Overview on Toxins as Weapons Used By Pathogens to Invade Plants Tissues

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ABSTRACT
In the history of phytopathology, microbial toxins have been the objects of extensive studies as possible pathogenicity or virulence factors for the producer pathogens. Some of the most potent phytotoxins are synthesized by microbes. A few of these share molecular target sites with some synthetic herbicides, but many microbial toxins have unique target sites with potential for exploitation by the herbicide industry. Compounds from both non-pathogenic and pathogenic microbes are discussed. Microbial phytotoxins with modes of action the same as those of commercial herbicides and those with novel modes of action are covered. Some examples of the toxin compounds used by plants to invade their host tissues are discussed in the light of tentoxin, AAL-toxin, auscaulitoxinaglycone, hydantocidin, thaxtomin, and tabtoxin and many more.

KEYWORDS: *Microbial, pathogens, bacteria, phytotoxins, herbicides, inhibitors.*

INTRODUCTION

In general, a plant becomes diseased when it is continuously disturbed by some causal agent that results in an abnormal physiological process that disrupts the plant's normal structure, growth, function, or other activities. This interference with one or more of a plant's essential physiological or biochemical systems elicits characteristic pathological conditions or symptoms.

Plant diseases can be broadly classified according to the nature of their primary causal agent, either infectious or non-infectious. Infectious plant diseases are caused by a pathogenic organism such as a fungus, bacterium, mycoplasma, virus, viroid, nematode, or parasitic flowering plant. An infectious agent is capable of reproducing within or on its host and spreading from one susceptible host to another. Non-infectious plant diseases are caused by unfavourable growing conditions, including extremes of temperature, disadvantageous relationships between moisture and oxygen, toxic substances in the soil or atmosphere, and an excess or deficiency of an essential mineral. Because non-infectious causal agents are not organisms capable of reproducing within a host, they are not transmissible.

In nature, plants may be affected by more than one disease-causing agent at a time. A plant that must contend with a nutrient deficiency or an imbalance between soil moisture and oxygen is often more susceptible to infection by a pathogen; a plant infected by one pathogen is often prone to invasion by secondary pathogens. The combinations of all disease-causing agents that affect a plant make up the disease complex. Knowledge of normal growth habits, varietal characteristics, and normal variability of plants within a species - as these relate to the conditions under which the plants are growing - is required for a disease to be recognized.

The study of plant diseases is called plant pathology. Pathology is derived from the two Greek words *pathos* (suffering, disease) and *logos* (discourse, study). Plant pathology thus means a study of plant diseases.

Microbes are a lucrative source of phytotoxins, e.g., Duke, *et al*., (2012). The evolutionary pressure for phytotoxin production is obvious with microbial plant pathogens, but many non-pathogenic soil microbes also produce potent phytotoxins, and the role of these compounds in chemical ecology is less clear. An example of the latter case is the production of bialaphos by several *Streptomyces* species (Strobel *et al*., 1991; Barazani & Friedman, 2001). Most of the previous reviews of microbially-produced phytotoxins have focused on aspects of the compounds other than their modes of action. The reviews by Duke *et al. (2012)*, Shinko et al.,2001 and Cutler *et al.*2004 are not exceptions. Any review that focuses on mode of action leaves out many microbial phytotoxins for which we have little or no information on their molecular target site. We also exclude larger phytotoxic peptides (>10 amino acids).

Diseases constitute a major setback in crop production world-wide and especially in the tropics. Diseases affect plants right from the planting stage to harvesting and storage of the produce. Amagasin *et al.*, (1994) reported that diseases accounted for world-estimated losses of 7 million tones. Anthracnose diseases of cassava and yam have resulted in an annual loss of 30-70% in both crops (Nishomo, 1983 and Sores, 1994). The effect of plant diseases is not only on the market value of the produce, but also on the availability of planting materials. Rando (1977) reported that the most significant effect of cassava anthracnose disease is the reduction of healthy planting materials available to farmers. Several methods have been employed to manage plant diseases in crops, (Rajaram*et al*., 2008). But the most effective approach would be the selection and breeding for diseases resistance varieties (Rosellini *et al*., 2007). Most of the existing techniques for selecting resistant varieties include evaluation for disease incidence and severity in the field and green houses.

