Prevalence and controlling mechanisms of mycotoxin

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Abstract: Fungi grow everywhere in agricultural produce, food and surface of indoor and outdoor environment. The aim of this paper is to expand the growth and synthesis contributing factors and prevention mechanisms of fungi and its metabolites. Fungi, grouped as hydrophilic, mesophilic and xerophilic, grow under a wider range of water activity, temperature, pH, gases and substrate. Besides the beneficial properties, the harmful fungi species are gaining attention due to their toxicity effect on consumer and economic losses. Taking into consideration their prevalence, food group, daily intake, sampling, analytical techniques and consumer type’s regulatory limit have been established and promising prevention mechanisms discovered. Prevention of growth and production of toxic metabolites includes good practices, use of plant extracts/probiotics, oxygen-reactive scavenging substances and molecular silencing technology for a wide range of commodities. Nevertheless, application and commercialization of those techniques are limited.

Subjects: Food Chemistry; Food Analysis; Food Microbiology; Nutrition; Food Engineering; Food Packaging; Preservation; Processing; Product Development; Food Laws & Regulations

Keywords: Food value chain; fungi; mycotoxin; health; tolerable limit; detoxification

1. Introduction

Spore-forming fungi are a microbial hazard (Gacem & Hadj-khelil, 2016) that produce toxic metabolites known as mycotoxins which cause economic and public health problems in human and livestock (Bhat, Rai, & Karim, 2010; Fountain et al., 2015; Pitt, 2000). The spore-forming fungi grow everywhere in the indoor and outdoor environment where humidity, temperature, hygienic condition and product composition are conducive (Kumar, Mahato, Kamle, Mohanta, & Kang, 2017). Studies show that fungi
and mycotoxins exist at high dose levels in soils and walls (Diba, Rezaei, & Mahmoudi, 2007; Visagie et al., 2014a, 2014b), mixed mycotoxicosis in water, damaged buildings (Gray et al., 2003), in agricultural commodities (Fountain et al., 2015; Lai, Zhang, Liu, & Liu, 2015; Thathana, Murage, Luther, & Abia, 2017), fresh and stored sorghum (Taye, Ayalew, Chala, & Dejene, 2016), livestock (EFSA, 2013) and food stuffs such as sun-dried potato chips (Amri & Lenoi, 2016), edible oils (Yang et al., 2011), sesame oil (Idris, Hassan, & Mariod, 2013; Kolliia, Tsourouflis, & Markaki, 2016); groundnut, sesame and cottonseed oils (Idris, Mariod, Elnour, & Mohamed, 2010), groundnut and sunflower oils (Mariod & Idris, 2015) dried vine fruits (Kolliia, Kanapitsas, & Markaki, 2014), wheat flour (Li et al., 2016), and melon seeds when consumed raw (Somorin, Akinyemi, Bertuzzi, & Pietri, 2016).

Fungi are categorized into three major groups based on their stage of occurrence and moisture content for their growth (Egmond Van & Jonker, 2003; Hassane et al., 2017; Iram et al., 2016; Mannao & Kim, 2017; Nayak, Agarwal, Pandey, Sudini, & Jayale, 2017; Perczak, Goliński, Bryła, & Waśkiewicz, 2018). First, fungi are grown in the field in the early stage of form at high moisture content (aw = 1) referred to as hydrophilic or also called pre-harvest fungi such as Alternaria, epicoccum and fusarium species. Second category are the mesophilic or intermediate fungi which occur at the optimal maturation for harvesting at water activity (aw = 0.95–1.0) such as aureobasidium species, cladosporium species and verticillium species. Third, xerophilic post-harvest fungi occur during handling and processing at water activity level (aw = 0.6–0.95) such as aspergillus species, eurotium species and penicillium species. However, not all fungi species are harmful.

Visagie et al. (2014a) identified species of fungi of aspergillus (1160 species), penicillium (1459 species) and talaromyces (98 species) isolates in house dust from around the world using extraction-2-dilution method (e2d), and Visagie et al. (2014b) identified 339 aspergillus isolates using different agar medias in the indoor environments. Diba et al. (2007) identified more than 205 isolates of aspergillus species from the surface (wall, floor, beds and trolleys), environment (air) and other surfaces of teaching hospitals in Iran with higher fungi dose in the indoor environment. Thathana et al. (2017) identified 43 aspergillus flavus isolates in maize and soils in Jomo Kenyatta University of Agriculture and Technology in Kenya. Those fungi isolates and strains significantly impact biotechnology, food production, environment and human health. More than 37% of rice was contaminated by aflatoxin B1 (175–30,797 µg/kg) and B2 (70–10,329 µg/kg) (Lai et al., 2015) and heavily contaminated maize supplied to local mills by aflatoxin B1 (≤155.6 µg/kg), fumonisin (≤9,638 µg/kg) and deoxynivalenol (≤7,394 µg/kg) in China due to prolonged and inappropriate storage conditions, lack of restrict receiving and inspection, and poor processing practices (Liu et al., 2016).

