

Chapter 9

Chemical and Physical Treatments for Reducing Mycotoxin Contaminations



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Abstract In most cases, enzymes, antifungal microbial, and various bio-sourced methods were effective for the control of mycotoxin contaminations, while it has a common deficiency that not all of the mycotoxins were desirably controlled when treating with these abovementioned means. Herein, we concluded multiple physical and chemical agents to control mycotoxins and also the most widely used way in the factory production. All of the physical and part of the chemical treatments aimed at the reduction of the mycotoxins themselves, which means destroying or transformation of their molecular structures. Most chemical reagents were used in the field experiments where they aimed at the resources of these mycotoxins, i.e., fungal pathogens. Of course, some antifungal reagents are especially absorbed or combined with these mycotoxins just like multiple bio-resourced agents. After all, these two methods played an important role in the front of food processing procedures, due to their low cost, simplicity, high efficiency, and sufficient universality.

Keywords Chemical treatment · Physical treatment · Contaminations · Reduction · Mycotoxins

9.1 Physical Treatments for Reducing Mycotoxin Contaminations

Before the appearance of variable chemical reagents and specific biogenic enzymes, physical processing was the most effective way to remove mycotoxins during the production practice, and it is still under extensive uses till now. Among these, thermo-treatment is seemed to be the simplest and operable method. Gbashi et al. (2019) suggested parameters of 210.85 °C/54.71 min for mycotoxin-contaminated maize flour as the optimum degradation conditions. Siciliano et al. (2017) also

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tested the heat exposure of 140 °C for 40 min, and it was effective for detoxification of aflatoxin with no effects on lipid profile and the nutritional quality in foodstuffs. Furthermore, during food processing at high temperature, ochratoxin A (OTA) could be turned to its thermal isomerization product 2'R-Ochratoxin A, showing different metabolic characteristics in human body (Sueck et al. 2018) (Fig. 9.1).

Besides heat, plasma and various waves were also attempted to be widely applied for mycotoxin control. The treatment of *Penicillium verrucosum* on barley after an incubation of 5 days using a CO₂ + O₂ plasma and air plasma resulted in a reduction of the ochratoxin A (OTA) content from 49.0 (untreated) to 27.5 (1 min) and 25.7 (1 min), respectively (Durek et al. 2018). In addition, Shi et al. (Shi 2017) confirmed the disappearance of the C8=C9 double bond in the furofuran ring of aflatoxin B1 (AFB1) after treatment of high-voltage atmospheric cold plasma (Shi 2017). Very recently, the cold atmospheric pressure plasma may overcome multiple weaknesses associated with the classical methods, and most mycotoxins exposed to this plasma were degraded almost completely within 60 s (Hojnik et al. 2017; Ten Bosch et al. 2017). Hernández et al. compared three treatments during milk storage, non-treatment, pasteurization, and thermoultrasound (Hernandez-Falcon et al. 2018), suggesting that 10 min-thermoultrasound unhomogenized milk 1 day after storage kept the lowest aflatoxin M1 (AFM1) level of 0.15 ± 0.05 pg/mL. Similarly, oven roasting and microwaving of chicken breast muscles can reduce the content of ten prevalent mycotoxins, reducing their increased bioaccessibility (Sobral et al. 2019) (Fig. 9.2).

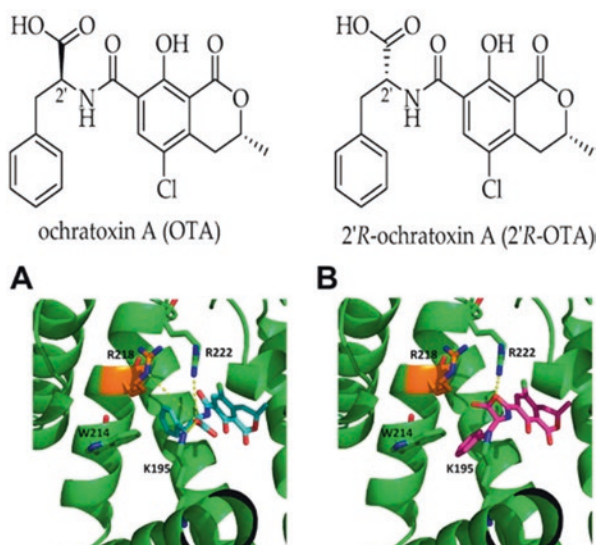


Fig. 9.1 The hypothetical molecular structures of ochratoxin A (OTA) and its thermal isomer 2'R-OTA. Important interacting residues are shown as sticks, OTA can form salt-bridge interactions with R218, R222, and K195; 2'R-OTA can only form these interactions with R222. (Sueck F et al. 2018)

