Microbial Pathogenesis 142 (2020) 104095

Contents lists available at ScienceDirect

Microbial Pathogenesis

journal homepage: www.elsevier.com/locate/micpath

Review

# Mycotoxin contamination and control strategy in human, domestic animal and poultry: A review

Md Atiqul Haque[a,b], Yihui Wang[a], Zhiqiang Shen[c], Xiaohui Li[a], Muhammad Kashif Saleemi[d], Cheng He[a,*]

[a] Key Lab of Animal Epidemiology and Zoonoses of Ministry of Agriculture, College of Veterinary Medicine, China Agricultural University, Beijing, 100193, China
[b] Department of Microbiology, Faculty of Veterinary & Animal Science, Hajee Mohammad Danesh Science and Technology University, Dinajpur, 5200, Bangladesh
[c] Binzhou Animal Science and Veterinary Medicine Academy of Shandong Province, Binzhou, 256600, China
[d] Department of Pathology, Faculty of Veterinary Science, University of Agriculture, Faisalabad, 38040, Pakistan

ARTICLE INFO

*Keywords:*
Mycotoxin
Biological detoxification
Toxigenic fungus
Nanotechnology

ABSTRACT

Mycotoxins are secondary metabolites produced mainly by fungi belonging to the genera *Aspergillus*, *Fusarium*, *Penicillium*, *Claviceps,* and *Alternaria* that contaminate basic food products throughout the world, where developing countries are becoming predominantly affected. Currently, more than 500 mycotoxins are reported in which the most important concern to public health and agriculture include AFB1, OTA, TCTs (especially DON, T-2, HT-2), FB1, ZEN, PAT, CT, and EAs. The presence of mycotoxin in significant quantities poses health risks varying from allergic reactions to death on both humans and animals. This review brings attention to the present status of mycotoxin contamination of food products and recommended control strategies for mycotoxin mitigation. Humans are exposed to mycotoxins directly through the consumption of contaminated foods while, indirectly through carryover of toxins and their metabolites into animal tissues, milk, meat and eggs after ingestion of contaminated feeds. Pre-harvest (field) control of mycotoxin production and post-harvest (storage) mitigation of contamination represent the most effective approach to limit mycotoxins in food and feed. Compared with chemical and physical approaches, biological detoxification methods regarding biotransformation of mycotoxins into less toxic metabolites, are generally more unique, productive and eco-friendly. Along with the biological detoxification method, genetic improvement and application of nanotechnology show tremendous potential in reducing mycotoxin production thereby improving food safety and food quality for extended shelf life. This review will primarily describe the latest developments in the formation and detoxification of the most important mycotoxins by biological degradation and other alternative approaches, thereby reducing the potential adverse effects of mycotoxins.

## 1. Introduction

Mycotoxins are naturally occurring toxins produced by certain species of *Aspergillus*, *Fusarium*, *Penicillium*, *Claviceps*, and *Alternaria*. Recently about 100,00 fungi have been identified, among these more than 500 mycotoxins have been reported as potentially toxigenic, major mycotoxins influencing human and animal health include aflatoxins (AFTs), ochratoxins (OTs), trichothecenes (TCTs), fumonisins (FUMs), zearalenone (ZEN), patulin (PAT), citrinin (CT) and ergot alkaloids (EAs) [1–3]. These compounds produced by mould infection at pre- and post-harvest crops under natural conditions worldwide. The historical evidence of the mycotoxicological risk has existed since the first stage of organized agricultural production. The first report on human mycotoxicoses dates back to Middle Ages, “St. Anthony's Fire” which was associated with toxicity of both gangrenous and convulsive form due to ergotism from *Claviceps purpura* related to moldy rye [4]. The mycotoxins may induce acute to chronic effects resulting in carcinogenic, mutagenic, teratogenic, immunosuppressive and endocrine-disrupting effects both on humans and animals [5]. The acute toxicity may result in consuming a moderate toxin causing deterioration of liver or kidney functions extremely leading to death. Chronic toxicity may result in consuming moderate to low quantity of toxins causing production loss in the form of poor growth rate, reduced productivity and inferior market quality. Consumption of low quantity of toxins often susceptible to various infectious diseases specially secondary bacterial infections or a heavy progression of some often encountered parasitic

* Corresponding author.
*E-mail address:* hecheng@cau.edu.cn (C. He).

https://doi.org/10.1016/j.micpath.2020.104095
Received 10 December 2019; Received in revised form 17 February 2020; Accepted 21 February 2020
Available online 22 February 2020

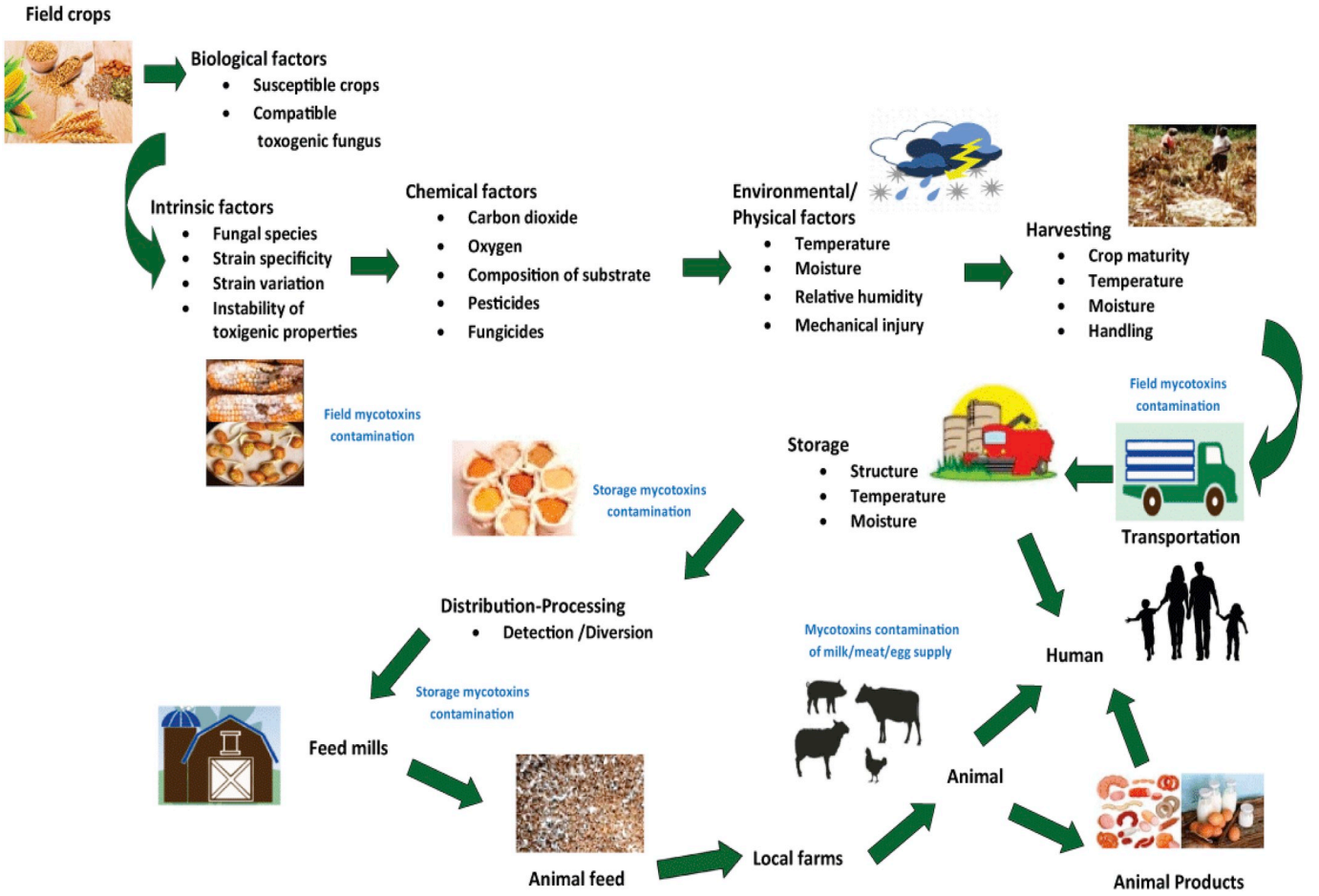


**Fig. 1.** Factors affecting mycotoxin occurrence in the food and feed chain [9,10].

diseases [6]. The predisposing conditions for toxin production are mainly related to biological, chemical, physical or environmental factors (Fig. 1). It is estimated that approximately 25–50% of cereal products produced world-wide are significantly contaminated with mycotoxins to a varying degree and 5–10% of which are irreversible causing huge economic losses [7]. Mycotoxins cause mortality of human and animal, or increased health and veterinary care cost, or decreased production efficiency, or by rendering commodities unacceptable for national or international trade [8]. Regulatory guidelines and limits for mycotoxins have been set by the European Union (EU), Food and Drug Administration (FDA) of the USA and other countries for both import and export of affected commodities. In this review, we discussed the recent evidence on mycotoxicity associated risks to human and livestock health, prevention and control strategies to ensure consumer's health and safety.

## 2. Occurrence and types of mycotoxins

Mycotoxins are small and quite stable toxic molecules, extremely difficult to remove or eradicate present in agricultural and animal products. The origin, available food, affected species, pathological effects, and toxicities are summarized in Table 1 and tolerable limits of different mycotoxins in the food chain by different countries and authorities are shown in Table 2. Mycotoxin contamination usually exists in the field by foods and feeds following infection of toxogenic fungus in the pre-harvest period, then suitable environmental conditions for spoilage fungi during processing, storage and distribution of harvested products in post-harvest period. Mycotoxin can enter to human food chain directly by consuming contaminated plants and food products and indirectly through residues in milk, meat, eggs, and their derivates. The mycotoxin occurrence in the food chain and their residual effect on human and animal health has been shown in Fig. 2.

