M, Felton GW (2020) Induction of defensive proteins in Solanaceae by salivary glucose oxidase of *Helicoverpa zea* caterpillars and consequences for larval performance. Arthropod-Plant Interact 14:317–325

Lin PA, Chen Y, Chaverra-Rodriguez D, Heu CC, Zainuddin NB, Sidhu JS, Peiffer M, Tan CW, Helms A, Kim D, Ali J (2021) Silencing the alarm: an insect salivary enzyme closes plant stomata and inhibits volatile release. New Phytol 230:793–803

Lindroth RL (1988) Hydrolysis of phenolic glycosides by midgut β-glucosidases in *Papilio glaucus* subspecies. Insect Biochem 18(8):789–792

Lindroth RL (1989) Host plant alteration of detoxication activity in *Papilio glaucus glaucus*. Entomol Exp Appl 50(1):29–35

Liu F, Cui L, Cox-Foster D, Felton GW (2004) Characterization of a salivary lysozyme in larval *Helicoverpa zea*. J Chem Ecol 30(12):2439–2457

Louis J, Peiffer M, Ray S, Luthe DS, Felton GW (2013) Host-specific salivary elicitor (s) of European corn borer induce defenses in tomato and maize. New Phytol 199(1):66–73

Maffei M, Bossi S, Spiteller D, Mithöfer A, Boland W (2004) Effects of feeding *Spodoptera littoralis* on lima bean leaves. I. Membrane potentials, intracellular calcium variations, oral secretions, and regurgitate components. Plant Phys 134(4):1752–1762

Magalhães DM, Da Silva ITFA, Borges M, Laumann RA, Blassioli-Moraes MC (2019) Anthonomus grandis aggregation pheromone induces cotton indirect defence and attracts the parasitic wasp *Bracon vulgaris*. J Exp Bot 70(6):1891–1901

Malik G, Chaturvedi R, Hooda S (2021) Role of herbivore-associated molecular patterns (HAMPs) in modulating plant defenses. In: Singh IK, Singh A (eds) Plant-Pest Interact Mol Mech Chem Ecol. Springer, Singapore, pp 1–29

Matsui K, Koeduka T (2016) Green leaf volatiles in plant signaling and response. In: Nakamura Y, Li-Beisson Y (eds) Lipids in plant and algae development. Springer, Berlin, pp 427–443

Mattiacci L, Dicke M, Posthumus MA (1995) beta-Glucosidase: an elicitor of herbivore-induced plant odor that attracts host-searching parasitic wasps. Proc Natl Acad Sci 92(6):2036–2040

Melotto M, Underwood W, He SY (2008) Role of stomata in plant innate immunity and foliar bacterial diseases. Annu Rev Phytopathol 46:101–122

Merkx-Jacques M, Bede JC (2005) Influence of diet on the larval beet armyworm, *Spodoptera exigua*, glucose oxidase activity. J Insect Sci 5(1):48

Mikó I, Rahman SR, Jones AC, Townley MA, Gominho B, Paudel S, Stupski SD, Hines HM, Schilder RJ (2019) From spinning silk to spreading saliva: mouthpart remodeling in *Manduca sexta* (Lepidoptera: Sphingidae). Insect Syst Divers 3(6):2

Mithöfer A, Boland W (2008) Recognition of herbivory-associated molecular patterns. Plant Phys 146(3):825–831

Mori N, Yoshinaga N (2011) Function and evolutionary diversity of fatty acid amino acid conjugates in insects. J Plant Interact 6(2–3):103–107

Mori N, Alborn HT, Teal PE, Tumlinson JH (2001) Enzymatic decomposition of elicitors of plant volatiles in *Heliothis virescens* and *Helicoverpa zea*. J Insect Phys 47(7):749–757

Mori N, Yoshinaga N, Sawada Y, Fukui M, Shimoda M, Fujisaki K, Nishida R, Kuwahara Y (2003) Identification of volicitin-related compounds from the regurgitant of lepidopteran caterpillars. Biosci Biotech Biochem 67(5):1168–1171

Morishima I, Suginaka S, Bougaki T, Inoue M, Ueno T (1988) Induction and partial characterization of antibacterial proteins in the hemolymph of the silkworm, *Bombyx mori*. Agric Bio Chem 52(4):929–934

Mumm R, Schrank K, Wegener R, Schulz S, Hilker M (2003) Chemical analysis of volatiles emitted by *Pinus sylvestris* after induction by insect oviposition. J Chem Ecol 29(5):1235–1252

Musser RO, Hum-Musser SM, Eichenseer H, Peiffer M, Ervin G, Murphy JB, Felton GW (2002) Caterpillar saliva beats plant defenses. Nature 416(6881):599–600

Musser RO, Cipollini DF, Hum-Musser SM, Williams SA, Brown JK, Felton GW (2005) Evidence that the caterpillar salivary enzyme glucose oxidase provides herbivore offense in solanaceous plants. Arch Insect Biochem Phys Publ Collab Entomol Soc Am 58(2):128–137