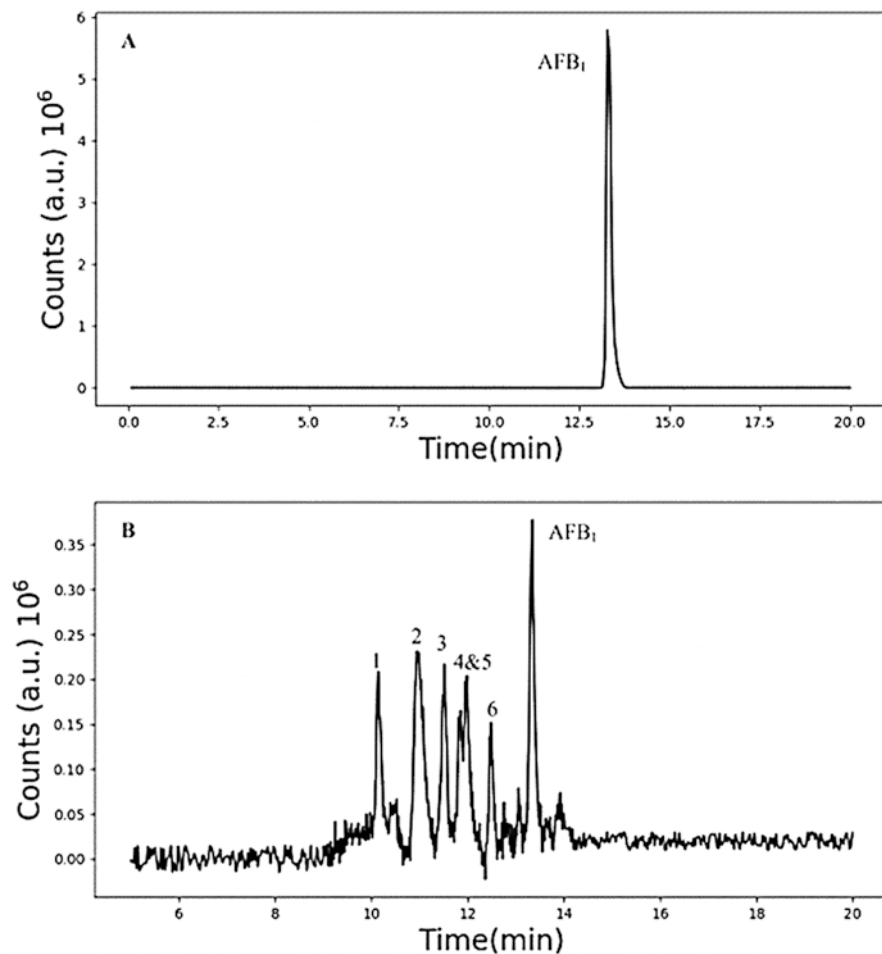


Fig. 9.2 Chromatograms of AFB₁ untreated (5 $\mu\text{g}/\text{mL}$) in 50% ethanol solution (a) and AFB₁ sample treated by HVACP in ambient air for 5 min (b). (Shi et al. 2017)

Interestingly, the light might be connected with mycotoxin production. As demonstrated, the optimized combinational treatments of radiation and essential oil were very effective in reducing the fungal growth and mycotoxins content (Kalagatur et al. 2018a). Also, Wang et al. found that high intensity of blue light decreased the accumulation of citrinin (CIT) production in *Monascus ruber*, providing a unique mentality of mycotoxin reduction in the field production (Wang et al. 2016) (Fig. 9.3).

Specially for mycotoxins of *Alternaria* toxins, improved food processing methods, such as milling process (Janic Hajnal et al. 2019) and extrusion processing (Janic Hajnal et al. 2016), can affect the residue of tenuazonic acid (TeA), alternariol (AOH), and alternariol monomethyl ether (AME), suggesting the demands of

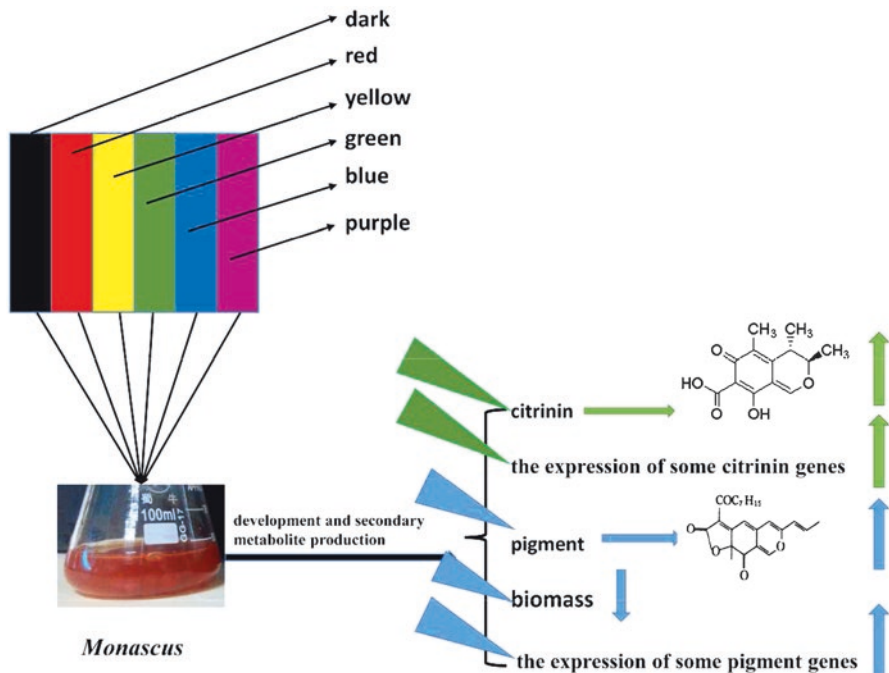


Fig. 9.3 The principles of light affect the production of citrinin (CIT). (Wang L et al. 2016)