### 2.1. Aflatoxins (AFTs)

AFTs are difuranocoumarins or furanocoumarins mainly produced by *Aspergillus* spp. (*flavus* and *parasiticus*) [15–17]. There are >20 types of AFT molecules, the most prominent are difurocoumarocyclopentenone group (AFB1, AFB2, AFM1, and AFM2) and difurocoumarolactone group (AFG1 and AFG2) [18]. AFB1, AFB2, AFG1, and AFG2 are ubiquitous in food and feedstuff while, AFM1 derived from AFB1 in the liver by hepatic microsomal cytochrome P450, can enter through blood circulation and be excreted into milk [19,20]. The toxicity profile of AFTs is B1 > M1 > G1 > B2 > M2/G2 etc. Among all discovered mycotoxins, AFTs are the most potent mycotoxins with acute toxicological and chronic hepatocarcinogenic effects in the liver based on their reactivity with DNA, RNA, enzymes, and proteins [21]. Cumulative evidence links chronic aflatoxicosis with hepatocellular carcinoma (HCC) or liver cancer while, acute aflatoxicosis with abdominal pain, vomiting, edema, and death have been reported in China, India, Malaysia and Kenya [22,23]. Recent research revealed that the global burden of AFT may contribute to the occurrence of 4.6–28.2% of all global HCC, the third leading cause of cancer deaths globally and is also susceptible to lung, GI tracts and cause kidney injury in mice and calf models [19,24]. In poultry, ducks are the most sensitive to AFTs followed by turkey, quails, broiler, and layers; toxicity includes fatty liver, kidney disorder, leg, and bone deformity, reduced weight gain and productivity, immunosuppression, small and poor quality eggs,

**Table 1**
Major food-borne mycotoxins, their main producing fungal species, the commodities most frequently contaminated, and their primary health effects on animals and humans.

| Mycotoxin | Fungal species | Food commodity | Affected species | Pathological effects and toxicities | Ref. |
|---|---|---|---|---|---|
| Aflatoxins (AFB1, AFB2, AFG1, AFG2, AFM1, AFM2) | *Aspergillums (flavus, nomius, parasiticus, arachidicola, bombycis, pseudotamarii, minisclerotigenes, rambellii)* *Emericella (astellata, venezuelensis, olivicola)* | Maize, wheat, rice, spices, sorghum, ground nuts, tree nuts, almonds, oilseeds, dried fruits, cheese, spices, milk & dairy products, eggs, meat | Birds: duck, turkey, pheasant, chicken, quail Mammals: pig, dog, cattle, sheep, cat, monkey, human Fish: Laboratory animal | Carcinogic, mutagenic, hepatoxic, teratogenic, nephrotoxic, immunosuppressive | [20], [28–32], [34] |
| Ochratoxins (OTA, OTB, OTC) | *Aspergillus (alutaceus, alliaceus, niger, auricomus, glaucus, steynii, citricus, fonsecaeus, ochraceus, carbonarius, cretensis, meleus)* *Neopetromyces muricatus,* *Penicillium (viridicatum, verrucosum, cyclopium, carbonarius, verrucosum)* | Cereals, barley, wheat, dried vine fruit, wine, coffee, oats, spices, rye, raisins, grape juice | Pig, dog, duck, chicken, rat, human | Nephrotoxic, hepatotoxic, neurotoxic, mutagenic, teratogenic, immunodepressants, carcinogenic (urinary tract tumors), inhibition of protein synthesis | [20], [28–33] |
| Trichothecenes (T-2, HT-2, DAS, NIV, DON) | *Fusarium (sporotrichioides, graminearum, cerealis, moniliforme, myrothecium, lunulosporum, culmorum, equiseti, poae) Cephalosporium sp., Myrothecium sp., Trichoderma sp., Verticimonosporium sp.* *Phomopsis sp., Stachybotrys sp.* | Cereals, cereal products | Pig, cattle, chicken, turkey, horse, rat, dog, mouse, cat, human | Cytotoxicity, immuno-depressants, mutagenic, neurotoxic, anorexia & diarrhea, weight loss, neuroendocrine changes, leukocytosis, hemorrhaging, or circulatory shock, oral lesions, dermatitis, infertility | [20,28], [29,31–33] |
| Fumonisins (FB1, FB2, FB3) | *Fusarium (anthophilum, moniliforme, dlamini, globosum, napiforme, proliferatum, nygamai, verticillioides, oxysporum), Alternaria alternate* | Maize, maize products, corn based products, sorghum, asparagus, rice, milk | Horse, pig, rats, chicken human | Hepatotoxic, immunotoxic, cytotoxicity, carcinogenic, apoptosis, pulmonary edema, immune-depressants | [20,28,29,31–33] |
| Zearalenone (ZEN) | *Fusarium(graminearum, culmorum, crookwellense, equiseti, sporotrichioides, cerealis, incarnatum)* | Barley, oats, wheat rice, sorghum, sesame, soybeans, cereal-based products | Pig, dairy cattle, chicken, turkey, lamb, rat, mouse, guinea pig, human | Carcinogenicity, immunotoxicity, genotoxicity, reproductive & developmental toxicity, oestogenic effects, prolapse of vagina, abortion | [20,28,29,31,32] |
| Patulin (PAT) | *Aspergillums(clavatus, ongivesica, terreus),* *Penicillium (expansum, patulum, crustosum, griseofulvum)* *Byssochlamys sp.* | Apples, apple juice, cherries, cereals, apricots, grapes, pears, peaches, olives, bilberries | Birds: chicken, chicken embryo, quail Mammals: Cat, cattle, mouse, rabbit, rat, human Others: Brine shrimp, guppie, zebra | Neurotoxicity, embryotoxicity, teratogenicity, immunotoxicity, convulsions, dyspnea, pulmonary congestion, edema, ulceration of GI tract | [28], [30–32] |
| Citrinin (CT) | *Penicillium citrinum, P. expansum, P. radicicola, P. verrucosum* *Monascus purpureus, M. ruber* | stored grains and grain-based products, cheese, sake, and red pigments as well as in spices | Chicken, pig, human | Reproductive toxicity, nephrotoxic, embryotoxic, teratogenic, hepatotoxic, immunotoxic, carcinogenic | [28,32,34] |
| Ergot alkaloids (Ergometrine, ergotamine, ergosine, ergocristine, ergocryptine & ergocornine) | *Claviceps (africanana, purpurea, fusiformis, paspali)* *Neotyphodium coenophialum* | Wheat, rye, hay, barley, millet, oats, sorghum, triticale, grass | Fish larvae, pigs, cattle, swine, horses, swine, human | Neurotoxicity, endocrine disruption gangrenous form: edema of the legs, paraesthesias, gangrene at the tendons convulsive form: nausea, vomiting, drowsiness, ataxia, convulsions, blindness, paralysis | [28] |

**Table 2**
Maximum tolerable limit (MTL) and maximum residue limit (MRL) of mycotoxin in the food chain [50–56].

| Country/authority | Mycotoxins | Food commodities | Limit (μg/kg) | |
|---|---|---|---|---|
| | | | MTL | MRL |
| USA | Total AFT | Meat | 20 | 20 |
| | | Egg | 20 | 20 |
| | AFM1 | Milk, milk products | 0.5 | – |
| | ZEN | – | 30 ng/kg BW TDI | – |
| EU | Total AFT | Meat | 4 | 4 |
| | | Egg | 4 | 4 |
| | | Milk | 4 | – |
| | AFB1 | Milk | 2 | – |
| | AFM1 | Milk | 0.05 | – |
| | | Infant milk | 0.025 | – |
| | OTA | Pork | ≤25 | – |
| | | Milk | 5 ng/kg BW TDI | – |
| | | – | 120 ng/kg BW TWI | – |
| | DON | – | 1 μg/kg BW/TDI | – |
| | FB1, FB2, FB3 | – | 2 μg/kg BW/PMTDI | – |
| | ZEN | – | 60 to 200 | – |
| | PAT | – | 0.4 μg/kg BW/PMTDI | – |
| WHO | AFM1 | Milk | 0.50 | |
| | FB1 | – | 2 μg/kg/BW PMTDI | |
| Joint FAO/WHO | ZEN | – | 0.5 μg/kg BW MTDI | |
| | OTA | – | 100 ng/kg PTWI | |
| | FUM | – | 2 μg/kg/BW PMTDI | – |
| | DON | – | 1 μg/kg/BW PMTDI | |
| Canada | ZEN | – | 20 ng/kg BW TDI | – |
| Norway | ZEN | – | 20 ng/kg BW TDI | – |
| Italy | OTA | Pork meat and derived products | 1 | – |
| Estonia | OTA | Pig liver | 10 | |
| Denmark | OTA | Pork | – | 25 |
| | | Pig kidneys | 10 | 10 |
| | | Pig liver | – | 25 |
| | ZEN | – | 20 ng/kg BW TDI | – |
| France | AFM1 | Infant milk (<3 years) | 0.03 | – |
| | | Milk powder | 0.5 | – |
| | | Infant milk powder (>3 years) | 0.3 | – |
| | FB1 | Avian kidney and liver | – | 100 |
| China | AFM1 | Milk and milk products | 0.5 | – |
| Japan | Total AFT | Meat | 10 | – |
| | | Egg | 10 | – |
| | AFM1 | Milk | 0.5 | – |
| Korea | AFM1 | Milk | 0.5 | – |
| Malaysia | AFM1 | Milk | 0.5 | – |
| | | Infant milk | 0.025 | – |

TDI = tolerable daily intake; TWI = tolerable weekly intake; PMTDI = provisional maximum tolerable daily intake; BW = bodyweight

pigmentation problems, etc. [25,26]. In an experimental study, it is found that AFB1 causes severe kidney and liver damage in broiler birds along with concurrent infection with Fowl Adenovirus-4, leading to severe hydropericardium syndrome [27].

### 2.2. Trichothecenes (TCTs)

TCTs consist of approximately 200 structurally related compounds, are divided into 4 types (A-D), importantly type-B: deoxynivalenol (DON) and nivalenol (NIV) and type-A: T-2 toxin and its major metabolite HT-2 toxin [35,36]. The most acutely toxic TCT in animals is T-2 while, sensitivity varies among animal species especially in dairy cows, it has been related to feed refusal, gastroenteritis, intestinal hemorrhages, and death while in poultry it causes intestinal lesion and weight loss [37,38]. In research reports it is found that DON concentrations of 1–7 mg/kg diet significantly decreasing absorption area of villus surface and also altering the permeability of the gastrointestinal tract resulting both immunosuppressive and immunomodulating effects in poultry [39–41]. DON toxicity has been associated with animal and human gastroenteritis outbreak resulting in typical acute symptoms such as nausea, vomiting, abdominal pain, diarrhea, headache, dizziness, or fever thereby also called it vomitoxin [42]. Several outbreaks of acute DON toxicity in humans have been reported in India, China, and the USA to strengthen the potential risk for humans [22].