However, these screening procedures are very cumbersome, time consuming, labor intensive and require a large amount of land space (CRAC, 1996 & Evidente *et al.*, 1998). Typical symptoms of most plant diseases revealed the involvement of phytotoxic metabolites, which therefore suggest a role for toxic metabolite secreted by the pathogen in the disease development. Metabolites ofmany fungi may have adverse or stimulatory effects on plants (Berestetskiy, 2008; Mobius & Hertwerk, 2009, Duke *et al.*, 2011) such assuppression of seed germination, malformation, andretardation of seedling growth (Strange, 2007; Brunner *et al*., 2007).Conti *et al.*, (2003) reported that some fungal pathogens often produce phytotoxins that affect seed germinationand seedling growth. Mallik, 2001 and Natsumeda *et al*., (1989) reported that some fungi on the surface of seeds often produce mycotoxins that affect food quality. Abbas & Duke, 1995; Rodriguez-Surez *et al.*, (2007) reported that the foliar symptoms of Eutypa infected grapevines are not the direct result of the fungus, but rather that of a toxin, eutypine, produced by the fungus and transported through vascular tissue to the affected shoot. Pathogenic fungi and bacteria often damage their host plants by producing toxins, which cause various symptoms including necrosis, chlorosis, wilting, water soaking and eventually the death of plants (Cutler, 1995; Williams *et al*., 2009). One criterion of the importance of a toxin in a disease syndrome caused by a pathogen is that toxigenicity is often related to pathogenicity or virulence (Evidente, 2006).

Several phytotoxic metabolites have been found associated with bacteria and fungal pathogens, which, causes symptoms similar to those caused by the pathogen. Such toxic metabolites include pinolidoxin from *Ascochytapinodes* (Lydon and Duke, 1998), deoxyradicin and maculosinfrom *Alter-nariahelianthi*and *Alter-nariaalternata* (Wild and

Ziegler, 1989, Ziegler, 1989). Identified metabolites from other pathogens includes piricularin from *Piriculariaoryzea*, victorin from *Cochliobolusvitoriae*(Kato *et al.*,1991), phaseolotoxin from *Pseudomonas syringae*pv*phaseolicola*, toxin from *Periconiacircinata*, saccharitoxin from *Helmithosporiumsacchari* (Strobel *et al.*, 1991), cercosporin from *Cercospora*spp. (Strange 2007). Phytotoxic metabolites of most of these pathogens have been reported to play a significant role in pathogenesis (Duke *et al.*, 2011). Phytotoxic metabolites have been employed in screening crops for disease resistance (Lydon and Duke, 1998). Considering the importance of phytotoxic metabolites in crop protection management's practices, this paper reviews the use of phytotoxic metabolites of pathogens in plant disease management.

TYPES OF MICROBIAL PHYTOTOXINS AND THEIR MODES OF ACTION

A. Tabtoxin

Tobacco leaves diseased by infection with wildfire bacteria result in a small necrotic spot containing bacterial cells, surrounded by a chlorotic zone that is free from bacteria. The wildfire bacterium *P. syringae*pv. *Tabaci* produces a pathogenic toxin called tabtoxin. When a tobacco leaf was treated with tabtoxin, this toxin caused chlorotic spots similar to the halos on leaves infected with the wildfire bacteria. Thus it has been suggested that the formation of disease symptoms by the attack of *P. syringae*pv. *Tabaci* is directly correlated to the toxic effect of tabtoxin on plant cells (Cutler, 1995).

The first isolation of tabtoxin was reported by Evidente *et al*. (1998), and an acceptable structure was published by Stewart (1971). The structure of tabtoxin is composed of tabtoxinine-b-lactam [2- amino-4-(3-hydroxy-2-oxoazacyclobutan-3-yl) butanoic acid] and threonine. Another type of tabtoxin is also produced at a minor amount as a derivative containing a serine molecule in place of threonine, called [2-serine] tabtoxin (Williams *et al*., 1972). Although both types of tabtoxin are synthesized in a biologically inactive form, they are readily converted to the active moiety of tabtoxinine-b-lactam by the cleavage of threonine or serine with some aminopeptidases present in either the bacteria or the plant. The active moiety tabtoxinine- b-lactam inhibits the target enzyme glutamine synthetase, which catalyzes the synthesis from glutamic acid to glutamine in amino acid metabolism. This inhibition results in the abnormal accumulation in tobacco cells of ammonia causing the characteristic chlorosis (Mobius and Hertwerk, 2009).

