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A Review of Post-harvest Approaches to Reduce Fungal and Mycotoxin Contamination of Foods

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Abstract: Contamination of agricultural and food products by some fungi species that produce mycotoxins can result in unsafe food and feed. Mycotoxins have been demonstrated to have disease-causing activities, including carcinogenicity, immune-toxicity, teratogenicity, neurotoxicity, nephrotoxicity and hepatotoxicity. Most of mycotoxins are heat stable and cannot be easily destroyed by conventional thermal food processing or domestic cooking methods. Post-harvest approaches to prevent growth of mycotoxin-producing fungi and detoxify mycotoxins from contaminated food are important topics in food safety research. Physical, chemical and biological methods have been applied to prevent fungal growth or mycotoxin production, or to reduce mycotoxin content in the post-harvest period and contribute towards mitigating against the effects of mycotoxins on human health. This literature review aims to evaluate post-harvest approaches that have been applied to control both fungi growth and mycotoxin content in food and discuss their potential for upscaling to industrial scale.

Key words: Mycotoxin; Fungi; Contamination; Post-harvest; Food Safety; Anti-Fungal, Reduction, Prevention or Mitigation approaches.

Words: 13131

1 Introduction

Agricultural and food products can be contaminated by fungi, most particularly during the post-harvest period. Some fungi can produce toxic metabolites, named mycotoxins, which have a negative impact on the safety of food and feed. Dietary exposure to mycotoxins cause health issues due to their biological activities which include carcinogenicity, immune-toxicity, teratogenicity, neurotoxicity, nephrotoxicity and hepatotoxicity (Dalié, Deschamps, & Richard-Forget, 2010; Jard, Liboz, Mathieu, Guyonvarc'h, & Lebrihi, 2011). Some of these toxicities can be acute (WHO, 2015, 2017), resulting in illness or death within a few days of exposure to heavily contaminated food. Meanwhile, mycotoxins can have cumulative effects at lower doses, resulting in chronic health effects that manifest over several months or years (Tola, Kebede, & Yildiz, 2016).

More than 100 fungi species have been found to produce over 400 poisonous metabolites (Jard, Liboz, Mathieu, Guyonvarc'h, & Lebrihi, 2011). The most common agricultural mycotoxins comprise aflatoxins (AFB_1, AFB_2, AFG_1, AFG_2 and AM_1), fumonisins (FB_1, FB_2), ochratoxin A (OTA), the trichothecene mycotoxins (type A: T-2 and HT-2, type B: deoxynivalenol (DON), nivalenol (NIV)), and zearalenone (ZEN), patulin (PAT) and egot

alkaloid. Minor mycotoxins include cyclopiazonic acid, sterigmatocystin, gliotoxin, citrinin and citreoviridin. Mycotoxins are produced primarily by *Aspergillus* sp., *Penicillium* sp., *Fusarium* sp. and *Claviceps* sp. (CAST, 2003; Hathout & Aly, 2014; Petruzzi et al., 2014; Schaarschmidt & Fauhl-Hassek, 2018).

Mycotoxin producing fungi are prevalent worldwide. According to recent report published in 2011, more than a quarter of the world's agricultural products are contaminated by mycotoxins at levels above the European Union (Table 1) and *Codex Alimentarius* limits (Jard, Liboz, Mathieu, Guyonvarc'h, & Lebrihi, 2011). Moreover, a more recent report indicates that mycotoxins are detected in 60–80% of agricultural products. The increase is likely due to a combination of the improved sensitivity of analytical methods and impact of climate change (Eskola et al., 2019). Moreover, more than 50% of food products are showing co-occurrence of more than one mycotoxin (BIOMIN, 2015). Mycotoxin contamination may occur during pre- and/or post-harvest periods. The occurrence of mycotoxins in different crop products is shown in Table 1. It appears that cereals (such as wheat, maize, rice, barley and sorghum) are the most commonly contaminated products, although mycotoxins can also be found in animal products (meat, eggs and milk), pulses, oilseeds, dry fruits and nuts. The most important agricultural pathogens are *Aspergillus*, *Fusarium* and *Penicillium* sp. *Aspergillus* sp. exists in warm (25 to 42°C) environments, which can be humid or dry (even down to -35 MPa water potential). These conditions are common in soil, food storage areas and manufacturing facilities (Klich, 2007; Tola, Kebede, & Yildiz, 2016). In *Aspergillus* sp., the production of aflatoxins is related to spore production (Klich, 2007; Tola, Kebede, & Yildiz, 2016). In temperate regions *Aspergillus* sp. also contributes to OTA production. *Penicillium* sp. can produce ochratoxins at temperatures as low as 5℃ (Tola, Kebede, & Yildiz, 2016).

As some mycotoxins are highly toxic, maximum limit (MLs) standards have been established to protect the consumers' health. In the early 21th century, approximately 100 countries in the world (covering about 85% of inhabitants) have set MLs to regulate the maximum amount of mycotoxins permitted in human and animal feed (van Egmond, Schothorst, & Jonker, 2007). The MLs of main mycotoxins set by the European Commission are shown in Table 1. However, these limits exert an impact on the agricultural export market, where least contaminated crops are exported to generate income, while more contaminated foods may be traded in the producing country, especially in low income countries where regulations are poorly enforced. As a result, it is critical for the food and economic security of low income countries to reduce fungal and mycotoxin contamination of foods.

Because of the different distinct hazards caused by fungi (microbiological) and toxins (chemical), the risk control strategies should be addressed simultaneously and where possible synergistically. Prevention of fungal growth is usually considered as an early step during production and post-harvest storage. If fungal growth cannot be avoided, approaches to de-contaminate the food of the toxin through processing must be considered.

This is a comprehensive review of post-harvest approaches that have been applied to reduce fungal growth and mycotoxin contamination in foods. The review includes a comparative evaluation of the efficacy of different approaches, including physical, chemical, biological and their combination, on fungal growth and mycotoxin content. The review discusses the

feasibility of these different approaches to be upscaled from laboratory to industrial scales within different food systems.

2 Control of fungal growth and prevention of mycotoxin production

The most effective way to reduce the mycotoxins in the food chain is to prevent the fungus growing in the first place, and if fungi do happen to be present in the food, then to prevent the toxin from being produced. A range of physical, chemical and biological approaches have been applied, both at industrial and laboratory scale.

2.1 Physical approaches

2.1.1 Temperature and humidity control

Storage of crops causes a mini ecosystem containing the biotic factors (crops, microorganisms, etc.) and abiotic factors (water, air, temperature, etc.) suitable to fungal growth (W. X. Peng, Marchal, & van der Poel, 2018). Similar to other living organisms, fungi require water and an optimal temperature to survive and thrive. Moisture content and storage temperature can be controlled to be outside of the microorganisms' optimum to reduce metabolic activity and decreased growth. Moreover, water content and temperature are one of the easiest factors to control during food storage, at both industrial and domestic scale. Although both relative humidity (RH) and moisture content (MC) are used to reflect the water content of food, it is better to use equilibrium RH, because the impact of equilibrium RH on spoilage organisms is consistent across different foods, regardless of their composition (Bradford et al., 2018). When the equilibrium RH is below 65%, microorganisms stop growing, meaning food is safe for at least one year of storage at ambient temperature. Storage temperature can also contribute to crop longevity (Bradford et al., 2018). In stored rice, both raising temperature (10 to 40℃) and RH (12 to 98%) significantly increased the growth of both *Aspergillus* sp. and *Penicillium* sp. by about 4 to 6 log colony forming units per gram (CFU/g) from about 3.8 log CFU/g. According to the result of multiple linear regression analysis, changing one unit of temperature resulted in stronger impacts on fungal populations than changing humidity (Mannaa & Kim, 2018). Additionally, Choi et al. (2015) showed that both 21℃ with 97% humidity and 30℃ with 85% humidity were associated with an increase of population of *A. flavus* by about 3 log CFU/g and the production of aflatoxins during the 120-day storage period, while when the rice was stored at 21℃ with 85% humidity, *A. flavus* population could be constant and no aflatoxins were produced. For *F. graminearum*, 97% humidity encouraged fungal growth from 2.5 to 4 log CFU/g at 21℃. When the humidity was reduced to 85%, *F. graminearum* and DON production could be controlled. Thus, dry (below 85% RH) and low temperature (below 21^{o}C) are good strategies for controlling fungal growth. However, these conditions may be difficult to maintain in warm and humid countries where a refrigerated and ventilated store may not be available. Moreover, vegetable foods tend to respire, causing moisture and temperature rises during post-harvest storage, and thus the environmental conditions must be regularly monitored.

2.1.2 Modified atmosphere treatment

Modified atmosphere (MA) approaches includes modification of the gas composition (e.g. O_2, CO_2, N_2) considering temperature, RH, MC and competing microorganisms (Magan and Olsen 2004), and is usually applied for fresh food preservation (Bouletis et al., 2016; de

Siqueira Mendes, Aguayo, de Oliveira Pessoa, Nastaro, & Kluge, 2019; Putnik et al., 2017). Fungi have a different sensitivity to atmosphere compositions. In general, high CO_2 and low O_2 content can contribute to inhibition of foodborne fungi. *P. roqueforti* and *A. flavus* could not grow in both 40% and 60% CO_2 environments balanced with N_2 and less than 0.5% O_2, but weakly grow (about 30mm in 30-day incubation) in 20% CO_2 (Taniwaki, Hocking, Pitt, & Fleet, 2009). MA at a large scale can be expensive, and there may be issues in displacing and replacing the gases during the storage period.

Modified atmosphere packaging (MAP) is a strategy that controls gas composition immediately surrounding the food within gas-impermeable packaging. Wheat and rye bread artificially inoculated with several fungi were packaged with 0%, 50%, 75% or 100% CO_2, 1%, 0.03% O_2 or in the presence of O_2 -absorber, and balanced with N_2. Notably, the gas composition would be changing during the storage of the bread. MAP was more effective against fungal growth on rye bread, as fewer fungi grew with the increase of CO_2. But for *P. roqueforti*, this main contaminant of rye bread was inhibited only in the presence of O_2 -absorber. For wheat bread, the most resistant to CO_2 was *P. commune* which could grow in 99% CO_2. *A. flavus* grew in the lowest O_2 concentration and 75% CO_2 (Suhr & Nielsen, 2006). So far, MAP has become a widely used way of food preservation because of its efficiency, convenience and safety. It is cheaper and easier that large scale MA as it is only necessary to fill the packaging with modified gas. MAP requires suitable packaging which is generally plastic-based, and will inevitably cause usage and disposal of a large number of plastic packaging.

2.1.3 Irradiation treatment

Irradiation of food for safety is based on the utilization of ionizing energy to inactivate microorganisms by changing their cellular structure or physiological functions, including DNA strand breakage, cell membrane rupture/leakage, or mechanical damage of cell walls (Calado, Venâncio, & Abrunhosa, 2014). The effectiveness of the irradiation method depends on many factors, such as irradiation dose, the microbial attributes (e.g. morphological structures, physiological stage) and the environmental condition of the irradiated materials (e.g. temperature, pH) (Magan & Olsen, 2004).

Aziz, El-Far, Shahin, and Roushy (2007) treated wheat, maize and barley collected from Cairo (Egypt) markets with gamma-irradiation and evaluated the occurrence of 4 *Fusariums* strains and FB_1 production. At 5 kGy, both *Fusarium* sp. counts and FB_1 production on barley samples were completely decontaminated. Same results could be observed on wheat and maize under 7 kGy irradiation. When the dose was below 5 kGy for barley or 7 kGy for wheat and maize, the growth of *Fusarium* sp. and production of FB_1 could be inhibited by up to 85% and 97% respectively. Similar observations were later reported by Akueche et al. (2012) who studied the effect of gamma-radiation treated on sesame grains sampled from Abuja (Nigeria) markets. In this study, 135 fungal strains including *Aspergillus* sp., *Penicillium* sp., and *Fusarium* sp. were isolated from non-irradiated sesame grains. But only 34 strains were found on grains after 3 kGy gamma-irradiation, and no of fungal species was found on grains irradiated between 6 to 15 kGy.

In an experiment aimed at preventing fungal infection in fruits and vegetables, fungi were usually artificially inoculated on the fruits or vegetables, and then treated with various doses of irradiation. In general, the results showed better fungal inhibition comparing to control

group with the increasing irradiation dose in peppers, oranges, broccoli, cabbage, tomato, bean sprout and papaya (Bari et al., 2005; Cia, Pascholati, Benato, Camili, & Santos, 2007; Jeong, Chu, Lee, Cho, & Park, 2016; Yoon et al., 2014). The irradiation could not only reduce the fungi, but also affected the production of mycotoxins. For instance, the total fungi isolated from packed hot peppers were 4.8×10^3 CFU/g, total *Aspergillus* count were 4.7×10^2 CFU/g and aflatoxin level was 1.14 ppb on average. After 2, 4, 6 kGy irradiation treatment, over 90% fungi could be reduced. But only a non-significant reduction of 6% on aflatoxin levels was observed at 6 kGy gamma radiation (Iqbal, Amjad, Asi, & Arino, 2012). In addition, as the fruits and vegetables tend to easily lose their sales value, the effect of irradiation treatment on product qualities should be considered. In a study of Bari et al. (2005), appearance, texture, color, taste and overall acceptability were used as sensory indicators to determine the quality of broccoli, mungbean sprouts, cabbage and tomato in both untreated and treated groups. Of all indicators, texture was the worst affected parameter after irradiation treatment in the four tested vegetables, and the sensory evaluation of other indicators gradually got worse with increasing dose (maximum 1.0 kGy). Despite this, with 1.0 kGy, less than 7 days storage was acceptable for each vegetable at refrigeration temperature.

The primary advantages of irradiation are non-residual chemicals and high efficacy, so that it can be considered as an environment friendly mycotoxin reduction approach. Nevertheless, the nutrient loss, high costs and secondary products of uncertain safety in treatment are not negligible as well (Calado, Venâncio, & Abrunhosa, 2014), added to the deterioration of sensory quality that can be caused by irradiation.

