

Review

Mycotoxins: Producing Fungi and Mechanisms of Phytotoxicity

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Academic Editor: Anna Andolfi

Received: 19 May 2015 / Accepted: 16 July 2015 / Published: 23 July 2015

Abstract: Mycotoxins are secondary fungal metabolites, toxic to humans, animals and plants. Among the hundreds of known mycotoxins, aflatoxins, citrinin, patulin, penicillic acid, tenuazonic acid, ochratoxin A, cytochalasins, deoxynivalenol, fumonisins, fusarin C, fusaric acid, and zearalenone are considered the types that most contaminate cereal grain. The majority of the mycotoxins in these groups are produced by three fungal genera: *Aspergillus*, *Penicillium* and *Fusarium*. These metabolites primarily affect the seed quality, germination, viability, seedling vigour, growth of root and cleoptile. Additionally, since the fungi responsible for the production of these mycotoxins are often endophytes that infect and colonize living plant tissues, accumulation of mycotoxins in the plant tissues may at times be associated with development of plant disease symptoms. The presence of mycotoxins, even in the absence of disease symptoms, may still have subtle biological effects on the physiology of plants. Several studies highlight the toxic effects of mycotoxins on animals and cell lines but little is known about the mode of action of most of these metabolites on plant cells. The most important mycotoxins with phytotoxic effects and their producers in addition to their discovery are briefly outlined below and will be addressed in this article.

Keywords: mycotoxins; producing fungi; phytotoxicity

1. Introduction

The term mycotoxin was first used in the 1960s to describe the toxin associated with contaminated peanuts in animal feed and the loss of turkeys in England (Turkey-X-disease). This mycotoxin was later identified as the *Aspergillus flavus* toxin aflatoxin B1. Bennett [1] defined mycotoxins as “natural products produced by fungi that evoke a toxic response when introduced in low concentrations to higher vertebrates and other animals by a natural route”. Mycotoxins are secondary metabolites, defined by Bennett and Bentley [2] as “metabolic intermediates or products, found as a differentiation product in restricted taxonomic groups, not essential to growth and life of the producing organism, and biosynthesized from one or more general metabolites by a wider variety of pathways than is available in general metabolism”. The term was later applied to other toxic fungal natural products [3].

Traditionally, toxigenic fungi contaminating agricultural grains have been conventionally divided into two groups those invade seed crops have been described as “field” fungi (e.g., *Cladosporium*, *Fusarium*, *Alternaria* spp.), which reputedly gain access to seeds during plant development, and “storage” fungi, (e.g., *Aspergillus*; *Penicillium* spp.), which proliferate during storage [4]. Currently, this division is not so strict because according to Miller [5] four types of toxigenic fungi can be distinguished: (1) Plant pathogens as *Fusarium graminearum* and *Alternaria alternata*; (2) Fungi that grow and produce mycotoxins on senescent or stressed plants, e.g., *F. moniliforme* and *Aspergillus flavus*; (3) Fungi that initially colonize the plant and increase the feedstock’s susceptibility to contamination after harvesting, e.g., *A. flavus*; (4) Fungi that are found on the soil or decaying plant material that occur on the developing kernels in the field and later proliferate in storage if conditions permit, e.g., *P. verrucosum* and *A. ochraceus*.

The involvement of *Aspergillus* spp. as plant pathogens has been reported and aflatoxin-infected crops have from time to time been returned to agricultural soils. This practice may prove hazardous, since both *A. flavus* and *A. parasiticus* can infect crops prior to harvesting [6]. The phytotoxic effects of the aflatoxins have been investigated, with respect to seed germination, and the inhibition of root and hypocotyl elongation [7,8]. Aflatoxin has been reported to occur within apparently healthy, intact seeds which suggest that the toxin can be transported from contaminated soil to the fruit [9]. Aflatoxin B1 (AFB1) can be translocated from the roots to the stems and leaves. If the soil microorganisms do not rapidly degrade the aflatoxin contained within the plowed under stover and grains, the possibility that the roots of the seedlings of the following year’s crop will both absorb and translocate the aflatoxins to both the stems and leaves exists [10]. This could be hazardous to the plant’s growth and development as well as to the consumer’s health.

The *Penicillium* genus dominated the fungal flora, with mycotoxigenic species such as *P. crustosum*, *P. chrysogenum*, *P. hirsutum*, *P. expansum*, *P. roqueforti*, *P. viridicatum*, *P. commune*, *P. aurantiogriseum*, *P. citrinum*, *P. verrucosum*, *P. cyclopium*, *P. canescens*, *P. madriti*, *P. palitans*, *P. thomii*, *P. baarnense*, *P. fennelliae*, *P. frequentans*. These fungi have been reported to produce a number of toxins as citrinin (CTN), cyclopiazonic acid (CPA), ochratoxin A (OTA), patulin (PAT), penicillic acid (PA), penitrem A (PNT), roquefortine (RQF), frequentin (FRE), palitantin (PAL), mycophenolic acid (MPA), viomellein (VIM), gliotoxin (GT), citreoviridin (CIV), rubratoxin B (RB) [11–17]. These fungal species and their mycotoxins contaminate harvested seeds causing losses of agricultural commodities in many zones of the world. Such contaminants are fearsome, since they affect the seeds

before harvest time and may find optimal developing conditions when the seeds are stored, leading to alteration of the germination quality of these seeds [18,19].

Alternaria, *Helminthosporium*, *Pyrenophora* (sexual state: *Drechslera*), *Phoma*, and *Zygosporium* are genera of saprobic and plant pathogenic dematiaceous fungi with a world wide distribution, commonly associated with leaves, wood, cereals and other grasses. The species of these fungal genera are known to produce some dangerous mycotoxins such as cytochalasins and tenuazonic acid (TA).

Members of the genus *Fusarium* produce a range of chemically different phytotoxic compounds, such as fusaric acid (FA), fumonisins (fumonisin B1, FB1), beauvericin (BEA), enniatin (ENN), moniliformin (MON) and trichothecenes. These possess a variety of biological activities and cause morphological, physiological and metabolic effects including necrosis, chlorosis, growth inhibition, wilting, inhibition of seed germination and effects on calli [20–23]. Table 1 summarizes the general classes of mycotoxins with their producing fungal genera/species and chemical groups. Some of these mycotoxins are phytotoxic and others are non-phytotoxic. Mycotoxins with phytotoxic properties will be addressed below on the basis of their producing species. This review provides insight into characterization and evaluation of mycotoxins as phytotoxins. For each of the diverse groups of mycotoxins, we will give examples indicating history and fungi production with a focus on their modes of action and phytotoxic effects on several morphological and biochemical processes.

Table 1. Summary of the mycotoxins mentioned in the text. For references please refer to the text. The genus of the first isolation/description/main relevance is given.

Name	Abbreviation	Species/Genus/Group	Chemical Group
citreoviridin	CIV	<i>Penicillium citreo-viride</i>	pyranone derivative
citrinin	CTN	<i>Penicillium</i> , <i>Monascus</i> , <i>Aspergillus terreus</i>	benzopyran compound
cyclopiazonic acid	CPA	<i>Penicillium</i> , <i>Aspergillus</i>	indole tetramic acid
frequentin	FRE	<i>P. frequentans</i>	carbocyclic compound
gliotoxin	GT	<i>A. fumigatus</i>	epipolythiodioxopiperazine
mycophenolic acid	MPA	<i>Penicillium</i>	meroterpenoid compound
ochratoxin A	OTA	<i>Aspergillus</i> , <i>Penicillium</i>	benzopyran compound
palitantin	PAL	<i>Penicillium</i>	cyclohexane derivative
patulin	PAT	<i>Penicillium</i> , <i>Aspergillus</i>	benzopyran compound
penicillic acid	PA	<i>Penicillium</i> , <i>Aspergillus</i>	isopropylidene tetronic acid
penitrem A	PNT	<i>Penicillium</i>	indole diterpene alkaloid
roquefortine	RQF	<i>Penicillium</i>	diketopiperazine compound
rubratoxin B	RB	<i>Penicillium rubrum</i>	alpha, beta unsaturated lactone
viomellein	VIM	<i>Penicillium</i>	benzopyran compound
3-acetyldeoxynivalenol	3-ADON	<i>Fusarium</i>	trichothecenes, sesquiterpenoid
4-deoxynivalenol	DON	<i>Fusarium</i>	trichothecenes, sesquiterpenoid
beauvericin	BEA	<i>Fusarium</i>	hexadepsipeptide compound
diacetoxyscirpeno	DAS	<i>Fusarium</i>	trichothecenes, sesquiterpenoid
enniatin	ENN	<i>Fusarium</i>	cyclic depsipeptide
fumonisins	e.g., FB1	<i>Fusarium</i>	monoterpenes

Table 1. Cont.

Name	Abbreviation	Species/Genus/Group	Chemical Group
fusaric acid	FA	<i>Fusarium</i>	picolinic acid derivative, carboxylic acid
HT-2 toxin	-	<i>Fusarium</i>	trichothecenes, sesquiterpenoid
moniliformin	MON	<i>Fusarium</i>	cyclobutane compound, dione
nivalenol	NIV	<i>Fusarium</i>	trichothecenes, sesquiterpenoid
T-2 toxin	-	<i>Fusarium</i>	trichothecenes, sesquiterpenoid
zearalenone/F-2 toxin	ZEA	<i>Fusarium</i>	estrogenic compound
aflatoxin	e.g., AFB1	<i>Aspergillus</i>	difuranocoumarin derivative
tenuazonic acid	TA	<i>Alternaria tenuis</i>	3-acetyltetramic acid
cytochalasin	e.g., CB	<i>Phoma</i>	polyketide-amino acid hybrid

2. Mycotoxins Produced by *Aspergillus* and *Penicillium* spp.

2.1. Aflatoxins

2.1.1. Historical Perspective

The discovery of aflatoxin has revolutionized research on molds and mold metabolites because of its potency as a toxin and carcinogen. The term “mycotoxin” has nearly become a household word, and aflatoxin has served as the model for research on and control of other mycotoxins that might otherwise have been unrecognized or neglected. In 1910, K uhl [24], a German pharmacologist, stated that Brazil nuts often were molded by *Aspergillus flavus*; the fungus was known to be toxic and probably made the nuts toxic. The discovery of aflatoxins began immediately after an outbreak, termed the Turkey-X-disease, appeared in England in the early months of 1960. In the course of a few months, deaths were reported of more than 100,000 young turkeys on poultry farms in England but deaths were also reported of thousands of ducklings and young pheasants on nearby farms [25]. Larger animals such as calves and pigs were also affected as well. Veterinarians and scientists of all kinds, pathologists, microbiologists, nutritionists, and chemists, were called on to seek a solution. All results of an intensive investigation were negative. None of about 50 different known chemical poisons they tested for could be found; no virus or bacterial infection and no new microorganism could be found. Eventually, the toxicity was traced to the feed, and more specifically to one ingredient in the feed, a peanut meal imported from Brazil [25]. Fortunately, a considerable quantity of this meal remained unused. During this time, the problem with turkeys in England was related to a similar problem with ducklings in Kenya. As a result, a test for the toxin was developed using ducklings which were particularly suitable for evaluation of toxicity based on death or the appearance of characteristic liver lesions [26,27].