high-grade raw-food material and optimized machine process. Not just *Alternaria*, various physical postharvest treatments were deadly for pathogenic fungi, which obviously cause oxidative injury, protein impairment, and cell wall degradation, thus reduced mycotoxin contaminations (Liu et al. 2018; Karlovsky et al. 2016), for instance, extrusion and alkaline cooking of corn kernels reduced the fumonisin toxicity for mice (Voss and Ryu 2017). Also, processing methods such as color sorting reduced the levels of aflatoxin and can be practically utilized to monitor the occurrence of aflatoxins in some commercial products (Zivoli et al. 2016) (Fig. 9.4).

9.2 Chemical Treatments for Reducing Mycotoxin Contaminations

With the rapid development of traditional inorganic and synthetic chemistry, structural biologists applied the known interplay between multiple mycotoxins and diverse structures, eliminating mycotoxins from the molecular levels. The common removers normally include various acids, fungicides, organic oils, and little parts of other materials, while all of the compounds can be divided into two parts, some are the inhibitors of fungal growth, especially the essential metabolic pathways of mycotoxin synthesis, and the others act on the mycotoxins themselves, removing them by modification or completely degradation.

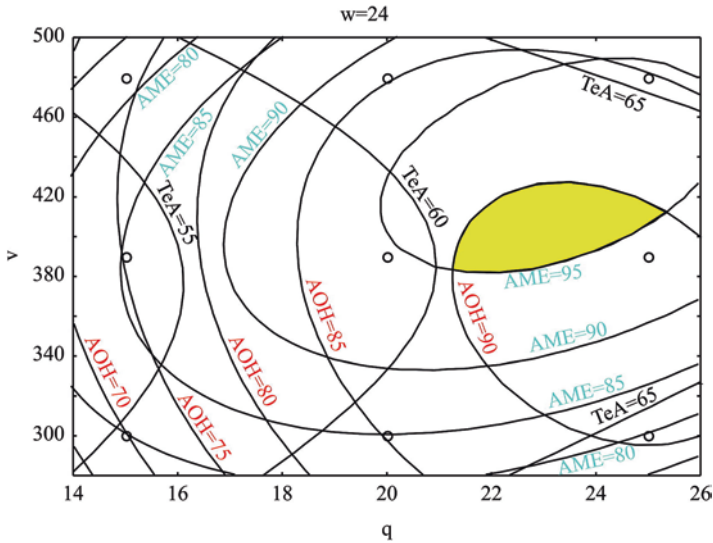


Fig. 9.4 Optimum region obtained after superimposing the contour plots of the system response. (Janic Hajnal et al. 2016)

Over the past decades, some scientists have found plenty of antifungal agents to control mycotoxin contamination. Moon et al. (2017) tested 38 coumarins and found that 4-hydroxy-7-methyl-3-phenyl coumarin was the most effective controller of aflatoxin for its downregulated function of aflD, aflK, aflQ, and aflR in the pathways of aflatoxin biosynthesis. Furthermore, coumarins can prevent the aflatoxin B₁ (AFB₁)-induced hepatotoxic effects via increasing antioxidant capacities and inhibiting the CYP450 isozyme-mediated activation (Zhang et al. 2016). One of the anthocyanins, delphinidin, showed great protection effects of gut from *Alternaria*-induced genotoxicity (Aichinger et al. 2018). Also, grape seed proanthocyanidin extract was found to be related to the activation of the Nrf2/ARE signaling pathway, which mRNA expression levels can be downregulated by zearalenone (ZEN), protecting the ZEN-induced hepatic injury (Long et al. 2016). Besides, more and more active substances, such as rutin and its derivatives (Huang et al. 2019), tannis (Peng et al. 2017) and validamycin (Li et al. 2019), were revealed to be connected with biocontrol efficiency and mycotoxin production of filamentous fungi. A similar group of biocontrol substances also includes piperine, and the main purpose was aimed at AFB₁. Results showed that piperine inhibits AFB₁ production while positively modulating fungal antioxidant status in *Aspergillus flavus* (Caceres et al. 2017), and thus it was demonstrated useful of its antigenotoxic effect in broiler chickens (da Silva Cardoso et al. 2016). Furthermore, researchers assessed several piperine-like synthetic compounds, in which 1-(2-methylpiperidin-1-yl)-3-phenylprop-2-en-1-one showed the most potential of antifungal and antiaflatoxigenic effects against *Aspergillus flavus* (Moon et al. 2016) (Fig. 9.5).

