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Biochemical Defense Agents Against Bacterial Pathogens

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Abstract

Plant diseases caused by bacterial pathogens place major constraints on crop production and cause significant annual losses on a global scale. The attainment of consistent effective management of these diseases can be extremely difficult, and management potential is often affected by grower reliance on highly disease-susceptible cultivars because of consumer preferences, and by environmental conditions favoring pathogen development. During their evolution, all plants have developed a real "immune system" capable of detecting a danger, whether the latter is of a biotic nature (pathogenic microorganism, insect pest) or abiotic (rain, hail, frost, wind). A plant's exterior protection can be compromised by mechanical damage, which may provide an entry point for pathogens. If the first line of defense is breached, the plant must resort to a different set of defense mechanisms which include structural and biochemical defense. The Biochemical defense mechanism includes the biochemical substances produced in the plant cells before or after the infection. These substances are considered as the agents of biochemical defense such as phytoanticipins which are described as "low molecular weight, antimicrobial compounds that are present in plants before challenge by micro-organisms", phytoalexins are lipophilic compounds in response to mechanical or chemical injury or infection, phenolic compounds are a large class of plant secondary metabolites that show a large diversity of structures (simples and polyphenols) and phytohormones (auxins, jasmonic acid, ethylene, etc). These defensive strategies, activated by aggression, leads to considerable changes in the metabolic activity of plant cells, resulting in a cascade of events designed to restrict the progression of infectious agents and reduce damage from injury.

Keywords: Bacterial diseases, Chemical defense, phenolic compounds, phytoalexins, phytohormones

INTRODUCTION

For successful infection to occur, the pathogen must overcome plant defense mechanisms, which it often does by injecting effector molecules directly into plant cells to suppress a host response. Virulence may also involve production of plant cell wall-degrading enzymes, toxins and/or plant hormones often under control of quorum sensing mechanisms. Some phytopathogenic bacteria actively move to their host via chemotaxis and enter the plant through natural openings such as stomata and lenticels or wounds caused by insect feeding, fungal infection, or mechanical plant damage. Host plants are internally colonized locally through intercellular spaces and systemically via the vascular system. (Lugtenberg, 2015).

To successfully invade host plants, phytopathogenic bacteria must cope with a number of plant defense mechanisms and have a means for acquiring water and nutrients for growth and colonization of plant tissues. (Van der Wolf and De Boer, 2015). Plants respond to pathogen attack by erecting a highly coordinated series of molecular, cellular and tissue-based defense barriers. All plants have the capacity to activate these defenses. However, if they are activated too little, too late, or in the wrong place, they will fail to restrict the pathogen and the plant will be susceptible. Pathogens respond by escaping or suppressing plant defense responses or by rendering these responses impotent, for example by detoxifying plant antibiotics (Guest and Brown, 1997). Plant disease resistance mechanisms may be divided into two categories: preformed resistance and induced resistance.

BIOCHEMICAL DEFENSE AGENTS AGAINST BACTERIAL PATHOGENS

Pathogens attack plants because during their evolutionary development they have acquired the ability to live off the substances manufactured by the host plants, and some of the pathogens depend on these substances for survival. Many substances are contained in the protoplast of the plant cells, however, and if pathogens are to gain access to them they must first penetrate the outer barriers formed by the cuticle and/or cell walls. Even after the outer cell wall has been penetrated, further invasion of the plant by the pathogen necessitates the penetration of more cell walls. Furthermore, the plant cell contents are not always found in forms immediately utilizable by the pathogen and must be broken down to units that the pathogen can absorb and assimilate. Moreover, the plant, reacting to the presence and activities of the pathogen, produces structures and chemical substances that interfere with the advance or the existence of the pathogen; if the pathogen is to survive and to continue living off the plant, it must be able to overcome such obstacles (Agrios, 2005).

Phytoalexins

Phytoalexins are natural products secreted and accumulated temporarily by plants in response to pathogen attack.

They have inhibitory activity against bacteria, fungi, nematodes, insects and toxic effects for the animals and for the plant itself (BRAGA, 1991). They are mostly lipophilic compounds that have the ability to cross the plasma membrane and act inside the cell. According to SMITH (1996) their toxicity in the plant occurs as a function of their acidic character, the high number of hydroxyl and substituents.

Phytoalexins are a heterogeneous group of compounds (Shinbo et al., 2006) that show biological activity towards a variety of pathogens and are considered as molecular markers of disease resistance. Synthesis of phytoalexin in response to pathogen attack can be modified with the influence of various factors as temperature, humidity and water availability. Several parts of the plant can produce phytoalexins such as leaves, flowers, stems, seeds and root tubers (Mikkelsen et al., 2003). Pisatin was the first chemically characterized phytoalexin from pea plants. After this discovery, other phytoalexins were isolated from various crops such as beans, rice, barley, banana, among others (BRAGA, 1991). Pisatin is a crystalline heterocyclic carbohydrate, $C_{17}H_{14}O_6$, produced by the pea (*Pisum sativum*) plant as an antibacterial phytoalexins (*Pseudomonas syringae* pv. *pisi*).

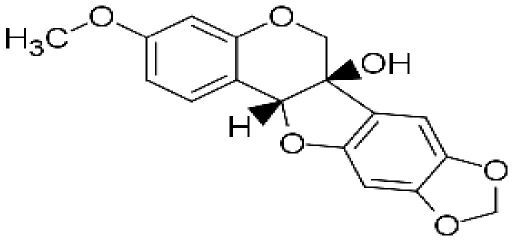

Figure 1: Chemical structure of Pisatin

Phytoalexins have been identified in several plant families such as Leguminosea, Solanaceae, Poaceae, Rutaceae and Compositae. Table 1 illustrates identified phytoalexins against some bacterial pathogens:

Table 1. Phytoalexins from different plant families and their targeted bacteria.