The test was used to effectively monitor the extraction and concentration of the toxin by classical chemical procedures. The toxic extracts emitted a characteristic bright blue fluorescence when illuminated with ultraviolet light. Furthermore, the intensity of fluorescence, as estimated visually, generally afforded a convenient guide to the toxicity of the sample. This observation provided for the first time the basis for a routine chemical assay for the toxin [28]. About this time, in relation to the outbreak in Kenya, it was determined that the toxin is produced by the common mold *Aspergillus flavus*. So, the name aflatoxin was coined from *Aspergillus flavus* toxin [29]. By 1963, the structures of

some of aflatoxins were being elucidated, culminating with the publication by Asao *et al.* of the currently accepted configurations [30].

2.1.2. Producing Fungal Species

Aflatoxins are difuranocoumarin derivatives produced in a polyketide pathway by many strains of *Aspergillus flavus* and *A. parasiticus*, in particular, *A. flavus* which is a common contaminant in agriculture. Among 18 different types of aflatoxins produced by *A. flavus* strains, aflatoxin B1 (AFB1, Figure 1) is the most extremely toxic, mutagenic and carcinogenic type [31,32]. Thus, numerous studies have been conducted to determine the effects of various food additives, preservatives, chemicals and environmental conditions to inhibit growth and aflatoxin production effectively [33–38].

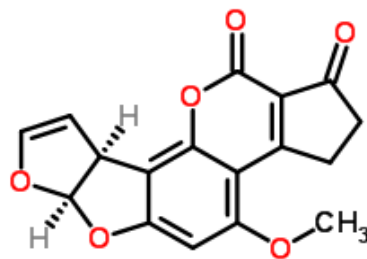


Figure 1. Chemical structure of Aflatoxin B1 (AFB1) (C₁₇H₁₂O₆), taken from ChemSpider [39], 162470.

2.1.3. Phytotoxicity

The phytotoxic effect of aflatoxin was observed on the basis of the remarkable inhibitory effect on chlorophyll and carotenoid synthesis and reduction of seed germination and seedling growth of lettuce [40], mung [41], mustard, gram [42], cowpea [43] and sesame [44]. Aflatoxin has been proposed to inhibit chlorophyll synthesis which results in the virescence or albinism in the affected plants [45]. The phytotoxic effects of AFB1 on *in vitro* cultures of regenerating plantlets of *Nicotiana tabacum* showed that root and leaf development, and root and leaf mass were significantly inhibited in a dose-dependent fashion with increasing AFB1 concentration above 0.5 µg·mL⁻¹, and root development was more seriously affected than leaf development [46]. The inhibition dose for 50% reduction (LD₅₀) in seedling viability was recorded by aflatoxins at 0.83 mg·L⁻¹ for barley, 1.74 mg·L⁻¹ for wheat and 2.75 mg·L⁻¹ for sorghum [47]. Aflatoxin at concentrations higher than 10 µg·mL⁻¹, induced the maximal reduction in the growth rate of hypocotyls after germination. This was discussed in relation to the effects of aflatoxin on DNA-dependent RNA biosynthesis [40]. Reduction in the number of tillers in plants treated with high concentrations of aflatoxin was also due to the accumulation of DNA damage in cells, which leads to apoptosis [48].

Electron microscopic studies also revealed the inhibition of grana formation in chloroplasts of maize leaves treated with aflatoxins [49]. At higher toxin concentrations, inhibition of root and shoot elongation was accompanied ultrastructurally by derangement of cytoplasmic constituents, dissolution of membranes, particularly the tonoplast, loss of ribosomes, organellar disruption and disappearance of

the endoplasmic reticulum. The increased inhibition of root and shoot extension as AFB1 concentration increased was suggested to be correlated with the increasing disruption of the organelles [8].

2.1.4. Mechanism of Action

Aflatoxin inhibition of chlorophyll *a*, chlorophyll *b* and protochlorophyllide biosynthesis in mung bean seeds (*Vigna radiata*) has been studied [41]. Suppression of protein and nucleic acid levels by aflatoxin has been also observed in germinating maize [50] and mung seeds [41]. Aflatoxin inhibits chromatin bound DNA-dependent polymerase activity. Inhibition of protein synthesis was attributed to the non-availability of m-RNA, whereas inhibition of DNA synthesis was due to the binding of aflatoxin to DNA during replication or due to the inhibition of DNA polymerase [50]. In tobacco plantlets (and also in *Zea mays* root tips), AFB1 has been immunolocated in the nucleus of stem cells [51]. Reduction in number of tillers in plants treated with aflatoxin may be due to the accumulation of DNA damage in cells, which leads to apoptosis [48]. Aflatoxin was reported to arrest cell cycle and induce apoptosis in cultured cells [48]. The apoptotic pathway is the only option for a cell when DNA repair systems are overburdened due to too many damages. Vogelstein and Kinzler [52] have shown that among its diverse functions, the p53 gene normally prevents DNA replication in cells that have DNA damage by maintaining the cell in G2/M phase allowing more opportunity for DNA repair. Cells with inactivated p53 might therefore survive abnormally and allow further DNA damage to accumulate [53], a situation, which favors carcinogenesis [54]. AFB1 exhibited genotoxic effect in wheat plants and several types of chromosomal aberrations have been detected during meiosis after application; these aberrations included chromosome stickiness, outside bivalents, bridges, laggards, unequal division and micronuclei [48].

2.2. Citrinin

2.2.1. Historical Perspective and Producing Fungal Species

Citrinin (CTN, Figure 2) is a benzopyran compound first isolated by Hetherington and Raistrick from a culture of *Penicillium citrinum* Thom [55]. Meanwhile, several other fungal species within the three genera, *Penicillium* (*P. expansum*, *P. verrucosum*), *Aspergillus* (*A. terreus*), and *Monascus* (*M. ruber*) were also found to produce this mycotoxin [56,57]. CTN contaminates maize [58], wheat, rye, barley, oats [59], and rice [60]. CTN has antibiotic properties against gram-positive bacteria, but it has never been used as a drug due to its high nephrotoxicity. The kidney is the major target organ of CTN toxicity, but other target organs such as liver and bone marrow have also been reported [61].

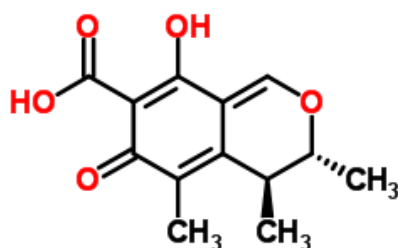


Figure 2. Chemical structure of citrinin (CTN) (C₁₃H₁₄O₅), taken from ChemSpider [39], 10222475.

2.2.2. Phytotoxicity

It was shown to be phytotoxic in several trials [62–65]. It was proved to have remarkable phytotoxic effects. Damodaran *et al.* [63] found that CTN exhibits a wilting effect on bean plants (*Dolichos lablab*, *Phaseolus vulgaris* and *Phaseolus mungo* Co-1), two types of cotton (*Gossypium arboreum* K6 and 0320-1) and sorghum (*Sorghum vulgare* Co-20). Maćias *et al.* [65] evaluated CTN ability to inhibit seed germination and seedling growth of *Amaranthus hypochondriacus* and *Echinochloa crusgalli*. These authors found that CTN reduced the radicle growth of both target species in a concentration-dependent manner recording IC_{50} of 5.5×10^{-5} M and 6.3×10^{-5} M, respectively.

2.2.3. Mechanism of Action

The data on the mechanism of its phytotoxicity are still controversial and most have been obtained *in vitro*. Damodaran *et al.* [63] interpreted CTN phytotoxicity on the basis of its ability to bind with the cellular components present along the vascular system, and possibly also in the leaves also, and thereby affecting the osmotic balance and translocation. Another interpretation suggests that CTN may affect respiration of germinating seeds and seedlings. The same explanation has been interpreted for alteration of mitochondrial function of the baby hamster kidney cells by CTN [66]. This was confirmed by electron microscopy studies that showed that CTN significantly affected normal mitochondria with swelling and cell death. Chagas *et al.* [67] have suggested that CTN decreases Ca^{2+} accumulation in the matrix by inhibiting its influx and increasing its efflux. In Japan, CTN is associated with yellow rice disease [3].

2.3. Patulin

2.3.1. Historical Perspective

Patulin (4-hydroxy-4H-furo[3,2-c] pyran-2(6H)-one) (PAT, Figure 3), was originally isolated by Chain *et al.* [68] and named as claviformin due to its isolation from *Penicillium claviforme*, later it was renamed PAT according to the PAT-producing mold, *Penicillium patulum* (later called *P. urticae*, now *P. griseofulvum*) that was isolated by Birkinshaw *et al.* [69]. Later, PAT was isolated under various names; clavicin, clavitin, expansin, gigantic acid, leucopin, mycoin, penicidin and tercinin [70–73]. The early findings that PAT had antibiotic activity led to its testing against the common cold in humans [74,75]. PAT was soon found almost useless in curing the common cold [76] and was too toxic for use as an antimicrobial agent. It causes several human health effects including convulsions, nausea, ulceration, lung congestion, epithelial cell degeneration, carcinogenic, genotoxic, immunotoxic, immunosuppressive, and teratogenic [75,77].

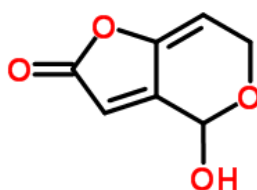


Figure 3. Chemical structure of patulin (PAT) ($C_7H_6O_4$), taken from ChemSpider [39], 4534.

2.3.2. Producing Fungal Species

Steiman *et al.* [78] found that PAT production is not a generic character, although *Aspergillus* and *Penicillium* are by far the most extensively represented. It has been isolated from *P. expansum* [79] (*P. leucopus* [80], *P. vulpinum* [17] (*P. claviforme* [68]), *P. griseofulvum* [79] (*P. patulum* [69]), *P. carneum*, *P. clavigerum*, *P. concentricum*, *P. coprobium*, *P. dipodomyicola*, *P. glandicola*, *P. gladioli*, *P. marinum*, *P. paneum*, *P. sclerotigenum* [81], *P. cyclopium* [82], *P. granulatum* (*P. divergens* [83]), *P. melinii*, *P. lapidosum* [82], *P. aurantiogriseum*, *P. canescens*, *P. chrysogenum*, *P. roqueforti*, *P. variable* [78], *P. purpurogenum* [84], *Aspergillus clavatus*, *A. giganteus*, *A. longivesica* [85], *A. terreus* [86], *Byssoschlamys fulva*, *B. nivea* and *Paecilomyces saturatus* [87,88]. PAT has been detected in apples and apple products, and occasionally in other fruits such as pears, apricots, peaches and grapes [77]. It has also become a quality indicator of fruit used for the production of apple juice concentrates [89]. It is mainly produced in rotten parts of the fruits after infestation with PAT-producing fungus that can occur at 0 °C during storage or develops rapidly when fruits are returned to room temperature [90]. PAT also appears to increase after storage when fruits remain at room temperature (20 °C) for short periods of time, a common procedure in fruit processing industries [91]. Apples are considered as an important source of PAT since they are easily infected by *Penicillium expansum* and also display optimum factors for PAT production [92]. The European Union has recommended levels of PAT for fruit juices and their products 50 µg·kg⁻¹; for solid apple products including apple compote, apple puree 25 µg·kg⁻¹, and 10 µg·kg⁻¹ for products intended for infants [93].