### 2.3. Fumonisins (FUMs)

There are 28 known important FUM analogs among which FB1 is the most prominent followed by FB2 and FB3 [36]. Consumption of corn-based feed containing FUMs are known to be responsible for fatal brain disease, equine leuko-encephalomalacia in horse and swelling of lungs and thorax, porcine pulmonary edema syndrome in pig [15]. The mode of action by which FUM causes toxicity in animals seems to be due to the collapse of sphingolipid metabolism [40]. The occurrence of FB1 is correlated with the presence of a higher incidence of esophageal cancer is related to the intake of corn grains containing FUMs in human have been reported in South Africa and China [36,43]. In other studies reported that esophageal cancer and neural tube defect has been linked to consumption of FB1 contaminated maize in human as well as numerous illness in animal have been observed along the US-Mexico border, in Guatemala, Egypt, South Africa and China [36,44,45].

### 2.4. Ochratoxins (OTs)

OTs were discovered as three secondary metabolite forms, A, B and C differ in that OTB is nonchlorinated and OTC is an ethyl ester form of

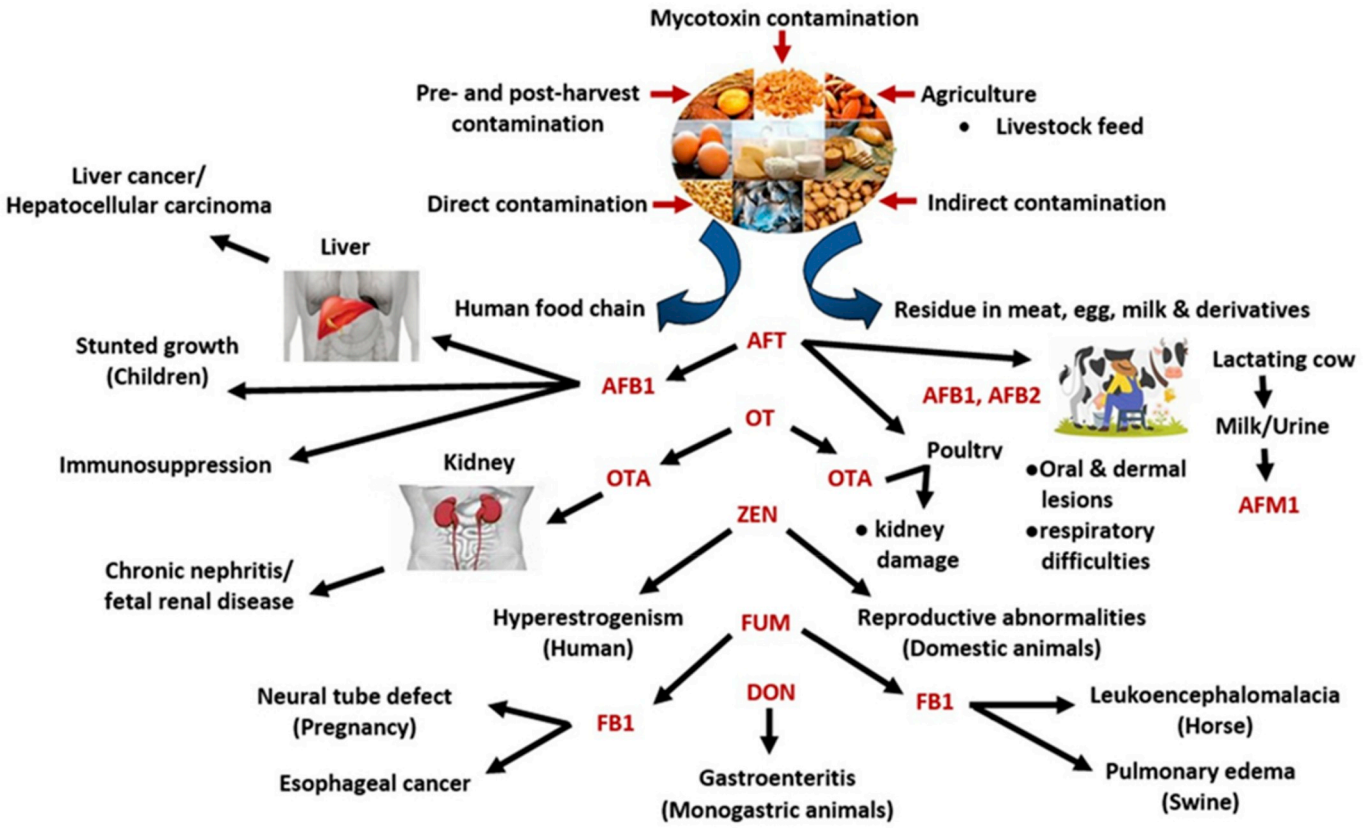


**Fig. 2.** Mycotoxins occurrence in the food chain and their residual effect on human and animal [11–14].

OTA [15,46,47]. OTA is found in beverages (beer and wine) contaminated with *Aspergillus ochraceus* and certain wines specially made from vine fruits such as grapes contaminated with *Aspergillus carbonarius* [48,49]. OTA is a nephrotoxin as well as a hepatotoxin, immune suppressant, potent teratogen and carcinogen to all animal species. OTA toxicity in poultry causes weakness, anemia, reduced feed consumption, decreased productivity, poor feathering, excessive mortality at high dietary concentration and hypocarotenidemia in broilers [40]. In human studies, OTA has been linked with fatal renal disease, such as Balkan endemic nephropathy, a progressive chronic nephritis and upper urothelial tract cancer [22,35]. It also causes porcine nephropathy (kidney damage) in pigs and tail necrosis in newborn piglets [46].

### 2.5. Zearalenone (ZEN)

ZEN is known as mycoestrogen, a subset of naturally occurring estrogenic compounds which is heat-stable and capable of binding estrogen receptors, causing adverse impact involved with reproductive disorders and hyperestrogenism, both in humans and farm animals [46,57]. Swine are reported as the most sensitive domestic animals affected on the farm compared to cattle and sheep, while it causes estrogenic syndrome, including enlarged mammary gland and genitalia, atrophy of ovaries and testes, abortion and stillbirths, reduced litter size and piglets viability [36,46]. Occurrences of swine estrogenic syndrome have frequently evident in North America and Europe but also high levels of ZEN have been reported from China and other Asian countries [36]. In laboratory animals (mice, rats, guinea pig, hamster, and rabbit) it causes reproductive toxicity and premature puberty syndrome [38,42].

### 2.6. Citrinin (CIT)

CIT is a secondary toxic benzopyran metabolite generally formed post-harvest condition and mainly found in stored grains, but also present in plant origin products such as rice, wheat, barley, rye, beans, pomaceous fruits, fruit juices, nuts and spices, and also in spoiled dairy products [34,58]. It represents a significant health hazard especially in tropical countries where it is a major source of food poisoning after fungal contamination. CIT is associated with yellowed rice disease in Japan and acts as a nephrotoxin in all animal species but acute toxicity differs in various species [46,49]. CIT is quickly absorbed and disseminated in the liver and kidney, the human toxicokinetic study showed that 40% of CIT was excreted via urine [42]. In a report, it is found that it has been related to pig nephropathy after the consumption of contaminated barley grains [59]. It can also act concurrently with OTA to depress the mechanism of RNA synthesis in murine kidneys [15,46].

### 2.7. Patulin (PAT)

PAT is considered a serious hazard for fruits at the post-harvest stage, first contacts the surface, then contaminates whole fruit and can spread to other fruits stored together, resulting in the disease known as “blue mould" which is common in apple, cherry, figs and other fruits [46]. Apples are found to be an vital source of PAT since they are readily infected by *Penicillium expansum* which is considered as the efficient natural source of PAT and its contamination in apple juice is a worldwide problem [46,60]. The report revealed that approximately 50% of the analyzed samples were comparatively high detectable PAT levels in apple juice globally while, organic apples have higher PAT contamination in baby food compared to conventional apples [35]. PAT represents various acute and chronic toxicity, such as nausea, vomiting, and gastrointestinal disturbances acutely, while in chronic cases, damage to kidney and liver, immunosuppression, carcinogenicity, and genotoxicity have been reported [61].

### 2.8. Ergot alkaloids (EAs)

EAs are compounds produced as a toxic mixture of alkaloids in the sclerotia (purplish or black structures) of *Claviceps* and *Neothyphodium* species, which are usually common pathogens of various grass species and cereal crops [62]. The recent development of grain cleaning methods notably mitigate ergotism in human whereas yet is an important veterinary issue since EAs have been used as pharmaceutical preparation [15,49]. The most prominents of EAs include compounds such as ergotamine, ergometrine, ergocristine, ergocryptine, ergocornine, and ergosine which usually co-appear in contaminated feed [62]. Toxicity of EAs in humans can cause hallucinations, convulsions, fever, distorted perception, acute burn, agalactia , such as gangrene, abortion, convulsions, suppression of lactation and hypersensitivity [47,62,63]. An outbreak of ergot toxicoses was reported the cause of death of eight calves fed a pelleted creep feed in the USA [64].

## 3. Current methods in the analysis and structural elucidation of mycotoxins

Analysis of mycotoxin in foods and feeds is a crucial practice to ensure food security and removal and control of health risks by contaminated foods and feeds. Several detection methods have been developed, among the most common methods currently used are described below.

### 3.1. Chromatographic techniques (CTs)

CTs represent a group of techniques most widely used for quantitative analysis of mycotoxin in food and feed samples which are highly, accurate, sensitive result and also assist the validity of other methods [31,65]. High-performance liquid chromatography (HPLC), Thin-layer chromatography (TLC), Gas chromatography (GC) and liquid chromatography-tandem mass spectrometry (LC-MS/MS) are commonly used for mycotoxin analysis. In China, HPLC coupled with ultraviolet (UV), diode array (DAD), fluorescence detector (FLD) or mass spectrometry (MS) detector has been used to detect AFT, OTA, DON, ZEN, FUM, CIT and PAT and by coupling Liquid chromatography techniques to mass spectrometry (LC-MS/MS) has been used for the simultaneous detection of multiple (hundreds) mycotoxins in various products [31,66]. TLC is cost-effective, simple and suitable for rapid screening of common mycotoxin, but the lack of automation limits its use; moreover, GC coupled with electron capture (ECD), flame ionization (FID) or MS detector have been applied for volatile mycotoxins (TCT and PAT) [31,67].

### 3.2. Immunological methods

#### 3.2.1. Enzyme-linked Immunosorbent Assay (ELISA)

ELISA has been a commonly used immunoassay method for the detection of major mycotoxins in a large number of food samples. It can be performed by direct, indirect and competitive inhibition method where an enzyme-labeled primary and secondary antibody reacts with antigen in direct and indirect detection, respectively; moreover, in competitive inhibition method, unlabeled antigens from samples and enzyme conjugated compete to bind with an antibody directed against the specific mycotoxin [65]. This method has the advantage of a relatively low limit of detection, highly specific, minimal cleanup procedure, high sample yield with low sample volume and ease of application; meanwhile possibility of a false positive and false negative result, single-use of kits and unsuitable for complex matrices restricts its use for field-testing [68].