B. Aminotransferases

Several microbial secondary compounds either inhibit an amino transferase or appear to have such a mode of action. Cornexistin, a fungal metabolite from *Paecilomycesvariotii*, was patented as a herbicide. The amino transferase inhibitor aminooxyacetate causes identical herbicidal symptoms in duckweed. Among these group include:

Cornexistin: inhibits aspartate amino transferase activity at high concentrations only after incubation in a plant cellular extract, suggesting that cornexistin is a proherbicide that must be metabolized to an amino transferase inhibitor. **Gostatin**, a product of *Streptomyces sumanensis*(Amagasa et al.,1994), is a potent amino transferase inhibitor that is phytotoxic.

Gabaculin: a product of *Streptomyces toyacaenis*(Sare, *et al.*,1984), is an inhibitor of several aminotransferases. In plants it strongly inhibits glutamate 1-semialdehyde aminotransferase, an enzyme required for 5-aminolevulinate synthesis and thus porphyrin and chlorophyll synthesis (Rando, 1977). This compound will be discussed in more detail under section 11 on porphyrin synthesis.

Ascaulitoxin aglycone: a product of *Ascochytacaulina*, a fungus being studied as a potential mycoherbicide (Rosellini*et al*.,2007), is a potent phytotoxin that has profound effects on amino acid metabolism as determined by metabolic profiling (Evidente, *et.al*., 1998). Feeding treated plants with most amino acids reversed the effects of the toxin. However, *in vitro* assays found that the toxin did not inhibit alanine aminotransferase nor alanine:glyoxylate aminotransferase, leading the authors to speculate that it might inhibit another amino transferase or one or more amino acid transporters.

C. Trichothecenes toxins

Trichothecenes are toxic secondary metabolites of *Fusarium* species that are pathogenic to economically important crops such as wheat, barley, and maize. They are the causal agents of moldy-grain toxicoses in animals such as feed refusal, dermatitis, anemia, immune suppresion, and hemorrhagicsepticemia. Some fungi that belong to other genera (e.g., *Myrothecium* and *Trichothecium*) also produce trichothecenes, including those with macrocyclic rings. These sesquiterpene epoxides are protein synthesis inhibitors of eukaryotes and constitute a large family of fungal antibiotics. They are conventionally divided into two classes based on the presence or absence of a keto group at C-8 of the trichothecene skeleton (i.e., 12,13-epoxytrichothec- 9-ene). Typical examples of type A and type B trichothecenes are T-2 toxin produced by *Fusariumsporotrichioides* and deoxynivalenol (DON) produced by *Fusariumgraminearum*, respectively. Disease development on tobacco leaves inoculated with *P. Syringae* pv. *tabaci.* (Left) untransformed tobacco with chlorotic symptoms; (right) transgenic tobacco with no chlorotic halo on the leaves.

A proposed trichothecene biosynthesis pathway of *Fusarium* and other fungi.t-Typetrichothecene is formed through a series of enzymatic reactions beginning with the cyclization of farnesyl pyrophosphate to trichodiene by trichodiene synthase (TRI5). Subsequent biosynthetic steps involve oxygenations, isomerization, and the second cyclization to give isotrichodermol, the first pathway intermediate that has a toxic trichothecene skeleton. The specific *O*-acetylation at C-3 occurs before oxygenations and esterifications at C-4, -7, -8, or -15 of the trichothecene skeleton.

The trichothecene biosynthesis pathway in *Fusarium* species starts with a cyclization of farnesyl pyrophosphateto trichodiene. After a series of oxygenationsand isomerization, the resulting bicyclic olefin trichotriolis converted to isotrichodermol, the first tricyclicintermediate that has the toxic trichothecene skeleton. Following this second cyclization, a diversity inoxygenation and esterification patterns arises basedon the genetic background of each producer *Fusarium*species. These biosynthesis pathways were established mainly through studies of blocked mutants and precursor feeding experiments by researchers in the United States (Barazani and Friedman, 2001; Williams *et al.*, 2009; Conti *et al*., 2003; Natsumeda *et al.*, 1989), Canada (Ziegler *et al*., 1989), England (Omura *et al*., 1984), and some other countries.