2.3.3. Phytotoxicity

The phytotoxicity of PAT has been studied by several investigators. PAT has been isolated from soils where phytotoxicity was observed [94,95]. The toxic effect has been observed on germinating seeds, young seedlings, isolated plant tissue of wheat and maize and plants which had continuous applications of PAT until maturity. Inhibition of plant elongation phases due to PAT effect accompanied with reduction in seed number, seed weight, number of flowers and gain in biomass was observed when PAT in aqueous solution was applied to these cultivated plants [17,96].

2.3.4. Mechanism of Action

The phytotoxic action of PAT may take place in several ways. The inhibition of protein, RNA and DNA synthesis occurs after intoxication of cell cultures, indicating a primary effect. The genotoxic effects might be related to its ability to react with sulfhydryl groups and induce oxidative damage [97]. Respiration seems to be inhibited by PAT at concentrations below toxic levels. Immediate respiratory inhibition in both germinating apple pollen and soybean suspension cultures by PAT was observed [98], but the effects on respiration are probably secondary. In a recent study [17], the mechanism of PAT phytotoxic action through its effect on the endogenous glutathione (GSH) concentration of maize seedlings was reported. Due to its electrophilic character, PAT has been reported to react *in vitro* with cellular nucleophiles such as proteins and GSH [17,99]. Various enzymes were inhibited by PAT, among them enzymes containing thiol groups, and alcohol and lactic dehydrogenases and muscle aldolase [100,101].

2.4. Penicillic Acid

2.4.1. Historical Perspective and Tautomeric Formulae

The mycotoxin penicillic acid (3-methoxy-5-methyl-4-oxo-2,5-hexadienoic acid) (PA) a secondary metabolite of *Penicillium puberulum* Bainier, was first isolated and named during the investigation of the possible connection between the incidence of pellagra and mold deterioration of maize [102]. These investigators showed that when *P. puberulum* was grown on corn-meal mush or on Raulin's medium, appreciable quantities of PA were formed. They described the general properties of PA, but did not determine its molecular constitution. In 1935, Oxford and Raistrick [103] found that cultures of *Penicillium cyclopium* Westling produced relatively large amounts of PA and this finding enabled Birkinshaw *et al.* [104] to prepare sufficient PA for a successful determination of its molecular constitution by analytical methods. In order to avoid confusion, it should be remembered that so far as is known at present, there is no relationship between PA and Fleming's penicillin, except the purely fortuitous choice of names for these two substances by their respective discoverers [105]. The properties and behavior of PA are adequately expressed (Figure 4) by the tautomeric formulae (I and II). The structural formula II may be rewritten as structure III, from which it appears that PA may be regarded as the β -methyl ether of γ -hydroxy- γ -isopropylidene tetronic acid. The biochemical importance of the tetronic acid structure has been discussed by Bentley and Keil [106]. They reported experiments designed to study the biosynthesis of PA (I). Their study was particularly interesting in view of the presence of an isopropylidene side chain in PA, a group occurring only infrequently in natural products. In aqueous solution, it exists completely in the pseudo acid form (cyclic form, II), whereas in alkali, the ionic form must be largely derived from the open structure (linear form, I) [18,107]. Its hazardous effects, carcinogenic nature and antibiotic activity made it a cause of concern [108–111].

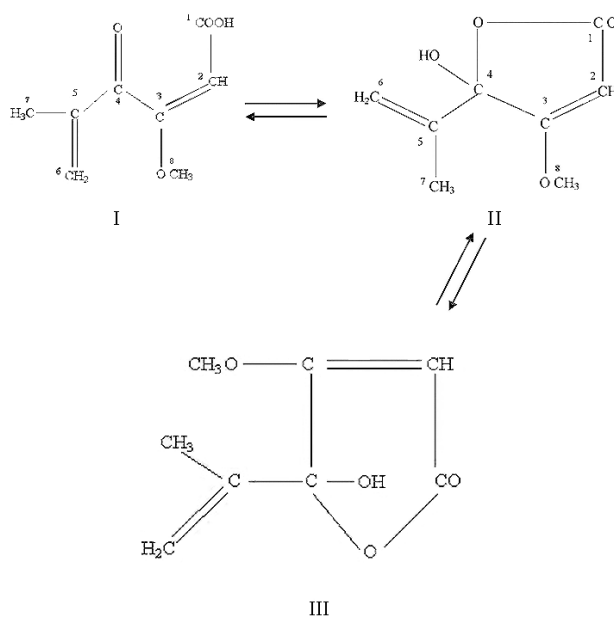


Figure 4. Structure of penicillic acid (PA) (C₈H₁₀O₄) showing tautomeric equilibrium with its lactone in aqueous solution, taken from [112].

2.4.2. Producing Fungal Species

Many fungi have been reported to be producers of PA, including the genus *Penicillium* and *Aspergillus* [113,114]. PA had been isolated from the following *Penicillium* species: *P. viridicatum* [115], *P. verrucosum* [116], *P. aurantiovirens* [117], *P. aurantiogriseum* [14], *P. tricolor* [117], *P. hirsutum* [11,110], *P. thomii* [118], *P. cyclopium* [86], *P. roqueforti* [13], *P. martensii*, *P. fenelliae*, *P. madriti*, *P. stoloniferum* [119], *P. canescens* [18], *P. melanocladium*, *P. frei*, *P. polonicum*, *P. radicum*, *P. tupliae*, *P. corneum* [14] and *P. frequentans* [16]. Different *Eupenicillium* species such as *E. bovis*, *E. baarnese* were also found to produce PA [120,121]. PA had been also produced by *Aspergillus* species such as: *A. ochraceus* [122], *A. auricomus*, *A. melleus* [119], *A. alliaceus* [123], *A. ostianus* [124], *A. cervinus*, *A. wentii* [109] and *A. sclerotiorum* [114]. The large number of strains capable of elaborating the mycotoxin PA indicates the ubiquity of penicillic acid-producing organisms in nature and the possibility for presence of this mycotoxin in stored high-moisture grains [119].

2.4.3. Phytotoxicity

The phytotoxicity of PA was discussed by its ability to lessen the seedlings respiration [125]. It was also reported to inhibit urease [126] and RNase [127] activity. Moreover, the toxic effects of PA have been considered to be caused by its reaction with enzymes and it has been shown to react with several amino acids to form less toxic products [128]. PA was reported to inhibit the growth of young plant roots of rice [129], *Amaranthus hypochondriacus* [130], corn [18], broad bean and pea [112]. PA was found to affect the overall turnover of the metabolites in *Zea mays* [131]. The phytotoxicity of PA was about 5% that of AFB1 [18]. Browning of *Picea glehnii* roots and collapse in the root structure of lettuce were the main anatomical changes induced by PA on seedlings [16].

2.4.4. Mechanism of Action

The fact that PA is readily inactivated by thiols [128] has led to the hypothesis that the mode of action of this mycotoxin is due to its interaction with the SH-residues in enzymes. It has been found that the PA inhibits alcohol dehydrogenase and lactic dehydrogenase which are thiol enzymes [100,132]. PA was found to occur in high quantities (up to 2% dry weight) in infected corn [133] that it must be considered seriously. The seriousness of PA as phytotoxin was reported to increase due to its accumulation at the low temperatures [18,134] of typical storage conditions.

2.5. Ochratoxin

2.5.1. Historical Perspective and Producing Fungal Species

Ochratoxin A (L-phenylalanine-*N*-[(5-chloro-3,4-dihydro-8-hydroxy-3-methyl-1-oxo-1*H*-2-benzopyran-7-yl)carbonyl]-(*R*)-isocoumarin) (Figure 5, OTA) is a mycotoxin that was discovered to be a metabolite of *Aspergillus ochraceus* in 1965 during a large screen of fungal metabolites designed specifically to identify new mycotoxins [135]. Subsequent studies revealed that a variety of mold fungus species, including *Aspergillus carbonarius* [136], *A. niger* [137] and *Penicillium verrucosum* [138]

were able to produce ochratoxins. Recently, *A. westerdijkiae* and *A. steynii*, two new species from the *Aspergillus* section *Circumdati* have been split from *A. ochraceus* and reported to be stronger OTA producers than *A. ochraceus* [139]. *Penicillium nordicum* and *P. verrucosum* are known to produce OTA, and have been frequently isolated from cereal crops, meat products and cheese varieties [140,141]. Because of its widespread occurrence on a large variety of agricultural commodities and the potential health risks, mainly toward humans, OTA has been classified as a possible human carcinogen (group 2B) by the International Agency for Research on Cancer [142]. Given the known human exposure and the abundance of toxicological data from animal studies, the European Union Scientific Committee has recommended the OTA levels below to $5 \text{ ng}\cdot\text{kg}^{-1}$ of body weight per day [143]. In the European Union, some regulatory limits have already been introduced for the levels of OTA in food products such as raw cereal grains ($5 \text{ }\mu\text{g}\cdot\text{kg}^{-1}$), products derived from cereals ($3 \text{ }\mu\text{g}\cdot\text{kg}^{-1}$), dried fruits ($10 \text{ }\mu\text{g}\cdot\text{kg}^{-1}$), roasted coffee and coffee products ($5 \text{ }\mu\text{g}\cdot\text{kg}^{-1}$), grape juice ($2 \text{ }\mu\text{g}\cdot\text{kg}^{-1}$) (EC No 123/2005) and also for all types of wine ($2 \text{ }\mu\text{g}\cdot\text{kg}^{-1}$) (amended Regulation EC No. 466/2001).

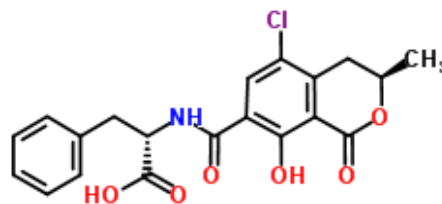


Figure 5. Chemical structure of ochratoxin A (OTA) ($\text{C}_{20}\text{H}_{18}\text{ClNO}_6$), taken from ChemSpider [39], 390954.

2.5.2. Phytotoxicity

Recent studies have suggested that OTA induces cell death in plants [144]. OTA exposure can cause significant inhibition in the growth of plants on media and induce necrotic lesions in detached leaves of *Arabidopsis thaliana*. Moreover, preferential inhibition of root growth by OTA of seedlings was observed [145]. When OTA solutions (2 mM, 1 mM, or control) were infiltrated into leaves of 4-week-old *A. thaliana* plants grown in soil, macroscopic lesions formed on the infiltrated leaves within 1–2 days [144]. In the presence of OTA, the growth of *A. thaliana* on media was significantly inhibited; in addition, cell death was observed with features resembling the hypersensitive response-type lesions in excised leaves that were infiltrated with this toxin. There was also evidence that cell death was induced by OTA, such as the occurrence of an oxidative burst and the deposition of callose and phenolic compounds (autofluorescence) [145]. McLean [146] investigated the effect of OTA on germinating *Zea mays* embryos. He found that the measured effects on root and shoot growth at $10 \text{ }\mu\text{g}\cdot\text{mL}^{-1}$ and $25 \text{ }\mu\text{g}\cdot\text{mL}^{-1}$ were stimulatory, while at $5 \text{ }\mu\text{g}\cdot\text{mL}^{-1}$ OTA, an inhibitory effect was observed.