#### 3.2.2. Lateral Flow Immunoassay (LFIA)

LFIA has designed using the principle of ELISA available as commercial kits for the visual qualitative detection of a specific mycotoxin. This method is a low-cost, very simple, rapid, one-step screening tool for mycotoxin analysis at the field level, besides the possibility of semi-quantitative detection using a portable photometric strip reader [65,69]. A multiplex LFIA has designed and optimized that provides both qualitative and quantitative for coinciding in situ determination of AFB1, ZEN, and OTA in grains [65].

#### 3.2.3. Fluorescence Polarization Immunoassay (FPIA)

As compared to ELISA and LFA, the FPIA needs only a few minutes without separation and washing methods and indirectly measure the quantitative detection of mycotoxin by determining the rate of a fluorophore (tracer) in the solution where free mycotoxin on the sample competes with mycotoxin labeled with the tracer towards a specific antibody [65,70]. Nowadays commercial FPIA kits are available which can be used for monitoring AFT, DON, and FUM in cereal at large-scale; besides FPIA could be used as a screening method for the simultaneous detection of the ZEN in naturally contaminated maize sample [70].

### 3.3. Biosensor methods

Compared with above conventional techniques, biosensors methods have been proved as potential to allow rapid, highly sensitive, robust, portability, real-time detection capability, high-throughput, and cost-effective quantitative technology in testing food samples [71,72]. Up to now development of new and emerging advancement in the analysis of mycotoxin, nanomaterials and biosensor fabrications technology as sensing receptors for mycotoxin, transducer technology at the micro/nanoscale as multiplex analysis and nano-tracking systems, micro and nanosystems as food tracking, electrochemical immunosensors, fluorescent nitrogen-doped carbon dots, lab-on-a-chip devices, microarray, and nanotechnology can be used [65,71].

## 4. Prevention and control of mycotoxins contaminations

It has been accepted that the prevention of different mycotoxins contamination is the primary measure and alternative over the other control methods. Still numerous physical and chemical detoxification control strategies have been established to prevent the growth of toxigenic fungus and mycotoxin contamination, few strategies fulfill the standards due to their heavy cost, bio-safety risk, losses in the nutritional quality and the palatability of the products or limited binding effect. Therefore it is necessary to develop appropriate detoxification methods to ensure food safety for human consumption. Table 3 summarizes the advantages and disadvantages of different mycotoxin detoxifying agents. In this article, we discussed below the biological detoxification methods and innovations for control and mitigation of mycotoxins problem.

### 4.1. Biological detoxification

Biological detoxification refers to the degradation or enzymatic transformation of mycotoxins into less toxic compounds comprising acetylation, glycosylation, ring cleavage, hydrolysis, deamination, and decarboxylation.

#### 4.1.1. Mycotoxin modifiers

Control of mycotoxicoses with the application of microorganisms and their enzymes is called mycotoxin modifiers which biotransform mycotoxins into less toxic metabolites. They are classified as -

*4.1.1.1. Use of microorganisms.* Biological approaches for mycotoxins decontamination by using microorganisms and specific kinds of isolated yeasts have been used effectively for the management of mycotoxins in food and feeds. Mechanisms in the removal of toxins by microorganisms are still investigated and successful results have been obtained related

**Table 3**
Comparison of different mycotoxin detoxifying products [18,92–96].

| Products | Bacteria | Fungus | Yeast | Enzymes | Chemicals | Physical |
|---|---|---|---|---|---|---|
| | *Bacillus licheniformis, B. natto, B. subtilis, Brevibacterium casei, B. linens, B. iodinum, Nocardia corynebacteroides, Mycobacterium fluoranthenivorans, Rhodococcus erythropolis, Mycococcus fulvus, Pseudomonas putida, Serratia* spp, *Stenotrophomonas maltophilia, Brevundimonas* spp, *Klebsiella* spp, *Cellulosimicrobium* spp, *Lactic acid bacteria, Pediococcus parvulus,* | *Aspergillus niger* | *Trichosporon mycotoxinivorans* | Peroxidase, Laccase, Myxobacteria aflatoxin degrading enzyme (MADE), Carboxylesterase B & aminotransferase, Cytochrome P450 system (Ddna + Kdx + KdR), Ochratoxinase, Lactono hydrolase, 2cys-peroxiredoxin | Ammonia/Ammonia with calcium hydroxid, Ozone, Sodium bisulphate, Hydrogen peroxide, Sodium bicarbonate, Sodium chloride, Calcium hydroxide | Automated removal of damaged kernels, Fluorescence sorting, Flotation, Pressure cooking, Microwave heating, Rinsing, Nixtramalization, Roasting, Wet-milling, Sunlight, heat processing, UV light irradiation, Gamma radiation, Pulsed light technology, Electron beam irradiation (EBI) |
| Toxin-specific Advantage | AFB1, OTA, FB1, DON, ZEN<br>● High specificity<br>● Safe<br>● Fermentation process<br>● Application for food and feed<br>● Comparatively rapid process<br>● Cheap | OTA | OTA, ZEN | AFB1, OTA, FB1, DON, ZEN<br>● High specificity<br>● Safe<br>● No loss of appearance or food quality | AFT, OTA, FUM, DON, ZEN<br>● Moderate specificity | AFT, OTA, FUM, DON, T-2, ZEN, PAT,<br>● Non-invasive<br>● Product stability<br>● Safe<br>● Rapid & highly effective |
| Disadvantage | ● Sometimes do not show good efficacies in field conditions<br>● Long incubation time was required for detoxification (more than 72 h)<br>● Incomplete degradation, non-adaptation to typical food fermentations & culture pigmentation<br>● Expensive at startup | | | ● Instability<br>● Not applicable for all types of mycotoxins | ● Toxic residue<br>● Loss of nutritional quality of food & feeds<br>● Corrosive<br>● Expensive<br>● Development of resistance | ● Incomplete<br>● Loss of quality of food or feed<br>● Discoloration & off-flavor<br>● Cross-contamination<br>● Not effective for all food items<br>● Development of mutant & resistant strains<br>● Expensive<br>● Residual effects |

to this method in recent years. A wide range of microorganisms including bacteria, fungi, and yeasts has proved biodegradation capacity.

*4.1.1.1.1. Bacteria.* Mycotoxin degrading bacteria have been isolated from different sources like rumen and intestinal flora, soil, and even water. Lactic acid bacteria (LAB) namely *Lactobacillus*, *Bifidobacterium*, *Propionibacterium*, and *Lactococcus* are significantly bound with AFB1 and AFM1, whereas, *Lactobacillus rhamnosus* was found as the excellent binding capability with AFB1 in contaminated wheat flour during the bread-making process [73,74]. Therefore special attention to LAB as they prevent the growth of molds and mycotoxins, and improve the feed utilization via specific hydrolytic enzymes production that decomposes carbohydrates and increases host's enzyme activity, such as β-galactosidases, saccharase, and maltase [75]. In recent reports *Bacillus licheniformis* CFR1 showed more than 90% degradation of AFB1 and a newly isolated bacterial strain *Lysinibacillus* sp. ZJ-2016-1 from chicken large intestine proved useful in the removal of ZEN in Luria Bertani (LB) broth within 48 h [76,77]. Interestingly, *B. subtilis* ANSB01G isolated from normal broiler intestinal chyme could efficiently reduce ZEN in naturally contaminated corn, distiller's dried grains with solubles (DDGS) and swine complete feed [78]. *Pseudomonas aeruginosa N17-1* were able to degrade AFB1, AFB2, and AFM1 in Nutrient Broth medium, while cell-free supernatants of *P. putida* DSM 291T and KT2442 were able to remove OTA [79,80]. In another report, *P. alcaliphila TH-C1* and *P. plecoglossicida TH-L1*, isolated from soil showed ZEN degradation ability [81]. A bacterium *Devosia mutans* 17-2-E−8 from an agricultural soil was capable of transforming DON to the less toxic product in vitro and in vivo studies [82]. A novel bacterium, *Eggerthella* sp. DII-9 has been isolated recently from chicken intestines that are capable of detoxifying TCTs (DON, HT-2, T-2 triol, and T-2 tetraol) with high de-epoxidation efficiency [83].

*4.1.1.1.2. Fungi and yeast.* Fungal species, *Aspergillus, Alternaria, Absidia, Armillariella, Candida, Dactylium, Mucor, Penicillium, Peniophora, Pleurotus, Trichosporon, Rhizopus* have been shown the ability to degrade different mycotoxins [84]. The appropriate quantity of yeast as feed additive decreases the bioavailability of mycotoxins in the GI tract which is removed through feces [85]. In vitro studies revealed that, yeast cell wall containing beta-glucans and mannan oligosaccharides can efficiently bind with AFB1 up to 90%, depending on the level [86]. Distillery yeast sludge (DYS), composed of *Saccharomyces cerevisiae*, *Candida parapsilosis*, and *Candida guilliermondii* are a rich source of proteins, lysine, tryptophan, phosphorus, crude fiber, iron, mannan, glucan and ascorbic acid that formed as a by-product of molasses fermentation. Research report suggested that DYS possesses the ability to prevent the absorption of mycotoxin in GI tract can be used as a poultry feed additive as it partially ameliorated the immunotoxic effects of mycotoxins [87]. *Aspergillus parasiticus* (NRRL 2999 and NRRL 3000) actively degraded AFTs*, A. tubingensis* NJA-1, isolated from soil, showed the ability to degrade DON, *A. niger* degrades OTA to the less toxic compound OTα, also capable to remove ZEN by incubation in contaminated culture medium after 24 h [88]. *Trichosporon mycotoxinivorans* and *Rhizopus* isolates (*stolonifer*, *oryzae, homothallicus*, and *microspores)* showed high potentiality to degrade ZEN and OTA as less toxic compound [89,90]. A new strain of *T. mycotoxinivorans* capable of degrading ZEN and OTA into the nontoxic OTα has been commercially used to detoxify OTA in animal and poultry diet [40,91]. *Yarrowia lipolytica* yeast showed the highest OTA degradation activity at 28 °C incubation temperature with pH level 4 [66]. *Phaffia rhodozyma* and *Xanthophyllomyces dendrorhous* yeasts also possess OTA degradation activity but their practical application yet limited due to lack of potential data.