2.2 Chemical approaches

2.2.1 Control by chemical antifungal agents

In general, many antifungal agents are low-molecular-weight organic acids and their salts (Magan & Olsen, 2004), and some of them are applied as food additives (1333/2008, 2017). Marín et al. (2000) revealed that *Penicillium* sp. had the highest sensitivity to both 0.5 and 1.0 g/kg propionates than *Aspergillus* sp. and *Fusarium* sp. at 25℃ in culture medium. The efficacy of propionates was higher at 7 days rather than at 14 to 21 days. In another study, Valencia-Chamorro, Palou, Río, and Pérez-Gago (2008) screened 15 chemicals and their mixtures in hydroxypropyl methylcellulose-lipid edible composite films on the effects of fungal growth. Amongst the chemicals, sodium bicarbonate, potassium sorbate (2%), sodium benzoate (2.5%), sodium salt of methyl paraben (1%/1.5%), sodium salt of ethyl paraben (1%) and sodium salt of propyl paraben (1%) and the mixtures of potassium sorbate (1.5%) with sodium propionate (0.5%), sodium benzoate (2%) with potassium sorbate (0.5%) and sodium benzoate (2%) with sodium propionate (0.5%) displayed the inhibition on growth of *P. digitatum* and *P. italicum* at all inoculation concentrations (10^3, 10^4 and 10^5 spores/mL). The inhibitory effects were dose dependent. Sodium salt of methyl paraben at the concentration of 1.5% showed the best performance, while no synergistic effect could be found in the mixtures of two antifungal agents. This edible coating displayed potential application prospects. In a recent research, a novel material, zinc oxide slightly coated with sliver nanoparticles, was demonstrated to inhibit the growth of *A. niger* (Tornero et al., 2018). Coating is one of the popular methods to preserve fresh fruits and vegetables. The coatings inhibit respiration, delay softening and color changes via controlling the internal gas composition and water vapor (Conforti & Totty, 2007; Mehyar, El Assi, Alsmairat, & Holley,

2014). When fungal inhibitors are added into the coatings, the counting of not only mycotoxin producing fungi but also other spoilage microorganisms, can be significantly reduced. For example, Salas-Méndez et al. (2019) compared antifungal effect of control group, edible nanolaminate coating (synthesized by the aminolysis of polyethylene terephthalate) (NL) and nanolaminate coating with added an extract from *Flourensia cernua,* a Mexican endemic plant growing in arid and semiarid areas (NL+ FcE). Fungi could be found from the beginning of storage in control and NL group at 20ºC, while NL+FcE coating could prevent the fungal infection for 6 days. On the 15th day, the counting of fungi and yeasts in control group was about 1000 times those in NL+FcE group, and was about 100 times those in NL group. Nevertheless, in a report of Mehyar, El Assi, Alsmairat, and Holley (2014), the coating of date palm cultivar with pea starch + carnauba wax and zein protein + carnauba wax could only reduce fungi and yeast about 1 log CFU/g after 14 days, but the coatings lost their effect in third week at 25ºC. Antifungal agent treatment, with or without coating are low-cost and easy-used control approaches, but the safety of the remaining fungicide residues in the treated products is also a major concern and this has highlighted the necessity of using antimicrobial compounds that are safe to humans and animals. Antifungal agents also tend to lose their effectiveness over time, putting into question their application for large scale crop and food storage.

2.2.2 Photodynamic treatment

Photodynamic treatment is a method that utilizes the interaction of a non-toxic photosensitizer and a particular wavelength of visible light (Al-Asmari, Mereddy, & Sultanbawa, 2018). This approach is mainly used in oncology, ophthalmology and dermatology (Preuß et al., 2014). In recent years, the photodynamic treatment has been investigated for its antimicrobial properties, as the photosensitizer, induced by light of specific wavelength, generates cytotoxic substances that cause biochemical and functional disturbances of the cell membrane component and leads the damage to microbial cells (Al-Asmari, Mereddy, & Sultanbawa, 2018; Temba, Fletcher, Fox, Harvey, & Sultanbawa, 2016). Curcumin is one of the most common photosensitizers in photodynamic studies. In a study by Temba, Fletcher, Fox, Harvey, and Sultanbawa (2016), about three log magnitudes of *A. flavus* spores counts were reduced by 84 J/cm^2 irradiation at 420 nm with both 15 and 20 μM of curcumin. When 5 log CFU/mL of spores were spiked into whole maize kernels, 1.9 log CFU/mL of spores were decreased at 60 J/cm^2 light with both 25 and 45 μM of curcumin, while 2.8 log CFU/mL of spores were reduced in milled kernels under same conditions. In another study by Temba et al. (2019), the effect of pH and temperature on *A. flavus* elimination under the reaction condition of 100 μM curcumin stock solution with irradiation at 420nm wavelength at 60J/cm^2 was investigated. Compared to the non-illuminated group, the *A. flavus* spores in the illuminated group were about two magnitudes lower at pH from 1.5 to 9, and showed a sharp decrease at pH in both groups. Similar pattern could be found on hyphae reduction. In the temperature-depending assay, although the counts in non-illuminated group were still higher than those in illuminated group, temperature (from 15 to 45ºC) did not have significant influence on *A. flavus* spores and hyphae. In addition, about 66.7% of produced AFB_1 was not detected under the light treatment with curcumin stock solution. Njoki, Okoth, and Wachira (2017) reported 6 plants extracts (*Solanum aculeastrum, Syzygium cordatum, Prunus africana, Ocimum lamiifolium, Lippia kituiensis*, and *Spinacia oleracea*) could inhibit the

growth of colony of *A. flavus* 4 to 47 mm (up to 42%) at concentration of 450 and 600 mg/mL. However, when *A. flavus* were treated with the increasing treatment dose and time of visible light (420 nm), the fungi were inhibited up to 95% at same concentration of plants extracts. Preuß et al. (2014) synthesized new photosensitizers and observed the prevention of growth of *A. niger* and *P. purpurgenum*. Besides, the new synthesized photosensitizer inactivated germination of conidia. As a novel method, the photodynamic treatment shows potential to control mycotoxin producing fungi. However, current studies mainly focus on fundamental research at laboratory scale, while the future research could consider the safety of photosensitizers and photolysis products and the application of photodynamic treatment in real and large scale food systems.

2.2.3 Electrolyzed oxidizing water treatment

Electrolyzed oxidizing water (EOW) is obtained from electrolyzed NaCl solution, transforming water molecules and chloride ions into chlorine oxidants (Cl_2, HOCl/ClO−) that are show antimicrobial properties. EWO contains two types of water: strongly acidic EOW and neutral electrolyzed water (NEW). The antimicrobial effect mainly depends on the level of ·OH. The radicals can break the normal morphological structure of spores, and is closely related to the damage of conidium cell wall and membrane, which leads to the spores losing their normal function. NEW is non-toxic and safe to humans, it can be applied to fungi decontamination (Gómez-Espinosa et al., 2017; Guentzel, Lam, Callan, Emmons, & Dunham, 2010; Xiong, Liu, Liu, & Li, 2010). Okull and Laborde (2004) used EOW to inactivate 1 to 4 magnitudes of *P. expansum* spores depending on concentration and exposure time. In an apple infection test, the apples were inoculated with 10^6 CFU/mL of spores and treated with 50% and 100% EOW for 5min, and stored at 25ºC for 6d. In non-treated apples, once wounds were infected by spores, the decay was in evitable (100% incidence). But when treatments were applied, decay in apple were only 18.4% for 50% EOW and 10.2% for 100% EOW. Therefore, the use of EOW can be considered as a potential method in an apple cleaning system. Xiong, Liu, Liu, and Li (2010) compared the elimination of *A. flavus* by both EOW and acidic EOW. The results illustrated the population of spore survival treated by acidic EOW was 5.77 log conidia/mL, which was 1.48 log conidia/mL less than control group, and no spores could be found in EOW group. This because that EOW showed a stronger signal on ·OH level than acidic EOW. With the addition of mannitol (a radical scavenger) in reaction system, the survival population was increased, which also provided a strong evidence that ·OH played the most important role in the inhibition of *A. flavus* spores.

2.2.4 Plasma treatment

Plasma is an ionized gas, with zero net electrical charge, that can be induced in any neutral gas at particular pressure and temperatures conditions. Examples of natural plasma are sun and polar gases, whereas artificial plasma include dielectric barrier discharges plasma, microwave plasma, inductively coupled plasma, radio-frequency and commercial ozone (Misra, Yadav, Roopesh, & Jo, 2019). These plasmas could inactivate a variety of mycotoxin producing fungi on a range of foods, including fruits, vegetables, herbs, spices, cereals, nuts and meat products in seconds. However, the effect of plasma on food quality depends on the type of plasma, the duration of treatment and plasma intensity (Misra, Yadav, Roopesh, & Jo, 2019).

Among the cold plasmas, ozone is one of the best documented plasma on antifungal activity.

This strong oxidant can progressively oxidise unsaturated lipids in the microbial membrane or cellular proteins, leading to a leakage or rapid death of the cell (Freitas-Silva & Venancio, 2010). In addition, ozone can reduce conidia germination (Savi, Bittencourt, et al., 2015). *A. flavus* artificially spiked on wheat was reduced by up to 96.6% with the 60 µmoL/moL O_3 gas treatment for 120min and 100% with the same concentration for 180min (Savi, Souza, et al., 2015), *P. citrinum* behaved in a similar way, while *F. graminearum* was more sensitive to the same concentration of O_3 gas, inhibited by up to 96.81% in 30min and completely inhibited in 180min (Savi, Bittencourt, et al., 2015). Naturally occuring *Aspergillus* sp. and *Penicillium* sp. on rice could be reduced up to 70% in short-time treatment (30min) at 10 mg/L O_3 gas (Beber-Rodrigues, Savi, & Scussel, 2015). Moreover, O_3 treatment can decrease also mycotoxin production. In one of above studies, produced AFB_1 degraded 69.5% and 72.2% exposed under 40 and 60 µmoL/moL of O_3 gas respectively for 180min (Savi, Souza, et al., 2015). Similar findings were reported by Savi, Piacentini, and Scussel (2015).

Although O_3 showed the highly efficient inhibition of fungi, the oxidation could still result in some negative effects on food quality. Savi, Souza, et al. (2015) reported that wheat could still germinate normally after 60 µmoL/moL of O_3 gas treated for 120min. However, seed germination of wheat, maize and paddy rice was significantly affected (up to 67%) when the seeds were exposed under 4.8 mg/L for 12h (S. Wang, Liu, Lin, & Cao, 2010). For the unmilled productions, ozone did not show a large impact on the total phenol content, antioxidant capacity and odor, but the colour of some grains could fade to somewhat white color (Santos Alexandre et al., 2018; S. Wang, Liu, Lin, & Cao, 2010). In contrast, for flour products, ozonation resulted in the degradation of starch in whole wheat flour decreasing viscosity and swelling capacity and increasing the pasting temperature (Alexandre, Castanha, Calori-Domingues, & Augusto, 2017; Alexandre et al., 2019). The ozonation process also contributed to the peroxide value, and accelerated the oxidation of unsaturated fatty acids (Alexandre et al., 2019). Plasma treatment has good potential as a strategy to control fungal growth and aflatoxin production, but more research is needed to understand undesirable effects, including potential production of toxic compounds.

2.3 Biological approaches

2.3.1 Inhibition by microorganisms and their metabolites

In nature, fungi often share habitats with plants and with other microorganisms, resulting in competition for space and nutrients. Therefore, fungal propagation would be weakened if outcompeted by other microorganisms (Abbas, Zablotowicz, Bruns, & Abel, 2007; Appell, Kendra, & Trucksess, 2009; Cavaglieri, Andres, Ibanez, & Etcheverry, 2005).

This natural competition phenomenon has been exploited by researchers to control fungi and their toxins though the direct use of certain antagonist microorganisms as biocontrol agents (BCAs) or the use of microbial metabolites. Biological control of mycotoxin-producing fungi has been largely covered by several reports (Bhat, Rai, & Karim, 2010; de Medeiros et al., 2012; Kagot, Okoth, De Boevre, & De Saeger, 2019; Kong, 2017; Mannaa & Kim, 2016). It appears that biological control using microbial antagonists such as bacteria, fungi and yeasts could be a feasible substitute to reduce the use of antifungal chemicals. Great successes in reducing aflatoxin contamination in fields of different crops by 70% to 90% have been achieved by application of atoxigenic strains of *Aspergillus*. For the biocontrol of *Fusarium*

and its associated fusariotoxins, species of *Trichoderma*, *Bacillus* and atoxigenic *Fusarium* have being tested as the most promising candidates. However, questions remain about the ability of the atoxigenic fungi to produce other mycotoxins, or to potentially exchange genetic material and become aflatoxigenic. The low efficacy of many antagonists in the field conditions, despite showing high potential in the lab is another concern. Overall, it is suggested that integrated management approaches should be considered, involving a combination of multiple BCAs, with reduced fungicide application, in conjunction with good agricultural practices, and coupled with good postharvest management. In this section, we focus on the inhibition of fungal growth and toxin production by microbial and plant metabolites.

Fungal growth and toxin production may be affected by metabolites produced by other microorganisms. Some proteins and peptides inhibit the growth of microorganisms and are therefore termed as antifungal proteins (AFPs) and antimicrobial peptides (AMPs). AFPs from molds show a high stability to pH and proteolysis and exhibit a broad inhibition spectrum against filamentous fungi, and thus have prospects to control hazardous molds in fermented foods. An AFP isolated from *P. chrysogenum* (PgAFP) at 4.9 μg/mL significantly reduced the growth of *A. flavus* with over 50% inhibition rate (Delgado et al., 2015).

A compilation of the antifungal peptides produced by molds by Delgado, Owens, Doyle, Asensio, and Nunez (2016) showed 16 compounds, produced by *Aspergillus*, *Penicillium*, *Fusarium*, *Monascus*, and *Neosartorya* sp., with molecular weights (MW) between 5773 and 10 000 Da. A peptide (MW 2500Da) isolated from *Bacillus* strain B-TL2 had strong inhibitory activity against mycelial growth of *A. niger*, as well as *Bipolaris maydis*, *Alternaria brassicae*, and *Cercospora personata.* Moreover, this peptide showed thermostability, which means the peptide could keep 100% activity at 100℃ (B. B. Zhang, Xie, & Yang, 2008). In addition, four AMPs, namely PPD1 (FRLHF), 66-10 (FRLKFH), 77-3 (FRLKFHF) and D4E1 (FKLRAKIKVRLRAKIKL) at concentrations between 1 to 40 μg/mL reduced the aflatoxin production by *A. flavus* and *A. parasiticus* in a dose-dependent manner. At near minimum inhibitory concentrations (MIC) the AMPs inhibited aflatoxins, without hindering the growth of the fungi. An almost 99% inhibition of aflatoxins produced by *A. parasiticus*. *Parasiticus* was observed. *Conidiation* of the fungi was also negatively influenced by the peptides (Devi & Sashidhar, 2019). A peptide purified from *Lactobacillus plantarum* with amino acidic sequence SGADTTFLTK reduced by 73% the growth of *A. parasiticus* in liquid medium after 48 h incubation (Luz, Saladino, Luciano, Mañes, & Meca, 2017). Similarly, three newly identified peptides from Bacillus megaterium (L-Asp-L-Orn (D1O), L-Asp-L-Asn (D1N) and L-Asp-L-Asp-L-Asn (D2N)) at concentrations above at 0.32 mg/well significantly inhibit the growth of *A. flavus*, but without any effect on spore germination. At concentrations ranging between 0.04 and 0.64 mg/mL, the reduction of AFB_1 by the peptides was from 70% to 80% (Chen, Kong, & Liang, 2019).

Efforts are being made to elucidate the mechanism of inhibition of AMPs. A single peptide is often capable of more than one mode of action, depending on the target cell type, and the antifungal activities of peptides cannot be inferred from studies on their antibacterial activities. AMPs usually act via membrane permeabilization, while antifungal activity for these peptides is generally more complex and often involves entry of the peptide into the cell (van der Weerden, Bleackley, & Anderson, 2013). As evidenced by confocal microscopy and

quantitative RT-PCR (qRT-PCR), three peptides from *B. megaterium* D1O, D1N and D2N could spontaneously enter into the hyphae of *A. flavus* and inhibited conidiation and aflatoxin production, but did not inhibit hyphae vegetative growth and spore germination (Chen, Kong, & Liang, 2019). A more detailed mechanism was proposed by Devi and Sashidhar (2019), which shows that the AMPs, at concentrations near MIC, induced membrane permeabilisation, without inducing cellular leakage. The AMPs also show antioxidant properties which interact with oxidative stress and impair aflatoxin production. At molecular level, the AMPs were responsible of down regulation of the aflatoxin gene cluster '*aflR*' (a regulatory gene for aflatoxin biosynthesis), and the expression of downstream genes. Similarly, a decrease in the expression of manganese-superoxide dismutase (Mn-SOD) has been shown to be correlated to aflatoxin synthesis, was obtained in peptide-treated samples.