2.5.3. Mechanism of Action

Several major mechanisms have been shown to be involved in the toxicity of OTA: inhibition of protein synthesis, interference with metabolic systems involving phenylalanine, promotion of membrane lipid peroxidation, disruption of calcium homeostasis, inhibition of mitochondrial

respiration, and DNA damage [147]. Wang *et al.* [144] investigated the possible mechanisms of OTA phytotoxicity on *A. thaliana* and analyzed after application of OTA gene and protein expression. The authors summarized OTA phytotoxicity, as follows: First, exposure of excised *A. thaliana* leaves to OTA rapidly causes the hypersensitive response, significantly accelerates the increase of reactive oxygen species (ROS) and malondialdehyde, and enhances antioxidant enzyme defense responses and xenobiotic detoxification. Secondly, OTA stimulation causes dynamic changes in the expression of transcription factors and activates the membrane transport system dramatically. Thirdly, a concomitant persistence of compromised photosynthesis and photorespiration is indicative of a metabolic shift from a highly active to a weak state. Finally, the data revealed that ethylene, salicylic acid, jasmonic acid, and mitogen-activated protein kinase signalling molecules mediate the process of toxicity caused by OTA. Wang *et al.* [148] studied the changes in biosynthesis and metabolism of GSH upon OTA stress in *A. thaliana* and found accumulation of GSH in the detached leaves of *A. thaliana* under OTA treatment. The authors revealed that OTA stimulated a defense response through enhancing glutathione-S-transferase, glutathione peroxidase, glutathione reductase activities, and the transcript levels of these enzymes were increased to maintain the total glutathione content. Moreover, the level of oxidized glutathione (GSSG) was increased and the ascorbate-glutathione cycle fluctuated in response to OTA.

3. Mycotoxins Produced by Dematiaceous Hyphomycetes

3.1. Tenuazonic Acid

3.1.1. Historical Perspective and Tautomeric Formulae

The tetramic acid derivative L-tenuazonic acid [(5S,8S)-3-acetyl-5-sec-butyl-pyrrolidine-2,4-dione] (TA) was first isolated by Rosett *et al.* [149], from *Alternaria tenuis*, a dematiaceous plant pathogen invading a series of plants involved in the postharvest decay of fruits, grains and vegetables. Its structure was established by Stickings [150] and later investigated by Wessels and co-workers [151] applying NMR spectroscopy and X-ray crystallography, also describing different tautomers of this 3-acetyltetramic acid. Nevertheless it was not possible to distinguish between different tautomers equilibrating fast on NMR scale and therefore the structure of TA is still not clear, especially in aqueous solution. Varying structures of TA are still widely used in the literature, resulting in different CAS registry numbers. Figure 6 shows the TA structures and tautomerism of 3-acetyltetramic acids which may lead to wrong structural information for further research. For a better understanding of the structure of TA, the tautomerism as well as important equilibria (fast and slow), all reasonable tautomers and rotamers of TA have been subjected to quantum chemical calculations at an adequate level of theory. NMR spectra were calculated and compared to experimental data, finally leading to a synergetic computational and spectroscopic approach for structural investigations of TA and 3-acetyltetramic acids in general [152]. Its biological activity was first described by Shigeura and Gordon [153]. Later, it was isolated from *Magnaporthe grisea* (the blast fungus, former name is *Pyricularia oryzae*) as a phytotoxin [154] and from *Alternaria longiceps*, *A. kikuchiana*, *A. mali*, *A. alternata*, *A. tenuissima* and *Phoma sorghina* as a mycotoxin [155–159]. Additionally, TA has been

made responsible for the outbreak of “onyalai” a human hematologic disorder disease occurring in Africa after consumption of sorghum [159].

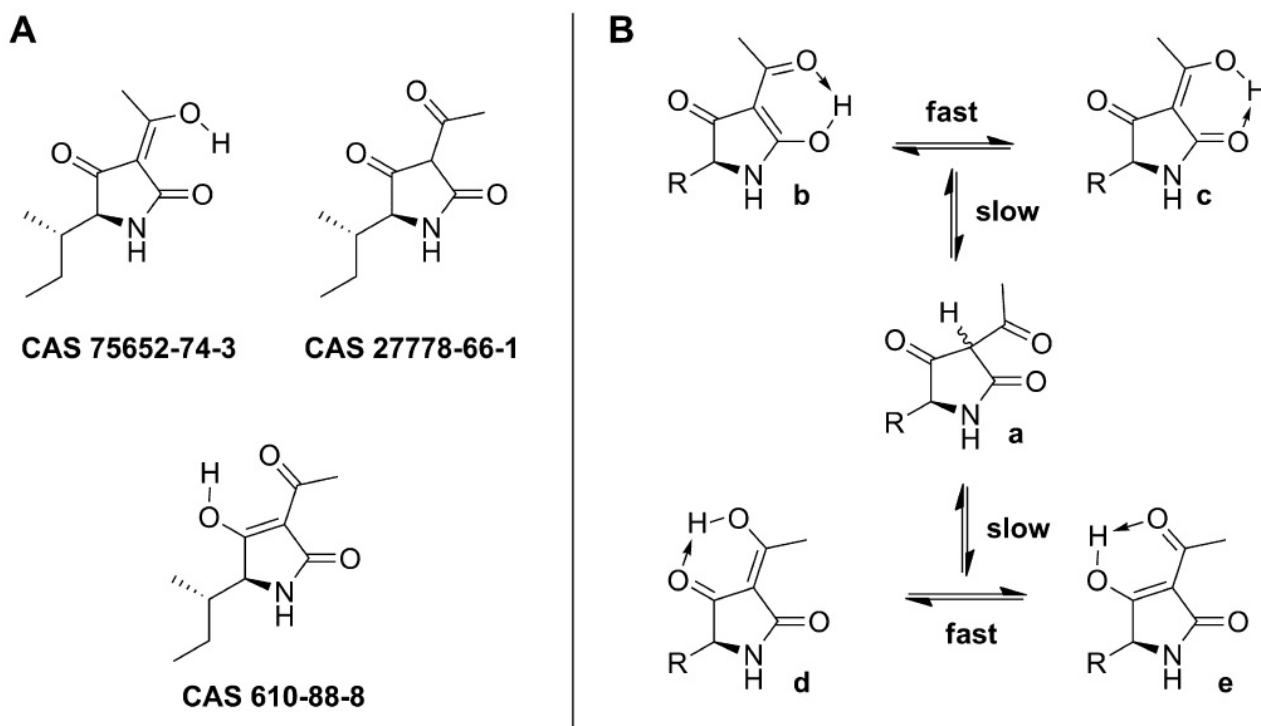


Figure 6. (A) Different structures of tenuazonic acid (TA) taken from [152] and (B) tautomerism of 3-acetyltetramic acids, taken from [152].

3.1.2. Phytotoxicity

TA exhibited significant phytotoxic effects on monocotyledonous and dicotyledonous plants and thus is a non-specific phytotoxin [160]. The relationships between the structures and the phytotoxicity of TA were assessed by Lebrun *et al.* [161]. These authors further showed that TA also induces a leaf necrosis on all rice varieties as well as the browning of the edges of dead areas on reactive varieties. Janardhanan and Husain [160] found that TA produced localized chlorotic spots in *Datura innoxia* which enlarged, turned to necrotic after 24 h of 200 $\mu\text{g}\cdot\text{mL}^{-1}$ TA application. Similar phytotoxic effects on leaves of *D. metel*, *D. stramonium*, belladonna, cowpea, wheat, rye and maize were observed at the same concentration of TA. The authors further indicated that TA inhibited growth of germinating seeds of *D. innoxia*, wheat, rye, lettuce and green gram at 100 $\mu\text{g}\cdot\text{mL}^{-1}$. TA was found to induce small brown necrotic spots on leaves and may also favor ROS production in *planta* [154].

3.1.3. Mechanism of Action

The inhibition of plant cells growth by TA is thought to be caused by the inhibition of protein synthesis [153,157] at the ribosome level [162]. It has been shown that TA has a ribosome binding site as it inhibits the binding of radioactive protein synthesis inhibitors (anisomycine and trichodermin) on the ribosome [163,164]. It was also reported that TA forms complexes with ions, including iron or copper [161]. TA showed no appreciable change in the rate of respiration of leaves, and the toxin

treatment had no significant effect on total sugar and phenol contents, however a reduction in chlorophyll and protein content of leaves was noticed [160]. Findings of Park [165] on the ultrastructure of parenchyma cells of Japanese pear leaves treated with TA supported the toxic effect of TA on the basis of degeneration of chloroplast and endoplasmic reticulum in leaf tissue near the treated area with toxin.

3.2. Cytochalasins

3.2.1. Historical Perspective and Producing Fungal Species

The metabolites isolated from a *Phoma* species have been called phomins. Those from *Zygosporium masonii* Huges were named zygosporins. The metabolites from *Helminthosporium* species were described as cytochalasins (cytos: cell; chalasis: relaxation). The three groups proposed a systemic nomenclature based on the generic name cytochalasan for the cytochalasins, phomins and zygosporins [166]. Phomin (phomine, cytochalasin B, CB), the first cytochalasin reported, was described in 1966 as a macrolide antibiotic with cytostatic activity produced by a *Phoma* species [167]. Later, in a more detailed investigation of the *Phoma* metabolites, a closely related compound with similar activity, dehydrophomin (cytochalasin A, CA), was isolated [168]. In 1967, Aldridge *et al.* [169] isolated CA and CB from *Helminthosporium dematioideum* (*Drechslera dematioidea*) and CD and CD from *Metarhizium anisopliae* (Metsch.) Sorok. Earlier, a French patent reported that CA and CB produced by *H. dematioideum* (*D. dematioidea*) contained nitrogen. These compounds are intraconvertible by oxidation-reduction reactions and had the empirical formulas of $C_{29}H_{35}NO_5$ and $C_{29}H_{37}NO_5$.

Cytochalasins are a group of polyketide-amino acid hybrid compounds belong to the cytochalasan family of fungal secondary metabolites, which have significant commercial and research values due to their diverse arrays of biological activities and complex molecular structures. Over 80 different cytochalasans have been isolated from a number of the fungal genera, including *Aspergillus*, *Phomopsis*, *Penicillium*, *Zygosporium*, *Chaetomium*, *Rosellinia*, *Metarhizium*, *etc.* [170]. Of these, CB (Figure 7) is the most widely studied and has been extensively used for cytological investigations [171–175]. It has been previously extracted from various phytopathogenic fungi such as *D. dematioidea* [169], *Helminthosporium solani* [176] and *Phoma exigua* strain 298, *P. exigua* var. *exigua* on potatoes [177], *Aschochyta heteromorpha* on chickpea [178] and from *Drechslera wirreganensis* and *D. campanulata* on cereal [179].