Family/Plant	**Phytoalexin**	**Bacteria**	**Bacterial Disease**
Leguminosea (*Phaseolus vulgaris*)	Phaseollin	*Pseudomonas syringae* pv. *phaseolicola*	Halo blight
Leguminosea (*Pisum sativum*)	Pisatin	*Pseudomonas syringae* pv. *pisi*	Pea blight
Solanaceae (*Solanum tuberosum*)	Rishitin	*Pectobacterium atrosepticum*	Black Leg of Potato
Poaceae (*Oryza sativa*)	Oryzalexins	*Xanthomonas oryzae* pv. *oryzae*	Rice bacterial leaf blight
Rutaceae (*Citrus sinensis*)	Hesperidin	*Xylella fastidiosa*	Citrus variegated chlorosis (CVC)
Compositae (*Lactuca sativa*)	Lettucenin A	*Xanthomonas campestris* pv. *vitians*	Bacterial Leaf Spot

Phytoalexins possess some antibacterial activity. Rishitin for instance decreased the viability of cells of *Erwinia atroseptica* by around 100% at a dose of 360 µg/L (Lyon and Bayliss, 1975). Rice (*Oryza sativa, Gramineae*) is among the most important crop in the world. Phytocassanes, Momilactones and Oryzalexins are compounds from the class of diterpenes (Solenoids) and Sakuranetin is from flavonoid's class. Figure 2 illustrates about this phytoalexins and their chemical structures.

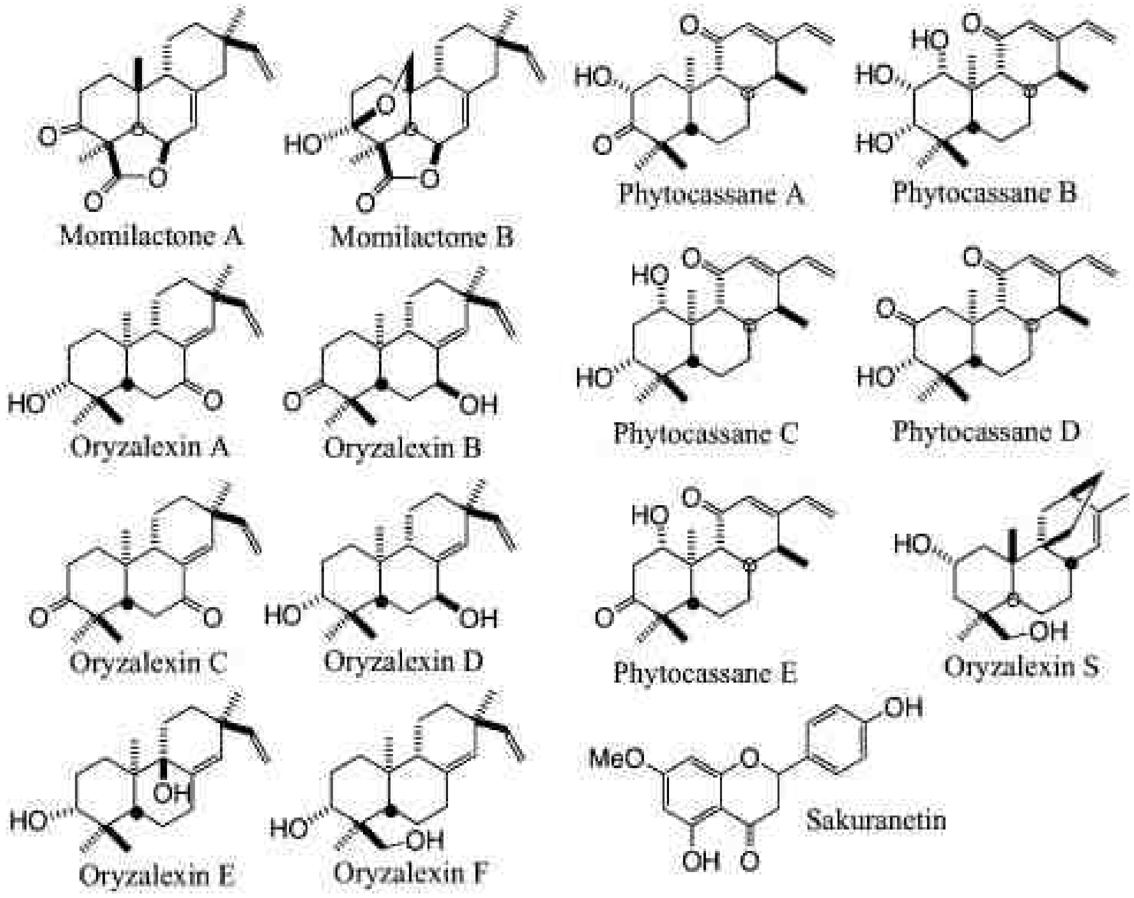

Figure 2. Structure of phytoalexins in rice plant.

Phenolic Compounds

Phenolic compounds are secondary metabolites, ubiquitous in plants and plant derived foods and beverages. They show a large diversity of structures, including rather simple molecules (e.g. vanillin, gallic acid, caffeic acid), and polyphenols such as stilbenes, flavonoids, and polymers derived from these various groups. For example, over 8,000 molecules have been reported in the flavonoid family alone and the list continues expanding (Andersen and Markham 2006). Although the term polyphenol is often used as a synonym of phenolic compound, it should be restricted to molecules bearing at least two phenolic rings (Quideau et al. 2011).

