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Plant defense system and phytoalexins

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Abstract
Plants generate phytoalexins, which are antimicrobial chemicals with a low molecular weight that are synthesized in response to biotic and abiotic stresses. The rate and amount of their accumulation are controlled by the release of immediate precursors from conjugates or de novo synthesis, as well as detoxification by plant or microbial enzymes. Phytoalexin is part of a battery of induced defensive mechanisms that include lytic enzymes like glucanases and chitinases, cell wall lignifications, oxidising agents, and a range of pathogenesis-related (PR) proteins and transcripts with unknown activities (Lamb *et al.*, 1989 Dixon and Lamb, 1990). It's important to remember that phytoalexin production is just one part of a complex defence mechanism in which anyone component may not be enough to keep pathogens at bay (Mansfield, 1999). In this review, we will focus on the description of secondary metabolites that the plant accumulates in response to pathogen invasion, both naturally occurring and pathogen-induced, with a particular focus on their biological role against microorganisms and biotechnological value as potential antimicrobials in plant protection and human health.

Keywords: Phytoalexin, Secondary metabolites, Antimicrobials, Plant protection, Detoxification

Introduction
Phytoanticipins and phytoalexins are two types of antimicrobial molecules found in plants (Mansfield, 1999), "Antimicrobial chemicals with low molecular weight which are present in plants before infestation by pathogens or are created after infection only from pre-existing precursors," these chemicals are referred to as phytoanticipins. Phytoalexins are toxic antimicrobial compounds generated in significant amounts in plants only in response to stimulation by different phytopathogenic microbes or chemical and mechanical harm. Borger and Muller suggested it in 1940 [34] while researching the interaction between *Phytophthora infestans* and potato. The majority of phytoalexins are harmful to plants and limit their growth, however, some are also hazardous to nematodes, bacteria, and other organisms. From around 30 plant families more than 350 phytoalexins have been chemically identified. From the Leguminosae family, the largest number of 130 has been identified (Joseph, 1995). Phytoalexins catalyzed by plants in the same family generally have similar chemical structures; e.g., in most of the legumes phytoalexins are isoflavonoids whereas terpenoids in case of Solanaceae. In plant defense the antimicrobial plant compounds that have received more attention are the phytoalexins. Phytoalexins are natural chemicals that plants release and accumulate as a reaction to pathogenic attack. They inhibit bacteria, fungus, nematodes, and insects, along with have harmful effects on animals and the plant on their own (Braga, 1991) [5]. Thus, they are a component of a complex defensive mechanism that allows plants to inhibit invading microbes, or the induced biochemical changes in host plants are the last line of host defence (Glazebrook & Ausubel; Ausubel, 1994) [16]. This can switch the genetic potential of plant or plant tissue from susceptible to resistant. Phytoalexins are antimicrobial and antioxidative compounds that plants produce on their own and accumulate significantly in regions where pathogens are present (Jeandet *et al.*, 2013) [22].

The physiological/biochemical basis of resistance of the plants to fungal, oomycte, and bacterial pathogens has been related with both infection-induced and preformed antimicrobial compounds [Van Etten (1994) [46], Hammerschmidt, & Schultz, (1996) [19], Mansfield, J. W. (2000)] [29]. For example, in the resistance of oats to *Gaumanomyces graminis* f.sp. *tritici* preformed antimicrobial compounds are involved (Osbourn & Clarke, 1994) [36] and onion bulbs to *Colletotrichum circinans* (Angell, Walker, & Link, 1930) [3]. However, the manifestation of resistance (i.e. defense) in most plant-pathogen interactions cannot be explained by the existence of preformed inhibitors. The majority of research on pathogen resistance mechanisms has demonstrated that the plant deploys defences that are engaged after

infection to halt pathogen development (Dixon & Harrison, 1990) [11]. After infection, plants undergo variety of biochemical changes, some of which have been linked to the expression of defence because they show antimicrobial action *in vitro*.

Phytoalexins are a type of lipophilic molecule that may penetrate the plasma membrane and function within the cell. Their toxicity in plants, according to Smith (2006) [42], is caused by their acidic nature, as well as the large quantity of hydroxyl and substituents. According to Cavalcanti *et al.* (2005) [8], phytoalexins' mode of action on fungi includes cytoplasmic granulation, disorganisation of cellular contents, rift of the plasma membrane, and hindering of fungal enzymes, which results in inhibition of seed germination and the germ tube elongation, and also the suppression of mycelial growth. According to Kokuban and Grayer (2001) [17], antifungal proteins and peptides can't employ phytoalexins because they're low-molecular-weight secondary metabolites generated by plants once their molecular weight has increased. The first chemically identified phytoalexin was pisatin which from to the pea plants. Following this finding, phytoalexins were extracted from a variety of crops, including barley, rice, beans, and bananas, to name a few (Braga, 1991) [5]. More than 300 types of phytoalexins have been characterized among various chemical compounds, including apigeninidin, coumarins, alkaloids, flavonoids, luteolinidin, apigenidin, phenolic compounds, and diterpenes (Harbone, 1999; Cavalcanti, 2005) [8], and these have been utilised as chemical markers in several studies. The accumulating rate of the phytoalexins is thought to be a crucial component in pathogen infection establishment. The effect of several parameters such as temperature, humidity, and water availability on phytoalexin synthesis against the pathogen infestation can be regulated. Phytoalexins are biosynthesized by a variety of plant elements, including stems, seeds, leaves, flowers, and root tubers (Mikkelsen *et al.*, 2003) [33]. Momilactone A,which appears constitutively in rice husks and stems (Lee *et al.*, 1999) [26], but is a phytoalexin in rice leaves, is an example of the chemical that may act as a phytoalexin in a plant organ and be constitutive in another (Cartwright *et al.*, 1981) [7]. Momilactone A is naturally generated and secreted from the root, in 2008 according to Toyomasu. Phytoalexins are thus characterized by the dynamics of their synthesis and function, rather than by the class of chemical structure or biosynthetic pathway by which they were produced. According to Ahuja *et al.*, (2012) [1] various plant families have phytoalexins, including Brassicaceae, Fabaceae, Solanaceae, Poaceae, and Vitaceae, in response to pathogen infection or elicitor treatment. The enormous production of cereals from the Poaceae family across the world, also their relevance in nutrition, has sparked research into phytoalexins in this family. subsequently, research has been conducted to analyse the phytoalexins secreted in diverse regions of this family of plants to defend against harmful microbes, as well as the usage of chemicals extracted from these plants to promote phytoalexin production (Chukwununso *et al.*, 2013).