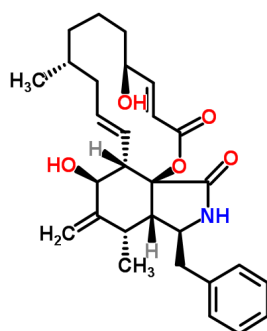


Figure 7. Chemical structure of cytochalasin B (CB) ($C_{29}H_{37}NO_5$), taken from ChemSpider [39], 4895549.

3.2.2. Phytotoxicity and Mechanism of Action

Carlier *et al.* [180] showed the mechanism of cell toxicity by cytochalasin, as follows: Cytoskeleton → disruption of endocytosis → cell deregulation → cell death. CB inhibited exudation in maize roots [181] and reduced fiber production of cotton ovules [182]. It significantly inhibited flax radical growth [183], stomatal movement in *Vicia faba* L. [184] and pollen tube growth in *Luffa cylindrica* (*L. aegyptiaca*) Mill. [185]. Kadota and Wada [186] found that the treatment of the tip growing protonemal cell of the fern *Adiantum* spp. with CB caused disruption of the microfilament strands, cessation of tip growth and stopping of nuclear movement. Treatment of the *Fasciola hepatica* spermatogenic cells with CB caused formation of bi- and multi-nucleated cells [187]. Tamagnini *et al.* [188] reported that treatment of *Pisum sativum* L. with CB decreased the respiration rate. They also observed that treated cotyledonary axis and cotyledons had higher contents of starch, soluble sugars and proteins but the phosphatase activity became lower than control. CB decreased the total respiratory rate in leaves of winter wheat cv. *Mironovskaya* 808 [189]. Cytochalasin was reported to have a morphogenetic effect on *Allium cepa* L. roots by producing a reversible inhibition of mitosis and axis elongation [176,190–192].

CA blocked the accumulation of phytoalexin and phenylalanine ammonia-lyase in pea tissues [193]. CD altered the actinomycin system of the onion epidermal cells, disintegrated the actin filaments and caused formation of large flat-sheet-like cytoplasmic reticulum sacs in the epidermal cells of onion [194]. Treatment of the microspores of *Brassica napus* L. cv. Topas with CD resulted in dislocated mitotic spindles, disrupted phragmoplasts, symmetric divisions and finally embryogenesis [195]. Traas *et al.* [196] found that CB and CD affected the organization of spindle microtubules, during meiosis in eggplant (*Solanum melongena* L.).

CE was found to be a phytotoxic metabolite to apple and lettuce plants [197,198]. It also inhibited seed germination of *Striga hermonthica* Lour. [199] and showed a direct effect on photosynthesis of young leaves of *Malus domestica* Borkh. (*Malus pumila*) as detected by chlorophyll fluorescence [200].

Pyrenophora semeniperda (a naturally occurring ascomycete seed pathogen) was reported to produce phytotoxins belonging to a different class of natural compounds when grown in solid culture on wheat seeds. This fungal species produced a large amount of the phytotoxic CB, as well as CA, CF, deoxaphomin, and the three novel cytochalasins, Z1, Z2, and Z3 [201]. Masi *et al.* [202] found that *P. semeniperda* was also able to produce phytotoxic sesquiterpenoid penta-2,4-dienoic acid, named pyrenophoric acid which showed strong phytotoxicity on cheatgrass, reducing coleoptile length relative to the control by approximately half at 10^{-3} M and by 23% at 10^{-4} M. CB at 10^{-4} M reduced coleoptile elongation 15%, and the combination of pyrenophoric acid and CB at 10^{-4} M reduced coleoptile elongation 36% relative to the control. The authors indicated that these two compounds exhibited an additive rather than a synergistic toxicity effect, as the combined effect was essentially the sum of the effects of the two compounds applied singly. The phytotoxicity of pyrenophoric acid helped them to explain why organic extract phytotoxicity was not correlated with CB concentration in their earlier study [203]. Pyrichalasin H (is another type of cytochalasins family), isolated from a *Digitaria* isolate (IFO 7287) of the blast fungus, inhibited the growth of rice seed and induced characteristic curling of the shoot at $1 \mu\text{g}\cdot\text{mL}^{-1}$, but did not induce any visible symptoms on the rice leaf [204]. Zygosporin D and two new cytochalasins were isolated from *Metarhizium anisopliae*. Of these cytochalasins, only zygosporin D was an effective inhibitor of shoot elongation of rice seedlings [205].

4. Mycotoxins Produced by *Fusarium* and Other Species

4.1. Trichothecenes

4.1.1. Historical Perspective and Producing Fungal Species

Trichothecenes belong to a major class of mycotoxins produced by a range of fungi from the order Hypocreales, including those of the genera *Fusarium*, *Myrothecium*, *Verticimonosporium*, *Stachybotrys*, *Trichoderma*, *Trichothecium*, *Cephalosporium*, and *Cylindrocarpon* [170,206–209]. More than 120 trichothecenes are known. These compounds have been isolated in the past thirty years. The first trichothecene to be isolated was trichothecin from *Trichothecium roseum*, in 1948 by Freeman and Morrison [210]. Diacetoxyscirpenol (DAS) from *Fusarium equiseti* was preliminarily characterized in 1961 by Brian *et al.* [211], and was later followed by nivalenol (NIV) [212] and T-2 toxin [213], both from *F. sporotrichioides*, although they were mis-identified as *F. nivale* and *F. tricinctum*, respectively, in the original articles [214]. However, it was the discovery of 4-deoxynivalenol (DON) from wheat in Eastern North America in 1980 [215], which truly sparked the research into the *Fusarium* species and led to the discovery of trichothecenes from other genera.

Trichothecenes are a large group of sesquiterpenoid fungal metabolites, which share a common core comprised of a rigid tetracyclic ring system (Figure 8) consisting of a cyclohexene, A-ring with a double C-C bond occurring between C-9 and C-10; a tetrahydropyranyl B-ring; a cyclopentyl C-ring, and an epoxide at C-12/13. The rigidity of this system results in a distinct stereochemistry for the A- and B-rings. The A-ring adopts a half-chair conformation, and the B-ring is most often found in the chair conformation (Figure 9a) [216,217], although there have been a few odd cases where the B-ring has been shown to adopt a boat conformation (Figure 9b) [218]. Shank *et al.* [219] reviewed the types of trichothecenes and showed that they fall into two main classes, simple and macrocyclic [170,220,221]. The simple trichothecenes are further divided into three types; A, B and C. Type A trichothecenes are the simplest group, being non-substituted, hydroxylated or esterified (Figure 10). Type B trichothecenes are characterized by a ketone present at C-8 (Figure 10) Type A and B trichothecenes, such as T-2 toxin and DON, respectively, are often associated with *Fusarium*-infected grain. Type C trichothecenes, such as crotocin [222], are less common than the others, and are distinguished by the presence of a second epoxide ring at C-7/8 (Figure 10). A fourth class (Type D), are characterized by the presence of a cyclic diester or triester linkage of C-4 to C-15 (Figure 10) (30). These macrocyclic trichothecenes include the satratoxins, verrucarins, roridins, myrotoxins and baccharinoids. While many of the Type D trichothecenes have been isolated from fungi, the baccharinoids were first isolated from the plant *Baccharis* spp. [223]. Although early reports suggested that the metabolites were produced by the plant itself, later studies indicated that the toxins were likely the product of a *Hypocrealean* endophyte (the order to which trichothecene-producing fungi such as *Fusarium*, *Myrothecium* and *Stachybotrys* belong) within the plants [224].

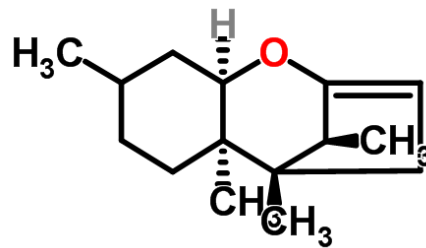


Figure 8. Chemical structure of the trichothecene core, taken from ChemSpider [39], 20004967.

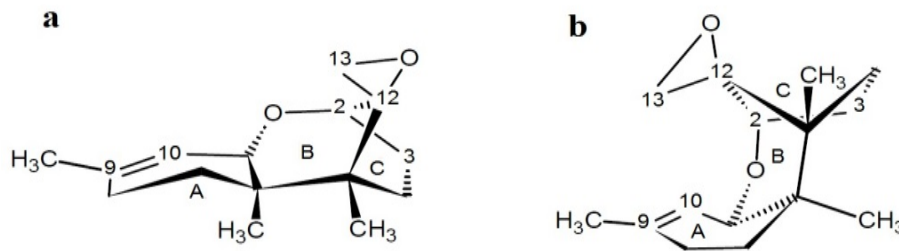


Figure 9. Three-dimensional stereochemistry of the trichothecene core when (a) the A-ring is in a half-chair, and the B-ring in a chair conformation; and (b) the A-ring is a half-chair, and the B-ring in a boat conformation, taken from Shank *et al.* [219].

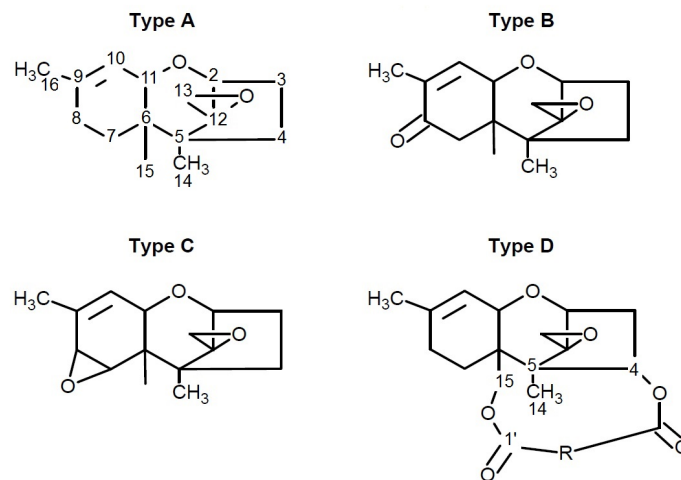


Figure 10. The general core structures for Type A, B, C, and D trichothecenes, taken from [219].