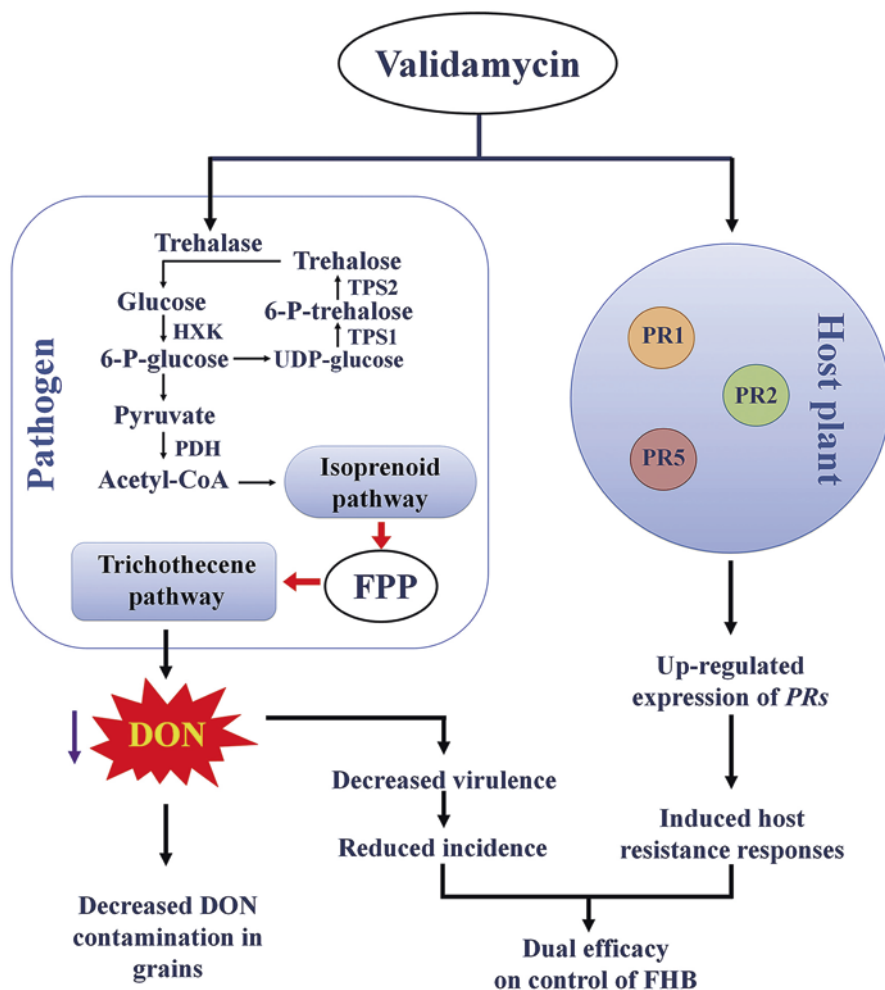


Fig. 9.5 The proposed working model of how validamycin affects the pathogen *F. graminearum* and the host wheat. (Li et al. 2019)

Fortunately, we can also see some valuable investigations aimed at the detoxification of mycotoxin *in vitro*. With the development of new macromolecular inorganic carbon matters such as activated carbon (Kalagatur et al. 2017), activated carbon fibers (El Khoury et al. 2018) make the mycotoxin absorption available. Similar eliminated artificial adsorbents include varied clays or bentonites. Cetylpyridinium chloride ions modified around organozeolites prepared by clinoptilolite and phillipsite are responsible for ZEN absorption (Markovic et al. 2016). Moreover, it was identified from two human cells that bentonite modified with zinc enhanced the antiaflatoxigenic ability (Nones et al. 2017). Researchers also evaluated the detoxification potential of both ZEN and AFB via multiple montmorillon-

ites (Wang et al. 2018a, 2019b) and surfactants (Wang et al. 2018b), plus, Kang et al. (2016) used the combined batch experiment with computational models, indicating that adsorption affinity of mycotoxins is dependent on the surfaces of clay aggregates. With the aid of micropore structure in chitosan derivatives (Yang et al. 2017), shrimp shells (Assaf et al. 2018), natural zeolites (Eroglu et al. 2017), and bentonite clay (Shannon et al. 2016), small molecules of mycotoxins were all sedimented and aggregated to the fixed microporous structure, reducing their toxicities to variable target organisms (Fig. 9.6).

There is also one part of important mycotoxin absorbents or antifungal agents, nanocomposites. Gao et al. (2019) synthesized an organic-inorganic P(DMDAAC-AGE)/Ag/ZnO composite for the usage of antibacterial cotton fabrics with laundering durability, showing more than 99.00% of anti-mildew performance even after 11 washing cycles. A kind of surface active maghemite nanoparticles was made to bind citrinin; mass spectroscopy and magnetization measurements showed that the material was an efficient and reliable mean for citrinin removal (Magro et al. 2016). Ag doped hollow TiO₂ nanoparticles were identified to be effective in protecting farm products affected by *Fusarium solani* or other fungi, where the Ag promotes the formation of stable Ag-S and disulfide bonds (R-S-S-R) in cellular protein, leading to cell damage (Boxi et al. 2016). Furthermore, nanocomposites mixed with other agents can significantly increase their antifungal property, such as chitosan nanoparticles encapsulated with essential oil (Kalagatur et al. 2018b), pyraclostrobin solid nanodispersion by self-emulsifying technique (Wang et al. 2019a).