Concept of Phytoalexin

Muller and Borger postulated in 1940 [34] that in response to infection, plants create defence chemicals termed phytoalexins. The name was coined after considering two key events in plant pathology, and it was adopted from Greek to imply "warding off agents in plants." First, many plants' cells respond actively to attempted infection; second, plants develop resistance after being exposed to an infecting organism. A fundamental component of this idea is the restriction of phytoalexins to molecules derived from distant origins via de novo enzyme production. Phytoantipicins and phytoalexins are two types of plant chemicals that work against microbes (Mansfield, 1999). Phytoantipicins are "low molecular weight antimicrobial chemicals that are present in plants before pathogens challenge them, or are created primarily after infection from pre-existing precursors." Phytoalexins are antimicrobial chemicals with a low molecular weight that are generated and accumulated in plants following exposure to microorganisms or abiotic factors (Purkayastha, 2017) [37]. Phytoalexins are a type of chemical or product that catalyses the triggered defence mechanisms that is used by plants, such as lytic enzymes like glucanases, and chitinases, oxidising agents, and cell wall lignifications, and several pathogenesis-related (PR) proteins and transcripts with unidentified activities (Dixon & Lamb, 1999) [12]. It's important to remember that the slow increase in phytoalexin might be part of a multi-pronged defence strategy, in which any single element might not be enough to keep the potential pathogen at bay.

Chemical Diversity of Phytoalexins

isoflavans, Isoflavones, coumestans, isoflavanones, pterocarpenes, and pterocarpans are the six isoflavonoid groups generated by Leguminosae. Pisatin, maackiain, glyceollin, medicarpin, and phaseollin are some of the well-known pterocarpan phytoalexins. Pisatin was the first phytoalexin isolated and identified from Pisum sativum, the garden pea (Cruickshank and Perrin 1960) [9]. Non-isoflavonoid phytoalexins such as furanoacetylenes and stilbenes are produced by a small number of legumes in addition to these chemicals.

Table 1: Phytoalexins from Different Plant Families

S. No.	Plant Families	Types of Phytoalexins
1.	Amaryllidaceae	Flavans
2.	Brassicaceae	Indol phytoalexins/camalexin Sulfur-containing phytoalexins/brassinin
3.	Chenopodiaceae	Flavanones/betagarin Isoflavones/betavulgarin
4.	Compositae	Polyacetylenes/safynol
5.	Convolvulaceae	Furanosesquiterpenes/Ipomeamarone
6.	Euphorbiaceae	Diterpenes/casbene
7.	Poaceae	Diterpenoids: Momilactones; Oryzalexins; Zealexins; Phytocassanes; KauralexinsDeoxyanthocyanidins/luteolinidin and Apigeninidin Flavanones/ sakuranetin Phenylamides
8.	Leguminosae	Isoflavones, Isoflavanones, Isoflavans, Coumestans Pterocarpans/pisatin, phaseollin, glyceollin and maiackiainFuranoacetylenes/wyerone Stilbenes/resveratrol Pterocarpens
9.	Linaceae	Phenylpropanoids/coniferyl alcohol
10.	Malvaceae	Terpenoids naphtaldehydes/gossypol
11.	Moraceae	Furanopterocarpans/moracins A-H
12.	Orchidaceae	Dihydrophenanthrenes/loroglossol
13.	Rutaceae	Methylated phenolic compounds/xanthoxylin
14.	Umbelliferae	Polyacetylenes/falcarinol Phenolics: xanthotoxin 6-methoxymellein

15.	Vitaceae	Stilbenes/resveratrol
16.	Rosaceae	Biphenyls/auarperin Dibenzofurans/cotonefurans
17.	Solanaceae	Phenylpropanoid related compounds Steroid glycoalkaloids Norsequi and sesquiterpenoids Coumarins

(*Source*: Singh, R., & Chandrawat, K. S. (2017) [41]