During food fermentation, some non-peptides metabolites have been shown to have antifungal activities. These compounds produced by lactic acid bacteria included organic acids, phenol compounds, hydroxy fatty acids, hydrogen peroxide and reuterin (Dalié, Deschamps, & Richard-Forget, 2010). For example, acetic and phenyl lactic acids produced by *L. plantarum* CRL 778, *L. uteri* CRL 1100, and *L. brevis* CRL 772 and CRL 796 displayed antifungal activity on *A. niger* (<40%), *Penicillium* sp. (40%-70%) and *F. graminearum* (>70%) isolated from contaminated bread. The effect of organic acids depends not only on the type of acid, but also on their concentration, the type of matrix, and pH of the matrix (Gerez, Torino, Rollán, & Font de Valdez, 2009). Selected *Lactobacillus* sp. (*L. fermentum* M107 and *L. fermentum* 223) and yeasts (*Hanseniaspora opuntiae* H17 and *Saccharomyces cerevisiae* H290) were used for to inhibit the growth of *A. flavus* S075, *P. citrinum* S005 and *Gibberella. moniliformis* S003 in cocoa bean fermentation. On average, *Lactobacillus* sp. (63% and 75% respectively) showed higher inhibition ability than yeast (25% and 31%), when they were cultural individually. Glucose, fructose, and citric acid in medium were converted to mannitol, acetic acid and lactic acid by *Lactobacillus* sp., whereas the glucose and fructose was metabolized to ethanol during culture. In the co-culture of *Lactobacillus* and yeasts, *A. flavus* S075 was inhibited completely after 10 to 14 days (Romanens et al., 2019). The antifungal interaction between fungi growth/mycotoxin production and lactic acid bacteria or yeasts was summarized by Hassan, Zhou, and Bullerman (2015) and Bourdichon et al. (2012). The application of AMPs and AFPs, as well as fermentation metabolites seems promising strategies for fungal and mycotoxin control. Further research is needed to elucidate the mechanism of action and potential negative effects of the microbes or microbial metabolites.

2.3.2 Inhibition by plant extracts

Higher plants can a produce a number of secondary metabolites that display wide biochemical and physiological functions (Prakash, Kedia, Mishra, & Dubey, 2015). A volatile substance containing secondary metabolites, obtained from distillation of plants is called an essential oil (EO). EOs have been used for antimicrobial and insecticidal applications in the pharmaceutical, cosmetic, agricultural and food industries (Bakkali, Averbeck, Averbeck, & Idaomar, 2008). The major compounds of EO are phenylpropanoids, phenolics, terpenoids, steroids, aromatic and alkaloids, whose content determine the properties of the EOs (Bakkali, Averbeck, Averbeck, & Idaomar, 2008; Prakash, Kedia, Mishra, & Dubey, 2015). The composition of EOs is highly variable and, depending on plant species, modes of extraction

and storage conditions. Different parts of one plant or even the same plant harvested from diverse regions or at different harvest time can vary in antifungal ability. Table 2 summarises and compares studies that studied the inhibition of mycotoxin-producing fungi by EOs. EOs from diverse plant species in eight countries showed inhibition effect from 58% to 100% under different concentrations. Leaf and aerial parts were the most common organs for extraction of EOs. As the EOs are at preventing fungi contamination, the safety assessment of EOs should be an important concern. In a number of studies, high LD_{50} values have been recorded, such as 11 mL/kg for *Ocimum gratissimum* (Prakash et al., 2011), 4 mL/kg for *Cinnamomum glaucescens* (Prakash, Singh, Yadav, Singh, & Dubey, 2013), 4.5 mL/kg for *Ocimum sanctum* L. (A. Kumar, Shukla, Singh, & Dubey, 2010), and 9 mL/kg for *Caesulia axillaris* roxb. (Mishra, Shukla, Singh, Prakash, & Dubey, 2012). Besides, the EOs of cinnamon, clove, lemon grass, oregano, thyme, nutmeg, and basil are confirmed as safe in America. In European countries, EOs components carvacrol, carvone, cinnamaldehyde, citral, p-cymene, eugenol, limonene, menthol, linalool, vanillin, and thymol are registered as flavour additives in foods (Prakash, Kedia, Mishra, & Dubey, 2015).

Apart from EOs, some plant AFPs and AMPs have also been identified (S. C. Park et al., 2017; Subramanyam et al., 2012; D. J. Yun et al., 1998). These components comprise defensins, lectins, chitinases, glucanases and other proteins obtained from seeds, bulbs, leaves, tubers, fruits, shoots, and roots (Yan et al., 2015). Both low molecular weight proteins and high molecular weight proteins could show fungal inhibition capability. For example, a 5.4 kDa highly homologous plant defensins peptide purified from *Phaseolus vulgaris* L. impeded the growth of *F. oxysporum* around paper discs containing this peptide (Chan & Ng, 2013). In the same way, a designated Chitinase A (Chit A) and Chitinase B (Chit B) of 28 kDa purified from maize seeds totally inhibited *F. oxysporum* (Huynh et al., 1992). A 35.7 kDa and 65 kDa lectin from seeds of *Archidendron jiringa* and *Pachira aquatic* respectively showed effective effect on the growth of *F. oxysporum* (Paiva, Vasconcelos, & Oliveira, 2014).

Plant antifungal metabolites are not limited to Eos, AFPs and AMPs. Polyphenols, flavonoids in particular, are a group of plant secondary metabolites that play important role on fungal defence (Bouarab-Chibane et al., 2019). The butanol extract and oxime derivative of fresh peppermint (*Mentha piperita*), which is rich in flavonoid, was found to inhibit the growth of *F. moniliforme* by (Ilboudo, Bonzi, Tapsoba, Somda, & Bonzi-Coulibaly, 2016). Butanol extract and oxime derivative at 5 mg/mL caused about 52% and 70% inhibition respectively. Conidial germination was delayed by the butanol extract by 1h compared with the control group, and less than 10% of spores germinated in total. Similarly, the oxime derivative group had less than 10% germinated spores at 2h, after which the quantity declined. In other studies, high-carotenoid content in maize could lead to low fumonisins and aflatoxins production by *Fusarium* sp. (Diaz-Gomez, Marin, Nogareda, Sanchis, & Ramos, 2016) or *Aspergillus* sp. (Diaz-Gomez, Marin, Nogareda, Sanchis, & Ramos, 2016; Suwarno et al., 2019) respectively. In a review of Atanasova-Penichon, Barreau, and Richard-Forget (2016), phenolic acids and tocopherols were mentioned as similarly active compounds.

The diversity of plant metabolites make plants promising sources of novel antifungal agents. Some of these can be extracted from agricultural by-products, making them potentially economically interesting. However, the variation in their composition may cause inconsistency in their performance. Purified compounds or synthetic mimetics could provide

more reproducible alternatives.

2.4 Combined approaches

Most approaches have limitations in terms of specificity to fungi and food matrices. For this reason, combinations of approaches have been tested by researchers, to offer an integrated management strategy that can target multiple microorganisms in various matrices.

The combination of MAP and antifungal additives can prolong the shelf life of food. For instance, pre-treatment with 3% potassium sorbate and 20% of ethanol solution decreased the incidence of molds and yeasts on table grapes by approximately 11%-30% higher than those only packed in MAP conditions (O_2:CO_2:N_2-6:5:89) at 4ºC until the end of shelf life. Meanwhile, 3000 ppm of citrus extract only caused a 9% decrease in the same system (Cristina, Annalisa, Amalia, Francesco, & Del Nobile, 2013). Similarly, the population of yeasts and molds on ready-to-cook poultry treated with 1.5% chitosan and 0.2% thyme extract under MAP conditions (30% CO_2 and 70% N_2) was 2.2 log CFU/g lower than that under the MAP only when stored at 4°C for 14d. The antifungal effect of chitosan and thyme was greater when used in combination compared to each individually (Giatrakou, Nizimani, & Savvaidis, 2010) .

Yoon et al. (2014) and Jeong, Chu, Lee, Cho, and Park (2016) used irradiation in combination with the chemical sodium dichloroisocyanurate (NaDCC) to reduce the activity of grey mold (*Botrytis cinerea*) and green mold (*P. digitatum*). Their results indicated that the decrease of quantity of grey mold relied on the increase of radiation (from 0.2 to 4 kGy) and increase in NaDCC (from 5 to 50 ppm) dose, but the great reduction (<5%) of green mold only occurred under the treatment of 0.4 kGy of gamma irradiation and 6 or 10 ppm of the NaDCC. Combining physical with chemical approaches appears to be effective at preventing fungal growth. More research is needed to understand the combined effects on a wider range of microbes and food matrices.

3 Reduction of mycotoxin content in contaminated food

The scale of food production makes control of fungal growth challenging. It is not always possible to prevent fungal growth or mycotoxin contamination. Therefore, approaches to remove mycotoxins from the edible part of the food must be considered.

3.1 Physical detoxification approaches

3.1.1 Cleaning, dehulling and milling

Sorting and cleaning are the most common and cost-effective mycotoxin removal processes. Matumba, Van Poucke, Njumbe Ediage, Jacobs, and De Saeger (2015) investigated the effect of sorting, flotation/washing or dehulling on the levels of 11 mycotoxins in white maize grown in Malawi. In general, hand sorting showed the greatest reduction of mycotoxins (more than 90%), followed by dehulling (more than 70%, except DON and AcDON). When the procedures were combined, less than 5% of mycotoxins could be detected. Similarly, it is reported that the level of aflatoxins, fumonisins, DON, NIV, and ZEN in washed food samples was lower than in original samples (Matumba et al., 2017; Tibola, Fernandes, & Guarienti, 2016; van der Westhuizen et al., 2011). According to Tibola, Fernandes, and Guarienti (2016), the lowest mycotoxin level could be obtained in milled flour products. Notably, the milling could cause a redistribution of mycotoxins in milling fractions. In general, lower mycotoxin

content are found in flour and semolina while the higher mycotoxins content are found in brans and flour shorts screenings These fractions were generally used for animal feeding (Cheli, Pinotti, Rossi, & Dell'Orto, 2013). An educational intervention trained women in Gambia to recognize and remove moldy groundnuts by hand sorting. The intervention resulted in a reduction of 42.9% AFB_1 (based on median AFB_1 levels at baseline and after hand sorting), and a reduction of 96.7% (based on the total AFB_1 in moldy and clean groundnuts), with a loss of only 2% of the groundnuts. By roasting the already clean sorted groundnuts, AFB_1 reduction of 39.3% was achieved (based on median levels) (Y. A. Xu et al., 2017). Due to the low cost and easy operation of sorting and cleaning, these procedures can be used not only before crop storage, but also during other processing operations and before food consumption. However, it is still necessary to consider the disposal of sorted contaminated seeds and waste water containing mycotoxin.

3.1.2 Heat treatment

The majority of mycotoxins are heat stable. Aflatoxins and OTA could be partially destroyed at the temperatures around 250℃ and 200℃ respectively. The complete degradation of fumonisins takes place at over 180℃ (Magan & Olsen, 2004; Vidal, Sanchis, Ramos, & Marin, 2015), and for DON degradation takes place at 210℃ (Milani & Maleki, 2014). In general, mycotoxin destruction is dependent on both the temperature and duration of exposure. For example AFB_1 and AFB_2, degradation in pistachio nuts was proportional to both temperature (90 to 150℃) and treatment time (30 to 120min) during roasting processing, although this degradation was more affected by temperature than by time (Yazdanpanah, Mohammadi, Abouhossain, & Cheraghali, 2005). In ground corn, Dupuy, Le Bars, Boudra, and Le Bars (1993) found a linear relationship between calculated half-lives of FB_1 and temperature, which were at 75, 100, 125 and 150, and for 8h, 175, 38 and 10 min respectively. For more efficient reduction of mycotoxins during food processing, high temperature can be combined with high pressure. Extrusion cooking is a food procedure that uses high temperature and high pressure to process foods in a short time, which usually applied in relatively dry viscous material (moisture contents around 20%), such as cereal grains, grits, and flours (Castells, Marín, Sanchis, & Ramos, 2006). In general, initial moisture content of food materials, extruded temperature, processing duration, screw speed and mycotoxins type are the main variables influencing the reduced efficiency of mycotoxins. In rice meal, aflatoxins were reduced by 51% to 95% during extrusion cooking. Broadly speaking, the longer the processing duration, the higher the reduction of aflatoxins content. In rice, 170℃ was the best temperature among three temperatures (140, 170, 200℃) for reducing AFB_1 and AFB_2, and no significant difference on AFG_1 reduction between 170℃ and 200℃ was observed, while AFG_2 was most reduced at 200℃ (Castells, Marín, Sanchis, & Ramos, 2006). For OTA in oat flakes, according to a central composite design analysis, the highest reduction of 28% could be obtained at 162℃, 30% moisture and 221 rpm of screw speed (Lee et al., 2017). Pleadin et al. (2019) compared the effects of different thermal treatment on reduction of DON and ZEN in cereals. The results showed the content of DON and ZEN only reduced by 11% in 30min by cooking at 96°C, while the DON and ZEN declined up to 40% and 46% when the roast temperature was increased to 220°C. The highest degradation of DON and ZEN were 75% and 80% by extrusion cooking (135-190°C).

3.1.3 Irradiation treatment

Ionizing radiation can not only inhibit growth and development of fungi, but also reduce some mycotoxins, and the effect is dose-dependent. In general, there is a positive correlation between irradiation dose and reduction effect in the same matrix (Herzallah, Alshawabkeh, & Fataftah, 2008; Jalili, Jinap, & Noranizan, 2012; Kumar, Kunwar, Gautam, & Sharma, 2012). Meanwhile, irradiation also shows diverse performance on mycotoxin detoxification between irradiation types. Kumar, Kunwar, Gautam, and Sharma (2012) obtained 93% of OTA reduction in aqueous coffee bean by gamma irradiation at 5 kGy. Herzallah, Alshawabkeh, and Fataftah (2008) achieved the destruction of about 30% of total aflatoxin and AFB_1 by microwave treatment at 2450 MHz and 1.45 kW for 10min. Sunlight (solar irradiation) reduced more than 60% aflatoxins under 30h exposure and about 40% aflatoxins under 3h exposure (Herzallah, Alshawabkeh, & Fataftah, 2008). Recently, electron beam irradiation (EBI) has been used for decontamination of ZEN and OTA in maize kernel and maize flour. At the dose of 50 kGy, the degradations of ZEN were approximately 60% and 71% for maize flour and maize kernel respectively, and those of OTA were about 60% and 73% respectively (Luo et al., 2017). PAT was successfully reduced using UV radiation. In a study on PAT degradation in apple juice or apple cider using UVC wavelengths, Zhu, Koutchma, Warriner, and Zhou (2014) found that UV exposure at 19.6, 84.3, 55.0, and 36.6 mJ/cm^2 resulted in 90% reduction of the toxin, with the order of efficiency of the three wavelength lamps were: far UVC (222 nm) > far UVC plus (282 nm) > UVC (254 nm). A non-significant increase in the L* (lightness) value and decreases in a* (redness) and b* (yellowness) values of the juices treated with 222 nm were obtained. The treatment also resulted in 36.5% loss of juice ascorbic acid. Assatarakul, Churey, Manns, and Worobo (2012) reported a reduction of PAT from 5.14% to 72.57% with UV exposure, ranging from 14.2 mJ/cm^2 (one pass) to 99.4 mJ/cm^2, respectively, from an initial PAT contamination of 1,000 ppb. The UV treatment did not significantly change titratable acidity and ascorbic acid of the juice, but there was modification of the pH, the degrees Brix and in the sensory perception for the finished apple juice. In a similar study, Kim, Shukla, Oh, Chung, and Kim (2018) observed that in PAT-spiked apple juice samples that were UV-irradiated at a range of 200–280 nm for different time intervals, PAT levels reduced from 94.11 μg/L to 69.28, 54.55, and 5.92 μg/L after 5, 10, and 30min, respectively. After 30 min of UV exposure, PAT was not detected in spiked apple juice samples. However, UV irradiation reduced the yellowness (b∗) of the apple juice.