Simple phenols (C6)

These are compounds with one (monophenol-like catechin) or several phenolic groups (di, tri- and oligophenols): phenol, benzoquinone, pyrogallol, pyrocathecol, etc. (Lattanzio et al., 2006). Examples of simple phenols (C6) include catechol and phloroglucinol. Although most of the more complex plant polyphenols contain these two simple phenols as a parts of their structures, catechol and phloroglucinol are uncommon in plant tissues. Catechol has been found in leaves of Gaultheria species, while phloroglucinol has been found as glucoside in the peel of various Citrus fruits. Arbutin (figure 2) is found in leaves of various Vaccinium spp., such as blueberry, cranberry, cowberry, and pear trees (*Pyrus communis L., Rosaceae*) (Towers et al. 1966). The resistance of pear plants to *E. amylovora* seems to be associated with a high level of arbutin-hydroquinone, the antibacterial compound present in the exterior parts of the blossoms, where the plant is most susceptible to the bacterium (Schroth and Hildebrand, 1965).

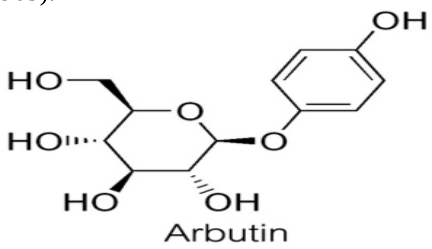

Figure 3: Chemical structure of Arbutin

Phenolic acids (C6-C1 or C6-C3)

These are benzoic or hydroxybenzoic acids (gallic acid, ellagic acid), and cinnamic or hydroxycinnamic acids such as caffeic, coumaric, ferulic, and chlorogenic acid (Manach et al., 2004; Macheix et al., 2005; Lattanzio et al., 2006). A group of small phenolic molecules is derived from the subclass of hydroxycinnamic acids and is called phenylpropenes.

Flavonoids (C6-C3-C6)

These are present in plant vacuoles, where they are sometimes water-soluble or sometimes act as pigments (Raven et al., 2003). Flavonoids are the most abundant phenolic compounds in nature and are classified according to the degree of oxidation and unsaturation of their heterocyclic ring (Scalbert et al., 2000). Two classes of flavonoids can be distinguished: 4-oxoflavonoids and anthocyanidins (Manach et al., 2004). Different subgroups of flavonoid compounds, including flavanone (naringenin), flavan-3-ol (catechin), flavonol aglycone (quercetin) and flavonol glycoside (rutin), were tested for anti-Xylella activities. Compared to phenolic acids, flavonoids generally have strong inhibitory activities against *X. fastidiosa* growth, except for rutin (quercetin glycoside), which is less active than the corresponding aglycone quercetin. Similar to flavonoids ($C_6 + C_3 + C_6$), stilbenes (such as resveratrol) are also derived from phenylalanine. However, due to the difference in condensation reactions, the core skeleton for stilbenes is $C_6 + C_2 + C_6$. Resveratrol exhibited very strong inhibitory activities (MIC = 200 μM) towards all four *X. fastidiosa* strains (Christina et al., 2010).

Lignins (C6-C3)n

These are extremely complex phenolic polymers. Of the biopolymers, lignins rank second in abundance after cellulose. The synthesis of these compounds results from a three-dimensional polymerization of three basic phenolic molecules (called monolignols): coumarylic, coniferylic and sinapylic alcohol, corresponding respectively to p-coumaric, ferulic and sinapic acid (Macheix et al., 2005). The complexity of lignins results from the potential association of these units via various chemical bonds, in a manner that is neither ordered nor repetitive, so as to generate an amorphous, hydrophobic polymer. Example of a phenolic compound that contributes to the plant’s defense mechanisms is lignin. Lignin is a phenolic polymer, which plays a fundamental role in solute conductance, mechanical support and disease resistance. In response to abiotic stress, to wounding or to pathogenic infection, the deposition of lignins, lignin polymers and other phenolic substances related to the cell wall are observed. This contributes to both a thickening of the cell wall (conferring greater rigidity and mechanical resistance) and to an increase in cell hydrophobicity. Lignin thus acts as a physical barrier against pathogenic invasion. In addition, lignin deposits reduce the diffusion of enzymes and toxins that the pathogen releases in order to facilitate host tissue colonization. Lignin also deprives the pathogen of the plant water and nutrients necessary to its proliferation (Macheix et al., 2005; Lattanzio et al., 2006).

Tannins (C6-C3-C6)n

These are found in several forms with different types of chemical reactivity and composition: water-soluble tannins, condensed tannins, catechic tannins and proanthocyanidins (Macheix et al., 2005). Proanthocyanidins have a high molecular weight and are a group of condensed (chain dimers or oligomers) flavan-3-ols often related to cell walls.