In another study, it was found that 11 of the fungi species (aspergillus flavus, niger, fumigatus, nidulans, tereus, parasiticus, penicilloid, tamarii, ochraceus, sojae and niveus) were found to be more toxigenic to humans, livestock, caused economic loss and affected the food market (Alberts, Van Zyl, & Gelderblom, 2016). The growth of fungi reduces the enzymatic activity, disorder of mitotic divisions of meristematic cells and restrained biosynthesis of proteins, and produces secondary metabolites (Podolska et al., 2017). The responses include oxygen-reactive stress, environmental stress and interaction of fungi species in the agricultural commodities and foods in the value chain (Fountain et al., 2015). The physical features of fungi are important for its identification and characterization, and vary depending on the type of media used to cultivate. The aspergillus flavus cultivated in potato dextrose agar (PDA) is wrinkled, olive to dark-green colored concentrated at the center with a colony diameter of 65–75 mm and have exudates; in Czapeck Dox Agar (SDA) is floccose isolated, yellowish-green and olive candida, with no exudates and 55–75 mm in diameter; in Rose-Bengal Chloramphenicol Agar (RBCA) is yellowish conidia turned to olive and dark green, tiny uncolored exudates with 50–70 mm diameter; in malt extract agar (MEA) is olive and dark conidia with variable shape and uncolored exudates visible at the center (Diba et al., 2007; Thathana et al., 2017). Isolates of A. flavus (28%) have the ability to produce aflatoxins B1, B2 and G1. Physical features of Aspergillus parasiticus are 250–500 µm in size, colorless, rough
surface and spherical in shape. They are inhibited by the application of a metabolite of streptomyces diocatia A (Dot A) (Diba et al., 2007; Yoshinari et al., 2007).

Mycotoxins are acute (single exposure) and chronic (repeated exposure) toxic metabolites (Darwish, Ikenaka, Nakayama, & Ishizuka, 2014; Krisko et al., 2008; Tola & Kebede, 2016), which play an important source of energy for the growth of other microorganisms. The toxicity of mycotoxin to human beings precipitates allergic responses to immunosuppression, potent carcinogens and results in different types of cancers and even mortality (Pitt, 2000; Zain, 2011). The occurrence of mycotoxins in food and feedstuffs are influenced by external and internal factors in the food value chain (Darwish et al., 2014). Their recoveries and level of detection (LOD) significantly influenced based on the extraction method, separation technique and type of food (Andrade, Da Silva, & Caldas, 2013; Frenich, Vidal, Romero-González, & Del Aguilera-Luiz, 2009). Several mycotoxins are known to have various physicochemical, morphological and physiological properties associated with food (Berthiller, Sulyok, Krisko, & Schuhmacher, 2007; Guchi, 2015; Krisko et al., 2016), prompt potential health risks and food insecurity to human. However, mycotoxins are gaining attention in the food value chain due to their toxicity, frequent occurrence and adverse health effect. Examples include aflatoxins, ochratoxins, fumonisins, trichotheccenes and Zearalenone, patulin and ergot alkaloids (Krisko et al., 2008; Pitt, 2000).

Aflatoxins-inducing fungi species are mostly grown in tropical and subtropical regions where optimal conditions such as temperature and humidity are conducive for their growth and toxin production (Krisko et al., 2017; Chowdhury, Hassain, & Ahmed, 2015). The tolerance limit of aflatoxins is less than 2 µg/kg in food; if it exceeds that, then it is potentially carcinogenic (Kollia et al., 2016). Aflatoxins B1, B2, G1 and G2 might be found in food and feed staffs, and M1 and M2 are the metabolites of B1 and B2 in dairy products and can cause mutagenic, teratogenic and carcinogenic problems (Kollia et al., 2016; Somorin et al., 2016; Taye et al., 2016; Mi, 2014; Idris et al., 2013; Torlak, Sert, & Serin, 2013; Yang et al., 2011; Idris et al., 2010; Chen et al., 2002). In a study by Garrido, Iha, Ortolani, and Favaro (2003), it was found that the incidence of aflatoxins M1 and M2 in dairy products exceeds the tolerable limit. Most studies conducted and ongoing, in particular, in developing countries are focusing on assessing their prevalence (Taye, Ayalew, Dejene, & Chala, 2018). Likewise, the conditions are conducive for the growth of fungi and production of toxin metabolites where the conditions of storage facilities are poor for its prevention.