The matrix is another factor to reflect different detoxification efficiencies. With gamma radiation dose of 10 kGy, OTA in methanolic suspension demonstrated 24% lower reduction than same concentration of the toxin in water. OTA powder the lowest reduction effect by gamma radiation (Kumar, Kunwar, Gautam, & Sharma, 2012). At gamma irradiation dose of 1 kGy, compared to practical degradation in distilled water, the degradation rate of PAT in 1% organic acid solutions (malic acid, citric acid, lactic acid, acetic acid), 1% amino acid solutions (aspartic acid, serine, threonine and glutamic acid, histidine), ascorbic acid and ethanol ranged from 31% to 98%. Therefore, in irradiated apple juice, 33% of PAT retention was due to its main elements of organic acid (5.68% of malic acid) and amino acid (0.08% of serine and 0.06% of threonine) (H. Yun et al., 2008). In another study, however, the detoxification of ZEN between distilled water and all orange juice, pineapple juice and tomato juice had no significant difference. While, the optimized model analysed by response surface

methodology (RSM) concluded that the determinant factors of detoxification was both irradiation dose and ZEN concentration in fruits juices. It was noted that irradiation-mediated detoxified ZEN showed lower toxicity than non-irradiated ZEN in cell line models. Furthermore, to assess the quality of fruit juices, the sensory profile, total phenolic content, total flavonoid content, total antioxidant activity and acidity were taken into account. In three fruit juices, the values of every parameter slightly decreased with increasing irradiation dose of 2.5, 5 and 7.5 kGy, while 10 kGy of irradiation had significant deterioration on quality parameters. Overall, irradiation with certain dose range could be used to reduce toxin content of fruits juices (Kalagatur, Kamasani, & Mudili, 2018).

When the irradiation is applied on foods, the primary reaction is the ionization of water, which decomposes the water molecules into positively charged water radicals and negatively charged free solvated electrons. Next, the water radical is split into hydroxyl radicals and hydrogen ions. The reaction ends until forming the final products of hydrated electrons, hydroxyl radicals, hydrogen ions, and hydrogen atoms. The radicals can be added into double bonds of mycotoxins, such as aromatic rings, heterocyclic rings and lactone rings, which leads to lower the mutagenicity and toxicity of mycotoxins (Di Stefano, Pitonzo, Cicero, & D'Oca, 2014; Jalili, Jinap, & Noranizan, 2012). Irradiation looks a promising approach to reduce mycotoxins content is fruit juices. Other matrices, including dried products, need to be considered and the degradation products assessed for their toxicity. Further development to prevent quality deterioration as a result of irradiation is nescessary.

3.2 Chemical detoxification approaches

3.2.1 Adsorption by chemical adsorbents

Some chemicals form weak interactions with mycotoxins due to their characteristics including polarity, solubility, molecular size, shape, surface area and, in the case of ionized compounds, charge distribution and dissociation constants (Jard, Liboz, Mathieu, Guyonvarc'h, & Lebrihi, 2011; Sabater-Vilar, Malekinejad, Selman, van der Doelen, & Fink-Gremmels, 2007; Sun, Song, Wang, Wang, & Zheng, 2018), causing adsorption between adsorbents and mycotoxins. Hydrated sodium calcium aluminosilicates (HSCASs) are one of the most popular clay-based adsorbents, obtained from natural aeolite (Şişman, 2006). The adsorption of pyrophyllite-type HSCAS, usually occurs in either or both octahedral and tetrahedral layers (the structure can be found in El Gaidoumi et al. (2019)) causing weak bonds of exchangeable cations in interlayer positions (Aly, Abdel-Galil, & Abdel-Wahhab, 2004). Apart from HSCAS, there are many other adsorbents, displaying diverse adsorption ability, shown in Table 3. These adsorbents included clay, activated charcoal, esterified glucomannan, cholestyramine and other modified polymers, showing 17% to 100% adsorption of AFB_1, FB_1, DON, ZEN, OTA and T-2 in liquid environments. There is no doubt that adsorbent adsorption is one of the most economical methods in mycotoxin reduction. Nevertheless, the safety of the absorbent materials, removal from foods and disposal of adsorption chemicals and adsorbent-mycotoxin complex are still under question. Some chemical adsorbents have been forbidden as detoxification materials in food industry by the European Union (Jard, Liboz, Mathieu, Guyonvarc'h, & Lebrihi, 2011).

Chemical adsorbents find more practical applications in mycotoxins detoxification of animal feeds. As a source of animal protein (milk, meat, eggs), the contaminated livestock products

can result in direct or indirect risk to human health (Halász, Lásztity, Abonyi, & Bata, 2009). For example, AFB_1 can be converted into aflatoxin M_1 (AFM_1) in cattle bodies, which is secreted in milk and consumed by humans, especially children (W. X. Peng, Marchal, & van der Poel, 2018). Adding additives into fodder is a low-cost and user-friendly detoxification method in animal feeding, and has been used in practical production. These additives mainly include aluminosilicate clays (with or without organic acid) and montmorillonite (Table 3), which are not always appropriate for human foods (Kolosova & Stroka, 2012). Although some in vivo studies have shown that the feeding additives decreased the impact of mycotoxins on growth and did not increase the toxicity in animals, adding additives could still cause the loss of essential nutrients and decline in growth performance to some extent. Thus, additives are not recommended for extensive use (Kolosova & Stroka, 2012).

3.2.2 Alkaline/acid treatment

Many major toxins are unstable in alkaline environments. Researchers have worked on the effect of common alkaline reagents on mycotoxin reduction. $Ca(OH)_2$, NaOH, KOH and $NaCO_3$ were found to reduce DON, ZEN, aflatoxins, OTA (Jalili, Jinap, & Son, 2011). In alkali treatment, ammoniation is one of the best documented methods of reducing toxins. So far, it has been demonstrated that ammonia could reduce almost all aflatoxins (Brekke et al., 1977), including 45% of FB_1 (Norred, Voss, Bacon, & Riley, 1991) and 64% of ZEN (Bennett, Shotwell, & Hesseltine, 1980). This treatment was more widely used in animal feeding from last century. In the 1970s, 1.5% ammonium hydroxide was added into aflatoxin-contaminated maize basal diet of rainbow trout, which caused the detoxification of aflatoxin in diet and decreased of hepatocarcinogenicity in rainbow trout (Brekke et al., 1977). Later, in the 1990s, Bailey, Price, and Hendricks (1994) reported that ammoniated aflatoxin-contaminated cottonseed, a kind of cattle feedstock, led to a 94% reduction in the content of AFB_1. When the rainbow trout (*Oncorhynchus mykiss*) ate the dried milk from the cattle fed by treated cottonseed meals, the incidence of hepatic tumors decreased by around 40%. Into the 21st century, ammonia vapor was used in decontamination of broiler chick diet. Broilers fed diets containing aflatoxin showed the high mortality rate (about 30% in 6 weeks) during the rearing period. Chicks fed ammonia-treated maize did not show significant differences on mortality rate, dietary intake, body weight gain, and feed conversion ratio of chicks (Allameh et al., 2005). Ammonia treatment did not significantly affect the detoxification of FB_1 in maize meal under air condition (Norred, Voss, Bacon, & Riley, 1991). This may be because ammonia could directly attack the lactone ring of aflatoxins and retain the difuran moiety, but had no direct reaction sites in FB_1 (Karlovsky et al., 2016; Norred, Voss, Bacon, & Riley, 1991; Temba et al., 2016).Furthermore, DON (Fig. 1) has been found to be mainly degraded to norDON A, norDON B, and norDON C (Fig. 2) in alkaline environments. These degraded compounds could be isolated from NaOH solution (75°C, 60min) and other processed samples, and have been shown to be less toxic than original DON. Other 4 new compounds, norDON D, norDON E, norDON F and 9-hydroxymethyl DON lactone (Fig. 2) were identified as degradation compounds (Bretz, Beyer, Cramer, Knecht, & Humpf, 2006). In many reports, alkaline ammonia treatment was mainly reported in the 1990s, and primarily used in animal feeding. This might be because the safety and applicability of alkaline ammonia treatment could not completely used in the food industry. However, in recent reports, baking soda has been shown to reduce the content of OTA in cereal-based foods. In a 85°C

direct steam injected process that exposes food to high temperature with high steam pressure, 19.8% of OTA in oat-based infant cereals was lost. In contrast, OTA reduced by 36.1% and 43.4% when 0.5% and 1% baking soda was added respectively (Lee, Gu, Ganjyal, & Ryu, 2019). Peng reported that a small decline of OTA (6.73% to 9.63%) occurred in Chinese fried bread sticks containing 0.4% soda during processing (C. H. Peng et al., 2015).

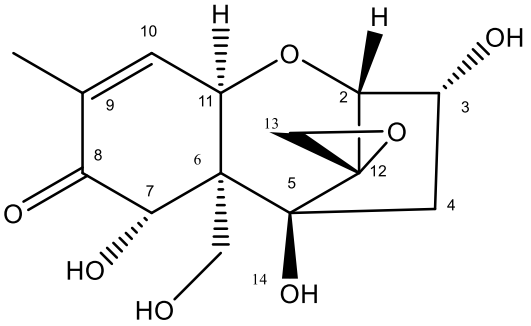


Fig. 1 Structure formula of DON (Wu, Kuca, Humpf, Klimova, & Cramer, 2017)

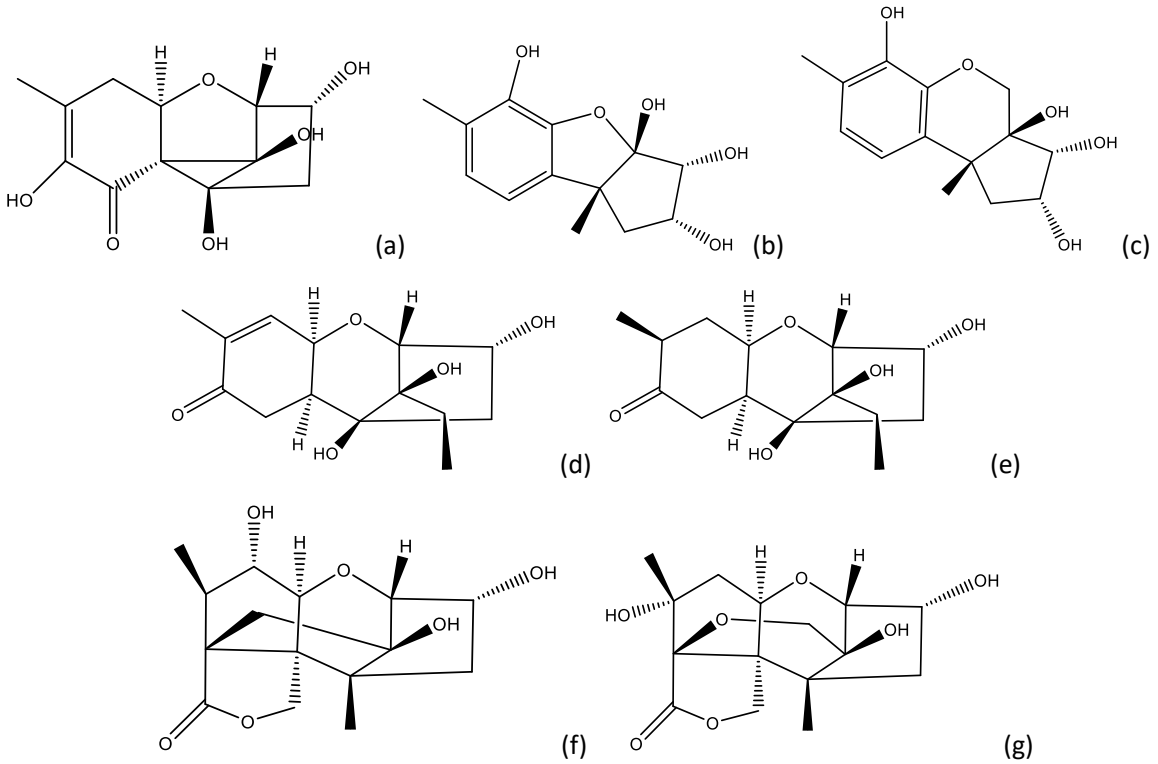


Fig. 2 Structure formula of norDON A (a), norDON B (b), norDON C (c), norDON D (d), norDON E (e), norDON F (f), and 9-hydroxymethyl DON lactone (g) (Bretz, Beyer, Cramer, Knecht, & Humpf, 2006)

Although the majority of mycotoxins are resistant to weak acids (Karlovsky et al., 2016), some acids also influence the presence of mycotoxins. Sulfuric acid, chloridric acid, phosphoric acid, benzoic acid, citric acid and acetic acid all displayed less than 30% reduction of AFB_1, AFB_2, AFG_1, AFG_2 and OTA in black and white pepper during washing, which was generally less effective than that in alkaline solutions (Jalili, Jinap, & Son, 2011). In another study, these five toxins were treated by 2% sodium hydrosulphite ($Na_2S_2O_4$) with atmospheric pressure (low pressure) and 100℃ for 30min or 1.5bar (high pressure) and 121℃ for 15min.

Except for AFB_2, other four samples under low pressure lost 64.8% to 83% of the toxin, and those under high pressure lost more than 96% (Jalili & Jinap, 2012). The use of 5% of both citric acid and lactic acid reduced DON about 20% to 40% in feeds soaked for more than 5h. Lactic acid showed the better performance than citric acid in this treatment (Humer et al., 2016). The detoxification of DON is considered to be due to the opening of the C12, 13-epoxy group (Fig. 1). In the extreme acidic environment (pH 1 to 2), DOM-1 (Fig. 3) might be degraded from DON (Wu, Kuca, Humpf, Klimova, & Cramer, 2017).

Sometimes, a combination of chemicals can reduce the level of mycotoxins. In the report of Rempe, Brezina, Kersten, and Danicke (2013), a mixture of methylamine, $Ca(OH)_2$ and sodium metabisulphite (2+4+1) caused the recession of 91% of DON and 79% of ZEN in naturally contaminated maize at 80°C. However, there is little evidence to show the safety of new derivatives produced from mycotoxins after treatment.