D. Toxins that affect β-Cystathionase

Rhizobitoxine: a phytotoxin produced by some *Bradyrhizobium*strains. It inhibits β-cystathionase, which is required for methionine synthesis. This toxin is phytotoxic enough to have been considered as a commercial herbicide. Since synthesis of the essential plant hormone ethylene is dependent on methionine, one could assume that ethylene synthesis

would be greatly inhibited in plants treated with this compound. However, rhizobitoxine also directly inhibits production of ethylene from methionine by inhibition of 1-aminocyclopropane-1-carboxylate synthase (Nishomo,1983)..

E. Toxins that affects Glutamate Synthase

Acivicin: is a product of *Streptomyces sviceu* that has been patented as a herbicide. It has not been well studied in plants, but has been well researched as a pharmaceutical. Acivicin is an analogue of glutamine and inhibits a number of glutamine-dependent enzymes, including glutamate synthase. It also inhibits amidophosphoribosyltransferase, phosphoribosylformylglycinamidine synthase, GMP synthase, and γ-glutamyltranspeptidase (Lydon and Duke,1998). Unfortunately, the effects of this toxin on these enzymes in plants are not published.

F Toxins that affect Glutamine Synthetase

Phosphinothricin and several other microbial products are inhibitors of glutamine synthetase (GS). This is perhaps the largest collection of microbial compounds that target a particular enzyme. Most of these compounds are of bacterial origin (from either *Pseudomonas syringae* plant pathovars or from soil-born *Streptomyces* species). These compounds are all analogues of glutamate, two of them are also produced from inactive di- or tripeptideprotoxins.
*Streptomyces hygroscopis*and *S. viridochromogenes*both produce bialaphos (Schinko *et al.*, 2009). This tripeptide does not inhibit GS, but must be metabolized in plants and microbes to L-phosphinothricin, the active GS inhibitor. Inhibition of GS causes accumulation of toxic levels of ammonium, as well as a disruption of amino acid and other primary metabolism. One of the earliest general physiological effects is cessation of photosynthesis. Both bialaphos and phosphinothricin are sold as commercial herbicides. Trialaphos and phosalacine, produced by *S. hygroscopicus*sp. KSB-1285 and *Kitasatosporiaphosalacinea*, respectively, also release phosphinothricin upon hydrolysis (Brunner *et. al.*, 2007 and Rodriguez-Surez *et al.*, 2007).

Bialaphos: is produced by fermentation. It has a very small market as a herbicide in Japan. Phosphinothricin is sold as a synthetic mixture of L- and D-phosphinothricin sold under several trade names, but given the herbicide common name of glufosinate. The D-isomer is inactive as a GS inhibitor. Glufosinate is one of the most successful commercial herbicides used throughout the world. Oxetin from *Streptomyces* sp. OM-2317 and the tripeptide L-(*N*5-phosphono) methionine-*S*-sulfoximinyl-L-alanyl-L-alanine from an unclassified strain of *Streptomyces* are also GS inhibitors. Oxetin is a very weak GS inhibitor. The latter compound is inactive as the tripeptide, but degrades into two known strong GS inhibitors, phosphor methionine sulfoximine and methionine sufoximine.
Several *Pseudomonas syringae* pathovars produce tabtoxin, a dipeptide prophytotoxin. Tabtoxin is not a GS inhibitor, but it is hydrolyzed*in planta*to form the potent GS inhibitor tabtoxinine-β-lactam. Analogues of tabtoxin, such as 2-serine-tabtoxin, valyl-alanyl-tabtoxin, alanyl-tabtoxin, and alanyl-analyl-tabtoxin have also been reported from various actinomycetes.

G, Toxins that Ornithine Transcarboxylase

Citrulline:The product of ornithine transcarboxylase (OCTase) is **citrulline**, a precursor of arginine. So, inhibition of this enzyme results in loss of arginine production.