*4.1.1.2. Use of enzymes.* Specific enzymes such as oxidase, peroxidase, laccase, reductase, esterase, carboxylesterase, aminotransferase, lactono hydrolase having the capacity of degrading mycotoxins have

been purified from microbial systems [95]. An enzyme peroxidase from *Aspergillus* (*flavus, parasiticus*) and a horseradish peroxidase enzyme from *Raphinus sativa* plant have been shown AFB1 degradation activity [69]. Enzymatic degradation by extracellular extract from *Rhodococcus erythropolis* culture along with laccase enzyme from several fungal species showed effective degradation of AFB1 [97]. In a study, two genes of soil bacteria *Sphingopyxis* sp. MTA 144 were identified and recombinant enzymes were produced which degraded FB1 by two consecutive steps, firstly FB1 is hydrolyzed to HFB1 by carboxylesterase and then it deaminated by aminotransferase to further less toxic compound [98]. A purified extracellular enzyme, myxobacteria aflatoxin degradation enzyme (MADE), from bacterium *Myxococcus fulvus* ANSM068 showed much degradation ability toward AFG1 (96.96%) and AFM1 (95.80%) [99]. The enzyme epoxidases detoxifies DON to its de-epoxy form DOM-1 [100]. *Brevibacterium* species (*B. epidermidis, B. iodinum and B. casei*) are capable of degrading OTA, due to release of highly active proteolytic carboxypeptidase enzymes [80]. A recent report revealed that OTA was significantly (74.8–84.9%) reduced by a carboxypeptidase and peptides present in liquid cultures of *Bacillus subtilis* CW14 [101].

#### 4.1.2. Mycotoxin binders

Mycotoxin binders also known as adsorbents or sequestering agents have been used to decontaminate animal feed by binding the mycotoxin and inhibit their absorption in the gastrointestinal tract, where the bounded toxins can be eliminated via feces or urine of animal [20,102]. Both inorganic (hydrated sodium calcium aluminosilicates, zeolites, bentonites, fuller's earth, diatomaceous earth, activated charcoal, kaolin, sepiolitic clay, cholestyramine) and organic binders (alfalfa fibre, oat fibers, extracted cell wall fraction of *Saccharomyces cerevisiae*, beta-D-glucan fraction of yeast cell wall) have been using for the control of toxin in diet [20,86,92]. Hydrated sodium calcium aluminosilicates inhibits the toxicity of AFTs in domestic animals along with decreases the AFM1 level in cow and goat milk whereas, zeolites can adsorb AFB1 and ZEA from feed [92]. Activated charcoal significantly removed OTA and PAT from contaminated wine and apple juice, respectively [12]. In the recent report, the body weight of broiler birds were increased 63%–100% by incorporation of activated charcoal, bentonite, and fuller's earth to aflatoxin-contaminated feed [102]. The binding efficiency of yeast has been mentioned earlier in section 4.1.1.1.2.

#### 4.1.3. Herbal products for the amelioration of toxic effects of mycotoxins

Herbal products such as spices, plant extracts, aromatic oils (lipophilic compounds from terrestrial herbs), primary olives (non-water solvents) are mixed with animal feed to increase growth performance and quality of the product. Research report showed that ethanolic extract of *Cassia Senna* (vegetable laxative) and methanol extract of *Cassia tora* (Naphtopyrone glycosides and anthraquinone aglycones) decreases the mutagenic effect of AFB1 in vitro; whereas methanol extract of *Piper argyrophyllum* leaves and *Thonninga sanguinea* extract found to be ameliorated the genotoxicity and hepatotoxicity effect of AFB1 in rat [103]. Natural herbs such as green tea, cinnamon, chamomile, ginger, black pepper, coriander, black seed, licorice, garlic, onion, fenugreek seeds, basil seeds, and roquette seeds can detoxify mycotoxins [104,105]. In a study report, it is found that turmeric extract (*Curcuma longa*) can ensure protection against the adverse effects of AFT on the performance of broiler birds [106]. In another study, herbal feed additives (*Silybum marianum*, *Withania somnifera*) showed hepatoprotective and nephroprotective effect on OTA-contaminated feed in broiler chicks [107]. The aqueous extract of *Ocimum tenuiflorum* (aromatic perennial plant) is found to be effective in inhibiting the AFB1 synthesis in the toxigenic strain of *A. flavus* whereas seeds of Ajowan [*T. ammi* (L.) Sprague ex Turrill] can degrade AFG1 [108,109]. Medicinal plants, black cumin (*Nigella sativa*), clove (*Eugenia caryophyllata*) and thyme (*Thymus vulgaris*) extracts have efficacy in suppressing fungal growth and toxin production by *Fusarium verticilloides* and *A. flavus* isolates [110]. In a recent report leaves extracts from sweet passion fruit (*Passiflora alata*), araçá (*Psidium cattleianum*), rosemary (*Rosmarinus officinalis*) and oregano (*Origanum vulgare*) efficiently degrade AFB1 in vitro [111].

## 5. Innovative approaches

### 5.1. Nanobiotechnology

This technique apparently a novel promising, effective and low-cost strategy that can offer eco-friendly for the control mycotoxigenic fungi and mycotoxins in the agriculture and food industry. The nanomaterials such as nanosilver (AgNPs), Zinc Oxide nanoparticles (ZnO-NPs), Selenium nanoparticles (SNP), Copper nanoparticles (CuNPs), magnetic nanoparticles like surface active maghemite nanoparticles (SAMNs), nano clay, nanogel, nano binders, and nanodiamonds can bind and remove mycotoxins or pathogens in food and feed [112]. AgNPs treatment was very effective against aflatoxigenic, ochratoxigenic fungi and AF and OTA accumulation in maize-based medium [113]. Selenium nanoparticles (SNP) derived from *Trichoderma harzianum* JF309 showed more inhibition of fungus and reduced DON (76%) and FB1 (63%) [114]. The application of ZnO-NPs in food systems is compelling in preventing the growth of mycotoxigenic fungi (*Aspergillus* spp., *Fusarium* spp., *Penicillium* spp.) and production of AFB1, OTA and FB1 [115]. The research demonstrated that CuNPs showed high antifungal activity against *Curvularia lunata, Alternaria alternata* and *Fusarium* (*culmorum, oxysporum, graminearum*) fungi [112]. SAMNs are efficient in CIT binding, magnetic carbon nano compound produced from maize waste was showed 90% adsorption of AFB1 and chitosan-coated Fe3O4 particles are promising adsorbents for patulin adsorption in the fruit juice industry [116,117]. Another nano-based approach could be the use of green nanofungicides formulations developed by phytochemicals (catechols, eugenol, essential oils, phloretin, hexanal, D-limonene, menthol, caffeic acid, thymol, tannins, etc.) extracted from plant materials with antibacterial and antifungal activity. The advantage of this method is cheap to prepare from natural constituents of plants that present no toxicity to human and animal health. Recent studies found that nanomaterials loaded with phytochemicals can be used to inhibit the production of toxigenic fungus and reduce the mycotoxin contamination in the food chain [118].

### 5.2. Antibody-mediated technology

Development of monoclonal and recombinant fungal-specific antibodies expressed in plants can limit the distribution of the fungal pathogens in the field and ultimately minimize the mycotoxin-production load. Monoclonal antibodies (Mabs 213,221) with high binding specificity to *Fusarium* mycotoxins were capable of binding to a wide variety of fumonisin-carbohydrate derivatives and were considered as an appropriate tool for detecting modified FB1 in maize [119]. Nevertheless, Mabs production and maintenance are difficult due to the high cost and specialized cell culture facilities are required. The phage display technology which generates recombinant single-chain antibodies specific to antigens displayed on the *Fusarium* cell surface similar to Mabs can be an alternative choice [120]. Research report revealed that these antibodies react strongly with cell wall-bound proteins and bind to the surface components of *F. asiaticum* [121]. In this method, antibody binding domain (Fv) of natural antibodies are formed, called a single-chain variable fragment (scFV) which has been used for the protection of plants against pathogenic fungi. A chicken-derived phage display Fusarium-specific antibody (scFv) is identified that reacts significantly with cell wall-bound proteins of Fusarium pathogens and remarkably enhanced in transgenic *Arabidopsis thaliana* plants [122]. In a recent report, the use of antibody-decorated magnetic nanoparticles were showed purification of an average of 80% of the ZEN and AFB1 from

mycotoxin-contaminated feed mixture [1]. Expression of antibody-mediated resistance in crops against initial infection in the field could be a control strategy for neutralizing and blocking fungal toxins.

### 5.3. Genetic improvement of crops

Mycotoxin contamination may both pre- and post-harvest stage which can be reduced greatly by developing disease-resistant traits through more sophisticated biotechnological approaches during the pre-harvest stage. Recently modern transgenic techniques such as Host-induce gene silencing (HIGS), RNA interference (RNAi), microRNA (miRNA)- or artificial microRNA (amiRNA)- mediated gene silencing, designer transcription activator-like effector (dTALE)-mediated up or down-regulation of gene expression, Zn-Finger nucleases, mega-nucleases, transcription activator-like effector nucleases (TALEN), clustered regularly interspaced short palindromic repeats (CRISPR)/Cas9, and oligonucleotide-directed mutagenesis (ODN)-based gene-editing techniques can be applied for development of mycotoxin resistant plant. In the HIGS method, pathogenic fungi are directed by the host plant to down-regulate the expression of its own genes, without requiring the host plant to express a remote protein [123]. An RNAi-based approach for mycotoxin resistance in the crop, use of RNAi as counteracting the vital gene is essential for fungus and toxin production. The transgenic crop would be developed with self-complementary hairpin RNAs of antifungal genes resulting in small interfering RNAs (siRNAs) by the host plant's DICER-like enzymes which have been efficiently taking up the transgenic tobacco generating *gus* siRNA by *Fusarium verticillioides* for silencing of the targeted *gus* gene [124]. In this method, using dual silence *Bc-Dcl1* and *Bc-Dcl2* genes revealed a substantial decrease of fungal pathogenicity and growth to a wide range of plant may be considered as a promising target for control of mycotoxins [125]. In another study silencing of five *AFT* genes by RNA interference (RNAi) in peanut plants was 100% reduction in AFB1 and AFB2 when inoculated with aflatoxigenic *A. flavus* [126]. In a study report, the role of miRNA was revealed that overexpression of Osa-miR7696 in transgenic rice plants gives rise to resistance against rice blast fungus *Magnaporthe oryzae* [127]. Zinc-finger nucleases (ZFNs) and transcription activator-like effector nucleases (TALENs) have been used for genome edition of many crops, CRISPR/Cas system which allows targeted modification of different crops genomic sequence to generate mycotoxin resistant varieties is superior TALENs approach because of its specificity and cheap, and it can be applied in crop improvement [128]. Genetically modified maize expressing the *Bacillus thuringiensis* (Bt) toxin anti-insecticidal cry1A(b) gene was showed efficacy to reduce its contamination with Fusarium mycotoxins (FUM, DON, ZEN) in grain [129].