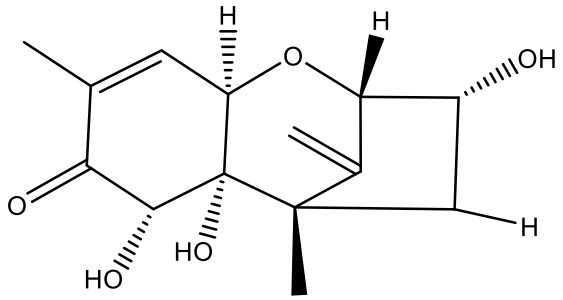


Fig. 3 Structure formula of DOM-1 (Wu, Kuca, Humpf, Klimova, & Cramer, 2017)

3.2.3 Plasma treatment

Plasma is an ionized gas, with zero net electrical charge, that can be induced in any neutral gas, and able to induce by innovative physical equipment at pressure and temperatures conditions (Misra, Yadav, Roopesh, & Jo, 2019). Many studies have suggested the mycotoxin detoxification effect of plasma. For instance, the effect of cold atmospheric plasma on aflatoxin contamination in both solution matrix (liquid) and hazelnuts matrix (solid) was evaluated by Siciliano et al. (2016). In this study, gas composition (proportion of N_2 and O_2), power of the generator, exposure time and reaction matrix were factors tested on detoxification efficiency. Among them, the power and exposure time were inversely proportional to aflatoxin loss. Besides, gas mixture with more N_2 and liquid matrices were more conducing to aflatoxin degradation. When AFB_1, DON and NIV were exposed to self-designed microwave-induced argon plasma system, the decrease of these toxins was significantly time-dependent, with complete degradation in 5s (B. J. Park et al., 2007). Ozone has the ability to degrade mycotoxins as well. 15min treatment by ozone on wheat bran contaminated with DON and ZEN caused approximately 29% and 52% degradation respectively, and no significantly difference in longer treatment times. Notably, ozonisation protected the quality of wheat bran at the greatest extent by preserving total phenolic compound content and antioxidant activity (Santos Alexandre et al., 2018). It was mentioned in the review of Misra, Yadav, Roopesh, and Jo (2019) that the plasma degrades mycotoxins by direct interaction of free radicals (e.g. O•, OH•) of plasma with the mycotoxin structure. With AFB_1 (Fig. 4), the degradation is trough epoxidation and oxidation by introducing water molecule, hydrogen atom, aldehyde group or hydroperoxyl radical (HO_2•) and leading the breakdown of C8 to C9 double bond of the dihydrofuran rings. Meanwhile, the toxicity and

carcinogenicity of AFB_1 would be reduced because of the loss of terminal furan ring.

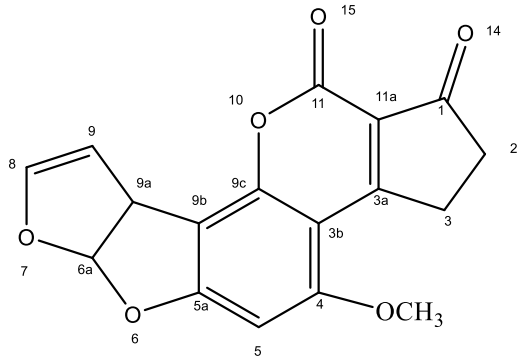


Fig. 4 Structure formula of AFB_1 (Luo et al., 2014)

Ozone was also used in the degradation of mycotoxins. For instance, highest reduction (48% and 64.3% respectively) of total aflatoxins and DON in soft wheat grains occurred at a concentration of 60mg/L for 300min (Trombete et al., 2017). ZEN in whole wheat powder quickly reduced by 62.3% in first 20 min at the condition of 51 mg/L of ozone (Alexandre et al., 2019). 15min-treatment by ozone on wheat bran contaminated with DON and ZEN caused approximately 29% and 52% degradation respectively, and no significantly difference in the longer treatment times. Notably, ozonisation protected the quality of wheat bran by keeping total phenolic compound content and antioxidant activity (Santos Alexandre et al., 2018). The effectiveness not only depends on exposure time and gas concentration, but also the physical characteristic of samples, moisture content and processing method (Trombete et al., 2017). L. Wang et al. (2016) showed that ozone treatment at same concentration was more effective in the flour than whole wheat with increasing of ozone concentration (from 0 to 100 mg/L), suggesting penetration into the kernels is not effective. Meanwhile, in the same study, higher moisture content (20.1%) of both whole wheat flour and wheat kernels showed greater degradation of DON (about 75% and 60% respectively), as high moisture content might promote oxidation power of ozone and its penetration ability. Similar result could be found in Alexandre, Castanha, Calori-Domingues, and Augusto (2017) study as well. S. Wang, Liu, Lin, and Cao (2010). They compared the degradation of AFB_1 by a dry method which involved delivering the O_3 gas to cereals, compared to an aqueous method which involved soaking cereals into ozone solutions and a semi-wet method which involved pumping ozone-rich steam into cereals. The results indicated that the ozonation reaction in aqueous or semi-wet conditions showed better effect than the dry method. The most effective reduction method for paddy rice and maize was semi-wet method, which reduced toxin content by about 92% and 85% respectively, while the aqueous method displayed the best performance on AFB_1 degradation (about 93%) in wheat.

Ozone preferentially attacks the unsaturated compounds in an electrophilic attack mechanism (Freitas-Silva & Venancio, 2010). The major mycotoxins including aflatoxins, FB_1, OTA, ZEN, DON and PAT could be degraded rapidly, within minutes. After ozone treatment, none of the by-products of OTA, ZEN and PAT could be detected by UV or fluorescence detector. However, a larger fraction of polar compounds were formed from ozonized AFB_1, and FB_1. For DON, ozone attacked at the C9 to C10 double bond (Fig. 1) with two additional atoms of oxygen but kept the rest of molecule (McKenzie et al., 1997; Young, Zhu, & Zhou, 2006). It was mentioned in the review of Misra, Yadav, Roopesh, and Jo (2019) that plasma interacts

with mycotoxins via free radicals (e.g. O•, OH•). With AFB_1 (Fig. 4) for example, the degradation is through epoxidation and oxidation by introducing water molecule, hydrogen atom, aldehyde group or hydroperoxyl radical (HO_2•) and leading the breakdown of C8 to C9 double bond of the dihydrofuran rings. Meanwhile, the toxicity and carcinogenicity of AFB_1 would be reduced because of the loss of terminal furan ring. In bioassay, apart from FB_1, all of treated aflatoxins, OTA, ZEN and PAT were not found to affect the activity of *Hydra Attenuate*, but treated FB_1 still kept the toxicity (McKenzie et al., 1997). In the induced toxicity assay of Caco-2 cells, ozone treatment weakened the cellular metabolic disorder by DON derivatives, but no impact on latent inflammation and oxidative stress effects, which shows some of the non-negligible toxicity of ozonised DON (Y. Xu et al., 2019). It is noteworthy that low O_3 concentration (below 0.05 ppm) had an enjoyable odor, while, when the concentration were above 0.05 ppm, O_3 affected human eyes and respiratory systems, which might be related to premature death, heart attack, bronchitis, asthma, and other cardiopulmonary problems (Jian, Jayas, & White, 2013). Therefore, when considering the application of ozone in cereal storage, attention should be paid to the harm caused by ozone to workers and the natural environment. Plasma, and in particular ozone, are effective at reducing mycotoxin content in foods. However, the toxicity of degradation products and impacts of ozone directly on human health need to be further considered.

3.2.4 Neutral electrolyzed oxidizing water (EOW)

Neutral electrolyzed oxidizing water is also an aflatoxin detoxifying substance. One view was that aflatoxin detoxified by hypochlorous acid from EOW eliminated the toxicity of double bond in the terminal furan ring and converted it to 8-chloro-9-hydroxy-aflatoxin B_1 (Fig. 5) (Escobedo-González et al., 2016). The derivative was shown to have significantly lower cytotoxicity and genotoxicity effects *in vitro* in a HepG2 cell model (Jardon-Xicotencatl, Díaz-Torres, Marroquín-Cardona, Villarreal-Barajas, & Méndez-Albores, 2015; Sakudo, Toyokawa, Misawa, & Imanishi, 2017). There was an ameliorative effect of EOW on the health and performance of turkeys fed on de-contaminated feed (Gómez-Espinosa et al., 2017).

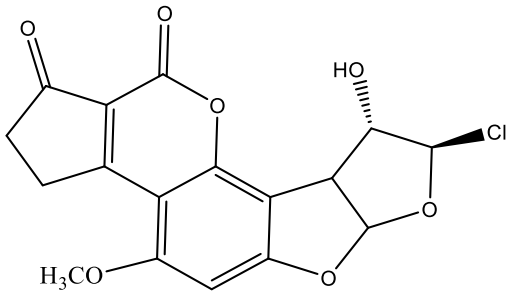


Fig. 5 Structure formula of 8-chloro-9-hydroxy-aflatoxin B_1 (Escobedo-González et al., 2016)

3.3 Biological detoxification approaches

3.3.1 Metabolite degradation

Biological enzymatic degradation reactions include acetylation, glucosylation, ring cleavage, hydrolysis, deamination, and decarboxylation caused by extra - or intra-cellular enzymes produced from bacteria and fungi (Hathout & Aly, 2014). In a report of Guan et al. (2008), *Stenotrophomona smaltophilia* was isolated from a selective medium containing coumarin as

the only carbon source and displayed reducing ability towards AFB_1 (82.5%) at 37℃ for 72h. After treatment of factors that could affect the enzymatic activity, reaction efficiency significantly drops, which indicated that reduced AFB_1 was produced by enzymatic degradation. Microbial species with similar functions were listed by Hathout and Aly (2014), including *Bacillus* sp., *Brevibacterium* sp., *Eubacterium* sp., *Flavobacterium aurantiacum*, *Mycobacterium fluoranthenivorans*, *Myxobacteria* sp., *Pseudomonas* sp., *Rhodococcus erythropolis*, *Trichosporon mycotoxinivorans*, *Aspergillus* sp., and *Rhizopus* sp.. The degraded toxins covered all major mycotoxins. Besides, some enzymes have been found in mushroom showing the detoxification ability. Manganese peroxidase (MnP) purified from the mushroom *Pleurotus ostreatus* detoxified AFB_1 by 6% at 0.1 U/mL enzyme activity for 8h, and by 90% at 1.5 U/mL enzyme activity for 48h (Sayed, 2014). In a review of Jard, Liboz, Mathieu, Guyonvarc'h, and Lebrihi (2011), the multiple degradation pathways of each major mycotoxin has been summarized. In simple terms, AFB_1 (Fig. 4) lactone ring or difuran ring could be opened resulting in loss of the toxicity. OTA was degraded to OTα and phenylalanine (Fig. 6); while ZEN could be transformed into oxidised, hydroxylated and methylated compounds, gluco- or sulfo-conjugates and hydrolysed compounds. Detoxification of DON was by opening the 12,13-epoxy ring (Fig. 1), and formed de-epoxidised DON and 3-keto-DON (Fig. 8). FB_1 has been found to be converted into polyolamine (Fig. 9) by extracellular carboxylesterase. Most degradation products showed no toxicity. However, the produced α-zearalanone (classified as hydroxyl compound) was more toxic than the original compound (ZEN) (Fig. 7).

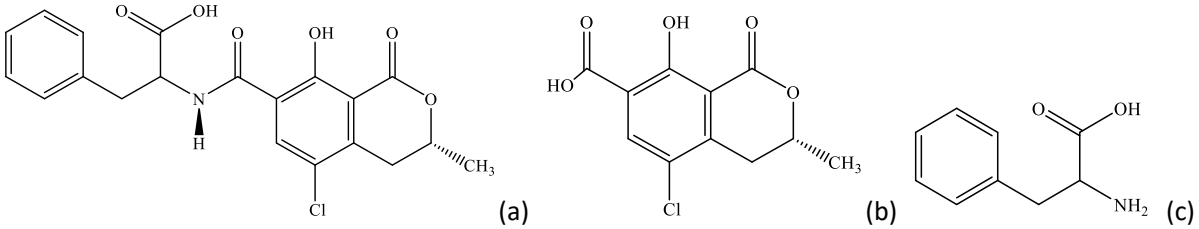
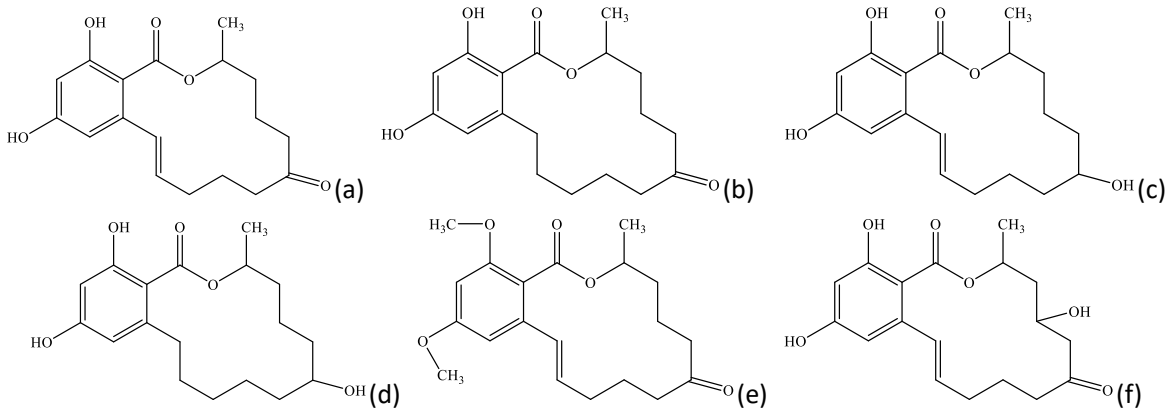


Fig. 6 Structure formula of OTA (a), OTα (b), andphenylalanine (c) (Jard, Liboz, Mathieu, Guyonvarc'h, & Lebrihi, 2011)



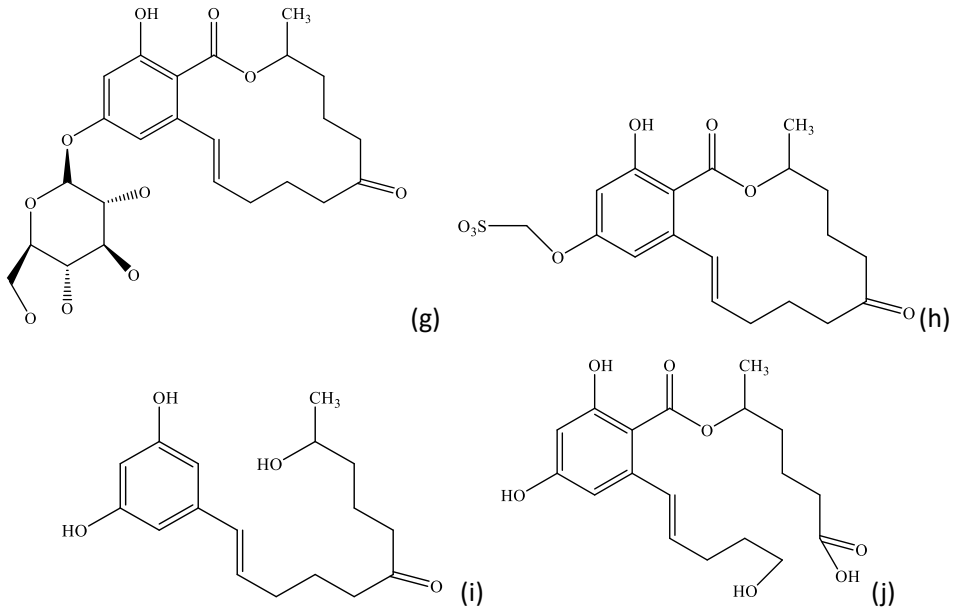


Fig. 7 Structure formula of ZEN (a), oxydised compounds: zearalanone (b), hydroxyled and methyl compounds: a-β zearalenol (c), a-β zearalanol (d), methoxy-ZEN(e), hydrocy-ZEN(f), gluco- or sulfo-conjugates: ZEN-4- β-glucopyranoside (g), ZEN-4-sulfate (h), and hydrolysed compounds: decarboxylated ZEN (i), Hydroxylated ZEN(j) (Jard, Liboz, Mathieu, Guyonvarc'h, & Lebrihi, 2011)