Ozone treatment was also effective for pathogen prevention and mycotoxin control. It has been concluded that ozone has great potential to improve the functional-

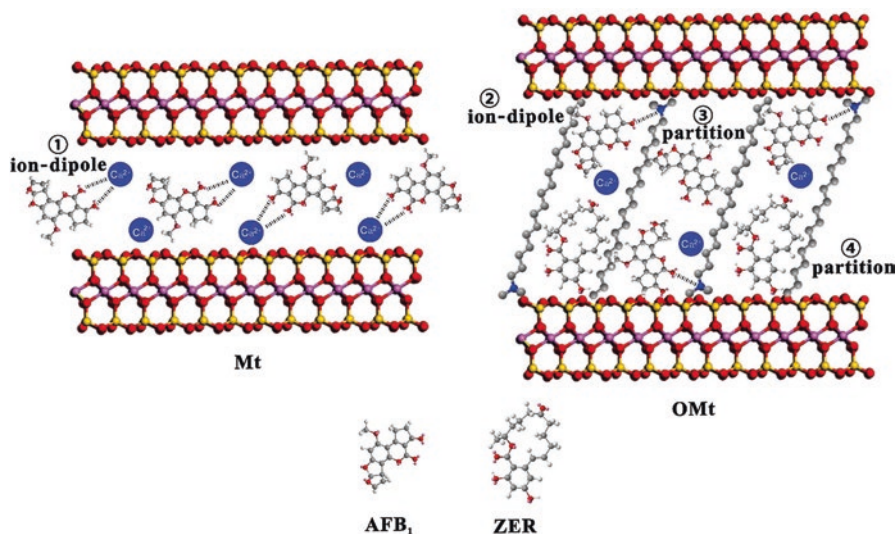


Fig. 9.6 Adsorption/partition mechanisms of adsorption of AFB₁ to natural Mt. (Wang et al. 2018a, b)

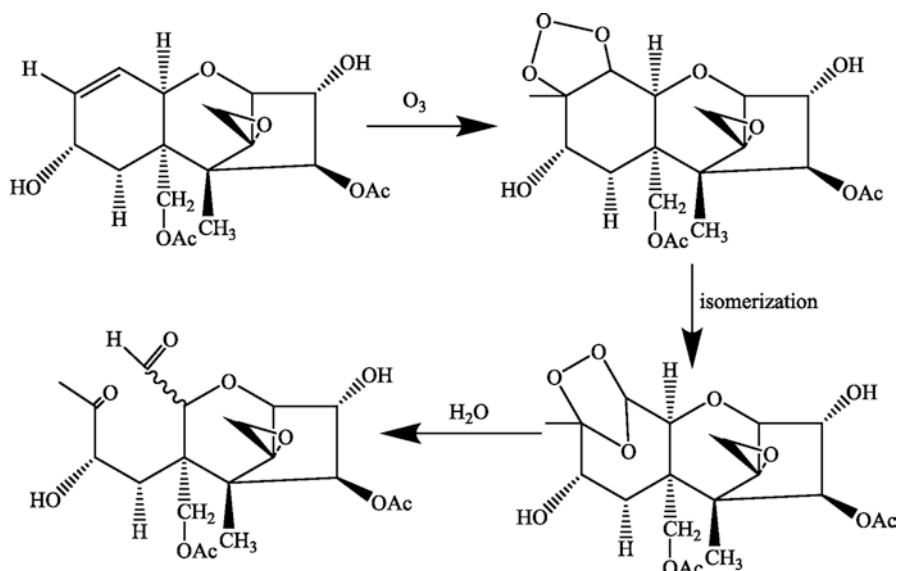


Fig. 9.7 The proposed mechanism of the reaction of ozone to the mycotoxin NEO. (Hua-Li et al. 2018)

ities of grain products while ensuring food safety (Zhu 2018). After treatment of ozone at 1.10 mg/L for 120 min, *Fusarium* rot development and neosolaniol accumulation in fruits were discriminately controlled (Hua-Li et al. 2018) (Fig. 9.7).

Interestingly, potassium may also relate to the antifungal attempt. *Penicillium expansum* under 5 mM potassium phosphite stress presented yield reduction of patulin and lower infectivity to apple fruit (Lai et al. 2017). Moreover, Chang et al. demonstrated that addition of triphenylphosphonium cation can enhance or at least restore compounds' antifungal activity, resulting in mitochondrial dysfunction and increased levels of intracellular reactive oxygen species (Chang et al. 2018).

Besides, other common chemical treatments to remove mycotoxins were varied organic active substances; among these organic acids, essential oils, aldehyde derivatives, organism extracts, and artificial fungicides were the substances with great representations.