### 5.4. Genetically Modified Animals (GMA)

Genetic engineering has the possibility to ameliorate the health and welfare of agricultural, food and laboratory animals such as cattle, pigs, chickens, goats, sheep, dogs, cats, fish, rats, and mice. The feasibility of creating GMA with the insertion of transgenes targeting specific pathogens into the genomes of host animals such as mastitis-resistant livestock, pigs resistant to African swine fever and chicks resistant to Avian influenza (H5N1) has been improved [130–132]. The new strategy genetic restoration where germ-line modification in host animals by generating targeted gene via ZFNs, TALENs or CRISPR-Cas9 could be a noble approach for the development of the disease-resistant animal. The TALENs method is very effective where specially coded enzymes called TALENs are used to split or cut out specific target DNA segments, thereby allowing the researchers to insert the preferred traits into the DNA of the subject. In the CRISPR/Cas9 method, a DNA-snipping enzyme called Cas9 involved in the defense mechanisms of bacteria and archaea is to cut specific segments of DNA and new segments are inserted to fill the gaps. This mutant cell can then divides and multiply through mitosis, creating more cells with the desired traits. The production of GMA can have a great impact on the livestock and food chains due to economic benefits for the farmers, producers, and consumers. However, consumer concerning genetically modified animals about their long-term impacts on health and environment should not be overlooked and such concerns are addressed seriously if society is to benefit from new developments.

## 6. Implication and outlook

Mycotoxins represent a major risks to the food chain associated with human and animal health aspects, therefore early and rapid detection will help in the elimination of toxins for preventing health problems and protecting life. Due to regulatory, toxicological and consumer protection, use of detoxification agent is limited in food and feed industries. So far most of the research focuses on the biological detoxification methods and more attention should be given for the practical evaluation of these microorganisms or their enzymes in food and feeds. However, conventional decontamination methods are continually improved, researchers are looking for innovative solutions. Therefore, it draws attention to the need for prevention and control strategies such as **A**. Control of mycotoxin by gene editing crops. **B.** Rapid and cheap test technology for detecting mycotoxins. **C.** Mycotoxin inhibits technology. **D.** Nano antibody that reduces contamination in the food chain. Development of fungi resistant crops by genetic engineering technology is to identify the mycotoxin detoxification gene and is to input transgenic resistance to mycotoxin. The new nanotechnology has the potential to many aspects of agriculture, livestock, and the food industry; specially nanoparticles can be applied as antifungal agents to minimize the health effects of mycotoxins. However, this technology is still in the preliminary stages, a clear perception of possible health outcome of nanoparticles is unknown, thereby limits its application in regards to food security and more research is needed to be investigated. Screening microbial population from various mycotoxin-contaminated environments is assumed to be a promising approach for mycotoxin degradation which can be improved by coupling innovative techniques and approaches, such as enrichments, highly selective media, PCR denaturing gradient gel electrophoresis, PCR-DGGE bacterial profiles and functional metagenomics [95]. It is also a noble approach to develop research focusing on probiotic bacteria and enzyme products for the effective detoxification of mycotoxin which can be applicable as feed additives in the commercial sector [133]. Considering this application of enzymes and cloning of genes through genetic engineering to develop genetically modified species suitable for the industrial scale of enzyme production and purification used in food production could be an alternative technology for mycotoxins detoxifications in the human and animal food chains [134]. Combined with the advanced biotechnology, antibody-mediated resistance to initial infection and spreading the fungal pathogen on susceptible grains offers new scope for the establishment of an environmentally friendly strategy for the control of mycotoxins. Special importance should be focused on the advancement of cost-effective, convenient and easy handling instruments and methods for the detection of mycotoxin at the field condition. Further research also needs to be highlighted on the epidemiological surveillance and generation of data dealing with the toxic effects of mycotoxin, especially in humans.

## Funding

This work was supported by the Taishan Scholar Foundation of Shandong Province Grant number: ts201511084, High-level Innovation and Entrepreneurship Talents of Jiangsu Province.

## Declaration of competing interest

The authors declare no competing interests.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.micpath.2020.104095.

## References


[1] P. Horky, S. Skalickova, D. Baholet, J. Skladanka, Nanoparticles as a solution for eliminating the risk of mycotoxins, Nanomaterials 8 (9) (2018) 727, https://doi.org/10.3390/nano8090727.

[2] M.U. Ukwuru, C.G. Ohaegbu, A. Muritala, An overview of mycotoxin contamination of foods and feeds, J Biochem Microb Toxicol 1 (2018) 101.

[3] B. Grenier, I. Oswald, Mycotoxin co-contamination of food and feed: meta-analysis of publications describing toxicological interactions, World Mycotoxin J. 4 (3) (2011) 285–313, https://doi.org/10.3920/wmj2011.1281.

[4] M.B. Levy, J.N. Fink, Toxic mold syndrome, Adv. Appl. Microbiol. (2004) 275–288, https://doi.org/10.1016/s0065-2164(04)55010-4.

[5] D.R. Milićević, M. Škrinjar, T. Baltić, Real and perceived risks for mycotoxin contamination in foods and feeds: challenges for food safety control, Toxins 2 (4) (2010) 572–592, https://doi.org/10.3390/toxins2040572.

[6] E. Eshetu, H. Adugna, A. Gebretensay, An overview on major mycotoxin in animal: its public health implication, economic impact and control strategies, Journal of Health, Medicine and Nursing 25 (2016) 64–73.

[7] Y. Wang, C. Zhao, D. Zhang, M. Zhao, D. Zheng, M. Peng, Z. Cui, Simultaneous degradation of aflatoxin B 1 and zearalenone by a microbial consortium, Toxicon 146 (2018) 69–76, https://doi.org/10.1016/j.toxicon.2018.04.007.

[8] J.I. Pitt, J.D. Miller, A concise history of mycotoxin research, J. Agric. Food Chem. 65 (33) (2016) 7021–7033, https://doi.org/10.1021/acs.jafc.6b04494.

[9] T.H. Fernandes, J. Ferrão, V. Bell, I.T. Chabite, Mycotoxins, food and health, J Nutrition Health Food Sci 5 (7) (2017) 1–10, https://doi.org/10.15226/jnhfs.2017.001118.

[10] V.E. Simion, A.T. Bogdan, V. Andronie, I. Ipate, M. Pârvu, B. Covaci, E. Mitrănescu, C. Andronie, Macro and microclimate – from beneficial to noxious action on the animals, 6th IASME/WSEAS International Conference on Energy & Environment (EE'11), Recent Researches in Energy & Environment Cambridge, 2011 UK February 23-25, 201. ISSN: 1792-8230 ISBN: 978-960-474-274-5.

[11] C.N. Fokunang, E.A. Tembe-Fokunang, P. Tomkins, S. Barkwan, Global impact of mycotoxins on human and animal health management, Outlook Agric. 35 (4) (2006) 247–253, https://doi.org/10.5367/000000006779398263.

[12] M. Zaki, Mycotoxins in animals: occurrence, effects, prevention and management, J. Toxicol. Environ. Health Sci. 4 (1) (2012) 13–28, https://doi.org/10.5897/jtehs11.072.

[13] D. Milićević, I. Nastasijevic, Z. Petrovic, Mycotoxin in the food supply chain—implications for public health program, Journal of Environmental Science and Health, Part C 34 (4) (2016) 293–319, https://doi.org/10.1080/10590501.2016.1236607.

[14] I. Vanhoutte, K. Audenaert, L. De Gelder, Biodegradation of mycotoxins: tales from known and unexplored worlds, Front. Microbiol. 7 (2016), https://doi.org/10.3389/fmicb.2016.00561.

[15] S. Ashiq, Natural occurrence of mycotoxins in food and feed: Pakistan perspective, Compr. Rev. Food Sci. Food Saf. 14 (2) (2014) 159–175, https://doi.org/10.1111/1541-4337.12122.

[16] J. Cary, K. Rajasekaran, J. Yu, R. Brown, D. Bhatnagar, T. Cleveland, Transgenic approaches for pre-harvest control of mycotoxin contamination in crop plants, World Mycotoxin J. 2 (2) (2009) 203–214, https://doi.org/10.3920/wmj2009.1138.

[17] Y. Gurbuz, A. Hussein, E. Ozkose, Determination of AFLD and AFLQ genes responsible for aflatoxin formation in some livestock concentrated feeds, Pak. Vet. J. 39 (2) (2019) 163–168, https://doi.org/10.29261/pakvetj/2019.057.

[18] A. Ismail, B.L. Gonçalves, D.V. de Neeff, B. Ponzilacqua, C.F.S.C. Coppa, H. Hintzsche, C.A.F. Oliveira, Aflatoxin in foodstuffs: occurrence and recent advances in decontamination, Food Res. Int. 113 (2018) 74–85, https://doi.org/10.1016/j.foodres.2018.06.067.

[19] H. Li, S. Li, H. Yang, Y. Wang, J. Wang, N. Zheng, l-Proline alleviates kidney injury caused by AFB1 and AFM1 through regulating excessive apoptosis of kidney cells, Toxins 11 (4) (2019) 226, https://doi.org/10.3390/toxins11040226.

[20] M.F. Abdallah, G. Girgin, T. Baydar, Occurrence, prevention and limitation of mycotoxins in feeds, Anim. Nutr. Feed Technol. 15 (2015) 471–490, https://doi.org/10.5958/0974-181X.2015.00048.7.

[21] D.N. Enyiukwu, A.N. Awurum, J.A. Nwaneri, Mycotoxins in stored agricultural products: implications to food safety and health and prospects of plant-derived pesticides as novel approach to their management, Greener Journal of Microbiology and Antimicrobials 2 (3) (2014) 032-048.

[22] W.-P.-P. Liew, S. Mohd-Redzwan, Mycotoxin: its impact on gut health and microbiota, Frontiers in Cellular and Infection Microbiology 8 (2018), https://doi.org/10.3389/fcimb.2018.00060.

[23] R.V. Bhat, Human health problems associated with current agricultural food production, Asia Pac. J. Clin. Nutr. 17 (Suppl 1) (2008) 91–94.

[24] Y. Liu, F. Wu, Global burden of aflatoxin-induced hepatocellular carcinoma: a risk assessment, Environ. Health Perspect. 118 (6) (2010) 818–824, https://doi.org/10.1289/ehp.0901388.