Most basic reaction of the plants to pressure, biotic (pathogen/insects) or abiotic (injuring) is the generation and amassing of substrates that can restrain the development and exercises of the biotic factors or may help in recuperating process. Hammerschmidt, 1999 [18] reported that in plants, continuous irritation by the pathogen is required for the production of an effective amount of these phenolic compounds. Kuc (1995) [24] defined phytoalexins as antibiotics produced in plant-pathogen interactions or as result of response to injury or other physiological stimulation. Wide variety of toxic chemicals was alleged to increase in concentration as a result of infection, thus phytoalexins are now considered as low molecular weight antimicrobial compounds produced de novo in the plants as a result of infestation or abiotic stress. This excludes the pre-existing phenols, example caffeic acid, chlorogenic acid and scopoletin. Plants from the families Gramineae (oats, rice, sorghum, and sugarcane), Solanaceae, Leguminaceae, Chenopodiaceae, Convolvulaceae, Compositae, Malvaceae, and Umbellifera have been demonstrated to contain phytoalexins (table 1). Phytoalexins are majorly synthesized by members of the Orchidaceae family.

Elicitors of Phytoalexins Accumulation

Elicitors are substances that inform plants when it's time to start synthesis of phytoalexins. Abiotic elicitors may not play a role in usual host-pathogen interactions, but biotic elicitors may play a function in the interaction between plants and suspected pathogens (Darvill and Albersheim, 1984) [10]. After being attacked by the pathogen, the production of phytoalexin compounds was considered to be initiated by either the pathogen's substance or the host-pathogen interaction. Numerous different pathogen and plant-produced molecules, known as elicitors (Ahuja, 2012) [1], will triggered phytoalexins and other defence responses. Several experiments have been carried out to see if plant cells exhibit receptors for these elicitors (Horsfall, 2012). Some elicitors have been reported to have the same specificity as the pathogen has with its host while most elicitors showed a lack of any specific connection to the outcome of a host-parasite interaction (Ahuja, 2012; Horsfall, 2012) [1]. Purkayastha (2017) [37] proposed a cutting-edge synthesis of the gene-for-gene hypothesis, which states that protection occurs only when the final product of a pathogen avirulence gene interacts with the final product of a plant resistance gene. Due to the high degree of specificity, the gene-for-gene system provides a good framework for determining if the outcome of the avirulence gene may also be used as a race-/cultivar-specific elicitor of defence responses, such as phytoalexin accumulations (Ahuja, 2012; Purkayastha, 2017) [1]. "Elicitors are molecular compounds that trigger plants to start producing phytoalexin." Plants and prospective pathogens may communicate through biotic inception elicitors, but abiotic elicitors are not involved in usual host-pathogen interactions (Purkayastha, 2017) [37]. In most cases, the boost is provided by the presence of microbes, whose recognition by the host initiates a cascade of events that leads to phytoalexin biosynthesis. "Exogenous" elicitors are those that originate from the attacking organism, on the other hand "endogenous" elicitors are those that come from the host plant and are formed by the communication between the microbe and the plant. Particles with elicitor action have been recognized in a broad range of structural forms, including lipopolysaccharides, polysaccharides, fatty acids, glycoproteins, oligosaccharides, and even enzymes, but their action is credited to their ability to discharge elicitor-active segments from the pathogen cell wall or host (Bostock *et al.*, 1992; Alghisi & Favaron, 1995) [6, 2]. Abiotic elicitors build a different assortment of chemicals that aren't naturally found, such as the pathogen's or host's tissues. They would not be detected by the plant in normal circumstances. Compounds such as purifiers, fungicides, important molecules such as histone and polylysine, heavy metal salts such as Hg2+ and Cu2+, and intercalated DNA reagents are included in this group (abiotic elicitors) (Purkayastha, 2017) [37]. Treatment of plant tissues with factors that cause stress for instance rehashed solidifying and defrosting, injuring or introduction to UV light (Liu *et al.*, 2015; Mert-Türk*et al.*, 1998) [27, 32] can likewise instigate phytoalexin synthesis.

Table 2: Common Phytoalexins Reported in Host-Pathogen Interaction

Type of Phytoalexin	Host Plant	Fungal Pathogen	References
Capsidol	*Nicotinia clvelandi, N. tabacum*	Tobacco necrosis virus (Capsicum)	Chaube and Pudhnir (2005)
Pistin	Pea (endocarp) pods, leaves	*Moniliniafructicols* non pathogen	Mazid*et al*. (2011)
Glutinosone	*Nicotinaglutinosa*	T.M.V	Burden *et al*. (1975)
Ipomeamarone	Sweet potato	*Ceratocystis fimbriata*	Mawalwa*et al.* (2014)
Wyerone	Pea	*Botrytis fabae*	Slusarenku*et al.* (2012)
Triflorrhizin	*Trifolium pretense*	*Monilia fructicola*	Chaube and Pudhnir (2005)
Glyceollin	Soyabean	*Pytophthoramegaspermav*ar. Sojae	Ng *et al.* (2011)
Rishitin, Phytuberin	Solanaceae	fungal sterol, ergosterol	Tugizimana*et al*. (2014)
Sativan, Vestitol	Alfalfa, *Lotus corniculatus*	*Helminthosporium turcicum Pass*	Bonde*et al.* (1973)
Isocoumarin	Carrot	-	Lafuente*et al*. (1996)
Vergosin and Hemigossypal	Cotton	-	Chaube and Pudhnir (2005)
AvenaluminI,II and III	Barley	*Puccinia caronata*f.sp. avenae	Chaube and Pudhnir (2005)