Biosynthesis of phenolic compounds occurs at various sites in plant cells, such as the chloroplasts, the cytoplasm and the endoplasmic reticulum membrane. Polyphenols (relatively hydrophilic) usually accumulate in the central vacuoles of guard cells, epidermal cells and the subepidermal cells of leaves and shoots. Some polyphenols are found covalently linked to the plant cell wall (lignin); others are found in waxes (related to lipidic structures) or on the external surfaces (cuticle) of plant organs (Lattanzio et al., 2006). The localization of a phenolic compound within a tissue reflects its physiological function or its participation in interactions of the plant with its environment (Macheix et al., 2005). For example, polyphenols with a role in signaling or defense are often stored at strategically important sites (Lattanzio et al., 2006). All phenolic compounds exhibit intense absorption in the UV region of the spectrum and those that are colored absorb strongly in the visible region as well. Each class of phenolic compounds has distinctive absorption characteristics. For example, phenols and phenolic acids show spectral maxima in the range 250-290 nm; cinnamic acid derivatives have principal maxima in the range 290-330 nm; flavones and flavonols exhibit absorption bands of approximately the same intensity at about 250 and 350 nm; chalcones and aurones have an absorption peak of great intensity above 350 nm and a much less intense band at 250 nm; anthocyanins and betacyanins show rather similar absorption in visible region (475-560 nm and 535-545 nm, respectively) and a subsidiary peak at about 270-275 nm (Harborne, 1964; Mabry et al. 1970).

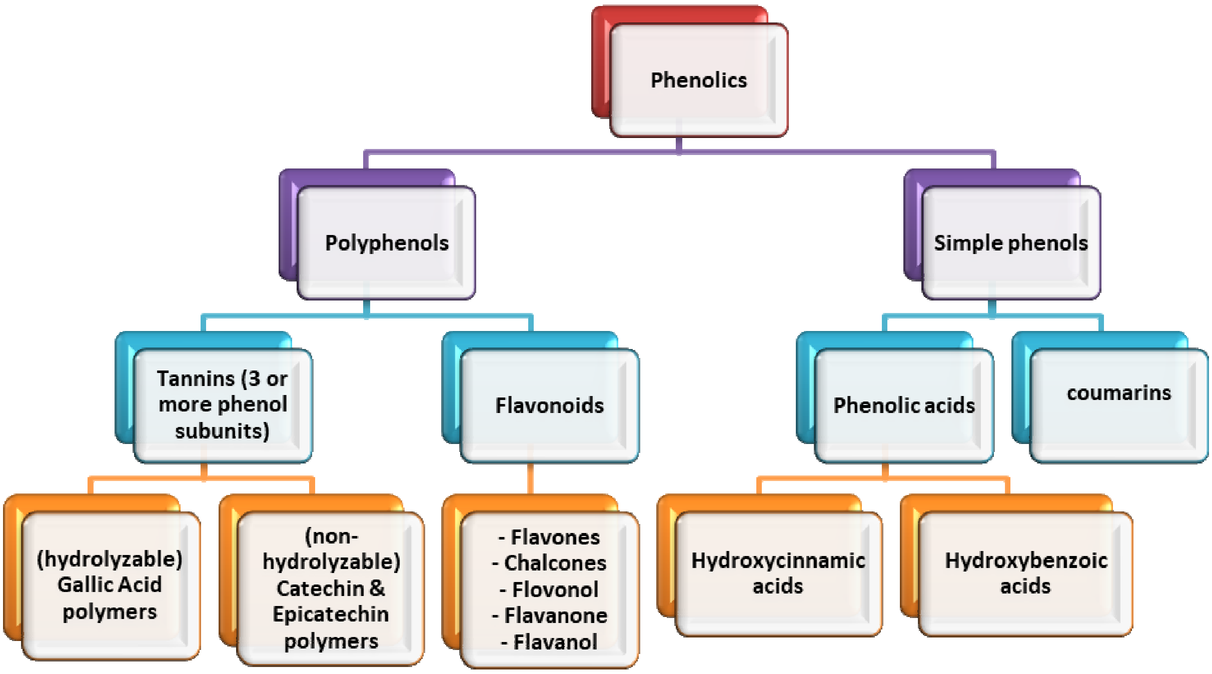

Figure 4: Chemical classification of phenolic compounds

X. fastidiosa colonizes exclusively in the xylem vessels (conductive tissue) of infected plants, and it is transmitted from diseased to healthy plants by insects that feed on xylem fluid (sap). Colonization of *X. fastidiosa* in the xylem vessel blocks water and nutrient transport from root to shoot, which results in disease and death of the infected plants. Axenic culture of *X. fastidios*a can be maintained in vitro in customized bacterial growth media (Davis et al, 1981). The anti-Xylella activity of 12 phenolic compounds, representing phenolic acid, coumarin, stilbene and flavonoid, was evaluated using an in vitro agar dilution assay. Overall, these phenolic compounds were effective in inhibiting *X. fastidiosa* growth, as indicated by low minimum inhibitory concentrations (MICs), In addition, phenolic compounds with different structural features exhibited different anti-Xylella capacities. Particularly, catechol, caffeic acid and resveratrol showed strong anti-Xylella activities. Differential response to phenolic compounds was observed among *X. fastidiosa* strains isolated from grape and almond (Maddox et al. 2010).

Phytohormones

Phytohormons contribute to all aspects of plant responses towards biotic and abiotic stimuli. They are also indicators of plant stress responses upon variation of light, salinity, temperature, radiation, pollutions (Vogt 2010; Kosova et al. 2012; Majláth et al. 2012). Phytohormones are small molecules produced within plants that govern diverse physiological processes, including plant defense. Among them, jasmonate (JA) and salicylic acid (SA) are major defense-related phytohormones ,Other phytohormones, such as ethylene (ET), abscisic acid (ABA), auxin, gibberellins (GAs), cytokinins (CKs), and brassinosteroids (BRs), are also involved in defense responses (Shigenaga and Argueso, 2016).