[25] M.C. Lozano, G.J. Diaz, Microsomal and cytosolic biotransformation of aflatoxin B1 in four poultry species, Br. Poultry Sci. 47 (6) (2006) 734–741, https://doi.org/10.1080/00071660601084390.

[26] S. Sana, A.A. Anjum, T. Yaqub, M. Nasir, M.A. Ali, M. Abbas, Molecular approaches for characterization of aflatoxin producing Aspergillus flavus isolates from poultry feed, Pak. Vet. J. 39 (2019) 169–174, https://doi.org/10.29261/pakvetj/2019.031.

[27] M.N. Naseem, M.K. Saleemi, R.Z. Abbas, A. Khan, A. Khatoon, A. Sultan, Hematological and serum biochemical effects of aflatoxin B1 intoxication in broilers experimentally infected with fowl adenovirus-4 (FAdV-4), Pak. Vet. J. 38 (2) (2018) 209–213, https://doi.org/10.29261/pakvetj/2018.028.

[28] Y. Man, G. Liang, A. Li, L. Pan, Recent advances in mycotoxin determination for food monitoring via microchip, Toxins 9 (10) (2017) 324, https://doi.org/10.3390/toxins9100324.

[29] N. Hojnik, U. Cvelbar, G. Tavčar-Kalcher, J. Walsh, I. Križaj, Mycotoxin decontamination of food: cold atmospheric pressure plasma versus "classic" decontamination, Toxins 9 (5) (2017) 151, https://doi.org/10.3390/toxins9050151.

[30] M. Eshelli, M. Qader, E. Jambi, A. Hursthouse, M. Rateb, Current status and future opportunities of omics tools in mycotoxin research, Toxins 10 (11) (2018) 433, https://doi.org/10.3390/toxins10110433.

[31] A. Alshannaq, J.-H. Yu, Occurrence, toxicity, and analysis of major mycotoxins in food, Int. J. Environ. Res. Publ. Health 14 (6) (2017) 632, https://doi.org/10.3390/ijerph14060632.

[32] S.A. Atanda, Fungi and mycotoxins in stored foods, Afr. J. Microbiol. Res. 5 (25) (2011), https://doi.org/10.5897/ajmr11.487.

[33] M.-C. Smith, S. Madec, E. Coton, N. Hymery, Natural Co-occurrence of mycotoxins in foods and feeds and their in vitro combined toxicological effects, Toxins 8 (4) (2016) 94, https://doi.org/10.3390/toxins8040094.

[34] D. Jh, The occurrence, properties and significance of citrinin mycotoxin, J. Plant Pathol. Microbiol. 6 (11) (2015), https://doi.org/10.4172/2157-7471.1000321.

[35] S. Marin, A.J. Ramos, G. Cano-Sancho, V. Sanchis, Mycotoxins: occurrence, toxicology, and exposure assessment, Food Chem. Toxicol. 60 (2013) 218–237, https://doi.org/10.1016/j.fct.2013.07.047.

[36] G.P. Munkvold, Fusarium species and their associated mycotoxins. Mycotoxigenic fungi: methods and protocols, in: Antonio Moretti, Antonia Susca (Eds.), Methods in Molecular Biology, vol. 1542, Springer Science + Business Media LLC, 2016, pp. 51–106.

[37] EFSA Panel on Contaminants in the Food Chain (Contam), Scientific Opinion on the risks for animal and public health related to the presence of T-2 and HT-2 toxin in food and feed, EFSA Journal 9 (12) (2011) 2481, https://doi.org/10.2903/j.efsa.2011.2481.

[38] F. Ben Taheur, B. Kouidhi, Y.M.A. Al Qurashi, J. Ben Salah-Abbès, K. Chaieb, Review : biotechnology of mycotoxins detoxification using microorganisms and enzymes, Toxicon (2019), https://doi.org/10.1016/j.toxicon.2019.02.001.

[39] W.A. Awad, M. Hess, M. Twarużek, J. Grajewski, R. Kosicki, J. Böhm, J. Zentek, The impact of the Fusarium mycotoxin deoxynivalenol on the health and performance of broiler chickens, Int. J. Mol. Sci. 12 (11) (2011) 7996–8012, https://doi.org/10.3390/ijms12117996.

[40] G.R. Murugesan, D.R. Ledoux, K. Naehrer, F. Berthiller, T.J. Applegate, B. Grenier, G. Schatzmayr, Prevalence and effects of mycotoxins on poultry health and performance, and recent development in mycotoxin counteracting strategies, Poultry Sci. 94 (6) (2015) 1298–1315, https://doi.org/10.3382/ps/pev075.

[41] A. Osselaere, M. Devreese, J. Goossens, V. Vandenbroucke, S. De Baere, P. De Backer, S. Croubels, Toxicokinetic study and absolute oral bioavailability of deoxynivalenol, T-2 toxin and zearalenone in broiler chickens, Food Chem. Toxicol. 51 (2013) 350–355, https://doi.org/10.1016/j.fct.2012.10.006.

[42] A. Vidal, M. Mengelers, S. Yang, S. De Saeger, M. De Boevre, Mycotoxin biomarkers of exposure: a comprehensive review, Compr. Rev. Food Sci. Food Saf. (2018), https://doi.org/10.1111/1541-4337.12367.

[43] C. Chilaka, M. De Boevre, O. Atanda, S. De Saeger, The status of Fusarium mycotoxins in sub-saharan Africa: a review of emerging trends and post-harvest mitigation strategies towards food control, Toxins 9 (1) (2017) 19, https://doi.org/10.3390/toxins9010019.

[44] J. Gelineau-van Waes, K.A. Voss, V.L. Stevens, M.C. Speer, R.T. Riley, Chapter 5 maternal fumonisin exposure as a risk factor for neural tube defects, Adv. Food Nutr. Res. (2009) 145–181, https://doi.org/10.1016/s1043-4526(08)00605-0.

[45] C.S. Ortiz, C. Richards, A. Terry, J. Parra, W.-B. Shim, Genetic variability and geographical distribution of mycotoxigenic Fusarium verticillioides strains isolated from maize fields in Texas, Plant Pathol. J. 31 (3) (2015) 203–211, https://doi.org/10.5423/ppj.oa.02.2015.0020.

[46] M. Edite Bezerra da Rocha, F. da C.O. Freire, F. Erlan Feitosa Maia, M. Izabel Florindo Guedes, D. Rondina, Mycotoxins and their effects on human and animal health, Food Contr. 36 (1) (2014) 159–165, https://doi.org/10.1016/j.foodcont.2013.08.021.

[47] P. Jeswal, D. Kumar, Mycobiota and natural incidence of aflatoxins, ochratoxin A, and citrinin in Indian spices confirmed by LC-MS/MS, International Journal of Microbiology (2015) 1–8, https://doi.org/10.1155/2015/242486 2015.

[48] C.E. Magnoli, A.L. Astoreca, S.M. Chiacchiera, A.M. Dalcero, Occurrence of ochratoxin A and ochratoxigenic mycoflora in corn and corn based foods and feeds in some South American countries, Mycopathologia 163 (5) (2007) 249–260, https://doi.org/10.1007/s11046-007-9005-z.

[49] J.W. Bennett, M. Klich, Mycotoxins, Clin. Microbiol. Rev. 16 (3) (2003) 497–516, https://doi.org/10.1128/cmr.16.3.497-516.2003.

[50] EC, No. 1881/2006. Setting maximum levels for certain contaminants in foodstuffs. Official Journal of the European Union L 364/5, https://www.fsai.ie/uploadedFiles/Reg420_2011.pdf, (2006).

[51] M.E. Zain, Impact of mycotoxins on humans and animals, Journal of Saudi Chemical Society 15 (2) (2011) 129–144, https://doi.org/10.1016/j.jscs.2010.06.006.

[52] V. Meucci, E. Razzuoli, G. Soldani, F. Massart, Mycotoxin detection in infant formula milks in Italy, Food Addit. Contam. 27 (1) (2010) 64–71, https://doi.org/10.1080/02652030903207201.

[53] S. Yazar, G. Omurtag, Fumonisins, trichothecenes and zearalenone in cereals, Int. J. Mol. Sci. 9 (11) (2008) 2062–2090, https://doi.org/10.3390/ijms9112062.

[54] S.M. Herzallah, Determination of aflatoxins in eggs, milk, meat and meat products using HPLC fluorescent and UV detectors, Food Chem. 114 (3) (2009) 1141–1146, https://doi.org/10.1016/j.foodchem.2008.10.077.

[55] FAO, Worldwide regulations for mycotoxins in food and feed in 2003. FAO food and nutrition papers, Rome, Italy, 81, 2004. http://www.fao.org/3/y5499e/y5499e00.htm.

[56] J.C. Leblanc, INRA (Ed.), Etude de l'alimentation totale en France: Mycotoxines, mineraux et aliments traces, 2004 (Paris).

[57] E. Streit, G. Schatzmayr, P. Tassis, E. Tzika, D. Marin, I. Taranu, I.P. Oswald, Current situation of mycotoxin contamination and Co-occurrence in animal feed—focus on Europe, Toxins 4 (10) (2012) 788–809, https://doi.org/10.3390/toxins4100788.

[58] K. Tanaka, Y. Sago, Y. Zheng, H. Nakagawa, M. Kushiro, Mycotoxins in rice, Int. J. Food Microbiol. 119 (1–2) (2007) 59–66, https://doi.org/10.1016/j.ijfoodmicro.2007.08.002.

[59] D. Flajs, M. Peraica, Toxicological properties of citrinin, Arh. Hig. Rada. Toksikol. 60 (4) (2009), https://doi.org/10.2478/10004-1254-60-2009-1992.

[60] S.A. Wright, Patulin in food, Current Opinion in Food Science 5 (2015) 105–109, https://doi.org/10.1016/j.cofs.2015.10.003.

[61] M.O. Moss, Fungi, quality and safety issues in fresh fruits and vegetables, J. Appl. Microbiol. 104 (5) (2008) 1239–1243, https://doi.org/10.1111/j.1365-2672.2007.03705.x.

[62] T. Grusie, V. Cowan, J. Singh, J. McKinnon, B. Blakley, Proportions of predominant Ergot alkaloids (Claviceps purpurea) detected in Western Canadian grains from 2014 to 2016, World Mycotoxin J. 11 (2) (2018) 259–264, https://doi.org/10.3920/wmj2017.2241.

[63] H. Hulvová, P. Galuszka, J. Frébortová, I. Frébort, Parasitic fungus Claviceps as a source for biotechnological production of ergot alkaloids, Biotechnol. Adv. 31 (1) (2013) 79–89, https://doi.org/10.1016/j.biotechadv.2012.01.005.

