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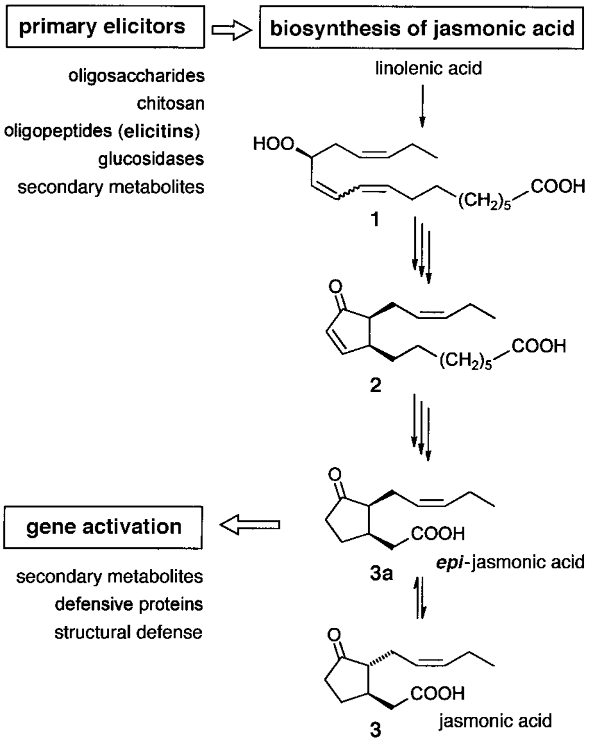
Induced Chemical Defense in Plants[**]

Frank Schröder[*]

The chemical defense of plants has been a most fascinating topic of natural product chemistry since its early beginnings. To date, a large number of secondary metabolites have been identified including alkaloids, anthocyans, flavonoids, and terpenoids, which are thought to have ecological functions related to plant defense against microbial, fungal, or herbivoral attack.[1] Additionally, several plant species have been shown to produce defensive proteins such as proteinase inhibitors.[2]

While many of the defensive compounds in plants are formed constitutively, recent results show that plants have highly sophisticated regulation mechanisms that control the production of defensive secondary metabolites or proteins. A growing number of examples demonstrates that the biosynthesis of defensive compounds may be induced by damage from pathogens or herbivores.[3] These induced plant defense reactions can be local, but very often extend systemically through the plant; that is, they are not limited to the site of damage.

The induced synthesis of defensive compounds, especially when the response of the plant is systemic, must rely on highly effective signaling systems that mediate a quick response to microbial or herbivoral attack. Although the understanding of defense systems in plants is still limited, and the signaling pathways may vary among plant species, recent results suggest a general underlying pattern for plant self-defense mechanisms (Scheme 1). Depending on the nature of the attacking



Scheme 1. General pattern of signaling systems involved in induced plant defense reactions and biosynthesis of jasmonic acid (**3**).

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pathogen, compounds from various classes of natural products have been found to function as the primary elicitors that activate the plant's signaling system. These can be oligosaccharide fragments generated from both plant or fungal cell walls,[4] small proteins (elicitins) secreted by infesting fungi,[5] secondary metabolites, or enzymes such as β-glucosidases in the saliva of herbivorous insects.[6]

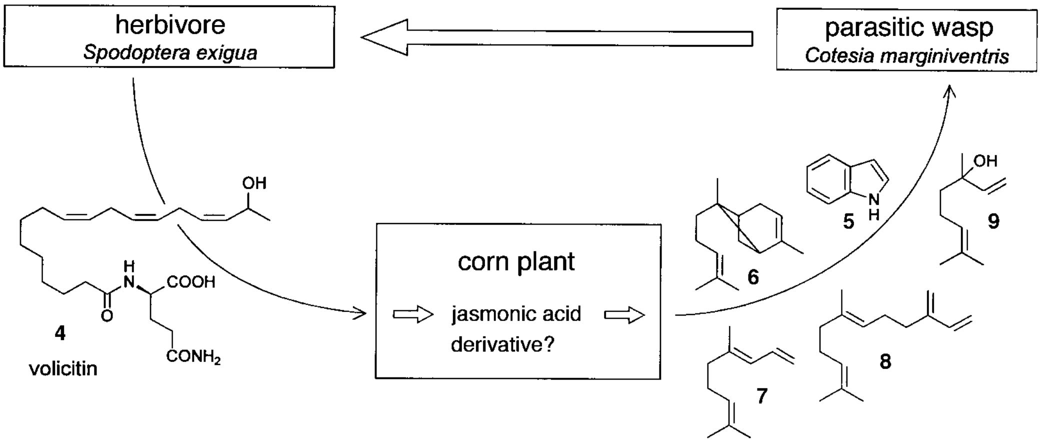
While there is a high degree of chemical diversity among the primary elicitors, defensive signaling in plants seems to rely on at least one common group of signal transducers. For a large number of species from different plant families it has been shown that recognition of the primary elicitors eventually induces the biosynthesis of jasmonic acid (**3**) or methyl jasmonate.[7] In plants jasmonic acid is produced from linolenic acid in a series of steps (the octadecanoic pathway) as described by Vick and Zimmermann (Scheme 1).[8] After lipoxidation, the intermediate (13*S*)-hydroperoxy-9,11,15-octadecatrienoic acid (**1**) is converted into 12-oxophytodienoic acid (**2**), which itself shows strong activity as a phytohormone. Reduction of **2** followed by three β-oxidation cycles finally leads to jasmonic acid (**3**).