4.1.2. Phytotoxicity and Mechanism of Action

In plants, trichothecenes produced by *Fusarium* spp. cause necrosis, chlorosis, and mortality enabling them to mediate a wide variety of plant diseases, including wilts, stalk rot, root rot and leaf rot in many important crop and ornamental plants [225–230]. Examples include kudzu [231], Orobanche [232], duckweed [233], and many grain crops [234,235]. The phytotoxicity of some examples of trichothecenes can be characterized, as follows:

4.1.3. Deoxynivalenol (Vomitoxin) (DON) and Nivalenol (NIV)

DON (3,7,15-trihydroxy-12-13-epoxytrichothec-9-en-8-one; *F. graminearum*; *F. culmorum*) and NIV (3 α ,4 β ,7 α , 15-tetrahydroxy-12,13-epoxytrichothec-9-en-8-one; *F. graminearum*; *F. sporotrichioides*; *F. crookwellense*) [22,217,236] play a role as virulence factors in disease development [237,238]. Wakulinski [239], using seedlings of three wheat varieties to assess the phytotoxic effects of six *Fusarium* metabolites, found DON and 3-acetyldeoxynivalenol (3-ADON) to be the most inhibitory to germination and root development generally appeared to be the most sensitive to the metabolites. The phytotoxic effects of DON and 3-ADON were observed at 10 to 100-fold lower concentrations than those observed for ZEA, T-2 toxin and diacetyloxyscirpenol (DAS). Rocha *et al.* [240] summarized the phytotoxic effects of DON as growth retardation, inhibition of seedling and green plant regeneration. Shimada and Otani [241] measured similar inhibitory effects of DON on root development in seven varieties of wheat seedlings. A concentration of approximately 10 $\mu\text{g}\cdot\text{mL}^{-1}$ DON resulted in a 50% inhibition of shoot growth, while for roots, this value was five-fold lower (approximately 2 $\mu\text{g}\cdot\text{mL}^{-1}$) [241]. NIV was less phytotoxic: 100 $\mu\text{g}\cdot\text{mL}^{-1}$ and 48 $\mu\text{g}\cdot\text{mL}^{-1}$ caused a 50% inhibition of shoot and root growth, respectively [241]. DON was shown to be more phytotoxic to corn genotypes susceptible to gibberella ear rot than resistant genotypes [242]. Bottalico *et al.* [243] have reported DON to be more inhibitory of root growth than of shoot/leaf growth in tomato seedlings. In wheat seeds, 50 $\mu\text{g}\cdot\text{mL}^{-1}$ DON completely inhibited germination, while 10–25 $\mu\text{g}\cdot\text{mL}^{-1}$ significantly reduced plantlet growth [244].

The DON toxin caused greater damage to the membranes of the susceptible genotypes, as evidenced by the release of Na and K ions into solution [242]. DON concentrations above and including 50 ppm resulted in virtual suppression of calli regeneration (calli forming shoots) of three wheat genotypes, while 100 ppm DON was lethal to most calli [245]. Packa [246] found a decrease in the mitotic index of roots from germinated caryopses of rye, wheat, triticale and field bean treated with 10 $\mu\text{g}\cdot\text{mL}^{-1}$ a DON for 24 h. Inhibitory effects on mitosis were observed primarily in wheat and field bean. Chromosome and nuclear abnormalities included spirals of metaphase chromosomes and numerous ana- and telophase bridges [246]. In dividing root tip cells of onion, DON resulted in a decline in the mitotic index and relative division rate [247]. A toxin dose of 2.5 ppm reduced the relative division rate to 78% that of controls. DON (10 $\mu\text{g}\cdot\text{mL}^{-1}$ and 25 $\mu\text{g}\cdot\text{mL}^{-1}$) significantly inhibited both primary root and shoot elongation of excised, germinating *Zea mays* embryos following 9 days of toxin exposure. Seedling root mass was 43.5% and 45.6% of the control value for 10 $\mu\text{g}\cdot\text{mL}^{-1}$ and 25 $\mu\text{g}\cdot\text{mL}^{-1}$ DON, respectively. For shoot fresh mass, these values were slightly lower: 19.2% and 25.5%, respectively [246]. DON was demonstrated to interfere with the synthesis of kernel storage proteins (and presumably other processes, e.g., lignification) [248]. In wheat seedlings sensitive to both *F. culmorum* and DON, free proline level increases have been reported, but were influenced by cultivar and DON concentration [244]. The increased proline levels have been interpreted as a plant response to pathogen attack [244]. It is possible that elevated proline levels may reflect an inhibitory effect on protein synthesis (*i.e.*, failure to incorporate proline into proteins) [146]. Snijders and Kretzing (1992) showed that DON is essential for *F. graminearum* colonization of plants. DON, as an inhibitor of protein synthesis, would inhibit the production of host enzymes (normally elaborated in response to fungal presence), thereby allowing fungal spread [249].

Additionally, DON being water-soluble, may be distributed to the spike and kernel by phloem vessels, thus promoting fungal proliferation by inhibiting the plant response [238].

4.1.4. Diacetyoxyscirpenol (DAS)

DAS (3,4-diacetyoxyhydroxy-15-hydroxy-12,13-epoxytrichothec-9-ene; *F. graminearum*; *F. sambicinum*; *F. poae*; *F. equiseti*) [22,217,236]. It is known clinically as anguine [22]. DAS was reported to reduce seedling viability and the inhibition dose for 50% reduction (LD₅₀) was at 1.26 mg·L⁻¹ for barley, 3.98 mg·L⁻¹ for wheat and 10 mg·L⁻¹ for sorghum [47]. Germinating caryopses of rye and field beans, and to a lesser extent, triticale and wheat, were sensitive to 10 µg·mL⁻¹ DAS, resulting in a decrease in the mitotic index [246]. For rye and beans, the number of cells found in metaphase increased with respect to other stages, as did metaphase chromosome abnormalities (spiralisation, C-metaphases, increased chromosome number and stellate chromosomes) [246]. Such chromosomal abnormalities result from an interference with the mitotic spindle, which may in turn have arisen from a disruption of protein synthesis, particularly of spindle microtubular proteins [246]. Inhibitory effects of DAS on root growth were more marked than for leaf mass of wheat seedlings [239]. DAS was less toxic than DON, 3-ADON, MON and T-2 toxin on germination and root and leaf mass, however more toxic than F-2 toxin [239].

4.1.5. T-2 Toxin

T-2 toxin (4β,15-diacetoxy-3α-hydroxy-8α-(3'-methyl-butyloxy)-12,13-epoxytrichothec-9-ene; *F. sporotrichioides*; *F. poae*; *F. tricinctum*) [22,217,236]. It is frequently detected in grain products in combination with HT-2 toxin [250]. Both toxins are produced by *F. sporotrichioides*, which is generally regarded as a weak plant pathogen [251]. T-2 toxin is reported to be more toxic to animal cells than most of the other trichothecenes [252,253], and is implicated in human alimentary toxic aleukia, reported in Russia since the 19th century [22]. T-2 toxin, at 1 µg·mL⁻¹, significantly inhibited root and shoot growth (mass) of germinating wheat seedlings [239]. Germination was, however, affected only at a concentration of 100 µg·mL⁻¹. Maize callus growth was significantly inhibited from a dose of 2.15 µM (= 1 µg·mL⁻¹) T-2 toxin [20]. Chang and Xue [254] had previously reported a decreased activity of wheat protoplasts exposed to 30–50 ppm T-2 toxin. Vesonder [255], using a duckweed (*Lemna minor* L.) bioassay, found that a doubling of the T-2 toxin concentration (3.3 to 6.7 µg·mL⁻¹) decreased leaf (“frond”) growth rate and chlorophyll content ten-fold and 2.5-fold, respectively. At 6.7 µg·mL⁻¹ T-2 toxin, growth rate of duckweed and leaf chlorophyll content were reduced to 6% and 19% of the control values, respectively. Application of T-2 toxin to onion roots resulted in a more marked decrease in the relative division rate in cells than did DON [247]. At 2.5 ppm (2.5 µg·mL⁻¹) of toxin, relative division rate for T-2 toxin was 59%, while for DON, this value was 78%. The mitotic index of T-2 toxin-treated onion root cells was significantly reduced from (and including) a concentration of 1 ppm. A concentration-dependent decrease in cells found in prophase and metaphase divisions was also reported [247].

4.2. Moniliformin (MON)

4.2.1. Historical Perspective and Producing Fungal Species

MON (1-hydroxycyclobut-1-en-3,4-dione) (Figure 11) was discovered by Cole *et al.* [256] while screening for toxic products of a North American isolate of *F. moniliforme* Sheldon (*F. verticillioides* [Sacc.] Nirenberg) cultured on corn. MON production has been subsequently reported for two other North American isolates [257–259] and one South African isolate of *F. moniliforme* [260]. The toxin has since been shown [259] to be produced also by *F. moniliforme* Sheldon var. *subglutinans* Woilenweber and Reinking (*F. sacchari* [Butler] W. Gams var. *subglutinans* [Wollenweber and Reinking] Nirenberg). These two *Fusarium* species are common corn pathogens in most corn producing areas of the world [261]. Rable *et al.* [262] have found that isolates of *F. fusarioides* obtained from millet, sorghum, peanuts, dried fish, and soil are all capable of producing MON. Nine toxic strains of *F. avenaceum* (Corda ex Fries) Sacc. isolated from barley kernels and corn tassels in Europe all produce MON, as does the one toxic strain of *F. oxysporum* Schlechtendahl isolated from barley kernels [263]. McLean *et al.* [22] reported that MON is produced by *F. moniliforme*, *F. sporotrichioides*, *F. avenaceum*, *F. culmorum*, *F. oxysporum*.

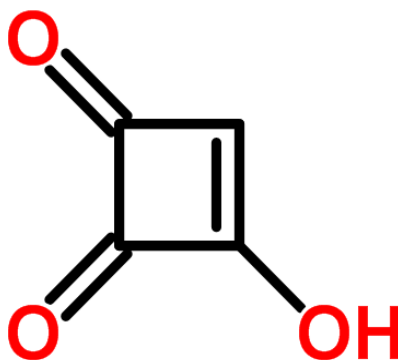


Figure 11. Chemical structure of moniliformin (MON) ($C_4H_2O_3$), taken from ChemSpider [39], 36957.

4.2.2. Phytotoxicity and Mechanism of Action

MON was less phytotoxic than FB1, butenolide, T-2 toxin or dihydroxyfusaric acid [255]. Wakulinski [239] reported that MON had a remarkable inhibitory effect on leaf than on root development in wheat seedling. This author further showed that $10 \mu\text{g}\cdot\text{mL}^{-1}$ generally resulted in a statistically significant decrease in leaf mass. Van Asch *et al.* [20] found that MON at $10 \mu\text{g}\cdot\text{mL}^{-1}$ and $100 \mu\text{g}\cdot\text{mL}^{-1}$ significantly reduced fresh mass accumulation. In *L. minor*, $66.7 \mu\text{g}\cdot\text{mL}^{-1}$ MON reduced growth to 84% of the control value, while for total leaf chlorophyll content, this value was 46% [255]. The toxicity of MON has been studied under *in vitro* and *in vivo* conditions. *In vitro* studies indicated an inhibition of multiple enzyme systems such as pyruvate dehydrogenase, transketolase, aldose reductase, glutathione peroxidase, and glutathione reductase [264–268]. Feeding studies with different avian species such as broiler chicks and ducklings using feed contaminated with MON resulted in symptoms such as acidosis and muscular weakness [269,270].