2. Factors influencing fungi growth and mycotoxin production

Most important influencing factors for the growth of fungi and the production of fungi metabolites are moisture, gas, temperature, time and composition (Hassane et al., 2017; Iram et al., 2016; Lahouar, Marin, Crespo-sempere, Saiid, & Sanchis, 2016; Leggieri, Decontardi, Bertuzzi, Pietri, & Battilani, 2017; Nayak et al., 2017). The optimal growth temperature varies by species, strain types and growth medium. Most fungi grow in the range of 5–35°C, optimal at 25°C (Hassane et al., 2017; Leggieri et al., 2017), influenced by the post-harvest drying temperature (Hawkins & Windham, 2005). Higher temperature inhibits the growth of fungi and the synthesis of mycotoxins by attacking the transcription genes (Gacem & Hadj-khelil, 2016).

Mycotoxins are synthesized at a wide range of temperature (5–40°C; 25°C) (Hassane et al., 2017; Leggieri et al., 2017), and even continue during cooking up to 110°C for 20 min (Sandoval-contreras, Villarruel-lópez, & Sierra-beltrán, 2017; Zhou, Chen, Kong, Ma, & Liu, 2017). The optimal temperatures of AFB and AFG synthesis in wheat induced by aspergillus flavus are 25°C and 28°C, respectively (Hassane et al., 2017). According to Hawkins and Windham (2005), aflatoxin synthesis in maize hybrids during post-harvest drying is high at a wide range of temperature (40–70°C), but no significant effect on aflatoxin concentration up to 100°C explains aflatoxins are resistant to a wide range of temperature. In conclusion, post-harvest drying of grains should not exceed 43°C to prevent the growth of fungi and synthesis of mycotoxins, to avoid loss of viability, minimize breakage susceptibility and quality reduction. Nevertheless, once the mycotoxin-inducing fungi are secreted in the food, it is hard to remove at moderate temperature treatment without affecting the physical and nutritional quality.
rate of AFB1 reduction was 0.71–7.8% during thermal treatment (25–60°C) and rate of AFB1 reduction with prolonged holding time of 6–72 h was 0.71–2.86% which is not practical from the economic, processing and nutritional value perspectives (Hassane et al., 2017; Hawkins & Windham, 2005). The basic condition, however, inhibits the growth of fungi and synthesis of the mycotoxins whereby the pH can be altered by mutation of the acid-tolerant enzymes or amino acid (Moreno-pedraza et al., 2015). Mutation of Xylanase in Aspergillus kawachii alters the pH condition, and hence the biosynthesis of mycotoxin and growth of fungi (Qiu et al., 2016).

Increased moisture content (5–25%) in the agri-value chain is susceptible to the growth of fungi and increased synthesis of mycotoxins (Hassane et al., 2017). Several species of fungi grow at water activities of 0.87–0.99, but no mycotoxins are detected at <0.93 water activity (Leggieri et al., 2010). The longer the incubation/storage time resulted, the higher the fungi colonies with bigger diameter at increased water activity. A combined significant Ochratoxin A accumulation with increased incubation time at high water activity and relatively elevated temperature due to Aspergillus carbonarius was observed (Lappa, Kizis, & Panagou, 2017). Mycotoxins are, in general, synthesized under acidic condition (Sandoval-contreras et al., 2017; Sulyok, Krska, & Schuhmacher, 2007), optimally active at 4.0–4.5 pH and reduction was observed at the pH of 5.5–8.0 (Brzonkalik, Hümmer, Syldatk, & Neumann, 2012; Iram et al., 2016), which explains they are acid tolerant. High gas (CO₂) concentration increases in fungi biomass without affecting the growth rate because fungi are facultatively anerobic (Brzonkalik et al., 2012; Gacem & Hadj-khelil, 2016). Similarly, the composition of the growth medium affects the growth of fungi and mycotoxin synthesis. Amino acids of tryptophan, alkaline condition and secondary plant metabolites such as octanal reduce the growth of fungi, hydrolyzable tannin; antioxidants such as phenolic compounds, ascorbic acid and caffeic acid inhibit or decreases the growth of fungi and toxin production. However, amino acids of tyrosine, lipids, organic C and N, simple sugars of glucose and fructose, acidity, increased water activity, increased CO₂, secondary plant metabolites such as octanal cause super enhancement of toxin production by encouraging the growth and synthesis of mycotoxins. Simple sugars of sorbose and lactose have no effect on either of the fungi growth or mycotoxin synthesis (Gacem & Hadj-khelil, 2016). In general, the combined effect of several parameters affects the fungi colonies and mycotoxin synthesis. The Aspergillus carbonarius strain type, optimal water activity, optimal incubation time and temperature show a significant increase in Ochratoxin synthesis (Lappa et al., 2017).