(*Source*: Usman & Ahmadu, 2018) [44]

The phytoalexins pisatin and phaseollin accumulated to fungitoxic levels not only in inoculum droplets applied to exposed pea or bean pods but also in tissues beneath the inoculum droplets (Cruickshank and Perrin, 1968) [9]. Treatment with sub-lethal dosages of resveratrol in *B. cinerea* conidia, asymetric development of the germ tube resulted in the formation of "curved-germ tubes." This cytological anomaly shows that stilbenic compounds may interact with

tubulin polymerization, which is a common mechanism of action for synthetic fungicides and anticancer drugs (Woods *et al.*, 1995) [47]. Furthermore, interactions between phaseollin or kievitone and *Rhizoctonia solani* have shown that phytoalexins can alter glucose absorption by fungus cells. After treatment with the stilbene phytoalexins resveratrol and pterostilbene, conidia of *B. cinerea* displayed disruption of the plasma membrane and full disarray of mitochondria. Camalexin in *B. cinerea*, has recently been implicated in the triggering of apoptosis (Shlezinger *et al.*, 2011) [40] (Table 2). The efficacy of various phytoalexins, including the coumarin phytoalexin scopoletin, in reducing green mould symptoms on oranges produced by *Penicillium digitatum* was demonstrated *in vivo* (Sanzani *et al.*, 2014) [38]. Similar to phenolic phytoalexins (umbelliferone, resveratrol, scoparone, and scopoletin) have been demonstrated to suppress *Penicillium expansum* growth and patulin buildup in apples. Phytoalexins also have antibacterial properties as well as to their antifungal properties. For example, the viability of *Erwinia atroseptica* cells is reduced by rishitin at a concentration of 360 g/L by roughly 100% (Bayliss and Lyon, 1975) [28]. Resveratrol also has antibacterial properties against *Enterococcus, Pseudomonas, Helicobacter, Neisseria*, and *Staphylococcus.* It is reported that phytoalexins are hazardous to a broad range of organisms, both eukaryotic and prokaryotic.

Phytoalexin: Biosynthetic Pathways

Various pathways are utilized for producing different phytoalexins. The majority of the phytoalexins discovered come from the phenylpropanoid biosynthetic pathway, which produces organic compounds from the amino acid phenylalanine. Phenylpropanoids are involved in a variety of functions and play an important role in the plant-environment interaction. Isoflavones, dihydrophenanthrene, stilbenes, coumarins, lignin, and other phenols are among the secondary metabolites implicated in plant disease resistance. Phenylalanine ammonia lyase (PAL), coenzyme 4-cumaraseligase, and cinnamate 4 hydrolase are enzymes that catalyse the formation of phytoalexins (Mateos & Leal, 2013). The understanding of phytoalexin biosynthetic pathways and the enzymes involved leads to an understanding of the expression of plant response to pathogen infection. Terpenoid phytoalexins can very well be found in a range of plants, including cotton *(Gossypium hirsutum*), tobacco (*Nicotiana tabacum*), elm (*Ulmus americana*), and sweet potato (*Ipomoea batatas*). Despite the wide range of monocots, which include orchids, ginger, lilies, palm trees, herbs, and onions the greatest collection of terpenoid phytoalexins in the Poaceae family has so far been found in the genera *Zea* and *Oryza* (Harborne, 1999) [20]. Isopentenyldiphosphate and dimethylallyl pyrophosphate (DMAPP) are isoprenoid precursors that may be made in plants from mevalonate or metileritritol phosphate. The production of geranyl-geranyldiphosphate and the biosynthesis of diterpenoid occurs via the methylerythritol phosphate (MEP) path (Okada, 2007) [35].

The most distinctive ones are:

1) Thephenylpropanoic-polymalonic acid route,
2) Themethylerythritol phosphate and geranyl-geranyldiphosphate pathway,
3) Theindolephytoalexin pathway.

1) Phytoalexins Produced by the Phenylpropanoic-

Polymalonic Acid Pathway: The universal phenylpropanoic-polymalonic acid route produces all flavonoid phytoalexins (isoflavans, isoflavones, isoflavonoids, pterocarpans, arylbenzofurans, and coumestans), as well as stilbene phytoalexins and derivatives (dihydrophenanthrenes). It all starts with phenylalanine and phenylalanine ammonia-lyase (PAL), or to a lesser extent, tyrosine and tyrosine ammonia-lyase (TAL). The resulting para-coumaric acid is activated in para-coumaroyl-CoA by 4coumaryl: CoA (C4L) ligase ligation to a coenzyme A.

Following that, chalcone synthase (CHS) and stilbene synthase (STS) utilise the same substrate and combine it with three consecutive units of malonyl-CoA, producing naringenin chalcone, the first C15 intermediate in the flavonoid pathway, and resveratrol, the precursor of all stilbenes, respectively (Jeandet *et al.*, 2014) [23]. The figure 1 depicts the biosynthetic pathways of the principal flavonoid and stilbene-like phytoalexins from the Leguminosae family.