Phaseolotoxin is a tripeptide produced by *Pseudomonas syringae* pv. *phaseolicola.* Phaseolotoxin is a protoxin, in that peptidases of the plant must convert it to *N*δ-*(N*1-sulfodiaminophospinhyl)-L-ornithine (PSorn), which is a potent inhibitor of OCTase (Mallik 2001).

H. Toxins that Cellulose Synthesis

Thaxtomin: belongs to a group of cyclic dipeptides (2,5-diketopiperazines) which arise from the condensation of 4-nitrotrytophan and phenylalanine groups. Structure-activity studies determined that the presence of a 4-nitroindole group is necessary to maintain phytotoxicity of these metabolites (Cutler, 1995). These potent toxins are produced by several species of the gram-positive filamentous bacteria in the genus *Streptomyces* (e.g., *S. scabies* and *S. eubacteria*) that cause scab disease in potato and in several taproot crops. Typical phenotypic responses of plants exposed to thaxtomin A include reduced seedling growth, cell swelling, and lignification of cell walls. Biochemically, thaxtomin inhibits cellulose synthesis. *Arabidopsis thaliana* seedlings treated with thaxtomin A have lower crystalline cellulose and higher content of pectins and hemicellulose in their cell wall, relative to untreated plants. This is accompanied by an alteration of the expression of genes involved in primary and secondary cellulose synthesis as well as genes associated with pectin metabolism and cell wall remodeling. Thaxtomin A affects the formation of the cellulose synthase complexes on the outside of the plasma membrane, leading to its dissociation from the cortical microtubule cytoskeleton (Sore, 1984).

I, Toxins that inhibits Energy Transfer

Tentoxin, a cyclic tetrapeptide from the plant pathogen *Alternaria alternata*, inhibits chloroplast development, which phenotypically manifests itself as chlorotic tissue (Rando,1977; Rajaram *et al.*,2008). These papers indicate that there is no direct effect of tentoxin on chlorophyll synthesis. Two fundamental processes are linked with this phenotype. This first is inhibition of energy transfer of the chloroplast-localized CF1 ATPase [19, 20]. One would think that this process alone could account for the chlorosis, but tentoxin also completely inhibits the transport of nuclear-coded enzyme polyphenol oxidase (PPO) into the plastid, even in etioplasts which should have no CF1 ATPase activity. Without this processing, PPO has no enzyme activity. Inhibition of these two processes seems to be linked, in that both processes are inhibited *in vivo* in tentoxin-sensitive plant species and not affected in insensitive species (Brunner *et al*. 2007). Nevertheless, the coding of the β subunit of proton ATPase at codon 83 seems to account for susceptibility of plants to tentoxin. Coding for glutamate at codon 83 correlates for resistance and aspartate coding results in susceptibility to tentoxin. Mutagenesis of *Chlamydomonas reinhardtii*to change gluamate to aspartate resulted in a change from resistant to susceptible. Later, tentoxin was suggested to exert its effect on chlorophyll accumulation through over energization of thylakoids, but this does not explain the profound effects of the compound on PPO processing in etioplasts without thylakoid membranes. The linkage of the β subunit of proton ATPase to PPO processing remains to be explained. Understanding this relationship may help to explain the role of PPO in the plastid, where enzymatic activity is latent (Evidente *et al*., 1998)]. The true physiological role of PPO in a functional chloroplast is still a mystery.

Nigericin: a product of *Streptomyces hygroscopicus*, is an uncoupler of photophosphorylation. It inhibits photosynthesis with decreased ATP/ADP ratios, decreased energy quenching, and hyper-reduction of QA (Strange, 2007).

Several microbial phytotoxins inhibit photosynthetic electron transport. These include cyanobacterin, fischerellinA, stigmatellin, and the aurachins. The first two of these compounds are produced by cyanobacteria.

Cyanobacterin: is a halogenated compound from the freshwater cyanobacterium *Scytonema hofmanni* that inhibits electron transport of photosystem II (Ziegler, 1989).

Fischerellin: from the cyanobacterium*Fischerellamuscicola*produces fischerellin A that inhibits PSII of green algae and higher plants (Kato *et.al*., 1991).