3. Health impact

Mycotoxin is a noiseless threat (Allen, 2017; Bhat et al., 2010; Karlovsky et al., 2016) where food and feed handling and storage condition are uncontrolled with prolonged storage (Pitt, 2000). Mycotoxins are chronic (Bryden, 2007; Knutsen et al., 2018), respiratory signs and neurological dysfunction due to mycotoxin exposure from building (Rea et al., 2003). More than half death and children malnutrition such as stunting, wasting and growth restriction are prevalent due to mycotoxins (Mitchell et al., 2017; Mupunga, Mngqawa, & Katerere, 2017; Tariku, Biks, Derso, Wassie, & Abebe, 2017). Children stunting in developing country (Wirth et al., 2017) is associated with frequent exposure to aflatoxin, fumonisin and deoxynivalenal in their staple foods through environmental enteric dysfunction (EED) and disturbance of the insulin-like growth factor (Smith et al., 2015). Deoxynivalenal (DON, vomitoxin) in wheat and wheat-based products is causing vomiting, diarrhea, gastrointestinal inflammation and immunomodulation (Kushiro, 2008) with frequent consumption and/or exceeding the tolerable limit (8 µg per kg body weight per day) (EFSA, 2013).

Aflatoxin is the most toxic, mutagenic and carcinogenic type affecting liver function, exacerbating malnutrition (Knipstein et al., 2015; Verheecke, Liboz, Anson, Díaz, & Mathieu, 2015) and increasing the susceptibility to hepatitis and liver cancer (Abrar et al., 2013; Šarkanj et al., 2018), immune system deficiency, reducing child growth and increasing incidences of stillbirth or newborn jaundice (Chen et al., 2018; Verheecke et al., 2015), and interfere with protein metabolism and multiple micronutrients leads to hepatocellular carcinoma (HCC) which may lead to death (Marchese et al., 2018). Aflatoxin is hepatocarcinogenic (Abebe et al., 2017; Egmond Van & Jonker, 2003) that binds nucleic acids and nucleoproteins which are essential to cellular viability and
buildup of hepatic lipids, causes enlargement of liver, proliferation of bile epithelium and necrosis (Abrar et al., 2013). Aflatoxin remains a global burden (Kumar et al., 2017). Aflatoxin exposure in sub-Saharan Africa (Mapunga et al., 2017), Latin America and Asia causes hepatocellular carcinoma, chronic growth impairment in childhood. Dietary aflatoxin and fumonisin exposure have an impact on children’s growth measured as stunting and underweight in Tanzania which is believed to be associated with breastfeeding and weaning practices (Chen et al., 2018). The AFB1-lysine concentrations in diets in Nigeria lead to stunting and acute child malnutrition (Mitchell et al., 2017), weight loss and mortality as a result of a significant reduction in packed cell volume, hemoglobin concentration, red blood cell and protein concentration (Hussein, 2015).