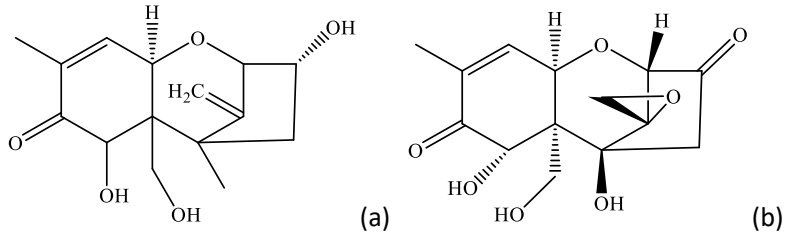


Fig. 8 Structure formula of de-epoxy DON(a) andketonic compound(b) (Jard, Liboz, Mathieu, Guyonvarc'h, & Lebrihi, 2011)

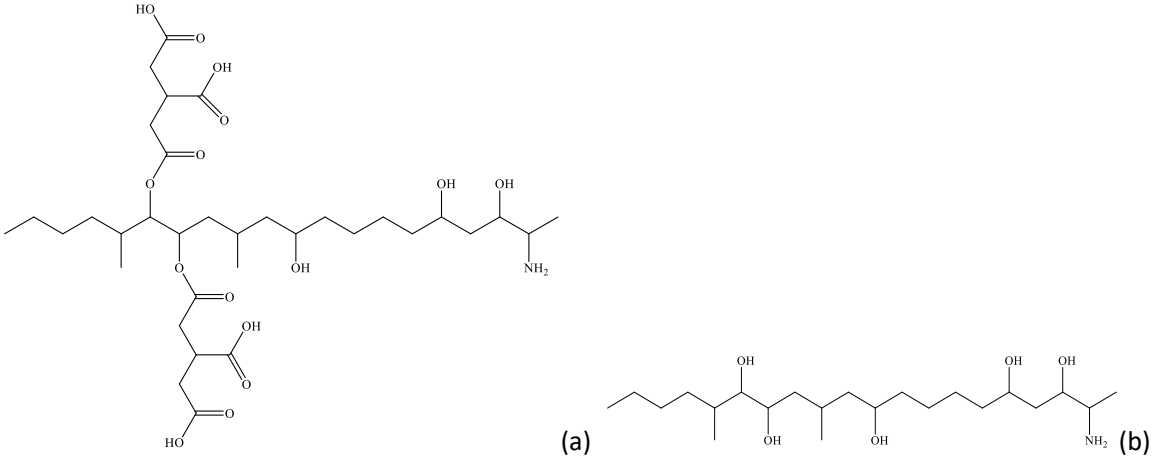


Fig. 9 Structure formula of FB_1(a) andpolyolamine (b) (Jard, Liboz, Mathieu, Guyonvarc'h, & Lebrihi, 2011)

3.3.2 Adsorption by biological polymer

Microorganism could not only degrade mycotoxins, but also remove them by adsorption to their cell walls. Most gram-positive bacteria and yeasts have demonstrated the adsorption capability. Recent studies are presented in Table 4. It could be observed that microorganism could adsorb 20% to 90% mycotoxins in different liquid food system or even body

environment. It has been suggested that heat-treated microorganisms (inactive microorganisms) showed similar or even higher mycotoxin adsorption capability when compared to live microorganisms in aqueous solution (El-Nezami, Polychronaki, Salminen, & Mykkanen, 2002; Turbic, Ahokas, & Haskard, 2002; Vosough, Sani, Mehraban, & Karazhyan, 2014). It was suggested that the adsorption was through physical adsorption rather than through a biological degradation mechanism. Thus, mycotoxins would not have the chemical reaction with binder during adsorption. This interaction usually occurs with the cell walls of microorganisms. For bacterial, cell walls or peptidoglycans (purified from cell walls) were isolated from lactic acid bacteria (Sreekumar & Hosono, 1998; Zhao et al., 2013; Zou et al., 2012), and were found to bind more toxins than cell pellets after removing the cell walls. The peptidoglycan played an important role in adsorption, and chemical methods can increase the number of adsorption sites and adsorption efficiency (e.g. acid-treatment, heat-treatment) (Zou et al., 2012). Haskard, Binnion, and Ahokas (2000) suggested that the addition of urea (an anti-hydrophobic agent) or organic solvent destroyed the cell wall-toxin complex, proving hydrophobic effect between the adsorption. For yeast, there were two layers in its cell wall, an inner layer of β-1,3-glucan and chitin and an outer layer of β-1,6-glucan with heavily glycosylated mannoproteins (Petruzzi et al., 2014). At the pH range of wine, mannoproteins had negative charges, and OTA carried a positive charge of the amine function (NH_3^+), so that cell wall and toxin could partially establish electrostatic and ionic interactions. Moreover, as a less polar mycotoxin, OTA could bind with hydrophobic surfaces of yeast cell wall through the phenol group and via interactions of two-π-electron orbital (Caridi, Galvano, Tafuri, & Ritieni, 2006). However, the adsorption was relatively weak, because toxin-microbe complexes would release toxins about 25-40% after washing with PBS buffer (Fernandez Juri, Dalcero, & Magnoli, 2015; Zou et al., 2012). This might indicate that the adsorption hardly occurs in nonpolar circumstances.

Most microorganisms with adsorption property belong to fermentation microorganisms, thus biological adsorption usually occurs in the process of fermentation in practical production. Food fermentation is a process of decomposing carbohydrates to alcohol or organic acids by microorganisms in aerobic or anaerobic environments, used in the production of fermented dairy products, wine, vinegar and bread-making. The raw food materials that are commonly used for fermentation cover most food groups including dairy, meat, fish, vegetables, fruits, legumes and cereals (Bourdichon et al., 2012), which could be contaminated by mycotoxigenic fungi or metabolic mycotoxins. Therefore, the mycotoxins are generally present in the fermentation process. The adsorption of mycotoxins by microorganisms during fermentation was summarized in Table 4.

Recently, more attention has been focused on the animal polysaccharides. Chitin, from shrimp shells, was investigated for its ability to bind with AFM_1. Assaf, El Khoury, Atoui, Louka, and Chokr (2018) demonstrated that chitin bound to 17% to 54% AFM_1 in PBS buffer, depending on concentration of both chitin and toxin and incubation time. High adsorption efficiency relied on high chitin concentration and long incubation. 0.15 g/mL of ground shrimp shell or 0.25g/mL of unground shrimp shell showed more than 90% of the adsorption rates when the incubation was up to 24h. By contrast, both ground and intact shrimp shell had lower adsorption rates than extracted chitin at same concentration and incubation time. However, the adsorption was not stable. After three times washing with buffer,

AFM_1adsorption rate decreased about 15% to 45% in different groups, which suggested the implication of electrostatic bounds (e.g. hydrogen bonds, Van der Waals interactions) in adsorption process.

Due to the presumed environmental and health friendliness of natural products (e.g. enzyme, microorganism cell wall), these approaches have attracted attention. However, biological control has shown lower effectiveness compared to other methods, and is also generally constrained to liquid media. Biological control tends to be more costly than physical and chemical approaches, and there is currently little evidence of the toxicity of enzymolysis products. However, reduction of mycotoxins during production of fermented products would permit the use of somewhat contaminated raw materials in their production.

3.4 Combined approaches

Pérez-Flores, Moreno-Martinez, and Méndez-Albores (2011) showed that the level of AFB_1 and AFB_2 in tortillas (a Mexican food) decreased 68% to 84%, according to different original concentration, by microwave treatment (1650 W, 2450 MHz, 5.5min) with added $Ca(OH)_2$ (0.5%). Kim, Shukla, Oh, Chung, and Kim (2018) reported that among food-grade additives (sodium bicarbonate, vinegar, mixture of sodium bicarbonate and vinegar, citric acid and baking powder), sodium bicarbonate yielded significantly higher PAT reduction in apple juice (from 94.11 to 7.55 μg/L), which was comparatively similar to 30min of UV irradiation. The authors suggested that since irradiation requires a special UV-irradiation apparatus and energy consumption, a food-grade additive sodium bicarbonate might be a useful alternative to UV radiation for reducing PAT content in apple juice samples. However, sodium bicarbonate treatment affected quality attributes including soluble solids, pH, and colour of apple juice. Nevertheless, the colour and door of juice treated with sodium bicarbonate could be recovered via addition of citric acid. The usage of some additives could contribute to the mycotoxin destruction in high-temperature processing. Sugars had a positive effect on FB_1 reduction of maize muffins baked at 200℃ for 30min. In this processing, the influence of glucose (40%) on the decrease of FB_1 was greater than that of fructose (27%) and sucrose (28%), and the effect of glucose concentration was more significant, from 40% reduction for 0.075g glucose/g maize meal to 52% reduction for 0.3 g glucose/g maize meal (Castelo, Jackson, Hanna, Reynolds, & Bullerman, 2001). Castelo, Jackson, Hanna, Reynolds, and Bullerman (2001) showed that when grits with added sugars of different concentration (2.5% and 5%) were extruded at a screw speed of 80, 100 or 120 rpm, the amounts of FB_1 remaining were around 40% to 80% at 140℃. 10% glucose with 40 rmp of extrusion at 160℃ led to about 90% reduction of FB_1, which was about 20% higher than the FB_1 treated without glucose (Voss et al., 2011). In another extrusion study with conditions of sample moisture (15% or 30%), screw speed (120 rmp), temperature (150℃ or 180℃) with or without 1% sodium metabisulphite addition, DON was significantly reduced (>95%) in maize flour treated under every condition, but AFB_1 content was not greatly affected (10% to 25%). Compared to glucose, sodium metabisulphite did not show a significant contribution to the reduction of both DON and AFB_1 (Cazzaniga, Basílico, González, Torres, & De Greef, 2001).With the addition of 30 mL of lemon juice and 6 g of citric acid, AFB_1 deceased up to 93.1% in 50 g pistachio nuts. When lemon juice and citric acid reduced to 15 mL and 2.25 g respectively, only 49.3% of AFB_1 could be detected (Rastegar et al., 2017). Furthermore, adding baking

soda under twin-screw extrusion could contribute to the reduction of OTA in oat-based food, and the degree of content reduction improved form about 40% to 65% with the increase of added soda from 0 to 1%. On the contrary, the baking soda did reduced OTA by a modest 10% in rice-based food (Ryu, Kowalski, Ganjyal, & Lee, 2019). The degradation of PAT with added ascorbic acid was predicted by nonlinear Weibull model to be higher than that without ascorbic acid, and the degradation increased with the raising of temperature. This might because the oxidized ascorbic acid formed free radicals, so that could attacked the lactone structure of PAT (Kokkinidou, Floros, & LaBorde, 2014).

The exploration of combined treatments is to pursue higher removal efficiency, taking advantage of the additional effect of integrated management. This is becoming a trend gradually. The combined treatments do reduce toxin contamination to a greater extent, and they can be better adapted to different food matrixes.

4 Evaluation of the feasibility of the approaches to be applied to food production

Several reports have shown the potential of various methods for preventing and reducing fungi or mycotoxins in foods. Here we perform a comparative evaluation of all the methods discussed in this review, on the basis of their technical advantages and disadvantages, the food matrices for which each method is suitable, the safety concern of a method, and the economical implication of large scale application. Using all these parameters, the potential for upscaling each method is then estimated as high, medium or low (Table 5).

In general, physical approaches, which include temperature and humidity control, MA treatment, irradiation treatment, cleaning, milling and sorting, and heat treatment, showed medium to high potential for using at a large scale. The advantages include versatility to use in various matrices, safety, and few changes to the nutritional and sensory properties of foods. However, the high cost of equipment and high energy required to operate over long times may limit the industrial deployment of these methods. Among the four methods, temperature and humidity control appears to have the highest upscaling potential.

Chemical approaches include photodynamic treatment, plasma treatment or ozonisation, EOW, chemical antifungal/anti-mycotoxins agents, and chemical removal of mycotoxin. Application of these methods in large scale also showed a medium to high potential. This can be justified by their high efficiency and their suitability for a wide range of food matrices. The limitations are mainly due to the negative impact on the quality and safety of foods. The use of EOW showed the highest potential for large scale application with low level of safety concern, once the cost of EOW production equipment and energy can be lowered.

Biological approaches include methods such as the use of biocontrol agents, use of antifungal plant metabolites and biological removal of mycotoxins. These approaches showed low to medium potential for upscaling. They are claimed to be environmental friendly, they have a high efficiency (although the replication of lab performance of biocontrol agents in the field remains a challenge), and they can be applied to various foods of plant and animal origin. However, these methods may actually deteriorate food quality; the binders are difficult to remove from food and feed, the potential toxicity can be high, and the cost of production of the biological or plant agent is also high. Among the three methods, the biological removal of mycotoxins, which is already largely used in feed industry, shows a great prospect.

5 Conclusion and perspectives

In order to reduce the contamination of foods by mycotoxins and minimize their negative effects on consumers health, 15 of strategies have been reviewed, which can be classified into physical, chemical and biological approaches, singly or in combination. These strategies are mainly focused on control of fungi growth in raw food materials and removal of mycotoxins from foods. Some new and efficient methods, such as plasma and EOW treatment show great potential but currently remain limited to laboratory applications. Currently physical approaches can be adapted into a wider range of food matrixes, including dry or liquid, raw or cooked foods. Physical approaches can be applied at large scale (e.g. crop storage) and small scale (MAP). Chemical and biological approaches are usually applied high humidity conditions (e.g. coating of fruits and vegetables) or liquid environment (e. g. mycotoxin binders in wine). However, so far no single approach is universal for all matrices or 100% effective at removing the risk of aflatoxin contamination. With the increasing demands in food safety and advances in technology, the mycotoxin reduction strategy has become to multi-dimensional, including a combination of multiple control methods as an integrated management strategy. Food safety concerns as a result of these treatments remain. It is critical when developing or applying a method, to test the toxicity of the applied agents and the derived secondary products. Nutrient loss and deterioration of sensory properties of foods by methods such as irradiation and plasma treatment must be tackled. For biological control methods, the efficacy of the biocontrol agents in field condition must be proven, and their short and long term toxicity be monitored. In methods involving plant-extracted metabolites, large amount of plant materials are needed to obtain sufficient amount of metabolites. Valorisation of plant waste can offer an alternative low cost source of the plant metabolites. On the other hand, the high cost of equipment and running, limits the industrial application of most of the methods, while low cost and easy operations such as sorting and cleaning can be upscaled if they are mechanized. This underlines the need of multidisciplinary collaboration involving engineering, physical and biological sciences in the fight against mycotoxins. Moreover, environmental aspects must be considered during the disposal of toxin-contaminated sorted seeds, waste water or binders.

Research usually remains at the laboratory level with little consideration for upscale applications. Physical approaches have shown the highest potential for upscaling, followed by chemical approaches, while biological approaches necessitate further improvements. Finally, in addition to developing mycotoxin reduction methods, educating producers and consumers on the toxicity of mycotoxins, improving the diversity of food choices (to prevent acute doses from single sources such as maize or rice) and guiding to change the food preferences (towards foods that are less prone to mycotoxin contamination) can also reduce the harmful effect of mycotoxins from human health.