Musser RO, Kwon HS, Williams SA, White CJ, Romano MA, Holt SM, Bradbury S, Brown JK, Felton GW (2005) Evidence that caterpillar labial saliva suppresses infectivity of potential bacterial pathogens. Arch Insect Biochem Phys Publ Collab Entomol Soc Am 58(2):138–144

Musser RO, Farmer E, Peiffer M, Williams SA, Felton GW (2006) Ablation of caterpillar labial salivary glands: technique for determining the role of saliva in insect–plant interactions. J Chem Ecol 32(5):981–992

Oliver JE, Doss RP, Williamson RT, Carney JR, DeVilbiss ED (2000) Bruchins—mitogenic 3-(hydroxypropanoyl) esters of long chain diols from weevils of the Bruchidae. Tetrahedron 56(39):7633–7641

Paré PW, Tumlinson JH (1997) De novo biosynthesis of volatiles induced by insect herbivory in cotton plants. Plant Phys 114(4):1161–1167

Paré PW, Tumlinson JH (1999) Plant volatiles as a defense against insect herbivores. Plant Phys 121(2):325–332

Peiffer M, Felton GW (2005) The host plant as a factor in the synthesis and secretion of salivary glucose oxidase in larval *Helicoverpa zea*. Arch Insect Biochem Phys Publ Collab Entomol Soc Am 58(2):106–113

Pohnert G, Jung V, Haukioja E, Lempa K, Boland W (1999) New fatty acid amides from regurgitant of lepidopteran (Noctuidae, Geometridae) caterpillars. Tetrahedron 55(37):11275–11280

Prajapati VK, Varma M, Vadassery J (2020) In silico identification of effector proteins from generalist herbivore *Spodoptera litura*. BMC Genom 21(1):1–16

Ray S, Gaffor I, Acevedo FE, Helms A, Chuang WP, Tooker J, Felton GW, Luthe DS (2015) Maize plants recognize herbivore-associated cues from caterpillar frass. J Chem Ecol 41(9):781–792

Ray S, Alves PC, Ahmad I, Gaffoor I, Acevedo FE, Peiffer M, Jin S, Han Y, Shakeel S, Felton GW, Luthe DS (2016a) Turnabout is fair play: Herbivory-induced plant chitinases excreted in fall armyworm frass suppress herbivore defenses in maize. Plant Phys 171(1):694–706

Ray S, Alves PC, Ahmad I, Gaffoor I, Acevedo FE, Peiffer M, Jin S, Han Y, Shakeel S, Felton GW, Luthe DS (2016) Turnabout is fair play: herbivory-induced plant chitinases excreted in fall armyworm frass suppress herbivore defenses in maize. Plant Physiol 171(1):694–706

Ray S, Basu S, Rivera-Vega LJ, Acevedo FE, Louis J, Felton GW, Luthe DS (2016c) Lessons from the far end: caterpillar frass-induced defenses in maize, rice, cabbage, and tomato. J Chem Ecol 42(11):1130–1141

Ray S, Helms AM, Matulis NL, Davidson-Lowe E, Grisales W, Ali JG (2020) Asymmetry in herbivore effector responses: caterpillar frass effectors reduce performance of a subsequent herbivore. J Chem Ecol 46(1):76–83

Ribeiro J (1987) Vector salivation and parasite transmission. Memórias do Instituto Oswaldo Cruz 82:1–3

Ribeiro JMC, Schneider M, Guimaraes JA (1995) Purification and characterization of prolixin S (nitrophorin 2), the salivary anticoagulant of the blood-sucking bug *Rhodnius prolixus*. Biochem J 308(1):243–249

Scala A, Allmann S, Mirabella R, Haring MA, Schuurink RC (2013) Green leaf volatiles: a plant's multifunctional weapon against herbivores and pathogens. Int J Mol Sci 14(9):17781–17811

Schmelz EA, Carroll MJ, LeClere S, Phipps SM, Meredith J, Chourey PS, Alborn HT, Teal PE (2006) Fragments of ATP synthase mediate plant perception of insect attack. Proc Nat Acad Sci 103(23):8894–8899

Schmelz EA, LeClere S, Carroll MJ, Alborn HT, Teal PEA (2007) Cowpea chloroplastic ATP synthase is the source of multiple plant defense elicitors during insect herbivory. Plant Physiol 144(2):793–805. https://doi.org/10.1104/pp.107.097154

Schmelz EA, Engelberth J, Alborn HT, Tumlinson JH, Teal PE (2009) Phytohormone-based activity mapping of insect herbivore-produced elicitors. Proc Nat Acad Sci 106(2):653–657

Schmelz EA, Huffaker A, Carroll MJ, Alborn HT, Ali JG, Teal PE (2012) An amino acid substitution inhibits specialist herbivore production of an antagonist effector and recovers insect-induced plant defenses. Plant Phys 160(3):1468–1478

Schröder R, Cristescu SM, Harren FJ, Hilker M (2007) Reduction of ethylene emission from Scots pine elicited by insect egg secretion. J Exp Bot 58(7):1835–1842