9.3 Organic Acids

Acids play a great role in control of pathogens and mycotoxins; single or multiple combined acids were proved effective in the food or food products protection. Researchers purified cuminic acid from the seeds of *Cuminum cyminum* L., which significantly distorted the mycelial morphology of *Fusarium oxysporum*; more importantly, synthetic genes of bikaverin (Bike1, Bike2, and Bike3) and fusaric acid

(FUB1, FUB2, FUB3 and FUB4) both were downregulated (Sun et al. 2017). Also, p-aminobenzoic acid was present in the secretions of rhizobacterium *Lysobacter* to show a broad spectrum of antifungal activities, which inhibits septation during cell division (Laborda et al. 2019). Most acids targeted in the membrane of fungal hyphae, ethyl p-coumarate, can cause severe lipid peroxidation and heavy oxidative damage to the cellular membranes and organelles of pathogens (Li et al. 2018). Chlorogenic and caffeic acids were also groups of antifungal micromolecular acids; both can be degraded into protocatechuic acid in the *Fusarium graminearum* and dramatically enhanced the counteraction of the fungal ability of mycotoxin production (Gauthier et al. 2016). Similar compounds including I-pyroglutamic acid (Bilska et al. 2018), sinapic acid (Kulik et al. 2017a), fluorinated dihydroguaiaretic acid (Yamauchi et al. 2017), etc. were all with antifungal potential. Meanwhile, gene expression revealed that *Tri* genes responsible for trichothecene biosynthesis were downregulated after acid treatment (Fig. 9.8).

Combination of multiple or even unknown acids seems like to have synergistic effects for the antifungal property. For example, the cell-free supernatant of *Lactobacillus plantarum* inhibits the production of aflatoxins by 91%, where lactic acid, phenyllactic acid, hydroxyphenyllactic acid, and indole lactic acid were detected in the metabolites and all were tested separately with antiaflatoxigenic property (Guimaraes et al. 2018). Combination of exogenous abscisic acid and gibberellic acid can also reduce head blight severity, as phytohormones, combining fungicidal agents and these acids may also be useful for the management of head blight infection (Buhrow et al. 2016). Phenolic acids were a group of organic matters with a phenolic hydroxyl group; caffeic, chlorogenic, ferulic, and p-coumaric

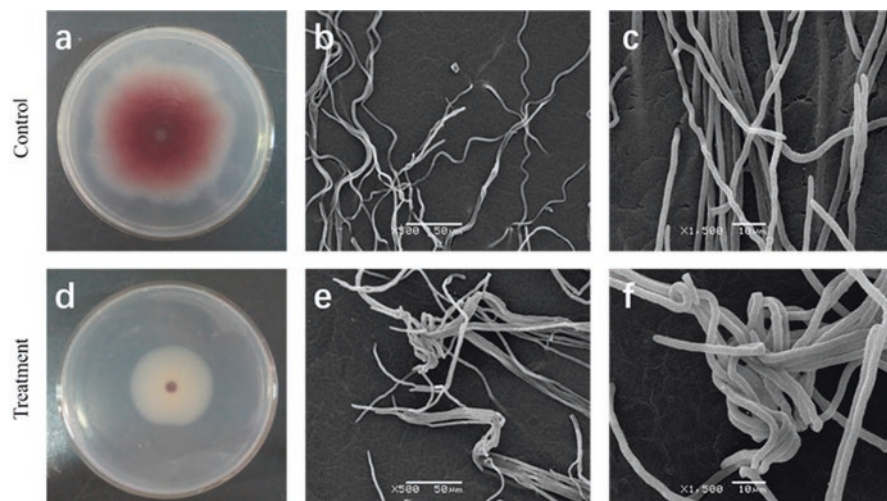


Fig. 9.8 Effect of cuminic acid on mycelia morphology of *Fusarium oxysporum* f. sp. *nivaeum*. (d–f) Untreated plates; (a–c) plates treated with cuminic acid at EC₅₀ value (22.53 $\mu\text{g}/\text{mL}$). Values are means and standard errors. (Sun Y et al. 2017)

acid were all tested. All those have somewhat variable effects on fungal growth and mycotoxin production, depending on the host strain and the concentration (Ferruz et al. 2016). Moreover, Ferruz et al. also proved that phenolic acids have the antifungal property and upregulated ergosterol biosynthesis by *Fusaria* (Kulik et al. 2017b).

9.4 Fungicides

Traditional fungicides were mostly aimed at pathogen growth inhibition, thus leading to the reduction of multiple mycotoxins. Wayne et al. (Jurick et al. 2019) tested the sensitivity of *Penicillium* spp. to difenoconazole and suggested a minimum limitation of 5 $\mu\text{g/ml}$ to fruit quality and mycotoxin control. A field experiment showed that prothioconazole could significantly reduce the total deoxynivalenol and zearalenone contents by applications at 18th leaf and R2 stages, while not visibly changing other mycotoxin contents (Limay-Rios and Schaafsma 2018).

And tebuconazole was also one efficient fungicide, the addition of tebuconazole significantly decreases the DON production, and meanwhile, TRI5 and TRI6 of biosynthetic genes were downregulated (Diao et al. 2018). Similarly, epoxiconazole (Duan et al. 2018), triticonazole (Zhang et al. 2018), arylpyrazole (Zhang et al. 2017), and varied triazoles (Hellin et al. 2017) were all verified to be effective to the pathogen prevention and mycotoxin control (Fig. 9.9).