4. Regulatory limit
According to the codex alimentarius report in 2003, 87% of the world inhabitant have had a forced mycotoxin regulation and the remaining 13% either do not have forced regulation or no information is available (Egmond, Schotthorst, & Jonker, 2007; Egmond Van & Jonker, 2003). The regulations of tolerable limit are settled based on the absence or level of occurrence, toxicological studies considering

Table 1. The tolerable limit of common mycotoxins in food considered to be consumed without further treatment or processing

| Toxin types | Food (µg/kg)(range: Average) | Feed (µg/kg) |
|-------------|-----------------------------|--------------|
| Total aflatoxin | 0–35: 4 | 0.01–50: 20 |
| AFB1 | 1–20: 2 | 5–50: 5 |
| AFM1 | 0.05–15 |
| Fumonisins | 2 |
| Patulin (fruit and fruit juice) | 5–100: 50 |
| Ocratoxin A (cereals and cereal products) | 3–50: 5 |
| Deoxynivalenol (Cereals and flours) | 300–2000: 750 |
| Zearalenone (estrogenic mycotoxin, cereals) | 50–1000 |

Figure 1. Prevention of potential health hazards and post-harvest losses in the food supply and value chain. GAP is good agricultural practices, MC is moisture content, and HACCP is hazard analysis and critical control point.
Table 2. Mycotoxin detoxification and/or reduction mechanisms in a wide range of agricultural/food produce

| Method                                          | Controlling, detoxification, reduction mechanisms                                                                                                                                                                                                 |
|-------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Good agricultural/handling/processing practices | • Strict receiving and inspection criteria (moisture content, visual quality and processing), appropriate storage conditions, and proper processing practices (Liu et al., 2016).                                                             |
|                                                 | • Cleaning, steeping, thermal treatment, dry size reduction and sifting reduce mycotoxin accumulation in food and feed (Karlovsky et al., 2016), acidulation and baking time in the baking industry reduces mycotoxin (25–68% during baking holding time of 4–10 min) (Generotti et al., 2017). |
|                                                 | • Microwave heating is effective in detoxification of aflatoxin in maize grain, maize dough and Tortillas (Moreno-pedraza et al., 2015).                                                                                                               |
|                                                 | • Aflatoxin detoxification by A. vasica extract showed that 69% of the toxin was degraded within 6 h and ≥95% degradation was observed after 24 h of incubation (Vijayanandraj et al., 2014).                                                      |
|                                                 | • Trachyspermum ammi oils (essential oils) are found to have strong antifungal activity. Absolute inhibition of mycelia was observed with the application 1 µL/ml oil, complete inhibition of spore germination with the application of 2 µL/ml of oil and significant anti- \ aflatoxigenic to aspergillus niger (0.5 µL/ml T. ammi oil) and aspergillus flavus (0.75 µL/ml T. ammi oil) (Gemeda, Woldeamanuel, Asrat, & Debella, 2014). |
|                                                 | • Poultry feed: Application of Pomegranate Peels (5%) and Clove Powders (2%) increase in chicken weight (36–61%) and decreases mortality (55%) explain the powders have the ability to detoxify AFB1 and OTA (Hussein, 2015). |
| Plant extracts                                   | • The aflatoxigenic aspergillus flavus growth inhibitory potential of Ocimum basilicum leaves and branch extract by the rate of 82.8–87.7% and 57–68.3%, and Cassia fistula leaves and branch extracts by the rate of 23.6–49.8% and 16.4–42.3%, respectively. The aflatoxins B1 and B2 detoxifying efficacy of Ocimum basilicum and Cassia fistula (leaves and branches) aqueous extracts at its optimal temperature (25°C) and increased with increased incubation time, is high. Detoxification rate after 72-h incubation time of Ocimum basilicum leaves extract by 77.9% and 76.7%, O. basilicum branch extract detoxification by 36.6–65.7% and 48.9–57.0% and C. fistula leaves extract 30.3, 43.9% for AFB1 and AFB2, respectively (Ram et al., 2016). |
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| Method                                                                 | Controlling, detoxification, reduction mechanisms                                                                 |
|----------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------|
| Probiotics (single or mixed microbial strains)                        | • Aflatoxin B1 degradation rate with single Bacillus subtilis (38.38%), lactobacillus casein (26.06%) and candida utilis (21.08%) and a combined probiotic degradation effect on AFB1 of Bacillus subtilis: Lactobacillus casein: Candida Utilis (1:1:1); 45.5% AFB1 reduction, combined aspergillus oryzae enzyme (3:2); 63.95% AFB1 reduction, alkaloids in methanolic extract of A. vasica leaves leaf (Adhatoda vasica Nees) degradation of AFB1 (≥98%) in food and feedstuff (Huang et al., 2018; Vijayanandraji et al., 2014).  
• ZEA degradation rate with single Bacillus subtilis (42.18%), lactobacillus casein (19.05%) and candida utilis (40.69%), combined probiotics degradation rate of Bacillus subtilis: Lactobacillus casein: Candida subtilis (1:1:1); 44.9%, combined with aspergillus oryzae enzyme (3:2); 73.51% reduction in food and feed (Huang et al., 2018).  
• Probiotic Lactobacillus plantarum have binding capacity of AFB1, improve the antioxidant capacity, reduce oxidative stress by improving the antioxidant enzyme and exposures of Glutathione S-transferase (GST) (Huang et al., 2017), biotransformation and adsorption by Kefir culture; Lactobacillus kefiri, Kazakhstania servazzii and Acetobacter syzygii (Taheur et al., 2017).  
• Lactobacillus plantarum in milk was shown AFB1 reduction by 29.6% after 24 h of incubation at 37°C but no change was observed during cold temperature incubation. Lactobacillus acidophilus, lactobacillus rhamnosus and streptococcus thermophilus show AFB1 significant reduction incubated at 4°C starting from 24 to 196 h (Marrez, Shahy, El-sayed, & Sultan, 2018).  
• The aflatoxin binding ability of non-saccharomyces cerevisiae which was commonly found and believed to have an inhibitory effect for the toxigenic fungal growth and production of mycotoxins of fermented products. Isolates of non-saccharomyces cerevisiae such as Pichiaamaladta, Clavispora lusitaniae and Candida tropicalis which have a binding effect of aflatoxins (Deepak, Jhanvi, & Anuappoiah, 2015).  
• Six streptomyces strains of aspergillus flavus and aspergillus parasiticus interaction have mutual antagonism and greatly reduces the fungal growth and production of aflatoxin (Verheecke et al., 2015).  
• Four yeast and four mold strains of Zygosaccharomyces rouxii from fermented soybean, yogurt treated at 80°C, PH 10 and 10-min holding time under aerobic solid-state fermentation in peanut meal showed 16.18–42.47% reduction of AFB1 (Zhou et al., 2017).  
• Aspergillus oryzae MAO103 and A. oryzae MAO104 beta-tubulin gene degrade more than 90% of AFB1 in fermented soybean (Lee et al., 2017).  
• Eleven lactobacillus and 11 yeast strains in Kefir culture were capable to biotransform AFB1, OTA and ZEA by 31%, 12% and 10%, and adsorbed by 84%, 94% and 100%, respectively, in milk and grains (Taheur et al., 2017). Kefir grain (10%) is effective by 96.8% to detoxify 20 ng/g of AFG1 during 6 h and 30°C incubation condition with the kinetics of reduction of 5.42 *10⁻³ h⁻¹ (Ansari, Khodaiyan, Rezaei, & Rahmani, 2015; Bedre, Rajasekaran, & Mangu, 2015).  
• Azole fungicides are effective to control the growth of fungi in particular and its toxic metabolites such as deoxynivalenol (DON). DON (1360 µg/kg) and Culmorin (875 µg/kg) mycotoxins in wheat were significantly reduced with azole fungicide application (Scarpino, Reyneri, Sulyok, Kiska, & Blandino, 2014). |
### Table 2. (Continued)