2) Phytoalexins Derived from Mevalonoid

Members of the carboxylic sesquiterpene, monoterpene, diterpene, and sesquiterpene families make up this group of phytoalexins. In elicitor-induced rice (*Oryza sativa*) cells, synchronised accumulation of seven MEP pathway gene transcripts (OsDXS3, OsDXR, OsCMS, OsCMK, OsMCS, OsHDS, and OsHDR) is expected, with the following stages of biosynthesis taking place in plastids. Diterpenoids are formed when a variety of enzymes react with GGDP as a starting material. Copalyldiphosphate synthases (CPS) are the first diterpene cyclases to act on GGDP, initiating the first cyclization of the latter to copalyldiphosphate (CDP). Class I diterpene synthases such as kaurene synthase-like (KSL) require CDP as a substrate. The olefin precursors of the main diterpene phytoalexin families are produced by the sequential action of CPS and KSL.

Following that, KSL uses stereochemically distinct isomers: the ent-CDP in the biosynthesis of phytocassanes A-E and oryzalexins A-F, as well as the syn-CDP in the synthesis of momilactones A and B. A range of cytochrome P450 (CYPs) enzymes are required for the synthesis of oryzalexins, momilactones, and phytocassanes with additional oxygen (figure 2).

3) IndolePhytoalexins:

In this type camalexin is an important example, this is the major phytoalexin of *Arabidopsis*. Camalexin's indolic ring is made up of tryptophan (Trp), which is made up of chorismate. Two cytochrome P450 homologues, CYP79B2 and CYP79B3, govern the first step in the pathway from Trp to camalexin, leading to indole-3-acetaldoxime. The cytochrome P450, CYP71A13 transforms the latter into indole-3-acetonitrile (IAN). A glutathione-S-transferase and, most likely, a cytochrome P450 is involved in the subsequent conjugation of IAN with glutathione. A phytochelatin synthase or into γ-glutamyl-cysteine IAN converts the IAN glutathionyl derivative into IAN cysteinyl-glycine, through the action of γ-glutamyltranspeptidases 1 and 3. The IAN cysteine conjugate is formed from both stages.The CYP71B15 (PHYTOALEXIN DEFICIENT 3, PAD 3) gene, which encodes a multifunctional enzyme that produces camalexin from dihydrocamalexic acid, regulates the last steps of this biosynthetic process (figure 3).

Phytoalexin Biosynthesis Regulation Networks

Many endogenous chemicals, including phytohormones (salicylic acid, jasmonic acid, abscisic acid, ethylene, auxins and to a lesser extent gibberellins), defense-related genes, transcriptional regulators, phosphorylation relays, and cascades, influence phytoalexin production. The type of the

infecting pathogen as well as the generated phytoalexin itself influence the regulatory mechanisms of phytoalexin production. Camalexin accumulation was observed to be independent of jasmonic acid (JA) in *Arabidopsis* plants treated with the fungal pathogen *Botrytis cinerea* in the *Arabidopsis Alternaria brassicicola* interaction. The use of rice mutants convincingly showed the existence of JA-dependent and independent pathways in the regulation of diterpenoid phytoalexins in the interaction between rice and the fungus agent *Magnaporthe oryzae*. Momilactone accumulation was hindered in these mutants missing a functioning allene oxide cyclase necessary for JA synthesis, although phytocassane production was unaffected. Furthermore, either salicylic acid (SA)-independent or SA-dependent signalling pathways influence camalexin synthesis in *Arabidopsis*. Indeed, SA-induction defective *Arabidopsis* mutants with decreased ethylene production when infected with *Pseudomonas syringae* have lesser manufacture of this phytoalexin. Other phytohormones have been implicated in phytoalexin production regulation mechanisms. Auxins and abscisic acid (ABA) appear to inhibit phytoalexin synthesis in general. Auxin signalling suppression has been found to boost *Arabidopsis* tolerance to biotrophic infections and reroute phytoalexin metabolism. ABA inhibits the formation of a variety of phytoalexins. ABA, for example, the accumulation of rishitin and lubimin in potatoes, inhibits the synthesis of kievitone in beans, and glyceollin in soybeans. Tobacco mutants lacking ABA produce twice the amount of capsidiol as wild-type plants. Overexpression of cytokinin, on the other hand, has been demonstrated to improve tobacco tolerance to *P. syringae*. The up-regulation of the synthesis of phytoalexins, capsidiol and scopoletin, corresponded well with the improved pathogen resistance. The stimulation of camalexin production in *Arabidopsis* plants after treatment with Microbe-Associated Molecular Patterns (MAMPs) has been linked to Mitogen-Activated Protein Kinases (MAPKs). MPK3 and MPK6 are two MAP kinases that have a role in the up-regulation of many enzymes involved in the camalexin biosynthesis pathway. For example, the Overexpression of these two MAPKs resulted in a 400-fold increase in expression of the CYP71B15 gene, which encodes the multifunctional enzyme that acts at the pathway's terminus. Camalexin synthesis was eliminated in Arabidopsismpk3/mpk6 double mutants, which also enhanced vulnerability to *B. cinerea*. Cell calcium transfers, which are decoded and conveyed by a toolbox of calcium-binding proteins, also govern protein phosphorylation-induced phytoalexin synthesis. The phytoalexin regulatory networks do involve several calcium sensor families. When the rice was treated with MAMP, overexpression of two genes producing calcineurin B-like protein-interacting protein kinase was shown to create two phytoalexin classes, phytocassanes and momilactones. Other phytoalexin biosynthesis regulators have been discovered. Rac protein overexpression resulted in disease resistance to bacterial blight in rice, as well as a 19- to 180-fold increase in the formation of the rice phytoalexin momilactone A. Selenium-binding protein also regulates the production of this phytoalexin.