Spiteller D, Pohnert G, Boland W (2001) Absolute configuration of volicitin, an elicitor of plant volatile biosynthesis from lepidopteran larvae. Tetrahedron Lett 42(8):1483–1485

Steinbrenner AD, Muñoz-Amatriaín M, Venegas JMA, Lo S, Shi D, Holton N, Zipfel C, Abagyan R, Huffaker A, Close TJ, Schmelz EA (2020) A receptor for herbivore-associated molecular patterns mediates plant immune responses to herbivore-associated molecular pattenrs. Proc Nat Acad Sci 117(49):31510–31518

Takai H, Ozawa R, Takabayashi J, Fujii S, Arai K, Ichiki RT, Koeduka T, Dohra H, Ohnishi T, Taketazu S, Kobayashi J (2018) Silkworms suppress the release of green leaf volatiles by mulberry leaves with an enzyme from their spinnerets. Sci Rep 8(1):1–14

Tang Q, Hu Y, Kang L, Wang CZ (2012) Characterization of glucose-induced glucose oxidase gene and protein expression in *Helicoverpa armigera* larvae. Arch Insect Biochem Phys 79(2):104–119

Tian D, Peiffer M, Shoemaker E, Tooker J, Haubruge E, Francis F, Luthe DS, Felton GW (2012a) Salivary glucose oxidase from caterpillars mediates the induction of rapid and delayed-induced defenses in the tomato plant. PLoS One 7(4):e36168

Tian D, Tooker J, Peiffer M, Chung SH, Felton GW (2012b) Role of trichomes in defense against herbivores: comparison of herbivore response to woolly and hairless trichome mutants in tomato (Solanum lycopersicum). Planta 236(4):1053–1066

Tripathi D, Zhang T, Koo AJ, Stacey G, Tanaka K (2018) Extracelluar ATP acts on jasmonate signaling to reinforce plant defense. Plant Phys 176(1):511–523

Truitt CL, Paré PW (2004) *In situ* translocation of volicitin by beet armyworm larvae to maize and systemic immobility of the herbivore elicitor in planta. Planta 218(6):999–1007

Truitt CL, Wei HX, Paré PW (2004) A plasma membrane protein from *Zea mays* binds with the herbivore elicitor volicitin. Plant Cell 16(2):523–532

Tumlinson JH, Engelberth J (2008) Fatty acid-derived signals that induce or regulate plant defenses against herbivory. In: Schaller A (ed) Induced plant resistance to herbivory. Springer, Dordrecht, pp 389–407

Tumlinson JH, Lait CG (2005) Biosynthesis of fatty acid amide elicitors of plant volatiles by insect herbivores. Arch Insect Biochem Phys Publ Collab Entomol Soc Am 58(2):54–68

Turlings TC, McCall PJ, Alborn HT, Tumlinson JH (1993) An elicitor in caterpillar oral secretions that induces corn seedlings to emit chemical signals attractive to parasitic wasps. J Chem Ecol 19(3):411–425

Turlings TC, Loughrin JH, Mccall PJ, Röse US, Lewis WJ, Tumlinson JH (1995) How caterpillar-damaged plants protect themselves by attracting parasitic wasps. Proc Nat Acad Sci 92(10):4169–4174

Ward Y, Gupta S, Jensen P, Wartmann M, Davis RJ, Kelly K (1994) Control of MAP kinase activation by the mitogen-induced threonine/tyrosine phosphatase PAC1. Nature 367(6464):651–654

Wu S, Peiffer M, Luthe DS, Felton GW (2012) ATP hydrolyzing salivary enzymes of caterpillars suppress plant defenses. PloS One 7(7):e41947

Yang KL (2017) Combined cross-linked enzyme aggregates of horseradish peroxidase and glucose oxidase for catalyzing cascade chemical reactions. Enzyme Microb Tech 100:52–59

Yoshinaga N, Aboshi T, Abe H, Nishida R, Alborn HT, Tumlinson JH, Mori N (2008) Active role of fatty acid amino acid conjugates in nitrogen metabolism in *Spodoptera litura* larvae. Proc Nat Acad Sci 105(46):18058–18063

Yoshinaga N, Alborn HT, Nakanishi T, Suckling DM, Nishida R, Tumlinson JH, Mori N (2010) Fatty acid-amino acid conjugates diversification in lepidopteran caterpillars. J Chem Ecol 36(3):319–325

Yoshinaga N, Ishikawa C, Seidl-Adams I, Bosak E, Aboshi T, Tumlinson JH, Mori N (2014) N-(18-hydroxylinolenoyl)-L-glutamine: a newly discovered analog of volicitin in *Manduca sexta* and its elicitor activity in plants. J Chem Ecol 40(5):484–490

Yu SJ (1989) Purification and characterization of glutathione transferases from five phytophagous Lepidoptera. Pestic Biochem Phys 35(1):97–105

Zunjarrao SS, Tellis MB, Joshi SN, Joshi RS (2020) Plant-insect interaction: the saga of molecular coevolution. In: Mérillon JM, Ramawat KG (eds) Co-evolution of secondary metabolites. Springer, Nature, pp 19–45