The phytohormones, salicyclic acid (SA), jasmonic acid (JA) and ethylene (ET) regulate responses to biotic and abiotic stresses (Baldwin et al. 1994; Leon-Reyes et al. 2010) and play central roles in coordinating various aspects of developmental processes throughout the life cycle of plants, including flower morphogenesis, fruit formation or ripening, seed germination and root elongation (Hause et al. 2000; Li et al. 2004), but they also play a major role in mediating defense responses against herbivores and pathogens (Pieterse and Van Loon, 1999; Spoel et al. 2003).

Salicylic acid

Plants synthesize SA via two pathways: the phenylalanine ammonium lyase (PAL) pathway and the isochorismate (IC) pathway, both of which utilize chorismate, the end product of the shikimate pathway, as a precursor (Dempsey 2011). The PAL pathway operates in the cytosol, and the IC pathway operates in chloroplasts.

SA signaling in plant defense should not be viewed as a linear pathway but rather as a complex network. Multiple stimuli can activate SA synthesis/signaling. SA can specifically bind to a variety of plant proteins affecting their activity (Dempsey, 1999). It can also activate gene expression/activity by multiple mechanisms and at different steps in plant defense signaling. In addition, SA influences a variety of other signaling mechanisms in plant defense (Kunkel, 2002). SA application increases resistance against the bacterial pathogen *Pectobacterium carotovorum* (formerly *Erwinia carotovora*) (Andersson, 2005).

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Palva et al. (1994) reported that addition of the SA to the growth medium of axenically-growing tobacco seedlings causes almost complete resistance to infection by *P. carotovorum subsp. carotovorum*, there is no information available on the effect of SA on Dickeya spp., particularly the *D. solani* infections of potato. Since 2005, the presence of *D. solani* has been reported in potato in many European countries including The Netherlands, Finland, Poland, Germany, Belgium, France, United Kingdom and Sweden, as well as outside Europe, in Israel and Georgia. The species has become the predominant pathogen responsible for the blackleg incidences in Europe (Van der Wolf et al. 2014).In a study of this bacterial pathogen, potato soft rot (*Dickeya solani*), exogenous SA application reduced disease symptoms in potatoes grown in tissue culture (Czajkowski et al., 2015).

Jasmonic acid

Jasmonic acid is an important signalling molecule for the activation of defense in response to wounding, herbivores and pathogen attack (Rosahl and Feussner, 2004). It is synthesized from α-linolenic acid by enzymes of the lipoxygenase pathway (Feussner and Wasternack, 2002). JA was first seen in Solanaceae species and recently in *Arabidopsis thaliana* (Gidda et al., 2003). In plants, the concentration of JAs ranges from 0.01 to 3.0 ng/g FW (fresh weight) with the exception of *Artemisia tridentata* in which MeJA level up to 95 μg g-1 fresh weight has been recorded (Preston et al., 2004). JA has been found in abundance generally in flowers and chloroplasts of illuminated plants (Creelman and Mullet, 1997; Yan et al., 2013). In soybean plant, organs like hypocotyl hook, axes, and plumules showed higher levels of JA as compared to the hypocotyl zone of elongated cells and the non-elongating roots and stems (Creelman and Mullet, 1995).

JA induces genes involved in phytoalexin biosynthesis (Chs, Pal, HMGR) (Choi D et al, 1994; Creelman, 1992) and phenolics (polyphenol oxidase) (Doares SH et al, 1995) that are involved in plant defense. The oxylipin pathway that leads to JA is also the source of other volatile aldehydes and alcohols that function in plant defense and wound healing. For example, the C6-aldehyde 2-hexenal completely inhibited growth of *Pseudomonas syringae* and E. coli (Deng et al, 1993) JA and ET have been shown to be involved in induced systemic resistance, which is activated by the nonpathogenic root-colonizing bacterium *Pseudomonas fluorescens* (Pieterse et al., 1996).

Auxin

The phytohormone auxin (from the Greek “auxein,” meaning to grow) regulates a whole repertoire of plant developmental processes. Perhaps less well known is the fact that some microorganisms also produce auxin (Costacurta and Vanderleyden, 1995; Patten and Glick 1996). In their interaction with plants, these microorganisms can interfere with plant development by disturbing the auxin balance in plants. This is best documented for phytopathogenic bacteria like *Agrobacterium* spp. and *Pseudomonas savastanoi* pv. *savastanoi*, causing tumors and galls, respectively (Jameson 2000; Mole et al. 2007), and plant growth promoting rhizobacteria (PGPR) such as *Azospirillum* spp. that impact on plant root development (Persello-Cartieaux et al. 2003; Spaepen et al. 2007a). The term rhizobacteria refers to the fact that their numbers are highly enriched in the rhizosphere, i.e., the narrow band of soil that surrounds the root (Hiltner 1904; Smalla et al. 2006; van Loon 2007), of more recent date is the observation that auxin (indole-3-acetic acid or IAA) is a signaling molecule in some microorganisms (Spaepen et al. 2007a).