1045 **Table 1.** The occurrence of main mycotoxins in raw and processed products and regulation of mycotoxins in European Communities

Mycotoxins	**Products**		**European Communities standards (ng/g)**	**Reference**
Aflatoxins	Raw products	Almonds, pistachios and apricot kernels,	10 (for human direct consumption)	de Medeiros et al. (2012)
		Oilseeds	15 (for oil production)	Milani and Maleki (2014)
		Cereals	10 (for processing)	Calado, Venâncio, and Abrunhosa (2014)
		Spices	10 (for human direct consumption)	Eskola et al. (2019)
		Milk	Cannot be detected	Cinar and Onbaşı (2019)
	Processed products	Dried fruits, copra	4 (for human direct consumption)	EU (2006)
		Maize grits	Cannot be detected	
		Cheese	Cannot be detected	
Fumonisins	Raw products	Germ, bran, rice, sorghum, legumes, cowpea seeds, triticale,	4000	de Medeiros et al. (2012)
		Maize	1000 (for human direct consumption)	Milani and Maleki (2014)
		Asparagus	NM	Calado, Venâncio, and Abrunhosa (2014)
		Milk	NM	Eskola et al. (2019)
	Processed products	Grits, maize-based products, wheat flour	800 (for adult direct consumption)	Cinar and Onbaşı (2019)
		Beer	200 (for human direct consumption)	EU (2006)
Deoxynivalenol	Raw products	Cereals	750 (for human direct consumption)	de Medeiros et al. (2012)
	Processed products	Wheat flour	750 (for human direct consumption)	Milani and Maleki (2014)
		Bread, pasta, pretzel, cookie	500	Eskola et al. (2019)
				Cinar and Onbaşı (2019)
				EU (2006)
Ochratoxin A	Raw products	Cereals, legumes, coffee beans, nuts, pulses, sesame seeds,	5 (for processing)	Larsen, Svendsen, and Smedsgaard (2001)
		Spices	15 (for human direct consumption)	Varga and Kozakiewicz (2006)
		Apples, peaches, strawberries, pears, oranges, figs, mangoes,	NM	Eskola et al. (2019)
		tomatoes, watermelons, yam, potatoes, garlic, onions,		Cinar and Onbaşı (2019)
		Milk, eggs, meat	NM	EU (2006)

	Processed products	Grape juices, wine vinegar	2.0 (for human direct consumption)	
		Breakfast cereals & snacks	3.0 (for human direct consumption)	
		Infant cereals	0.5 (for infant direct consumption)	
		Bread, pasta	0.5 (for human direct consumption)	
		Flour	0.5 (for human direct consumption)	
		Cocoa	5	
		Dried vine fruits	10	
		Sausage	NM	
		Cheese, milk-based products	0.5 (for human direct consumption)	
		Bottled water, plant food supplement, food colouring agent	NM	
Zearalenone	Raw products	Maize	350 (for processing)	de Medeiros et al. (2012)
		Cereals, sesame, soy beans, nuts	75 (for human direct consumption)	Calado, Venâncio, and Abrunhosa (2014)
	Processed products	Cereal-based products	50 (for adult direct consumption)	Eskola et al. (2019)
				Cinar and Onbaşı (2019)
				EU (2006)
Patulin	Raw products	Wheat straw residue	NM	CAST (2003)
	Processed products	Fruit juice	25 (for adult direct consumption)	EU (2006)

NM: Not mentioned

1056 **Table 2**.Examples of mycotoxin-producing fungi and their inhibition by plant essential oils

Fungal species	Plant species	Organ	Region	Concentration (μL/mL)	Main components	Inhibition (%)	Reference
A. flavus	*Hedychium* sp.	Leaf	USA	40000	NM	100	Rajasekaran, Sakhanokho, and Tabanca (2012)
	Ocimum gratissimum	Leaf	India	0.6	Methyl cinnamate; γ-Terpinene	91	Prakash et al. (2011)
	Origanum majorana	NM	India	3	NM	100	Prakash, Singh, Kedia, and Dubey (2012)
	Coriandrum sativum	NM	India	2.5	NM	100	
	Hedychium spicatum	NM	India	2.5	NM	100	
	Arachis hypogaea	Seed	India	1	NM	82	Prakash et al. (2012)
	Arachis hypogaea	Leaf	India	1	NM	62.5	
	Cinnamomum glaucescens	Berry	India	1	1,8-Cineole	58	Prakash, Singh, Yadav, Singh, and Dubey (2013)
	Salvia officinalis	Aerial parts	Jordan	5	1,8-Cineole	100	Abu-Darwish et al. (2013)
	Artemisia herba-alba	Aerial parts	Jordan	5000	Predominant; α-and β-Thujones	100	Abu-Darwish et al. (2015)
	Caesulia axillaris	Aerial parts	India	1	$_{DL}$-Limonene; Euasarone	100	Mishra, Shukla, Singh, Prakash, and Dubey (2012)
	Jamrosa	Leaf	India	0.4	Z-citral; Linalyl acetate	100	Mishra et al. (2012)
	Lippia rugosa	Leaf	Cameroon	1000	Geraniol; Nerol; Geranial	100	Tatsadjieu et al. (2009)
	Coleus aromaticus	Leaf	India	1	Z-citral; PrecoceneI	100	Jaya, Prakash, and Dubey (2011)
	Hyptis suaveolens	Leaf	India	1	Precocene I	93.8	
	Ageratum conyzoides	Leaf	India	1	Germacrene-D; Trans-caryophyllene	100	
	Ageratum conyzoides	Leaf	Brazil	1	PrecoceneI; PrecoceneII	63	Nogueira et al. (2010)
	Lavandula multifida	Aerial parts	Portugal	0.64	Carvacrol; *cis-β*-Ocimene	100	Zuzarte et al. (2012)
	Citrus sinensis var. Valencia	Orange peel	Mexico	16000	NM	100	Velázquez-Nuñez, Avila-Sosa, Palou, and López-Malo (2013)
A. niger	*Ocimum gratissimum*	Leaf	India	0.6	Methyl cinnamate; γ-Terpinene	85	Prakash et al. (2011)
	Origanum majorana	NM	India	3.5	NM	100	Prakash, Singh, Kedia, and Dubey (2012)
	Coriandrum sativum	NM	India	3	NM	100	
	Hedychium spicatum	NM	India	2.5	NM	100	
	Commiphora myrrha	NM	India	3.5	NM	100	

	Cananga odorata	NM	India	2	NM	100	
	Cinnamomum glaucescens	Berry	India	1	1,8-Cineole	63	Prakash, Singh, Yadav, Singh, and Dubey (2013)
	Salvia officinalis	Aerial parts	Jordan	5	1,8-Cineole	100	Abu-Darwish et al. (2013)
	Artemisia herba-alba	Aerial parts	Jordan	1250	Predominant; α-and β-Thujones	100	Abu-Darwish et al. (2015)
	Caesulia axillaris	Aerial parts	India	1	$_{DL}$-Limonene; Euasarone	100	Mishra, Shukla, Singh, Prakash, and Dubey (2012)
	Lavandula multifida	Aerial parts	Portugal	0.32	Carvacrol; *cis-β*-Ocimene	100	Zuzarte et al. (2012)
A. fumigatus	*Cinnamomum glaucescens*	Berry	India	1	1,8-Cineole	70	Prakash, Singh, Yadav, Singh, and Dubey (2013)
	Salvia officinalis	Aerial parts	Jordan	5	1,8-Cineole	100	Abu-Darwish et al. (2013)
	Artemisia herba-alba	Aerial parts	Jordan	2500	Predominant; α-and β-Thujones	100	Abu-Darwish et al. (2015)
	Caesulia axillaris	Aerial parts	India	1.25	$_{DL}$-Limonene; Euasarone	100	Mishra, Shukla, Singh, Prakash, and Dubey (2012)
	Lavandula multifida	Aerial parts	Portugal	0.32	Carvacrol; *cis-β*-Ocimene	100	Zuzarte et al. (2012)
A. terreus	*Caesulia axillaris*	Aerial parts	India	1	$_{DL}$-Limonene; Euasarone	100	Mishra, Shukla, Singh, Prakash, and Dubey (2012)
F. verticillioides	*Hedychium* sp.	Leaf	USA	40000	NM	100	Rajasekaran, Sakhanokho, and Tabanca (2012)
F. nivale	*Ocimum gratissimum*	Leaf	India	0.6	Methyl cinnamate; γ-Terpinene	100	Prakash et al. (2011)
	Origanum majorana	NM	India	2.75	NM	100	Prakash, Singh, Kedia, and Dubey (2012)
	Coriandrum sativum	NM	India	2	NM	100	
	Hedychium spicatum	NM	India	2.25	NM	100	
	Commiphora myrrha	NM	India	2.5	NM	100	
	Cananga odorata	NM	India	1.5	NM	100	
F. oxysporum	*Caesulia axillaris*	Aerial parts	India	0.75	$_{DL}$-Limonene; Euasarone	100	Mishra, Shukla, Singh, Prakash, and Dubey (2012)
P. italicum	*Ocimum gratissimum*	Leaf	India	0.6	Methyl cinnamate; γ-terpinene	100	Prakash et al. (2011)
	Origanum majorana	NM	India	2.5	NM	100	Prakash, Singh, Kedia, and Dubey (2012)
	Coriandrum sativum	NM	India	2.25	NM	100	
	Hedychium spicatum	NM	India	2.5	NM	100	
	Commiphora myrrha	NM	India	2.5	NM	100	
	Cananga odorata	NM	India	1.5	NM	100	
	Caesulia axillaris	Aerial parts	India	1	$_{DL}$-Limonene; Euasarone	100	Mishra, Shukla, Singh, Prakash, and Dubey (2012)

1057 NM: Not mentioned

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1060 **Table 3**. Mycotoxins detoxification by chemical adsorption to different matrices

Sorbents	Mycotoxin	Concentration (mg/mL)/(mg/mg)	Effects	Time	Matrix	Reference
Hydrated sodium calcium aluminosilicates (HSCASs)	AFB_1	40	>97% Adsorption	30min	Malt suspension	Aly, Abdel-Galil, and Abdel-Wahhab (2004)
		0.01	Retard of the decline in the total number of offspring	30d	*In vivo* (*Drosophilamelanogaster*)	Şişman (2006)
		2	No significant decrease on body weight gain; Retention on crude protein; Decrease on crude fat; No significant decrease on calcium; Retention on the proportion of breast muscle, thigh muscle and abdominal fat; Improvement of growth performance, digestibility, and immune function; Reduction of deleterious effects and tissue residues caused by AFB_1	42d	Broilers basal maize-soybean meal	Y. L. Liu et al. (2011)
		3		21d	Broilers maize meal	N. Liu, Wang, Deng, Gu, and Wang (2018)
	FB_1	40	>84% Adsorption	30min	Malt suspension	Aly, Abdel-Galil, and Abdel-Wahhab (2004)
	OTA	2	No significant decrease on body weight gain; Retention on crude protein; Decrease on crude fat; No significant decrease on calcium; Retention on the proportion of breast muscle, thigh muscle and abdominal fat	42d	Broilers basal maize-soybean meal	Y. L. Liu et al. (2011)
	ZEN	10	50% Adsorption	90min	Acetate/or citrate buffer	Yiannikouris, Kettunen, Apajalahti, Pennala, and Moran (2013)
		5	Reestablishment of haematological parameters, levels of serum biochemical	48h	*In vivo* (mice)	Abbès et al. (2006)

			enzyme activities and histological pictures of both liver and kidney			
	T-2	2	No significant decrease on body weight gain; Retention on crude protein; Decrease on crude fat	42d	Broilers basal maize-soybean meal	Y. L. Liu et al. (2011)
Hydrated sodium aluminosilicate	AFB_1	5	No effect on hepatic lesions	1 year	Rainbow trout diet meal	Arana et al. (2011)
Activated charcoal	FB_1	2	100% Adsorption	1h	Aqueous solution	Galvano et al. (1997)
	OTA	0.4	>95% Adsorption	1h	Aqueous solution	Galvano et al. (1998)
	DON	2	>90% Adsorption	1h	Aqueous solution	Galvano et al. (1998)
		1	67% Adsorption	90min	Phosphate buffer	Cavret, Laurent, Videmann, Mazallon, and Lecoeur (2010)
	ZEN	1	100% Adsorption	90min	Phosphate buffer	Cavret, Laurent, Videmann, Mazallon, and Lecoeur (2010)
Clay	AFB_1	0.002	Reduction of effects by mycotoxins on immune system and the liver; Improve pig growth	42d	Pig meal	Weaver et al. (2013)
	OTA	0.002	Reduction of effects by mycotoxins on immune system and the liver; Improve pig growth	42d	Pig meal	Weaver et al. (2013)
Egyptian montmorillonite	AFB_1	40	>97% Adsorption	30min	Malt suspension	Aly, Abdel-Galil, and Abdel-Wahhab (2004)
	FB_1	40	>80% Adsorption	30min	Malt suspension	Aly, Abdel-Galil, and Abdel-Wahhab (2004)
Esterified glucomannan	AFB_1	0.5	No significant decrease on body weight gain; Increase on crude protein; No significant decrease on calcium; Retention on the proportion of breast muscle, thigh muscle and abdominal fat	42d	Broilers maize-soybean meal	Y. L. Liu et al. (2011)
	OTA	0.5	No significant decrease on body weight gain; Increase on crude protein; No	42d	Broilers maize-soybean meal	Y. L. Liu et al. (2011)

			significant decrease on calcium; Retention on the proportion of breast muscle, thigh muscle and abdominal fat			
	T-2	0.5	No significant decrease on body weight gain; Increase on crude protein; No significant decrease on calcium; Retention on the proportion of breast muscle, thigh muscle and abdominal fat	42d	Broilers maize-soybean meal	Y. L. Liu et al. (2011)
Cholestyramine	DON	0.82	10% Adsorption	4h	Phosphate-citrate buffer	Döll, Dänicke, Valenta, and Flachowsky (2004)
		1	65% Adsorption	90min	Phosphate buffer	Cavret, Laurent, Videmann, Mazallon, and Lecoeur (2010)
	ZEN	0.82	94% Adsorption	4h	Phosphate-citrate buffer	Döll, Dänicke, Valenta, and Flachowsky (2004)
Modified aluminosilicate	DON	0.82	17% Adsorption	4h	Phosphate-citrate buffer	Döll, Dänicke, Valenta, and Flachowsky (2004)
	ZEN	0.82	81% Adsorption	4h	Phosphate-citrate buffer	Döll, Dänicke, Valenta, and Flachowsky (2004)
PVP-DEGMA-TAIC	FB_1	0.005	86% Adsorption	24h	Wine-like model solution	Carrasco-Sanchez, Kreitman, Folch-Cano, Elias, and Laurie (2017)
	FB_2	0.005	94% Adsorption	24h	Wine-like model solution	Carrasco-Sanchez, Kreitman, Folch-Cano, Elias, and Laurie (2017)
Poly(acrylamide-co-ethyleneglycol-methacrylate)	FB_1	0.005	82% Adsorption	24h	Wine-like model solution	Carrasco-Sanchez, Kreitman, Folch-Cano, Elias, and Laurie (2017)
	FB_2	0.005	100% Adsorption	24h	Wine-like model solution	Carrasco-Sanchez, Kreitman, Folch-Cano, Elias, and Laurie (2017)
Trimethylstearylammonium bromide	AFB_1	5.8	89% Adsorption	1h	Phosphate buffer	Sun, Song, Wang, Wang, and Zheng (2018)
	ZEN	5.9	86% Adsorption	1h	Phosphate buffer	Sun, Song, Wang, Wang, and Zheng (2018)