| Method                               | Controlling, detoxification, reduction mechanisms                                                                                                                                                                                                 |
|--------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| **Use of Oxygen reactive substance inhibitors** | • Ozonation: The DON level was reduced with 26.40%, 39.16%, 53.48% exposed to 75mg/L Ozone for 30, 60, 90 min. The Ozonation has no effect on the quality and nutritional value but exhibited higher tenacity and whiteness, as well as lower extensibility and yellowness (Wang et al., 2016).  
• According to Agriopoulou, Koliadima, Karaiskakis, and Kapolos (2016) the level of sensitivity to Ozone: aflatoxins were labeled as: AFG1 > AFB1 > AFG2 > AFB2. AFG1 and AFB1 has degraded their active sites of the aflatoxin furan ring with 2–10 ppb ozone during 3–7 min. Complete destruction of AFG2 and AFB2 with the application of 34.3 mg/l ozone during 50–60-min exposure at any temperature was achieved.  
• Effective for the detoxification in livestock food and human food in dry, watery and moist condition (Mallakian, Rezanezhad, Jalali, & Goobadi, 2017).  
• H₂O₂ induced by the fungicide Prothioconazole: H₂O₂ induced by sublethal doses of the Strobilurins and triazoles fungicide triggers DON biosynthesis from fusarium (Audenaert, Callewaert, Höfte, Saeger, & Haesaert, 2010).  
• Reactive oxygen species inhibitors such as superoxide dismutase in the cytoplasm and mitochondria of mammalians are antioxidants and endogenous enzymes such as catalase have the ability to detoxify or decreases its accumulation of patulin toxins (Liu, Wu, Yu, & Su, 2007). |
| **Molecular Technology**             | • RNA silencing Technology: The structural RNA and regulatory RNA targeting messenger (mRNA) on the growth of aspergillus flavus and aspergillus parasiticus and production of AFB1 shows a reduction by 98%, 97%, and 97% respectively (Abdel-hadi et al., 2011).  
• Nanotechnology: The Fe₃O₄ nanoparticles are capable to remove AFM1 from milk by magnet attachment by ≥95% (Jouni et al., 2018).  
• Silver nanoparticles of (10–40 µg, average size of 9.99 nm) have the inhibitory effect on Aspergillus parasiticus (24.2%) and A. ochraceous (28.2%) at the optimal concentration of 40 µg, highest inhibitory effect. Silver nanoparticles are potential for the reduction of AFB1, AFB2, AFG1 and AFG2 at the range of 12–78%, average by 58.76%) in honey. The level of reduction is higher when the AgNP concentration increases (1–3 mg) (El-desouky & Ammar, 2016). |
absorption and excretion, analytical methods, sampling, associated intake, direct consumption with or without treatment and requirements for further processing (Egmond et al., 2007; Solerizzo et al., 2018; Zhang et al., 2018). As a result, countries adopt the Codex standards or develop their own standards based on Codex standards considering the intake level and handling condition in a specified environment. However, in developing world, the existence of the regulation, implementation and monitoring is lagging behind (Alberts et al., 2016) where mycotoxin might be contributing to child malnutrition and associated health problems are higher. The set of regulatory limits as shown in table 1, are according to the maximal tolerable limit in food and feed, used as a guideline to avoid contamination, health risk to humans and animals, and promote food international trade (Egmond et al., 2007). However, depending on the daily intake of food or group of foods, consumer type and presences or absence of subsequent treatments, the limits can vary (Egmond Van & Jonker, 2003).