Overexpression of microbial virulence genes from the Nep1-like family of proteins has been linked to a significant transcriptional stimulation of genes involved in the camalexin pathway in Arabidopsis. Various sugars (fructose, sucrose, and glucose) have been demonstrated to operate as endogenous signals, influencing the production and accumulation of phytoalexins. Finally, it was shown that overexpression of non-expressor of pathogenesis-related genes-1, which is involved in systemic acquired resistance, causes the manufacture of the cotton phytoalexin polyphenols.

Understanding the Function of Phytoalexins

Phytoalexins are used by plants as part of a massive defence system against pests and illnesses. Plants develop and accumulate antimicrobial compounds with a low molecular weight in response to biotic and abiotic stresses. After discovering that infecting potato tubers with a strain of Phytophthora infestans capable of causing hypersensitive reactions significantly reduced the effect of subsequent infection with a different strain of P. infestans, Muller and Borger proposed the concept of phytoalexins over 70 years ago. This inhibition was linked to a phytoalexin-like "principle" produced by hypersensitive plant cells. Brassicaceae's major phytoalexin is camalexin (Cruciferae). Phytoalexins are chemicals that are synthesised from distant sources by enzyme de novo synthesis. Because of this characteristic, deciphering their biosynthesis and regulatory processes is extremely difficult. Phosphorylation cascades, defence-related marker genes, calcium sensors and elicitors, as well as hormone signalling, may all play a role in phytoalexin synthesis and pathogen resistance regulation. In a conclusion, comprehending the processes that govern phytoalexin accumulation has paved the way for genetic modification of those molecules in designed plants to improve disease resistance. The subject of whether phytoalexins are active *in vivo* and play a substantial part in plant defence systems has long been contested, with experts debating both phytoalexin antibacterial activity and their location surrounding invading organisms and plant tissues.These intriguing aspects are key to their postulated function as microbial growth regulators in diseased plant tissues. Despite this, there is substantial evidence that these chemicals cause *in vitro* toxicity in a wide range of prokaryotic and eukaryotic organisms. The capacity of pathogens to digest the phytoalexins to which they are exposed determines the nature of the interaction between plants and diseases. The involvement of fungal genes involved in phytoalexin detoxification in plants has been discovered by genetic engineering. Plant defence products and fungicides may be extruded by ATP-Binding Cassette (ABC) transporters in phytopathogenic fungus. These transporters operate as virulence factors, protecting the host against phytoalexin production. Many elements thus interact to influence the outcome of the plant-pathogen interaction. Phytoalexins have recently been discovered to have health-promoting properties in humans. For example, as a neuroprotective, a cardioprotective, anticancer, and antioxidant agent, as well as an antimicrobial and antifungal molecule, resveratrol generated by Vitaceae has been praised for its wonderful effects and wide spectrum of potential curative and preventative properties.

Phytoalexin Engineering and Their Role in Plant Defense Mechanisms

Gain- or loss-of-function genetic approaches for disease resistance in phytoalexin synthesis have provided direct and indirect evidence of their significance in plant-microbe interactions. Relatively simple genetic constructions involving the introduction of a single gene into plants are required in the case of the grapevine phytoalexin resveratrol, whose production is regulated by the stilbene synthase (STS)gene. The Kindl group was the first to show increased disease