4.3. Fumonisin B1 (FB1)

4.3.1. Historical Perspective and Producing Fungal Species

Fumonisin B1 (FB1) is produced by certain *Fusarium* spp. including *F. verticillioides* (Sacc.) Nirenberg, *F. proliferatum* (Matsushima) Nirenberg and *F. nygamai* Burgess and Trimboli [271,272]. FB1 (Figure 12) first isolated from *F. moniliforme* MRC 826 by Gelderblom *et al.* [273], is a hydroxylated long chain alkylamine with two tricarboxylic acid moieties attached. FB1 is responsible for several diseases: leukoencephalomalacia in horses [274]; pulmonary oedema and hydrothorax in pigs [275] and liver cancer in rats [273]. In addition, it has been implicated as an aetiological agent in human oesophageal cancer in certain regions of South Africa [276] and China [277].

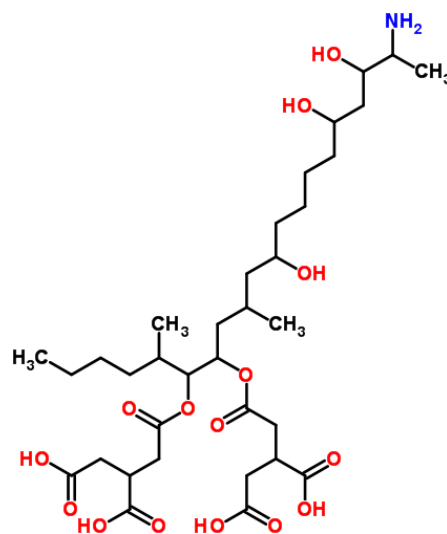


Figure 12. Chemical structure of fumonisin B1 (FB1) ($C_{34}H_{59}NO_{15}$), taken from ChemSpider [39], 3313.

4.3.2. Phytotoxicity

FB1 is known to exhibit phytotoxic effects towards different plants, including economically important crops [20,233,278–280]. Previous studies on other legume crops showed that soybeans (*Glycine max* L.) were severely damaged (necrosis and wilting) when sprayed with a $1000 \mu\text{g}\cdot\text{mL}^{-1}$ concentration of FB1 [281]. Doehlert *et al.* [282] showed that the presence of high levels of fumonisins in maize seeds might have deleterious effects on seedling emergence. An inhibitory effect on root elongation in germinating maize seedlings following FB1 treatment has been reported [282]. In maize and tomato seedlings, the fumonisins reduced root and shoot length and dry mass in a dose-dependent manner, and in a detached leaf assay, fumonisin application caused necrotic patches [280]. In comparing the fumonisins with AAL-toxin (TA, a host-specific pathotoxin of *Alternaria alternata* (Fr.:Fr.) Keissl. f. sp. *Lycopersici* causes stem canker disease of tomato) toxin, FB1 was found to be the most phytotoxic, especially in AAL-sensitive genotypes of tomato [280]. Several symptoms (chlorosis, necrosis, black leaf lesions, tissue curl, stunting, defoliation and death) developed, when FB1 was sprayed onto leaves of plantlets of a number of weed and crop plants, and the severity of which was varied with toxin concentration and plant species [281]. FB1 was implicated as an

aetiological agent in disease development since the response of jimsonweed plants treated with ground autoclaved fungal material was similar to symptoms (soft rot along leaf veins) caused by FBI application [278].

4.3.3. Mechanism of Action

When plants are contaminated by fumonisins, they could cause physiological damage, growth inhibition, and death in plants [283]. When the grains are infected, the starch granules of the endosperm are extensively degraded (pitted) [284] and the storage protein matrix that surround the starch granules were absent [285]. The germinability of bean, red gram, green gram and black gram seeds had vigorously reduced when soaked on culture filtrate of the toxic fungal strain [286]. Amylase production in the endosperm (specifically low pI amylases) was inhibited, suggesting that FB1 may interfere metabolically with germination [282]. FB1-treated maize callus cells exhibited dose-dependent deteriorative alterations in cell ultrastructure, which included cell wall thickening, the accumulation of what is presumed to be phenolics within vacuoles and the accumulation of large starch grains within swollen plastid [287]. The presence of extensive starch grains may reflect an interference with starch metabolism in the plant cell, as reported by Doehlert *et al.* [282]. FB1 was found to cause electrolyte leakage, photobleaching and a decrease in chlorophyll content [288]. The electrolyte leakage may be explained by the known membrane disruption effects of FB1 [289], while the photobleaching may arise from chloroplast membrane disruption that may inhibit photosynthesis, resulting in photobleaching of pigments or the photobleaching may be arise from accumulation of the inhibitory photodynamic metabolic intermediates [289].

4.4. *Fusarins and Fusaric Acid (FA)*

4.4.1. Historical Perspective and Producing Fungal Species

Fusarins are polyketides produced by many *Fusarium* species and by the entomopathogenic fungus *Metarhizium anisopliae* [290]. Fusarin A, B, C, and D were first described in 1981 by Wiebe and Bjeldanes in Berkeley, California [291]. The same authors already had isolated and partially characterized fusarin C [291], and its chemical structure was completed in 1984 [292]. The structure of fusarin C consists of a polyenic chromophore with a substituted 2-pyrrolidone (Figure 13a) [292]. Two other related compounds, fusarin A and D, with similar UV absorption properties were produced by *Fusarium*. A third kind of fusarin-like molecule was isolated from *F. moniliforme*, which was called fusarin F. [293]. Kleigrew *et al.* found out that this published structural assignment of fusarin F is incorrect, since fusarin C epimerizes to epi-fusarin C via the open-chain fusarin C structure [294]. Furthermore they discovered a new fusarin C-like structure called dihydrofusarin C.

FA (Figure 13b) was probably the first of the fungal toxins implicated in plant disease. In 1934, Yabuta, a Japanese agricultural chemist, was trying to isolate gibberellins when he separated a crystalline compound from the culture filtrate of *Gibberella fujikuroi* [295]. At that time the fungus was classified as *F. heterosporum* Nees. This compound was named FA and its chemical structure was 5-butylpicolic acid. The production of FA is broadly distributed among the entire genus *Fusarium*. Not only members of the *Gibberella fujikuroi* species complex (GFC), e.g., *F. fujikuroi*, *F. proliferatum*,

F. circinatum, *F. mangiferae*, *F. verticillioides*, and *F. subglutinans* but also more distantly related *Fusarium* species, such as *F. crookwellense*, *F. heterosporum*, *F. napiforme*, *F. oxysporum*, and *F. solani* are producers of FA [295–298].

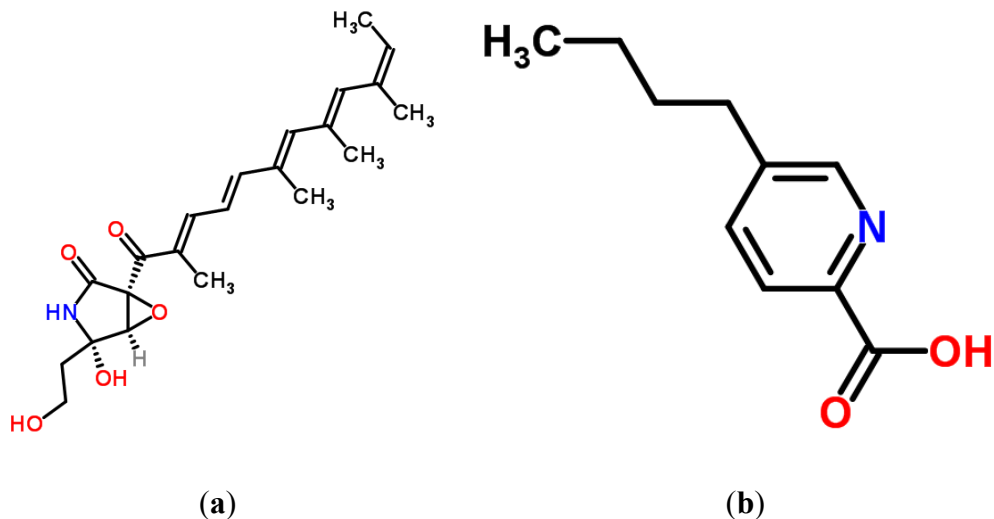


Figure 13. Chemical structure of (a) fusarin, taken from ChemSpider [39], 13085526; and (b) fusaric acid (FA), taken from ChemSpider [39], 3324.

4.4.2. Phytotoxicity and Mechanism of Action

Little is known about the phytotoxicity of the fusarins [22]. *F. moniliforme* was found to produce fusarin C on 7 varieties of maize, and on soybean, wheat, rye and barley [299]. In Taiwan, 83% of *Fusarium* isolates from maize were capable of producing fusarin C [300]. FA was one of the first fungal metabolites implicated in plant pathogenesis, in concrete in the tomato wilt symptoms caused by *F. oxysporum* f. sp. *lycopersici* Schlecht. emend. Snyder and Hans [301]. Phytotoxicity assays with FA and picolinic acid analogs revealed that the addition of alkyl groups to the 5-position of picolinic acid increased their phytotoxicity [302]. The toxic effects of FA on plants include alteration of membrane permeability (modification of cell membrane potential), decrease of mitochondrial activity and oxygen uptake, inhibition of ATP synthesis and inhibition of root growth [303–306]. These effects are observed at toxic concentrations ($>10^{-5}$ M). Nontoxic concentrations ($<10^{-6}$ M) of FA induce synthesis of the phytoalexin camalexin, which induces the formation of ROS and increases cytosolic Ca^{2+} . It has been suggested that FA could act as an elicitor of plant responses to pathogen attack [306]. The concentration of FA is positively correlated with *Fusarium* wilt index [307]. Infected plants had reduced stomata conductance and transpiration rate, which resulted in lower levels of water loss than in control plants [307].

4.5. Zearalenone (ZEA)

4.5.1. Historical Perspective

ZEA, also known as F-2 toxin (6-(10-hydroxy-6-oxo-trans-1-undecenyl)- β -resorcylic acid- μ -lactone) (Figure 14) is an estrogenic mycotoxin [308]. This mycotoxin causes hyperestrogenism, especially in swine [309]. The first report of moldy corn causing an estrogenic disturbance among swine appeared in 1928 [310]. Since then, other reports have come from the United States [311–313], Australia [314], and Ireland [315]. In 1962, Stob *et al.* [316] demonstrated that an anabolic uterotrophic compound, crystallized and partially characterized by them, was produced by *Gibberella zaeae*, the perfect stage of *Fusarium graminearum* (*F. roseum* “Graminearum”). Urry *et al.* [317] determined its chemical structure and named it ZEA. Partial characterization of the compound and environmental conditions suitable for its production were reported by workers at the University of Minnesota [313,318], who referred to ZEA as F-2.

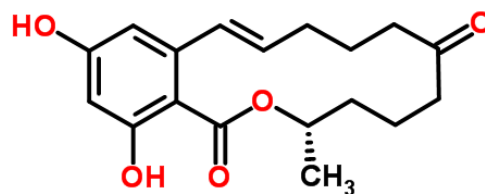


Figure 14. Chemical structure of zearalenone (ZEA) ($C_{18}H_{22}O_5$), taken from ChemSpider [39], 44448977.