In the next step of the signal-transduction chain, the jasmonic acid derivatives trigger the specific responses of the plant to the attacking pathogen or insect. For example, jasmonates induce genes encoding proteinase inhibitors, antifungal proteins, and enzymes involved in the biosynthesis of defensive secondary metabolites.[7] Thus, in addition to their well-established functions as regulators of plant growth and development,[9] jasmonates play a key role as phytohormones or signal transducers in the defense-signaling systems of plants.

So far, investigations of herbivore-induced chemical defense in plants have focused mainly on direct interactions between plant and herbivore. Recent studies have now demonstrated that plant response to herbivoral attack may include interaction with a third trophic level: Herbivore-damaged plants actively attract insect parasitoids or predators. Corn (*Zea mays*), for example, responds to injury inflicted by a caterpillar (*Spodoptera exigua*) with a systemic emission of a characteristic blend of volatile compounds, which attracts females of a parasitic wasp (*Cotesia marginiventris*), a natural predator of these caterpillars (Scheme 2).[10] Several components of this volatile mixture, including indole (**5**) and terpenoids **6**–**9**, are emitted only when the oral secretions of the herbivore comes into contact with damaged plant tissue, and are absent when the plants are just mechanically wounded. Furthermore, the timing of emission of these volatile compounds corresponds to the period of day when the parasitic wasps are foraging for their hosts. The plants are thus able to distinguish between mechanical wounding and damage caused by insects. Similar tritrophic interactions have been described for species from various other plant families, including cotton (*Gossypium hirsutum*),[11] beans (*Phaseolus lunatus*),[6] or cabbage (*Brassica oleracea*).[12] Tumlinson et al. showed that in cotton, the characteristic components emitted, indole (**5**) and terpenoids **7**–**9**, are synthesized de novo upon insect attack.[11] Therefore, elicitors present in the oral secretions of the feeding insects activate at least two different biosynthetic pathways. Until recently the nature of these primary elicitors was largely unknown. Hopke et al. have shown that in some plant species a mixture of β-glucosidases, when applied to freshly wounded leaves, induced the emission of volatile compounds.[6] Since β-glucosidases are also present in the oral secretions of many herbivores, it was concluded that β-glucosidases may represent one group of primary elicitors.

Recently Alborn et al. demonstrated that *N*-(17-hydroxylinolenyl)-L-glutamine (volicitin, **4**), isolated from oral secretions of *Spodoptera exigua*, acts as an elicitor of volatile emission in corn (Scheme 2).[10] Volicitin, presumably derived from linolenic acid, represents the first example of a secondary metabolite from insects that acts as an elicitor of a defensive reaction in plants. Its presence in the oral secretion of the caterpillars is not related to diet, and it thus appears to be produced de novo by the insect. Whether compounds related to **4** are present in the oral secretions of other insects and whether **4** acts as an elicitor of the defense reactions in other plant species remains unknown.

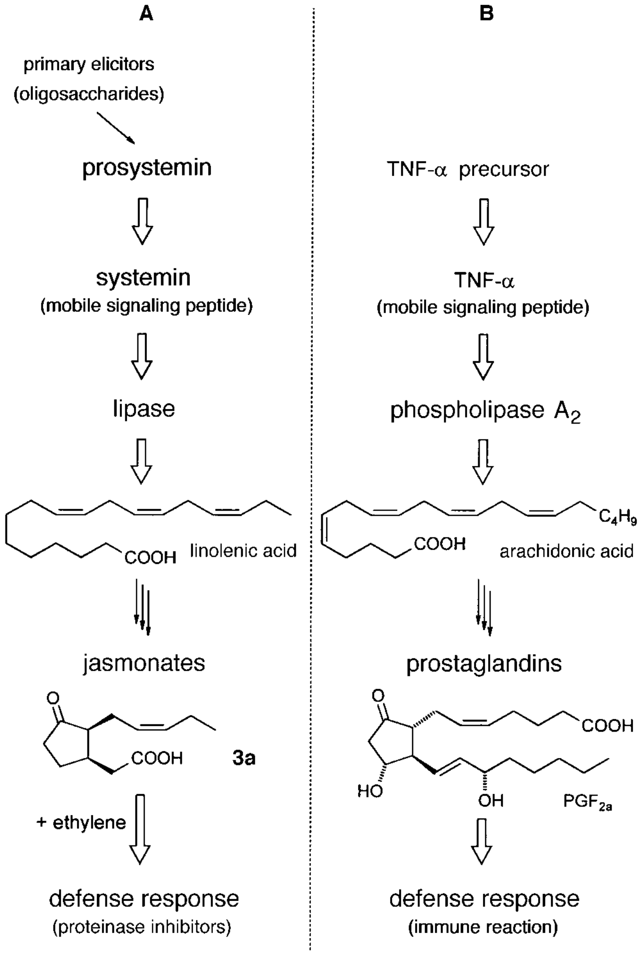
The signal-transduction pathways within the corn plant that lead from the recognition of volicitin to the systemic emission of volatile compounds have been only partially elucidated. As in the case of defensive reactions in other plant species,