5. Mycotoxin detoxification and reduction

Understanding of the location or distribution mechanism of mycotoxin in grains, fluid food and biosynthesis is important to identify the toxic-inducing part and their prevention methods. According to the Yu, Bhatnagar, and Cleveland (2004) investigation, the aspergillus parasiticus-induced AFB1, AFB2 and AFG1 synthesis involves 14–15 pathways and more than 25 enzymes which alter the genome sequences and facilitate the toxin synthesis process. The phytohormone signaling in the food or agricultural commodities is responsible for the activation of the calcium signaling which resulted oxidative stress to damage the tissues or nucleotides within few exposure time, while it can be prevented by calcium signaling blockers (channel blockers) such as LaCl3 (Li et al., 2019; Rentel & Knight, 2004). Extracellular hydrogen bonds are communication bridges where external fungi contaminates associate themselves to the crop/food (Fountain et al., 2015; Gacem & Hadj-khelil, 2016). Controlling the stress-inducing factors such as humidity, hotness and mechanical stress, quorum sensor understanding, protein signaling pathways (Gilbert et al., 2016) contribute to the prevention of aflatoxicogenic and mycotoxin occurrence (Gacem & Hadj-khelil, 2016). Studies showed numerous controlling mechanisms of fungi growth and its metabolites in the value chain as shown in Figure 1 and summarized Table 2.

6. Conclusion and future perspectives

In conclusion, fungi grow virtually everywhere which affects the quality, safety and productivity of agricultural produce, and produce toxic metabolites. Taking into consideration the consumption frequency, toxicity and bioavailability of mycotoxins, chemical, physical and biological prevention methods have been discovered. The chemical preservatives include high-oxidative power ozone with a wider spectrum, nanoparticles to bind/detoxify and fungicides. Physical prevention includes good practices from farm to fork; biological mitigation techniques include genome transcriptomes, mRNA silencing to advance disease-resistant breeds or monitor toxin biosynthesis, alerting the process condition and product composition by maintaining optimal quality. Commercialization and application of easily accessible, available, affordable and biologically safe bioactive plant extracts, single or mixed probiotics, enzyme extracts is a promising prevention in the food-value chain and promoting healthy consumption. However, the techniques, formulation and stability of the mitigation methods and substrates are not clear, and further investigations are required.

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Competing Interest
The authors declare no competing interest.

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