Stigmatellin: produced by the myxobacterium *Stigmatella aurantica*, inhibits photosynthetic electron transport at both the D-1 site of synthetic photosynthetic inhibitors and at the cytochrome b6/f-complex (Omura et al., 1984). The aurachins, a group of quinoline compounds from *Stigmatella aurantica*, also inhibit photosynthesis at the same two sites as stigmatellin.

Pyridazocidin: a cationic compound from soil *Streptomyces* species, causes rapid plant necrosis and chlorosis, much like that of bipyridinium herbicides like paraquat. Studies with isolated chloroplasts showed that its mode of action is exactly like bipyridiniums, diverting electrons from photosystem I to become reduced to a reactive radicle that subsequently generates superoxide radicle, resulting in a cascade of destructive oxidative processes. This is the only natural phytotoxin of which we are aware with this mode of action (Abbas & Duke, 1995).

J. Jasmonic Acid Analogues toxins

Jasmonic acid is a plant hormone derived from linolenic acid. It plays a major role in regulating growth and development, as well as responses to both abiotic and biotic stress. **Coronatine** is a jasmonate analog produced by *Pseudomonas coronafacience*. It usurps jasmonate-controlled signaling pathways, thereby deregulating many essential processes. The typical symptom of this toxin is chlorosis of developing tissues.

Cinnacidin: a product of the fungus *Nectria*sp. DA060097, has a similar mode of action to coronatine.

K. Toxins that impede Lipid Metabolism

A series of structurally related fungal metabolites specifically inhibit ceramide synthase (sphinganine-*N*-acyltransferase) in plants. These include several analogues of AAL toxin and fumonisin.

AAL toxins: are produced by *Alternaria alternata*tomato pathovars afumonisins are produced by *Fusarium* spp. AAL toxins were originally reported to be host specific, but they are phytotoxic to many plant species, as are their close structural analogues, the fumonisins. These compounds are analogues of the substrate for ceramide synthase, although australifunginis only a weak analog. When plant tissue is treated with these inhibitors, the sphingolipid precursors and precursor derivative levels are rapidly elevated to concentrations many fold more than found in untreated tissues. This precedes rapid loss of plasma membrane integrity. Kato *et al*., 1991, have sought to explain the action of this family of toxins by invoking induction of apoptosis (programmed cell death), but the effects are so rapid at even low doses, that this phenomenon seems unlikely to play a direct role except at very low doses. Treatment of plants with the sphingoid base precursors of ceramide synthase causes similar effects to those caused by the inhibitors of ceramide synthase (Schinko *et al*., 2009). They cause rapid, light-independent cellular leakage through dysfunction of the

plasma membrane. Sphingoid bases also cause generation of reactive oxygen species (ROS) in plant cells. Rapid formation of ROS in the plasma membrane can cause cell death unrelated to apoptosis, whereas slower formation can cause programmed cell death.

Thiolactomycin: is produced by unidentified species of *Norcardia*and *Streptomyces* and is an inhibitor of both plant and animal type II dissociated fatty acid synthetase. It is a very potent inhibitor of incorporation of acetate into fatty acids of chloroplasts.

Cerulenin: is a product of the fungus *Cephalosporium cerulens*, inhibits de novo fatty acid synthesis in plastids. Like thiolactomycin, it is an inhibitor of fatty acid synthetases, but it is not as active as an inhibitor (Strobel, et al., 1991)

The diphenyl ether compound cyperin, a metabolite of *Preussiafleischhakii*, *Phomasorghina*, and *Ascochytacypericola*, inhibits plant enoyl (acyl carrier protein) reductase (ENR), which is the target site of a syntheticdiphenyl ether called triclosan. Inhibition of ENR results in light-independent disruption of membrane integrity.