Auxins regulation of plant development can also cause indirect effects on plant defense response. For instance, IAA application can reduce rice resistance to *Xanthomonas oryzae* pv. *oryzae*. The possible reason of pathogen growth may be caused by cell wall expansion and loosening which are activated by IAA (Ding et al., 2008). Auxin is a central regulator of plant growth and development and controls apical dominance, stem and petiole elongation, root gravitropism and its architecture in response to light and temperature, plant vasculature, and flower formation, as well as root hair and lateral root formation (Kazan, 2013). Tryptophan is the main precursor for the biosynthesis of indole-3-acetic acid (IAA), a naturally occurring plant auxin, which is converted to indole-3-pyruvic acid through the action of amino transferases (Zhao, 2010) The metabolism of the auxin precursor tryptophan also leads to the synthesis of two important plant antimicrobial compounds, camalexins and glucosinolates, which selectively inhibit the growth of necrotrophic and biotrophic pathogens, respectively (Robert-Seilaniantz et al., 2011; Stotz et al., 2011).

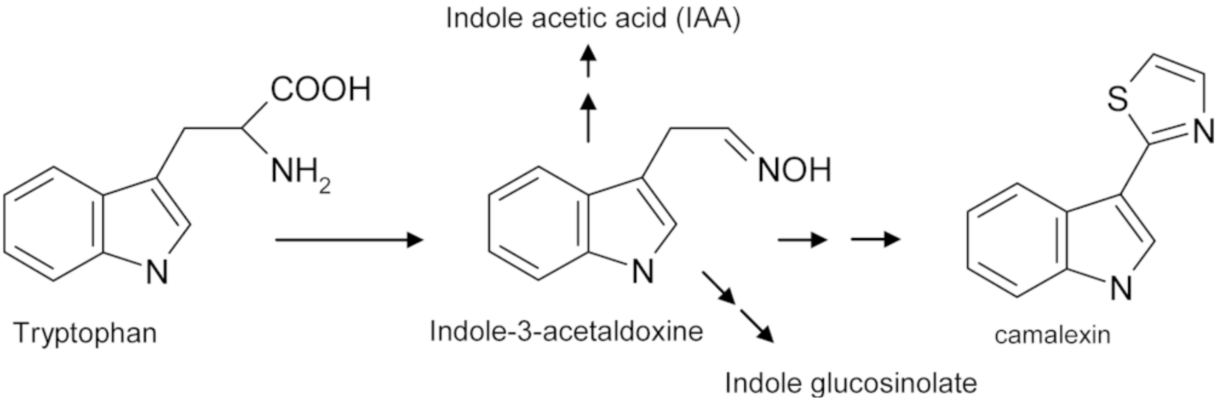

Figure 5: Schematic biosynthetic pathway of camalexin via indole-3-acetoaldoxime. Other important indolic compounds arise from the same route.

Tumor morphology is influenced by the levels of auxin and cytokinin in transformed plant cells. Inactivation of the *ipt* gene by Tn5 transposon mutagenesis produces"rooty" tumor morphology, whereas inactivation of either the *iaaM* or *iaaH* gene produces"shooty" tumor morphology (Akiyoshi et aI., 1983). Similarly, *ipt* placed under the control of a more active promoter, such as cauliflower mosaic virus coat protein 35S promoter, enhances endogenous cytokinin production and shoot growth (Smigocki and Owens, 1988).

Ethylene

Ethylene is a plant hormone that has been associated with the response of plants to wounding, pathogen attack, and other stresses (Arshad and Frankenberger, 2002). Ethylene produced after pathogen attack may be a stimulus for defense responses by regulating a wide range of defense-related genes, including those encoding pathogenesis-related (PR) proteins, such as chitinase and osmotin (Deikman, 1997).

From a molecular point of view, ethylene, produced by all organs, is the least complex plant hormone. It is a gaseous hormone that moves in free spaces between plant cells. This hormone is responsible for fruit ripening, growth inhibition and abscission (leaf drop).During plant development, endogenous ethylene production rates are highest in meristematic and ripening tissues (Abeles et al. 1992). High levels of ethylene production are found in young, developing organs that display rapid cell division, in ripening fruits and during senescence. Exogenously applied ethylene was demonstrated to either stimulate or inhibit cell division, depending on the plant species and tissue type. Generally, ethylene treatments promote processes related to aging and senescence, such as wilting and abscission of leaves and floral organs and ripening of fruits. Several biotic and abiotic stresses also trigger endogenous ethylene production (Abeles et al. 1992).

Ethylene is biologically active at very low concentrations of around 0.01 to 1.0 part per million (ppm). Lower or higher sensitivities have been observed depending on the species and the response. Some climacteric fruits, such as tomatoes and apples, can generate tens of ppm of ethylene. It is worth noting here that ethylene is a byproduct of partial combustion of organic fuels and is present, therefore, in the atmosphere due to such things as forest fires, volcanic eruptions and car exhaust (Abeles et al., 1992). It is well known that a large burst of ethylene is produced after the early steps of HR initiation and can induce defense-related genes (Boller, 1991). Treatment of plants with ethylene has long been known to increase either susceptibility or resistance, depending on the plant-pathogen interaction, and on the conditions of the interaction (Brown et al., 1993; Van Loon and Pennings, 1993; Diaz et al., 2002).

Cytokinins

Cytokinins are plant-specific chemical messengers (hormones) that play a central role in the regulation of the plant cell cycle and numerous developmental processes. Cytokinins were discovered by F. Skoog, C. Miller and co-workers during the 1950s as factors that promote cell division (cytokinesis). The first cytokinin discovered was an adenine (aminopurine) derivative named kinetin (6-furfurylaminopurine; Fig 6), which was isolated as a DNA degradation product. The first common natural cytokinin identified was purified from immature maize kernels and named zeatin (chemical name: 6-(4- hydroxy-3-methylbut-2-enylamino) purine. Several other cytokinins with related structures are known today. Cytokinins are present in all plant tissues. They are abundant in the root tip, the shoot apex and immature seeds. Their endogenous concentration is in the low nM range. Cytokinins may act also on the cell that produced them (autocrine signaling). Cytokinins are also produced by cyanobacteria, some plant pathogenic bacteria (e.g. *Agrobacterium tumefaciens, Pseudomonas savastanoi, Rhodococcus fascians*) and the slime-mold *Dictyostelium discoideum.* (Schmülling, 2004)

Cytokinins are plant hormones that may play essential role in biotrophic pathogenesis. Cytokinins are involved in the formation of "green islands" in infected leaves by redirection of host nutrients translocation to the site of pathogen ingress (Walters and McRoberts, 2006).