4.5.2. Producing Fungal Species

Fungi-producing ZEA contaminate corn and also colonize, to a lesser extent, barley, oats, wheat, sorghum, millet and rice. In addition, the toxin has been detected in cereals products like flour, malt, soybeans and beer. Fungi of the genus *Fusarium* infect cereals in the field. Toxin production mainly takes place before harvesting, but may also occurs post-harvest if the crop is not handled and dried properly [319]. ZEA is produced by a variety of *Fusarium* fungi, including *F. graminearum*, *F. culmorum*, *F. cerealis*, *F. equiseti*, *F. crookwellense* and *F. semitectum*, which are common soil fungi, in temperate and warm countries, and are regular contaminants of cereal crops worldwide [3].

4.5.3. Phytotoxicity and Mechanism of Action

ZEA has a less phytotoxicity. It was the least toxic of six metabolites to three varieties of wheat seedlings [239], where at $100 \mu\text{g}\cdot\text{mL}^{-1}$, ZEA did not significantly affect germination or the subsequent root and leaf development. Germinating caryopses of rye, wheat, triticale and field bean were found to differ in their response to treatment with $10 \mu\text{g}\cdot\text{mL}^{-1}$ ZEA for 24 h [246]. Mitotic activity increased in rye, but decreased in wheat and field bean. No abnormal metaphase chromosomes were observed [246]. ZEA at $5 \mu\text{g}\cdot\text{mL}^{-1}$, had an inhibitory effect on root and shoot elongation and fresh mass accumulation of germinating, excised embryos of *Z. mays*. Interestingly, 10 and $25 \mu\text{g}\cdot\text{mL}^{-1}$ ZEA stimulated these parameters measured [146]. When DON and ZEA were applied simultaneously, to give a final

combined toxin concentration of $25 \mu\text{g}\cdot\text{mL}^{-1}$, the inhibitory effects on root and shoot elongation and mass were similar to or exceeded the values measured for DON alone. This would suggest an additive and possibly a synergistic effect when ZEA and DON occur in combination [146]. In a study [320] to investigate the fate of ZEA in plant tissue, ZEA was found to be metabolized by *Z. mays* cell suspensions to the α - and β -zearalenol and the β -D-glucosides of ZEA and α - and β -zearalenol. This study showed that up to 50% of the mycotoxin became bound to starch, hemicellulose, and in particular, lignin fractions, suggesting binding of ZEA metabolites to cell wall components.

5. Remarks on the Phytotoxic Properties of Mycotoxins

After reviewing the literature on phytotoxicity of mycotoxins, several points can be drawn. Mycotoxins differ in structure which explains the great variation of disease symptoms and biological activities induced on plant cells and seed germination. Mycotoxins can cause these adverse toxicities in different seedlings and plants varieties. The resulting phytotoxic properties are dose-related and differ from a mycotoxin to another. Table 2 summarizes selected reports of mycotoxins with potentially phytotoxic properties at several doses (for comparison). The phytotoxic properties of mycotoxins varied from their role in causing plant diseases (wilt, necrosis, chlorosis, curling, browning, and lesions induction) to their inhibitory effect on seedling germination parameters. For all toxins, the inhibitory effects were generally more marked for root parameters than for shoot elongation or mass [46,146].

Table 2. Summary of the phytotoxic properties of mycotoxins and their effective doses on plants.

Mycotoxin	Dose	Affected Plants	Phytotoxic Effects	Ref.
Aflatoxin	$>10 \mu\text{g}\cdot\text{mL}^{-1}$	<i>Lepidium sativum</i>	Maximal reduction in the growth rate of hypocotyls after germination	[40]
	$0.83 \mu\text{g}\cdot\text{mL}^{-1}$	Barley	LD ₅₀ seedling viability	[47]
	$1.74 \mu\text{g}\cdot\text{mL}^{-1}$	Wheat	LD ₅₀ seedling viability	[47]
	$2.75 \mu\text{g}\cdot\text{mL}^{-1}$	Sorghum	LD ₅₀ seedling viability	[47]
CTN	10^{-3} – 10^{-4} M	Bean, cotton, sorghum	Symptoms of wilting	[63]
PAT	$25 \mu\text{g}\cdot\text{mL}^{-1}$	Maize	5% inhibition of radicle emergence	[17]
	$100 \mu\text{g}\cdot\text{mL}^{-1}$	Wheat	Decreases in internodal elongation, floret number, seed weight, and seed number	[96]
PA	250 – $500 \mu\text{g}\cdot\text{mL}^{-1}$	<i>Picea glehnii</i>	Browning of <i>Picea glehnii</i> roots without root destruction	[16]
		Lettuce	Growth inhibition of lettuce seedlings	[16]
	$500 \mu\text{g}\cdot\text{mL}^{-1}$	Corn	Growth of the main root was reduced 50%	[18]
OTA	1 – 2 mM	<i>Arabidopsis thaliana</i>	Formation of macroscopic lesions on leaves within 1–2 days.	[144]
	$50 \mu\text{M}$	<i>Arabidopsis thaliana</i>	Blocking of root elongation	[145]
TA	0.12 mM	Rice	Leaf browning and 80% root growth inhibition	[161]
	$100 \mu\text{g}\cdot\text{mL}^{-1}$	<i>Datura innoxia</i> , rye, wheat, lettuce and green gram	Growth inhibition of germinating seeds	[160]
	$200 \mu\text{g}\cdot\text{mL}^{-1}$	<i>Datura innoxia</i>	Localized chlorotic spots turned into necrotic after 24 h	[160]

Table 2. Cont.

CB	10 ⁻³ M	<i>Bromus tectorum</i>	Coleoptile elongation reduction to 34% of the control	[203]
CE	5 ppm	Apple	Limpness of shoot	[197]
	10 ⁻⁴ M	<i>Striga hermonthica</i>	LD ₅₀ seedling viability	[199]
Pyrenophoric acid	10 ⁻³ M	Cheatgrass	Coleoptile length reduction relative to the control by approximately half	[202]
Pyrihalasin H	1 µg·mL ⁻¹	Rice	Characteristic curling of the shoot	[204]
Zygosporin D	1 nmol/plant	Rice	Reduction of the second leaf sheath length of treated plants to 41% of control	[205]
DON	2 µg·mL ⁻¹	Wheat	50% inhibition of root growth	[241]
	10 µg·mL ⁻¹	Wheat	50% inhibition of shoot growth	[241]
	50 µg·mL ⁻¹	Wheat	Complete inhibition of germination	[244]
	10–25 µg·mL ⁻¹	Wheat	Plantlet growth reduction	[244]
	10 and 25 µg·mL ⁻¹	Maize	Significant inhibition of both primary root and shoot elongation of germinating embryos	[246]
NIV	48 µg·mL ⁻¹	Wheat	50% inhibition of root growth	[241]
	100 µg·mL ⁻¹	Wheat	50% inhibition of shoot growth	[241]
DAS	1.26 µg·mL ⁻¹	Barley	LD ₅₀ seedling viability	[47]
	3.98 µg·mL ⁻¹	Wheat	LD ₅₀ seedling viability	[47]
	10 µg·mL ⁻¹	Sorghum	LD ₅₀ seedling viability	[47]
T-2 toxin	1 µg·mL ⁻¹	Wheat	Significant inhibition of root and shoot growth of germinating seedlings	[239]
	1 µg·mL ⁻¹	Maize	Significant inhibition of callus growth	[20]
	6.7 µg·mL ⁻¹	Duckweed (<i>Lemna minor</i> L.)	Decrease of leaf growth rate	[255]
MON	10 µg·mL ⁻¹	Wheat	A significant decrease in leaf mass	[239]
	10–100 µg·mL ⁻¹	Maize	Significant reduction in fresh mass accumulation	[20]
	66.7 µg·mL ⁻¹	Duckweed (<i>L. minor</i> L.)	Growth reduction to 84% of the control	[255]
FB1	1000 µg·mL ⁻¹	Soybeans (<i>Glycine max</i> L.)	Necrosis and wilting	[281]
	100 ppm	Maize	Radicle elongation inhibition	[282]
	1–100 µM	Tomato	Leaves necrosis	[280]
	10–200 µg·mL ⁻¹	Jimsonweed	Chlorosis and necrosis and reduction in height and biomass	[281]
FA	10 ⁻³ M	Tomato	Symptoms of wilting	[301]
	10 ⁻⁵ M	<i>Arabidopsis thaliana</i>	Toxic effects such as alteration of cell growth, mitochondrial activity and membrane permeability	[306]
ZEA	5 µg·mL ⁻¹	Maize	Inhibitory effect on root and shoot elongation and fresh mass accumulation of germinating embryos	[146]

6. Conclusions

This review gives a comprehensive overview of the current knowledge on the phytotoxic effect of mycotoxins. Data about historical perspective and producing fungal species of each mycotoxin class

were also covered. Most mycotoxins of concern are produced by three genera of fungi, namely, *Aspergillus*, *Penicillium*, and *Fusarium* in addition to dematiaceous fungal genera (*Alternaria*, *Helminthosporium*, *Drechslera*, *Phoma*, *Zygosporium*). The major mycotoxin-producing fungi are not aggressive pathogens in plants; however, mycotoxins are produced by several genera in plants during the growing season when portals of entry are provided and environmental conditions are appropriate. Toxicogenic fungi in crops are divided into those which invade and produce their toxins before harvest which are often rather loosely called “field fungi” and those which becomes a problem after harvest “storage fungi”. Invasion by fungi before harvest is governed primarily by plant host-fungus and other biological interactions (e.g., insects), while growth by fungi postharvest is governed by crop (nutrients), physical (temperature, moisture) and biotic factors (insects, competition) factors. However, the original source of the fungi in both circumstances is the field. Within the genus *Aspergillus*, the major class of mycotoxins, are the aflatoxins. *A. flavus* is a common contaminant in agriculture, can infect crops prior to harvesting causing hazardous to the plant’s growth and development as well as to the consumer’s health since aflatoxin-infected crops have from time to time been returned to agricultural soils. *Penicillium* spp. are more typically associated with storage of crops and the production of mycotoxins such as CTN, PAT, PA, and OTA. Ochratoxin usually is formed in storage or during drying of certain commodities for processing. Within the genus *Fusarium*, there are a number of important mycotoxin-producing species. Some important plant pathogens are in this genus and are causes of wilts and scab or blight diseases of small grains. Ear rot also can be caused by *Fusarium* spp. *F. graminearum* is the major causative agent; however, other species such as *F. verticillioides*, *F. proliferatum*, *F. culmorum*, *F. sporotrichioides*, *F. moniliforme* and *F. subglutinans* may cause ear rot. These latter agents may produce DON, NIV, DAS, T-2 toxin, MON, FB1, fusarin C, FA and ZEA during the pathogenic state in different varieties of agriculture crops. Understanding the mechanisms of mycotoxin action on the host plants at the cellular and biochemical level is important in the overall goal to inhibit or decrease the action of mycotoxins.

Acknowledgments

This work was financially supported by a research grant from the Deutsche Forschungsgemeinschaft, Bonn, Germany (PA 764/19-1, AOBJ 618653).

Author Contributions

Most of the text was written by Ahmed A. Ismaiel, smaller contributions to all parts were done by Jutta Papenbrock.

Conflicts of Interest

The authors declare no conflict of interest.

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