L Toxins that affect Membrane Function

Syringomycin: from *Pseudomonas syringae*, is one of the many cyclic lipodepsinonapeptide microbial phytotoxins. Structurally related compounds from the same organism with similar modes of action are syringotoxin and syringostatins. These compounds are large molecules that typically have a polar peptide head and a hydrophobic 3-hydroxy fatty acid tail (Conti *et.al.,* 2003). This hydrophobic tail of varying length (from C10 to C14) is bound to the *N*-terminal serine residue via an amide bond. The *macrocyclic*lactone ring is obtained via an ester linkage to the *C*-terminal 4-chlorothreonine. Syringomycin often contains uncommon amino acids such as 2,3-dehydroaminobutyric acid, 3-hydroxyaspartic acid, and 4-chlorothreonine, as well as serine D-isomers and 2,4-diaminobutyric acid. Structure-activity relationship studies reported that chlorination of the molecule is important for biological activity. Syringomycin induces rapid necrosis in plant tissues by forming pores that are freely permeable to cations (e.g., K+, H+, and Ca2+) within the plasma membrane. Nanomolar amounts of syringomycin are sufficient to induce loss of membrane integrity and cell death.

Beticolins: a yellow group of toxins from *Cercosporabeticola*, self assemble into multimeric ion channels that disrupt membrane function. T-toxins are host-specific, trichothecenephytotoxins from the fungi *Cochiobolusheterstrophus*, *Phyllosticamaydis*, and *Bipolarismaydis.* They inhibit mitochondrial respiration by binding an inner mitochondrial membrane protein in sensitive plants, resulting in pore formation, leakage of NAD+, and other ions, as well as subsequentmitrochondrial swelling (Duke,et.al.,2011).

Fusicoccin: a product of the fungus *Fusicoccum*(*Phomopsis*) *amygdali*irreversibly activates the plant plasma membrane H+-ATPase, leading to inability of stomata to close and subsequent lethal wilting.

Victorin C: a fungal product of *Cochiobolusvictoriae*, induces a collapse of the mitochondrial transmembrane potential, which results in a mitochondrial membrane transition. It also binds the P protein of the glycine decarboxylase complex of the mitochrondria. All of this has been associated with programmed cell death, but it may also act at the cell surface to cause a hypersensitive response via plasma membrane ion fluxes.

Colletotrichin: is a highly phytotoxic compound from several *Colletotrichum* species, e.g.,. Ultrastructurally, the first effect of this compound is disintegration of the plasma membrane, accompanied by massive cellular leakage. The effect is not light dependent and could not be reversed with antioxidants, suggesting that it has a direct effect on the plasma membrane (Abbas & Duke, 1995).

Nigericin: a *Streptomyces hygroscopicus*product is a phytotoxic postassiumionophore. Zinniol, a product of several *Alternaria*species and one *Phoma*species, binds plant protoplasts

and stimulates Ca++ entry into cells. It may act on a specific class of plant calcium channel. There are a number of other compounds produced by plant pathogens that are structurally related to zinniol, but their mode of action has not been determined (Mallik,2001).

T-2 toxin: is a trichothecene that, unlike the other trichothecenes that inhibit protein synthesis, also causes plant plasma membrane leakage of electrolytes at low concentrations.

Ophiobolins: a tricyclic sesquiterpenephytotoxins from certain species of *Bipolaris*and other fungal genera, cause many symptoms on plants that were considered to be largely due to effects on the plasma membrane (Williams et.al.,2009). It effects on maize root ion leakage correlate well with its direct antagonism of calmodulin. Its effects on calmodulin cause inhibition of transport of nuclear-coded proteins into both the mitochondrion and the plastid.

CONCLUSION

This brief coverage of Phytotoxins should provide an appreciation for the amazing breadth of microbial toxin structures and modes of action. The number of potential useable herbicide target sites has been a matter of concern among companies involved in herbicide discovery. Molecular methods to discover new target sites have not been particularly fruitful. There are only about twenty molecular sites targeted by the hundreds of commercial herbicide active ingredients, and the last major target site was introduced to the marketplace over twenty years ago. However, it is clear from the many target sites of microbial phytotoxins, that nature has discovered many ways to kill a plant. The growing evolution of weed resistance to existing commercial herbicides has generated a new sense of urgency to discover and develop herbicides with new modes of action. Many of the compounds mentioned in this review have been studied as potential templates for new herbicides with new modes of action. We expect that the growing need for new modes of action will generate a stronger interest in the use of microbial phytotoxins to discover new herbicide target sites.

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