Application of highly active CKs such as kinetin or *trans*-zeatin also showed a strong inhibition of *P. syringae* growth mediated by CK-induced accumulation of antimicrobial phytoalexins (capsidiol and scopoletin) which is at least partially independent of salicylic acid (Großkinsky et al., 2011, 2013). In addition, an antagonistic relation between CKs and auxin in mediating resistance in *A. thaliana* against *P. syringae* has been demonstrated (Naseem et al., 2012).

Enzymes

Phenyl Ammonia Lyase (PAL)

PAL (E.C.4.1.3.5) is the primary enzyme in the phenylpropanoid pathway, which leads to the conversion of l-phenylalanine into trans-cinnamic acid with the elimination of ammonia. PAL has been demonstrated in metabolic activity of many higher plants and is the key enzyme in the synthesis of several defence-related secondary compounds like phenols and lignins (Hemm et al., 2004). The presence of phenolic compounds in plants and their synthesis in response to infection is associated with disease resistance. PAL is one of the most intensively studied enzymes in plant secondary metabolism because of its key role in phenylpropanoid biosynthesis (Whetten and Sederoff, 1995).

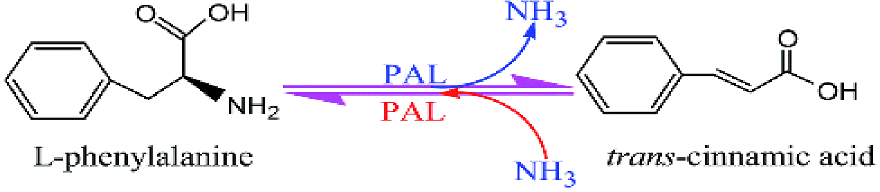

Figure 6: Forward reaction catalyzed by PALs

Peroxidases (Prxs)

In the literature, various abbreviations are used for class III plant peroxidases (POD, POX, Prx, Px, and PER) but, in accordance with gene annotations, the use of Prxs appears to be the most common choice. They are members of a large multigenic family, with 138 members in rice (Passardi et al., 2004a). Plant Prxs are involved in auxin metabolism, lignin and suberin formation, cross-linking of cell wall components, phytoalexin synthesis, and the metabolism of ROS (reactive oxygen species) and RNS (reactive nitrogen species) (Passardi et al., 2007).

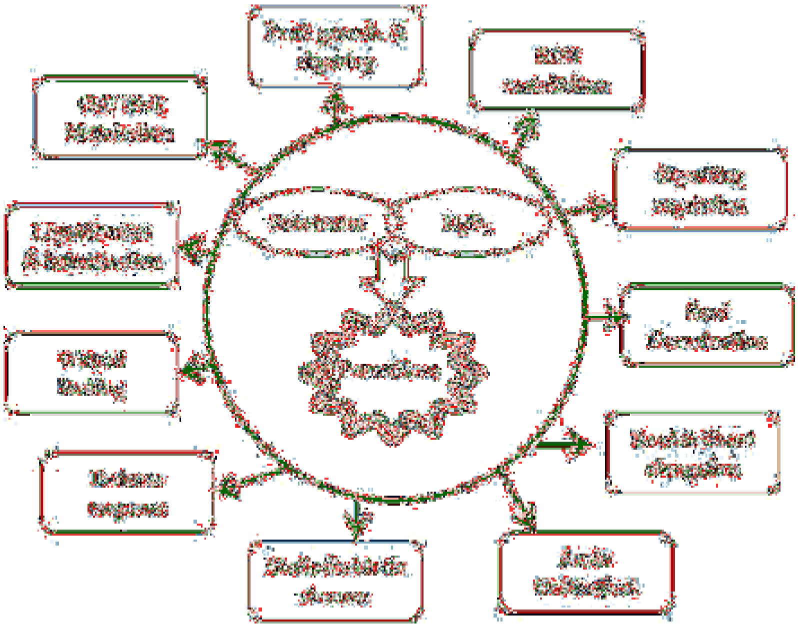

Figure 7: Various roles of plant peroxidases

Polyphenol Oxidase (PPO)

PPO (E.C 1.14.18.1) is a nuclear encoded, plastid copper-containing enzyme, which catalyzes the oxygendependent oxidation of phenols to quinones. Over-expression of PPO in transgenic tomato plants enhanced their resistance to Pseudomonas syringae (Li and Steffens, 2002).