PVP-DEGMA-TAIC:Resins of copolymerization of N-vinyl-2-pyrrolidinone with ethylene glycol dimethacrylate and triallyl isocyanurate

Table 4.Mycotoxinsdetoxificationby bacteria and fungi through adsorption in different matrixes

Micro-	Mycotoxin	Genus	Strains	Effects	Time	Matrix	Reference

organism							
Bacteria	AFB_1	*Lactobacillus*	*L. fermentum*	61% Adsorption	48h	PBS Buffer	Fazeli et al. (2009)
			L. plantarum	56% Adsorption	48h	PBS Buffer	
			L.casei	48% Adsorption	48h	PBS Buffer	
			L. paracasei LOCK 0920	Decreased the extent of DNA damage	14d	*In vivo* (Chicken Fodder)	Slizewska, Nowak, Libudzisz, and Blasiak (2010)
			L. brevis LOCK 0944	Decreased the extent of DNA damage	14d	*In vivo* (Chicken Fodder)	
			L. plantarum LOCK 0945 (mixed)	Decreased the extent of DNA damage	14d	*In vivo* (Chicken Fodder)	
			*L. rhamnosus*strain GG	70% Adsorption	24h	PBS Buffer	Vosough, Sani, Mehraban, and Karazhyan (2014)
		Bifidobacterium	*B. bifidum*	55% Adsorption	72h	PBS Buffer	Hamad, Zahran, and Hafez (2017)
			*B. lactis*CSCC 5094	35% Adsorption	24h	PBS Buffer	Peltonen, El-Nezami, Haskard, Ahokas, and Salminen (2001)
			B. longum CSCC 5304	38% Adsorption	24h	PBS Buffer	
			B.animalis CSCC 1941	46% Adsorption	24h	PBS Buffer	
			B.lactis CSCC 1906	49% Adsorption	24h	PBS Buffer	
		Enterococcus	*E. faecium* MF4	23% Adsorption	24h	PBS Buffer	Fernandez Juri, Dalcero, and Magnoli (2014)
			E. faecium GJ40	21% Adsorption	24h	PBS Buffer	
			E. faecium M74	19.3-30.5 % Adsorption	48h	PBS Buffer	Topcu, Bulat, Wishah, and Boyacı (2010)
			E. faecium EF031	23.4-37.5% Adsorption	48h	PBS Buffer	
	AFB_2	*Streptococcus*	P. *freudenreichii* spp. *shermanii* JS (mixed)	83% Adsorption	4 weeks	*In vivo* (human)	El-Nezami et al. (2000)
	AFM_1	*Lactobacillus*	*L. rhamnosus* GAF01	95% Adsorption	24h	PBS Buffer/Milk	Abbes et al. (2013)
			L. plantarum MON03	77% Adsorption	24h	PBS Buffer /Milk	
			L. plantarum MON03	16% Adsorption	14d	*In vivo* (mice)	
			L. bulgaricus	58.5% Adsorption	6h	Yogurt	El Khoury, Atoui, and Yaghi (2011)
			L. bulgaricus	55% Adsorption	6h	PBS Buffer	

	DON	*Lactobacillus*	*L. plantarum* strain 102	20% Adsorption	24h	PBS Buffer	Zou et al. (2012)
			L. rhamnosus GGATCC 53103	54% Adsorption	24h	MRS Medium	Niderkorn, Boudra, and Morgavi (2006)
			*L. delbruekii*ssp. *Bulgaricus*R0149	55% Adsorption	24h	MRS Medium	
	OTA	*Lactobacillus*	*L. rhamnosus*strain GG	47% Adsorption	2h	PBS Buffer	Turbic, Ahokas, and Haskard (2002)
			L. rhamnosus strain LC-705	36% Adsorption	2h	PBS Buffer	
	ZEN	*Lactobacillus*	*L. rhamnosus*GG	55% Adsorption	24h	MRS Medium	El-Nezami, Polychronaki, Salminen, and
			*L. rhamnosus*LC705	55% Adsorption	24h	MRS Medium	Mykkanen (2002)
	FB	*Lactobacillus*	*L. rhamnosus* GG ATCC 53103	54% Adsorption	24h	MRS Medium	Niderkorn, Boudra, and Morgavi (2006)
			L. plantarum R1039	40% Adsorption	24h	MRS Medium	
			L. plantarum R0011	30% Adsorption	24h	MRS Medium	
			L. brevis R0002	32% Adsorption	24h	MRS Medium	
			*L. acidophilis*R0052	34% Adsorption	24h	MRS Medium	
			L. delbruekii ssp. *bulgaricus* R0149	55% Adsorption	24h	MRS Medium	
			*L. casei*ssp. *casei* C3	36% Adsorption	24h	MRS Medium	
		Streptococcus	*Strep*. *thermophilus* B5	31% Adsorption	24h	MRS Medium	Niderkorn, Boudra, and Morgavi (2006)
		Lactococcus	*L. lactis* CS 43	23% Adsorption	24h	MRS Medium	Niderkorn, Boudra, and Morgavi (2006)
			*L. lactis*CS 202	40% Adsorption	24h	MRS Medium	
			L. lactis CS 197	23% Adsorption	24h	MRS Medium	
		Leuconostoc	*L. mesenteroides*R1107	46% Adsorption	24h	MRS Medium	Niderkorn, Boudra, and Morgavi (2006)
		Lactobacillus	*L. rhamnosus* 6149	51.1-52.0% Adsorption	24h	Physiological saline solution (0.85%, w/v)	S. Hatab, T. Yue, and O. Mohamad (2012)
		Bifidobacterium	*B. bifidum* 6071	52.9-54.1% Adsorption	24h	Physiological saline solution (0.85%, w/v)	S. Hatab, T. Yue, and O. Mohamad (2012)
		Enterococcus	*E. faecium* 21605	64.5% Adsorption	24h	Apple juice	S. Hatab, T. Yue, and O. Mohamad
			E. faecium M74	15.8-41.6% Adsorption	48h	PBS Buffer	(2012)
			E. faecium EF031	9.5-45.3% Adsorption	48h	PBS Buffer	Topcu, Bulat, Wishah, and Boyacı (2010)
Fungi	AFB_1	*Saccharomyces*	*S. cerevisiae*	48% Adsorption	1h	PBS Buffer	Campagnollo et al. (2015)

DON	*Saccharomyces*	*S. cerevisiae*	12% Adsorption	1h	PBS Buffer	Campagnollo et al. (2015)
PAT	*Saccharomyces*	*S. cerevisiae*strain YS3(laboratory-prepared)	70% Adsorption	24h	Apple Juice	Guo, Yue, Hatab, and Yuan (2011)
		*S. cerevisiae*strain YS3(commercial)	76% Adsorption	24h	Apple Juice	Yue, Dong, Guo, and Worobo (2011)
		S. cerevisiae YS1-YS10	50-7% Adsorption	24h	Apple Juice	Guo, Yue, Hatab, and Yuan (2012)
		S. cerevisiae YS3	100% Adsorption	36h	Apple Juice	Coelho et al. (2008)
		S. cerevisiae	90-96% Adsorption	143h	Apple Juice	
OTA	*Saccharomyces*	*S.cerevisiae var. boulardii* ATCC MYA-796	39% Adsorption	1h	PBS Buffer	Petruzzi, Corbo, Sinigaglia, and
		S. cerevisiae BM45	39% Adsorption	1h	PBS Buffer	Bevilacqua (2016)
		S.cerevisiae W13	39% Adsorption	1h	PBS Buffer	
		*S.cerevisiae*W28	39% Adsorption	1h	PBS Buffer	
		S.cerevisiae W47	42% Adsorption	4d	YPG Medium with Ethanol	
		S.cerevisiae Y28	37% Adsorption	4d	YPG Medium with Ethanol	Petruzzi, Sinigaglia, Corbo, Beneduce, and
		*S.cerevisiae*Malaga LOCK 0173	85% Adsorption	10d	Grape/Blackcurrant Juice	Bevilacqua (2012)
		*S.cerevisiae*Syrena LOCK 0201	83% Adsorption	10d	Grape/Blackcurrant Juice	
		S. cerevisiae bakery BS strain	64% Adsorption	10d	Grape/Blackcurrant Juice	Piotrowska, Nowak, and Czyzowska
		S. cerevisiae RC008	57% Adsorption	1h	PBS Buffer	(2013)
		S. cerevisiae RC009	67% Adsorption	1h	PBS Buffer	
		S. cerevisiae RC012	71% Adsorption	1h	PBS Buffer	
		S. cerevisiae RC016	74% Adsorption	1h	PBS Buffer	Armando et al. (2012)
		S. cerevisiae	76% Adsorption	90d	White Wine	
		S. cerevisiae	86% Adsorption	90d	Red Wine	
		S. cerevisiae	90% Adsorption	90d	Rose Wine	
		S. cerevisiae	59% Adsorption	1h	PBS Buffer	Csutorás et al. (2013)
		S. cerevisiae	30% Adsorption	1h	Dough Fermentation	
						Campagnollo et al. (2015)
						Valle-Algarra et al. (2009)
ZEN	*Saccharomyces*	*S. cerevisiae* RC008	21% Adsorption	1h	PBS Buffer	Armando et al. (2012)

	S. cerevisiae RC009	33% Adsorption	1h	PBS Buffer	
	S. cerevisiae RC012	29% Adsorption	1h	PBS Buffer	
	S. cerevisiae RC016	34% Adsorption	1h	PBS Buffer	
	S. cerevisiae	75% Adsorption	1h	PBS Buffer	Campagnollo et al. (2015)

Table 5. Evaluation of fungi/mycotoxin decontamination approaches

Classification	Treatments	Technical advantages	Technical disadvantages	Suitable food matrix	Safety	Economical concerns in large	Potential for using in	Reference

						scale production	large scale	
Physical approaches	Temperature and humidity control	Easy-operated; less colour, odor and nutrition changes; shelf life extension	Inconvenient transportation	Almost all food types	No reported toxic substance induced and formed	Cost of temperature and humidity equipment; high energy consumption	High	-
	Modified atmosphere treatment	Less colour, odor and nutrition changes; shelf life extension	Large consumption of packaging material	Packed foods	No reported toxic substance induced and formed	Cost of gas generator equipment and food packaging material	Medium	-
	Irradiation treatment	High efficiency; environmental friendly; agrees with the legislations of food application in 55 countries	Food quality change (e.g. colour, odor); nutrition loss (e.g. oxidization of vitamin) at high dose	Packed foods; frozen foods; liquid foods; cereals; fruits and vegetables	No residual irradiation; may cause mutations to fungi	Low consumption of water and electrical energy (exception of electron beam and X-ray); high cost of food irradiation facilities	High	Calado, Venâncio, and Abrunhosa (2014)
	Cleaning, milling and sorting	Easy-operated; effective with water-soluble mycotoxins	Less effective with organic-soluble mycotoxins	Raw food materials	No other introduced chemicals and new mycotoxin-derivative	High consumption of water	High	Temba et al. (2016)
	Heat treatment	Already a necessary processing method in food production	Change of the desired physical properties of food	Cooked foods (e.g. roasted foods); sterilized food	Lack of studies on transformation mechanisms	Cost of heating equipment; high energy consumption	Medium	Rastegar et al. (2017)

Chemical approaches	Photodynamic treatment	Environmental friendly; biochemically stable; photosensitizer adequately activated by using easy-available visible light	Limited light penetration	Cereals; fruits; sea foods; animal feeds	Food grade photosensitizer (e.g. curcumin); lack of studies on safety after treatment	Cost of light generator and photosensitizer; relative cost-effective		Njoki, Okoth, and Wachira (2017) Al-Asmari, Mereddy, and Sultanbawa (2018) Temba et al. (2019)
	Plasma treatment (Ozonisation)	High efficiency; rapid; no significant change of nutritional components to whole cereals	May cause the loss of nutrition in other foods; change of colour; production of undesirable odor	Cereals; meat; fruits and vegetables; herbs and spices; animalfeeds	Lack of studies on safety of degraded residue	Low energy consumption; high cost of cold plasma production equipment; less maintenance and dust cleaning	Medium	Savi, Bittencourt, et al. (2015) Temba et al. (2016) Misra, Yadav, Roopesh, and Jo (2019) Alexandre, Castanha, Calori-Domingues, and Augusto (2017)
	Electrolyzed oxidizing water	High efficiency; environmental friendly; easy-operated	Loss of antifungal activity without continuous electrolysis; Cl_2 production; possibility of metal corrosion	Fruits and vegetables; meat products; cereals	Safe to degrade mycotoxins; no not corrosive to skin, mucous membrane and organic material	High cost of EOW production equipment, electrical and water consumption; low cost of each litre	High	Okull and Laborde (2004) Q. Zhang, Xiong, Tatsumi, Li, and Liu (2012) Huang, Hung, Hsu, Huang, and Hwang (2008)
	Chemical antifungal/anti-mycotoxins agents	Effective; easy-operated	Unpleasant chemical residue	Coating; animal feeds; specific food conforming to food additives (e.g. soda in Chinese baking)	Lack of studies on transformation mechanisms; toxicity of induced chemicals at high concentration to human and	Cost of agents	Medium	Bretz, Beyer, Cramer, Knecht, and Humpf (2006) Temba et al. (2019)

					environment			
	Chemical removal of mycotoxin	Effective; easy-operated; some commercial clay materials enhance nutrition and digestibility of animal feeds	Difficult removal of mycotoxin-binder complex; need to be in aqueous environment	Animal feeds; clay capsules for human (potential)	Toxicity of released mycotoxins from mycotoxin-binder complex	Cost effective	Medium	Di Gregorio et al. (2014)
Biological approaches	Biological control agents/mycotox in degradation	High efficiency in lab experiments; easy-operated (e.g. soak, spray); environmental friendly	Less evidence on the correlation between laboratory inhibition assay and field performance; need to be under strict conditions (e.g. pH, solution, temperature)	Cereals; fruits and vegetables; fermented foods	Less toxicity shown on degraded residue	Cost of bacterial high density culture; used as antagonist solution cost of materials and equipment for production of the biocontrol agent	Low	Jard, Liboz, Mathieu, Guyonvarc'h, and Lebrihi (2011) de Medeiros et al. (2012)
	Antifungal plant metabolite	High efficiency; a wide range of sources	Change of colour and odor; mainly used in aqueous environment	Meat products; dairy products; vegetable and fruits; cereals	Potential toxicity (e.g. carcinogenicity) at high concentration	Large amount of plant materials needed; high cost of production equipment and energy consumption	Low	Burt (2004) Bakkali, Averbeck, Averbeck, and Idaomar (2008)
	Biological removal of mycotoxin	High efficiency; from food source; environmental friendly	Difficult removal of mycotoxin-binder complex; need to be in aqueous environment	Fermented foods; animal feeds	Toxicity of released mycotoxins from mycotoxin-	Cost of bacterial high density culture	Medium	Hathout and Aly (2014)

	bacteria complex

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Data Availability

The data supporting the conclusions of this manuscript will be made available by the authors, without undue reservation, to any qualified researcher.

Conflict of Interest Statement

The authors declare no potential conflict of interest.

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Author contributions

YL performed the literature review and evaluation of literature data. YL drafted the manuscript. All authors contributed ideas to the design and organisation of the work. All authors edited and reviewed the manuscript.

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