Scheme 2. Chemical signals in the tritrophic interaction between corn (*Zea mays*), herbivore (*Spodoptera exigua*), and parasitic wasp (*Cotesia marginiventris*). The absolute configuration at position 17 in volicitin (**4**) has not yet been determined.

jasmonic acid derivatives appear to play an important role. Interestingly, in many plant species *N*-jasmonoyl amino acids ("amino acid conjugates" of jasmonic acid) act as highly active phytohormones.[7d] Since jasmonic acid is produced from linolenic acid, Alborn et al. proposed that an elicitor such as volicitin (that is, an octadecatrienoate conjugated to an amino acid) may be involved with the octadecanoic pathway in the herbivore-damaged corn plant.[10]

Although defensive reactions of plants appear to be induced by jasmonic acid derivatives, jasmonates may not generally represent the systemic signal that travels through the plant and induces defense reactions in its undamaged parts.[13] Interestingly, in one of the most extensively investigated defense mechanisms, the systemic response of tomato plants to herbivore attack, a polypeptide factor was established as the systemic signal (Scheme 3 A).[2, 14]



Scheme 3. A: Defense signaling in tomatoes in response to wounding (simplified).[2, 14] B: Analogies in the defense signaling systems of animals.

Tomato plants (*Lycopersicon esculentum*) respond to wounding with a systemic production of proteinase inhibitor proteins (PINs), which interfere with the digestive systems of the attacking herbivores, reducing the availability of essential amino acids and retarding the growth and development of the herbivores.[2] In this case, oligosaccharides from the plant cell walls act as primary elicitors. However, these oligosaccharides can induce the production of PINs only locally at the sites of pathogen attack, and therefore do not represent the systemic signal which induces the defense reaction in other parts of the plant. Finally, Pearce et al. showed that the systemic reaction is induced by a mobile polypeptide made up of 18 amino acids (systemin), which is produced from a precursor with 200 amino acids (prosystemin) at the sites of wounding.[2b] Systemin travels to distal leaves, where it induces the biosynthesis of jasmonic acid; this then triggers the biosynthesis of PINs. Recently Bowles et al. showed that jasmonic acid activates the PIN genes only in the presence of ethylene.[15] Whether ethylene is directly induced by the mobile signal systemin is not clear, yet ethylene and jasmonic acid influence each other's level in the plant and together act to regulate PIN gene expression.[15]

The biochemical mechanisms involved in the activation of jasmonic acid biosynthesis by systemin remain largely unknown. In the model proposed by Ryan et al. systemin activates a lipase in receptor cell membranes, resulting in the release of linolenic acid and thus the production of jasmonic acid and finally the activation of the PIN genes (Scheme 3 A).[14]

The important role that jasmonates and other intermediates of the octadecanoic pathway play as signal transducers in the defense signaling systems of plants seems to parallel the role of the structurally related prostaglandins, which have key functions in the response of animals to parasitic or pathogenic attack (Scheme 3 B).[14] While in plants jasmonic acid is produced from linolenic acid by the octadecanoic pathway, in animals important signal transducers such as the prostaglandins are synthesized from arachidonic acid. Plant and animal defense signaling may show even further analogies. The systemic induction of jasmonate biosynthesis in plants by phloem-transported polypeptides such as systemin may correspond to the activation of prostaglandin biosynthesis in animals by the polypeptide cytokine tumor necrosis factor α (TNF-α) transported in blood.[16] TNF-α triggers the activation of a phospholipase, which releases arachidonic acid from cell membranes. This is analogous to the activation of a lipase in tomatoes by systemin, which leads to the release of linolenic acid. Further investigations of the intracellular biochemical mechanisms including identification of the lipase and the mode of its activation are needed to prove whether these analogies of plant and animal defense signaling are significant.

Although the underlying signaling pathways have only partially been revealed, it is apparent that the regulatory systems of chemical defense in plants show a high degree of complexity and sophistication. In addition to the defense strategies discussed here, several other mechanisms of inducible plant defense have been described, including a response known as "systemic-acquired resistance", in which plants can become immune to attack by a wide range of fungal, bacterial, or viral pathogens after surviving an initial infestation.[3] Moreover, it seems likely that only a small fraction of plant defense mechanisms has so far been discovered.

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