resistance due to foreign phytoalexin synthesis in a new plant after transferring two grapevine STS genes (Vst 1 and Vst 2) into tobacco. It was discovered that adding these two genes increased B. cinerea resistance. Following that, various changes in alfalfa, wheat, papaya, rice, barley, tomato, and Arabidopsis, giving resistance to various diseases utilising the same STS genes or STS genes from other plants sources. All of these findings demonstrated that phytoalexins can play a role in the development of plant defence mechanisms against phytopathogenic bacteria, although STS overexpression is not always related to disease resistance. Other phytoalexin genes have undergone genetic modifications as a result of the study on stilbene phytoalexins. Surprisingly, phytoalexin engineering appears to have been restricted to a few phytoalexin biosynthetic genes. The use of a tobacco glucosyltransferase working on scopoletin has mostly been used to manipulate phytoalexin glycosylation genetically. Overexpression of the isoflavonoid-7-O-methyltransferase enzyme in alfalfa, which plays a key role in the manufacture of the phytoalexin maiackiain, has also been related to the plant's improved resistance to *Phoma medicaginis*. Soybean hairy roots were transformed with the peanut resveratrol synthase 3 AhRS3 gene and the resveratrol-O-methyltransferase ROMT gene, which catalyses the transition of resveratrol to pterostilbene, resulting in resistance to *Rhizoctonia solani*. In many situations, it is not possible to construct the full phytoalexin biosynthesis process, therefore the challenge for researchers is to find the correct enzyme to catalyse the route's limiting step. Phytoalexins have a role in plant-microbe interactions, as revealed by loss-of-function genetic techniques. Phytoalexin-deficient mutants were shown to be more susceptible to infections in practically every experiment. Reduced pisatin levels in hairy roots of peas modified with antisense 6-α-hydroxymaiackiain-3-O-methyltransferase were linked to lower resistance to the fungus *Nectria haematococca*. RNAi suppression of isoflavone synthase or chalcone reductase in soybeans reduced daidzein and glyceollin accumulation as well as disease resistance to *P. sojae* by 90%. In Sorghum, loss-of-function alleles of the yellow seed1 gene, which encodes CHS, chalcone isomerase, dihydro flavonol reductase, and flavonoid-3'-hydroxylase, resulted in a reduction in the accumulation of 3-deoxyanthocyanidin, which appeared linked to severe anthracnose symptoms. The effect of a phytoalexin-deficient mutation on camalexin in *Arabidopsis* was discovered to be dependent on the pathogen infecting the plant. This mutation was not linked to enhanced susceptibility to *P. syringae, Perenospora parasitica, Erysiphae oronti, or B. cinerea*, however, it did have a significant impact on *A. brassicicola* susceptibility. Finally, the importance of phytoalexin glycosylation in plant-pathogen interactions has been highlighted through loss-of-function genetic techniques. Scopolin levels were reduced by 70% to 75% in transgenic tobacco leaves downregulated for a tobacco-specific phenylpropanoid-glucosyltransferase, which was related to a 63 percent increase in TMV lesion surface. The involvement of phytoalexins in plant defence systems was further proven by indirect modification of phytoalexin levels by manipulating hormone signalling, phosphorylation cascades, or defence-related marker genes. Overexpression of cytokinins in tobacco, for contrast, resulted in greater resistance to *P. syringae*, which was significantly linked to increased production of phytoalexins, capsidiol and scopoletin. In *Arabidopsis*, mutations in two MAP kinases, MPK3 and MPK6, reduced camalexin synthesis and disease resistance to *B. cinerea*. Though phytoalexin engineering appears to be confined to a few genes, mostly stilbene and isoflavonoid genes, indirect regulation of phytoalexin accumulation via transcriptional regulators or components of upstream regulatory networks might be a valuable technique to increase plant disease resistance.

Phytoalexins' Role in Plant Disease Control

Phytoalexins accumulate at infection sites and limit the growth of fungi and bacteria *in vitro*, suggesting that they could be utilised to protect plants from fungi and bacteria-caused illnesses. Phytoalexins are significantly less toxic than chemical fungicides. The effect of resveratrol on B. cinerea, the pathogen that causes grey mould in grapevines, inhibits germ-tube elongation, radial mycelial growth, and mycelia dry weight increase, demonstrating phytoalexin fungitoxicity. Phytoalexins may alter the physiological, morphological, and cytological characteristics of fungal cells. The activity of four phytoalexins from the Solanaceae family (phytuberin, rishitin, solavetivone, and anhydro—rotunol) caused zoospore motility loss, cell rounding, moderate swelling, cytoplasmic granulation, and cell membrane splitting in three Phytophthora species (Harris and Dannis, 1997) [21].

Phytoalexins to Control Fungi

The available evidence concerning the contribution of phytoalexins to the restriction of fungal growth at different stages of colonization include;

1. Inhibition on plant surfaces

Fungal spores often fail to germinate following their deposition on leaf surfaces (Friend, 2012) [14]. A striking example of this concern is the behaviour of saprophytes in the phyllosphere. Ahuja (2012) [1] have described the increased growth of epiphytic fungi coincident with the onset of senescence. The ability to produce phytoalexins declines during senescence (Friend, 2016) [15] and it has been proposed that fungal growth on young leaves may be restricted by phytoalexins produced by underlying cells in response to fungal metabolites diffusing from germinating spores (Van Wees *et al.*, 2003) [45]. However, the limited evidence available does not support this attractive hypothesis. Thus, Mansfield *et al.*, 1982 [4] found that germination of saprophytes *Aureobasidiumpullulans, Cladosporium herbarum* and *Epicoccum nigrum* on pea leaves did not induce formation of the phytoalexin pisatin. The apparent absence of influence of phytoalexins on microbial proliferation in the phyllosphere could be explained if the cuticle functions as a barrier, preventing chemicals stimulating phytoalexin biosynthesis from diffusing to underlying cells.

2. Inhibition during attempted penetration into the plant cells

Protection from fungi is as often as possible communicated by the failure of disease hyphae to enter into or through the plant cell walls (Mellersh and Heath, 2003) [31]. Different sorts of deposit (Papillae) have been discovered to aggregate inside living cells underneath destinations of endeavored entrance. It has been shown that papilla development and other confined changes in the cell wall structure including lignification (Friend, 2016) [15] and silicification (Mellersh and Heath, 2003) [31] may give simply physical boundaries to the continued advance of attacking hyphae. Friend (2016) [15] isolated a fungitoxic flavonoid (which may be considered a

phytoalexin) from papillae formed in resistant barley leaves in response to *Erysiphe graminis* f. sp. *hordei*. It is possible that other phytoalexins may also be incorporated into papillae or cell walls, thereby producing a localized, fungitoxic barrier to penetration.

3. Inhibition after penetration:

Following penetration of resistant plants, fungal growth may be restricted at numerous sites:- 1.)within the partially degraded walls of epidermal cells (for example *Botrytis* spp. in non-host plants); 2.)intracellularly, either within the epidermis (*Colletotrichum* spp. in non-host plants or resistant cultivars) or in mesophyll cells (restricted development of hautoria of rust fungi); 3.)in intercellular spaces (*Cladosporium fulvum* in resistant tomato leaves; and within xylem vessels (*Verticillium* and *Fusarium* spp. in wilt resistant plants). In other to prove whether or not inhibition of hyphal growth at these sites is caused by phytoalexins, it would necessary to measure the concentrations of inhibitors to which hyphae are exposed at the time they stop growing and also to examine activity of what may be a mixture of the phytoalexins at the site of exposure (Mansfield, 1999).