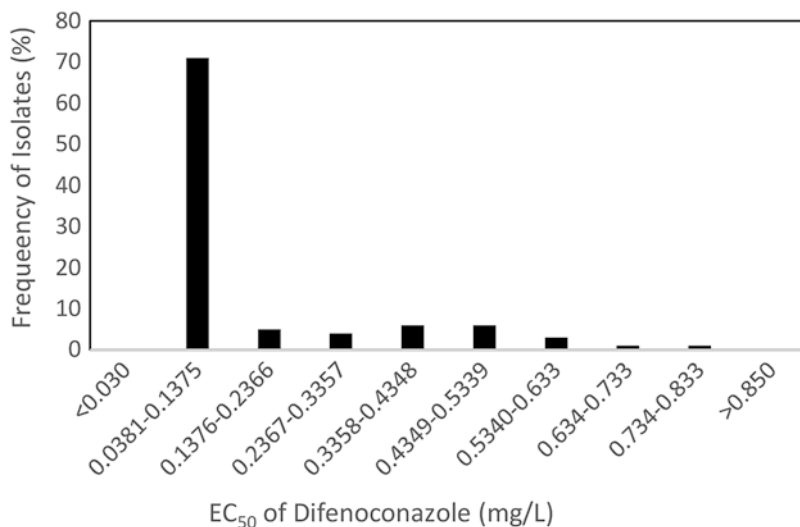


Fig. 9.9 Frequency distribution of isolates in fungicide concentration that inhibit mycelial growth by 50% for technical grade difenoconazole for *Penicillium* isolates. (Jurick et al. 2019)

As a powerful and simple method to control fungal pathogens, fungicides were always compared with other emerging antifungal agents, but no doubt, fungicides were still the most widely used field method. Scaglioni et al. (Scaglioni and Blandino 2018) compared the inhibition effects of fumonisin production between tebuconazole and microalgal phenolic extracts, and both showed antifungal potential, while either would directly control the fumonisin contents. Moreover, a direct comparison of the synthetic commercial antifungal compound and the antifungal protein PgAFP showed that both were with fungal growth inhibition. Furthermore, the presence of PgAFP produced a significant reduction in mycotoxins accumulation (da Cruz Cabral et al. 2019). Additionally, researchers investigated the effects of two fungicides, quinone outside inhibitors and demethylation inhibitors, on *Fusarium* head blight and deoxynivalenol production, and results suggested that the combination effect of two fungicides depended on the active ingredients and whether the two were applied as a mixture at heading or sequentially (Paul and Bradley 2018). Anyway, new emerging antifungal agents were always tested by making comparison with these commercial fungicides, which represents a dominance of fungicides in fungal pathogens and mycotoxins control in a very long period (Fig. 9.10).

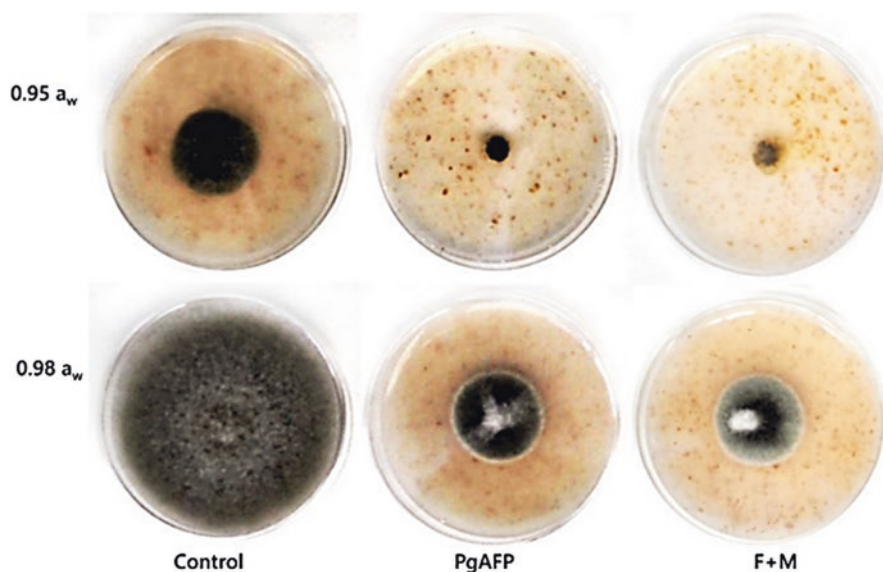


Fig. 9.10 The changes on the colonies of *Alternaria tenuissima* sp. grp. grown on wheat media in the presence of two antifungal treatments (PgAFP and F + M) at two water activity (a_w) levels, 0.95 and 0.98 after 6 days of incubation at 25 °C. (da Cruz Cabral L et al. 2019)

9.5 Aldehydes, Essential Oils, and Organism Extracts

Besides organic acids, aldehydes and their derivatives were also popular for mycotoxin control, and most of them were derived from plants, especially herbs. Harohally et al. (2017) tried to enhanced the antiaflatoxigenic activity of 2-hydroxy-4-methoxybenzaldehyde, cinnamaldehyde and the molecules with similar chemical structures, and the productions, Schiff bases, which showed great commendable antiaflatoxigenic activity. Plus, the antiaflatoxigenic potential of cinnamaldehyde was attributed to alleviate oxidative stress, which was possibly induced by modifications of cellular structure (Sun et al. 2016). Meanwhile, cuminaldehyde thiosemicarbazone was structurally modified, and then it was testified to be more special for aflatoxin control via yeast experimental model (Degola et al. 2017).