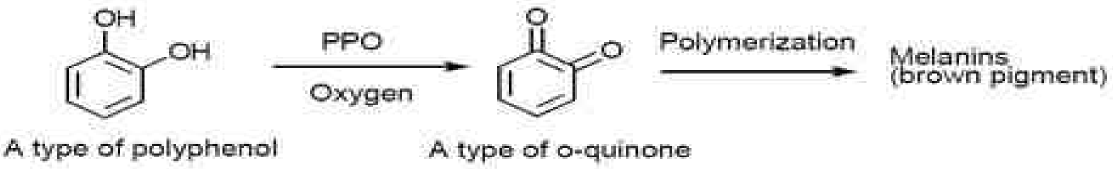

Figure 8: Reaction catalyzed by PPO

Note: PAL and PPO were involved in development of tomato resistance to bacterial wilt and could be used as biochemical markers to screen the resistance ⁄susceptibility of tomato to *Ralstonia solanacearum*. (Vanitha S.C et al., 2009)

Peptide Toxins

The antimicrobial peptides (AMPs) are biologically active molecules produced by wide variety of organisms as an essential component of their innate immune response. The primary role of the AMPs is host defense by exerting cytotoxicity on the invading pathogenic microorganisms, and they also serve as immune modulators in higher organisms (Zanetti. M., 2004). The smaller size of AMPs facilitates the rapid diffusion and secretion of peptide outside the cells, which is required for eliciting immediate defense response against pathogenic microbes (Nissen-Meyer and Nes, 1997). Currently, more than 3,000 AMPs have been reported in antimicrobial peptide database, (http://aps.unmc.edu/AP/main.php/). The main families of AMPs comprise thionins and plant defensins.

Thionins

The first AMP isolated from plants was a thionin from the endosperm of wheat (Balls et al., 1942). The protein moiety of a proteolipid was later shown to be a mixture of two forms, purothionins a and b (Nimmo et al. 1968). Additional thionins were isolated, including a- and b-hordothionins from barley endosperm (Bohlmann and Apel 1991)

Table 2. Antimicrobial properties of selected thionins against bacteria.

Proteins	**Susceptible species**	**References**
Wheat endosperm crude purothionin	Bacteria: *Pseudomonas solanacearum* *Xanthomonas phaseoli* *Xanthomonas campestris* *Erwinia amylovora* *Corynebacterium fascians* *C. flaccumfaciens* *C. michiganese* *C. poinsettiae* *C. sepedonicum*	Fernandez De Caleya et al. (1972)
Nicotiana attenuate PR-13 thionins	Bacteria: *Pseudomonas syringae* pv. *tomato*	Rayapuram et al. (2008)

Defensins

Defensins are the largest groups of AMPs. These peptides are cysteine-rich and have diverse sequences and structures, stabilized into compact shapes by three or four conserved cysteine disulfide bridges. They have at least two positive charges (lysine or arginine residues) and are small, ranging approximately from 12 to 50 amino acid residues (2–6 kDa) (Ganz, 2003) Plant defensins include over 100 members from a wide range of plants, including wheat, barley, tobacco, radish, mustard, turnip, arabidopsis, potato, sorghum, soybean, cowpea, and spinach, among others (Padovan et al., 2010)

Antibiotics produced by soil- and plant-associated bacteria

Soils presumably harbor the most diverse populations of bacteria of any environment on this planet because of the extensive heterogeneity in soil texture and the large spatiotemporal variations in abiotic and biotic conditions (Davies, 1990). Over the past four decades, numerous studies have demonstrated that metabolites, including antibiotics, enzymes, and volatiles produced by soil- and plant-associated bacteria, are key factors in the suppression of plant pathogens (Lugtenberg and Kamilova, 2009) According to Webster's English Dictionary, an antibiotic is defined as "a substance produced by a microorganism and able, in dilute solution, to inhibit or kill another microorganism."

Fluorescent pseudomonads play an active role in the suppression of pathogenic microorganisms by secreting antibiotics. These antibiotics are low molecular weight organic compounds and are deleterious to the growth and metabolism of pathogenic microorganisms, even at low concentrations. Production of antibiotics by fluorescent pseudomonads is an important factor in the disease-suppressing ability of this group of bacteria (Thomashow et al. 1990). *Pantoea agglomerans* a Gram-negative bacterium that belongs to the family *Enterobacteriaceae* (synonym: *Erwinia herbicola*) strain Eh318 produces through antibiosis a complex zone of inhibited growth in an overlay seeded with *Erwinia amylovora*, the causal agent of fire blight. This zone is caused by two antibiotics, named pantocin A and B. (Wright et al, 2001)

CONCLUSION

Plants have been developed physiological, biochemical, or molecular mechanisms to overcome effects of stress. Phenolic compounds represent a large group of molecules with a variety of functions in plant growth, development, and defense. Phenolic compounds include signaling molecules, pigments and flavors that can attract or repel, as well as compounds that can protect the plant against insects, fungi, bacteria, and viruses. Most phenolic compounds are present as esters or glycosides rather than as free compounds. Tannins and lignin are phenolic polymers. Tannins are used commercially as dyes and astringents, and lignin accounts for structural rigidity of cells and tissues and is essential to vascular development. Phytohormones such as auxin, cytokinin, abscisic acid, jasmonic acid, ethylene, salicylic acid, gibberellic acid, and few others, besides their functions during germination, growth, development, and flowering, play key roles and coordinate various signal transduction pathways in plants during responses to environmental stresses.

Hormone signaling crosstalks can be a target for crop improvement to increase disease resistance using pharmaceutical, genetic, or transgenic approaches. Such strategies include strengthening resistance induced by a particular signaling pathway via suppressing its antagonistic pathway or exploiting synergistic interactions. Engineering of these compounds is increasingly enabled by new technical developments in biochemical analysis, DNA sequencing, bioinformatics, gene expression methodology and, more recently, the possibility of genome editing. Hopefully, these and other novel strategies will see more progress in the coming decade than we have witnesses in the last one.

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