Phytoalexins to Control Bacteria

Studies in the role of phytoalexins in bacterial resistance have been mainly concerned with the restriction of bacterial multiplication within intercellular spaces. *Pseudomonads* and French bean and soyabeans.- The French bean plant and the resistance of leaves of particular cultivars to halo blight induced by *Pseudomonas phaseolicola* and pods to avirulent isolates of *Pseudomonas syringae* are the subjects of the most extensive research of phytoalexins' role in bacterial diseases. The multiplication of compatible and incompatible races of *P.phaseolicola* in bean cv. Red Mexican, as well as the onset of symptoms, are investigated (Schmelz *et al.,* 2014) [39]. The compatible race is to multiply rapidly causing water-soaked lesions to develop between two and four days after inoculation; these lesions become brown and desiccated after five days. The incompatible race multiplies less rapidly and causes a hypersensitive reaction, inoculation sites collapsing to form localized desiccated brown lesions within two days. Collapse of tissue throughout the hypersensitive reaction is closely linked with the cessation of bacterial multiplication (Schmelz *et al.,* 2014) [39].

Phytoalexins to Control Nematodes

Researchers have studied the resistance of legume roots to nematodes. For example, lima bean roots exhibit a hypersensitive resistance response to *Pratylenchus scribneri*. *Jeandet et al.* (2014) [23] found that tissue bearing necrotic lesions caused attempted feeding of the nematode inside the epidermis and cortex accumulated the fluorescent isoflavonoids coumestrol and psoralidin. These compounds were present only in low concentrations in uninoculated roots. Coumestrol inhibited *P.scribneri* movement at concentrations lower than those reported in infected roots, prompting Jeandet *et al.* (2014) [23] to believe that induced accumulation of the coumestan phytoalexin provides the chemical basis for lima bean root resistance to *P.scribneri*. The relevance of glyceollin in the expression of soybean cv. Centennial's resistance to the root-knot nematode Meloidogyne incognita has also been investigated.

Phytoalexins to Control Viruses

Antifungal phytoalexins accumulate during the development of local necrotic lesions by viruses in leaves of legumes and *Nicotiana* spp. but they are absent from systematically infected plants (Jeandet *et al.*, 2012). There have been few attempts to decide if phytoalexins suppress viral replication and thereby restrict lesion size. Hammerschmidt (1999) [18] found that incubation of tobacco necrosis virus (TNV) in soyabean leaf extract containing low concentrations of glyceollin had no effect on viral infectivity. However, they postulated that the presence of phytoalexin in tissues close to lesions would make them unsuitable for virus multiplication in the future. Glyseollin was not translocated and was not involved in systemic protection against TNV afforded by the prior inoculation of soybean leaves with the virus.

Conclusion

The multiple instances of plant secondary metabolites (phytoalexins) discussed here show that they are an essential mechanism for preventing phytopathogen spread in plants, serving as antifungals or elicitors of other defence responses. More intriguingly, several of the examples shown here suggest that phytoalexins can be used as "antifungal potentiators" and are active against therapeutically important infections. The significance of research operations aimed at collecting and identifying plant secondary metabolites, as well as gaining a better knowledge of the mechanisms involved in plants' natural defences against fungal aggressors. The discovery of phytoalexins in a specific species helps future elicitors of active chemical synthesis in plant defence against biotic stimuli. The search for PR proteins in other related plant species that can be isolated in high concentrations and utilised to induce the production of these compounds in other plants is an efficient strategy for providing better protection to all of these plants. The vegetable crude extract contains a complex of secondary metabolites that work together to battle plant diseases. They additionally be utilised as a matrix for the separation and production of specific active compounds, making large-scale use easier. Because these are plant-derived chemicals, they may contain phytoalexins, which help to boost the expression of these compounds in the plants utilised in the study.

Because the method for synthesis of phytoalexins has yet to be established, the single way to obtain them is through the isolation and the identification process, which takes longer and yields less. Due to high cost and time required to complete the insolation method, few researchers can establish phytoalexin identification, due to scarcity of defined standards. Apart from the necessity of obtaining these standards, study into the optimum elicitors for each species studied becomes important, because secondary metabolic products require components for induction. Advanced approaches such as metabolomics and proteomics, which aim to quantitatively measure the set of metabolites created or modified, are being used. Advanced techniques such as proteomics and metabolomics, which aim to identify and quantify the group of metabolites secreted or modified by a body, are tools that can be used to provide a more comprehensive analysis of phytoalexins. Because knowledge of expressed genes facilitates the identification of species with similar defence response properties and allows the retrieval and identification of these phytoalexins through a bank of genomic data, molecular biology research has become a strategy that has been studied extensively. Further research to evaluate the discovery of new phytoalexin identification techniques, as well as research to prove their functions and the application procedures for this mechanism to diminish

production losses of significant crops for human consumption, such as the Poaceae family, can work together to enhance the quality of product lines supplied to the population.

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