Similarly, essential oils were mainly separated from medical plants, different from other antifungal agents; most of these oils were mixtures with complicated composition. As reported, the bioactive ethylene-vinyl alcohol copolymer (EVOH) films, containing cinnamaldehyde, linalool, isoeugenol, or citral, showed strong inhibition of OTA biosynthesis in corn at very low concentrations (Tarazona et al. 2018). And Mateo et al. (2017) compared several oils contained in EVOH films; the result showed that EVOH-cinnamaldehyde film showed the most inhibition of fungal growth and aflatoxin control. Natural essential oil derived from turmeric was used as an eco-friendly antifungal agent. Moreover, expression of mycotoxin genes in aflatoxin biosynthetic pathway was relatively downregulated (Hu et al. 2017). The essential oil of rosemary was also applied to the investigation of multiple pathogens, including *Alternaria* spp., *Fusarium* spp., *Colletotrichum* spp., and *Penicillium* spp., all with good control practice (Waithaka et al. 2017). Moreover, similar essential oils with antifungal properties were extracted from other plants, such as *Hedychium spicatum* L. (Kalagatur et al. 2018a), *Mentha cardiaca* L. (Dwivedy et al. 2017), and so on. Clove oil-in-water nanoemulsions were one new material with different oil composition, and addition of corn oil or triacylglycerol would reduce its antifungal potential to this material, while the inhibition activity would be enhanced when clove oil was encapsulated in nanoemulsions (Wan et al. 2018).

Actually, all the pure antifungal agents were from multiple organisms; as a result, extractions from these can also be of antifungal potential. Researchers investigated the reduction rate of grape pomace to varied mycotoxins, and it can reduce the gastrointestinal absorption of mycotoxins, as well as be a natural binder for multiple mycotoxins (Gambacorta et al. 2016). In the extraction of peanut, peanut stilbenoids could provide the new strategies for preventing plant invasion and production of aflatoxin (Sobolev et al. 2018). Furthermore, the fermentation liquid of *Bacillus subtilis* also showed great growth inhibition to varied fungal pathogens, for its volatile organic compounds in the metabolites (Gao et al. 2018) (Fig. 9.11).

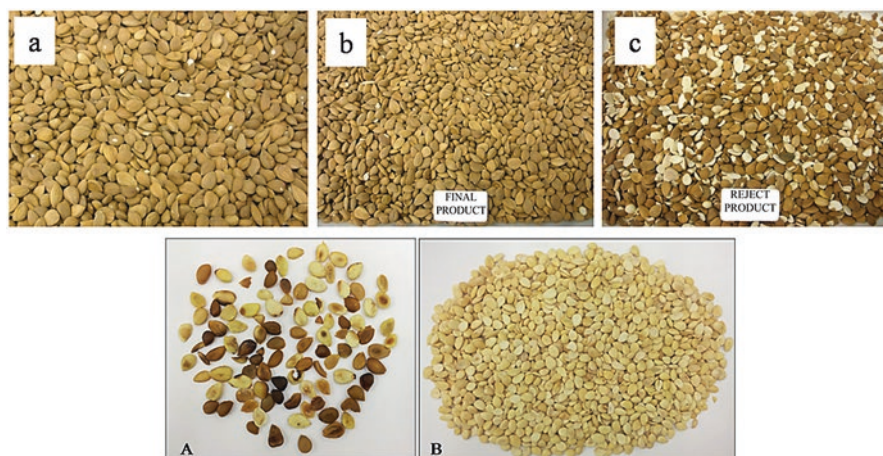


Fig. 9.11 Initial apricot kernels (a), final product (b) and reject product (c) obtained by e-sorting and discolored apricot kernel (a, b) and healthy apricot kernels. (Zivoli et al. 2016)

9.6 Conclusion

To sum up, physical treatments for control of mycotoxin contamination were aimed at the molecular structure of mycotoxins; change of multiple physical parameters leads to the destruction or modification of their carbon skeleton, resulting in the removal of origin mycotoxins. On the other hand, for chemical treatments, most detoxifiers were aimed at the antifungal property, thus leading to the reduction of mycotoxins. Chemical reagents are too large of a group; some are broad antifungal agents, and some are specific, also with little certain microstructures to absorb mycotoxins. Unlike other emerging bio-sourced enzymes, physical and chemical detoxifiers were always the direct, simple, and broad ways to remove mycotoxins, or we can conclude that pretreatment of foodstuffs would always be these traditional ways to remove mycotoxins and protect food safety. Industrial production should be a processing chain, from treatment to the early generation and then to the final package and delivery; among these, before treatment, either the physical or chemical pretreatments show their indispensability in practical uses.

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