[64] S. MacDonald, D. Chan, K. Lumb, H. Scott, L. Randall, S. Edward, ... C. Elliott, Mycotoxin Contamination: Assessment of Risk in Livestock Systems. Research Review No. 85 AHDB Cereals & Oilseeds, Agriculture and Horticulture Development Board (AHDB), 2016.

[65] C. Santos Pereira, S.C. Cunha, J.O. Fernandes, Prevalent mycotoxins in animal feed: occurrence and analytical methods, Toxins 11 (5) (2019) 290, https://doi.org/10.3390/toxins11050290.

[66] H. Shi, S. Li, Y. Bai, L.L. Prates, Y. Lei, P. Yu, Mycotoxin contamination of food and feed in China: occurrence, detection techniques, toxicological effects and advances in mitigation technologies, Food Contr. 91 (2018) 202–215, https://doi.org/10.1016/j.foodcont.2018.03.036.

[67] A. Roseanu, L. Jecu, M. Badea, R.W. Evans, Mycotoxins: an overview on their quantification methods, ROM, J. Biochem. 47 (1) (2010) 79–86 http://journal.biochim.ro/archive/n47-1/pdfs_47-1/rjb47-1_06.pdf.

[68] L. Xie, M. Chen, Y. Ying, Development of methods for determination of aflatoxins, Crit. Rev. Food Sci. Nutr. 56 (16) (2015) 2642–2664, https://doi.org/10.1080/10408398.2014.907234.

[69] V. Aiko, A. Mehta, Occurrence, detection and detoxification of mycotoxins, J. Biosci. 40 (5) (2015) 943–954, https://doi.org/10.1007/s12038-015-9569-6.

[70] X. Zhang, S.A. Eremin, K. Wen, X. Yu, C. Li, Y. Ke, Z. Wang, Fluorescence polarization immunoassay based on a new monoclonal antibody for the detection of the zearalenone class of mycotoxins in maize, J. Agric. Food Chem. 65 (10) (2017) 2240–2247, https://doi.org/10.1021/acs.jafc.6b05614.

[71] I. Tothill, Biosensors and nanomaterials and their application for mycotoxin determination, World Mycotoxin J. 4 (4) (2011) 361–374, https://doi.org/10.3920/wmj2011.1318.

[72] R. Eivazzadeh-Keihan, P. Pashazadeh, M. Hejazi, M. de la Guardia, A. Mokhtarzadeh, Recent advances in Nanomaterial-mediated Bio and immune sensors for detection of aflatoxin in food products, Trac. Trends Anal. Chem. 87 (2017) 112–128, https://doi.org/10.1016/j.trac.2016.12.003.

[73] S.H. Ahlberg, V. Joutsjoki, H.J. Korhonen, Potential of lactic acid bacteria in aflatoxin risk mitigation, Int. J. Food Microbiol. 207 (2015) 87–102, https://doi.org/10.1016/j.ijfoodmicro.2015.04.042.

[74] R.M. Elsanhoty, M.F. Ramadan, S.S. El-Gohery, M.F. Abol-Ela, M.A. Azeke, Ability of selected microorganisms for removing aflatoxins in vitro and fate of aflatoxins in contaminated wheat during baladi bread baking, Food Contr. 33 (1) (2013) 287–292, https://doi.org/10.1016/j.foodcont.2013.03.002.

[75] K. Śliżewska, S. Smulikowska, Detoxification of aflatoxin B1 and change in microflora pattern by probiotic in vitro fermentation of broiler feed, J. Anim. Feed Sci. 20 (2) (2011) 300–309.

[76] K. Raksha Rao, A.V. Vipin, P. Hariprasad, K.A. Anu Appaiah, G. Venkateswaran, Biological detoxification of Aflatoxin B 1 by Bacillus licheniformis CFR1, Food Contr. 71 (2017) 234–241, https://doi.org/10.1016/j.foodcont.2016.06.040.

[77] J.Q. Wang, F. Yang, P.L. Yang, J. Liu, Z.H. Lv, Microbial reduction of zearalenone by a new isolated Lysinibacillus sp. ZJ-2016-1, World Mycotoxin J. 11 (4) (2018) 571–578, https://doi.org/10.3920/WMJ2017.2264.

[78] Y.P. Lei, L.H. Zhao, Q.G. Ma, J.Y. Zhang, T. Zhou, C.Q. Gao, C. Ji, Degradation of zearalenone in swine feed and feed ingredients by Bacillus subtilis ANSB01G, World Mycotoxin J. 7 (2) (2014) 143–151, https://doi.org/10.3920/wmj2013.1623.

[79] L. Sangare, Y. Zhao, Y. Folly, J. Chang, J. Li, J. Selvaraj, Y. Liu, Aflatoxin B1 degradation by a Pseudomonas strain, Toxins 6 (10) (2014) 3028–3040, https://doi.org/10.3390/toxins6103028.

[80] H. Rodriguez, I. Reveron, F. Doria, A. Costantini, B. De Las Rivas, R. Muñoz, E. Garcia-Moruno, Degradation of ochratoxin A by brevibacterium species, J. Agric. Food Chem. 59 (19) (2011) 10755–10760, https://doi.org/10.1021/jf203061p.

[81] H. Tan, Y. Hu, J. He, L. Wu, F. Liao, B. Luo, J. Deng, Zearalenone degradation by two Pseudomonas strains from soil, Mycotoxin Res. 30 (4) (2014) 191–196, https://doi.org/10.1007/s12550-014-0199-x.

[82] J.W. He, G.S. Bondy, T. Zhou, D. Caldwell, G.J. Boland, P.M. Scott, Toxicology of 3-epi-deoxynivalenol, a deoxynivalenol-transformation product by Devosia mutans 17-2-E-8, Food Chem. Toxicol. 84 (2015) 250–259, https://doi.org/10.1016/j.fct.2015.09.003.

[83] X. Gao, P. Mu, J. Wen, Y. Sun, Q. Chen, Y. Deng, Detoxification of trichothecene mycotoxins by a novel bacterium, *Eggerthella* sp. DII-9, Food Chem. Toxicol. 112 (2018) 310–319, https://doi.org/10.1016/j.fct.2017.12.066.

[84] O.A. Adebo, P.B. Njobeh, S. Gbashi, O.C. Nwinyi, V. Mavumengwana, Review on microbial degradation of aflatoxins, Crit. Rev. Food Sci. Nutr. 57 (15) (2015) 3208–3217, https://doi.org/10.1080/10408398.2015.1106440.

[85] M.K. Saleemi, K. Ashraf, S.T. Gul, M.N. Naseem, M.S. Sajid, M. Mohsin, A. Khan, Toxicopathological effects of feeding aflatoxins B1 in broilers and its ameliosration with indigenous mycotoxin binder, Ecotoxicol. Environ. Saf. 187 (2020) 109712, , https://doi.org/10.1016/j.ecoenv.2019.109712.

[86] N.F. Yalcin, T. Avci, M.K. Isik, H. Oguz, In vitro activity of toxin binders on aflatoxin B1 in poultry gastrointestinal medium, Pak. Vet. J. 38 (1) (2018) 61–65, https://doi.org/10.29261/pakvetj/2018.012.

[87] A. Khan, M.M. Aalim, M.Z. Khan, M.K. Saleemi, C. He, A. Khatoon, S.T. Gul, Amelioration of immunosuppressive effects of aflatoxin and ochratoxin A in White Leghorn layers with distillery yeast sludge, Toxin Rev. 36 (4) (2017) 275–281, https://doi.org/10.1080/15569543.2017.1303781.

[88] C. He, Y. Fan, G. Liu, H. Zhang, Isolation and identification of a strain of Aspergillus tubingensis with deoxynivalenol biotransformation capability, Int. J. Mol. Sci. 9 (12) (2008) 2366–2375, https://doi.org/10.3390/ijms9122366.

[89] E. Vekiru, C. Hametner, R. Mitterbauer, J. Rechthaler, G. Adam, G. Schatzmayr, R. Schuhmacher, Cleavage of zearalenone by Trichosporon mycotoxinivorans to a novel nonestrogenic metabolite, Appl. Environ. Microbiol. 76 (7) (2010) 2353–2359, https://doi.org/10.1128/aem.01438-09.

[90] J. Varga, Z. Péteri, K. Tábori, J. Téren, C. Vágvölgyi, Degradation of ochratoxin A and other mycotoxins by Rhizopus isolates, Int. J. Food Microbiol. 99 (3) (2005) 321–328, https://doi.org/10.1016/j.ijfoodmicro.2004.10.034.

[91] O. Molnar, G. Schatzmayr, E. Fuchs, H. Prillinger, Trichosporon mycotoxinivorans sp. nov., A new yeast species useful in biological detoxification of various mycotoxins, Syst. Appl. Microbiol. 27 (6) (2004) 661–671, https://doi.org/10.1078/0723202042369947.

[92] M. Peraica, A. Domijan, Ž. Jurjević, B. Cvjetković, Prevention of exposure to mycotoxins from food and feed, Arh. Hig. Rada. Toksikol. 53 (3) (2002) 229–237 https://hrcak.srce.hr/452.

[93] J. He, T. Zhou, J.C. Young, G.J. Boland, P.M. Scott, Chemical and biological transformations for detoxification of trichothecene mycotoxins in human and animal food chains: a review, Trends Food Sci. Technol. 21 (2) (2010) 67–76, https://doi.org/10.1016/j.tifs.2009.08.002.

[94] T. Calado, A. Venâncio, L. Abrunhosa, Irradiation for mold and mycotoxin control: a review, Compr. Rev. Food Sci. Food Saf. 13 (5) (2014) 1049–1061, https://doi.org/10.1111/1541-4337.12095.

[95] M. Loi, F. Fanelli, V. Liuzzi, A. Logrieco, G. Mulè, Mycotoxin biotransformation by native and commercial enzymes: present and future perspectives, Toxins 9 (4) (2017) 111, https://doi.org/10.3390/toxins9040111.

[96] S.K. Pankaj, H. Shi, K.M. Keener, A review of novel physical and chemical decontamination technologies for aflatoxin in food, Trends Food Sci. Technol. 71 (2018) 73–83, https://doi.org/10.1016/j.tifs.2017.11.007.

[97] J.F. Alberts, W.C.A. Gelderblom, A. Botha, W.H. van Zyl, Degradation of aflatoxin B1 by fungal laccase enzymes, Int. J. Food Microbiol. 135 (1) (2009) 47–52, https://doi.org/10.1016/j.ijfoodmicro.2009.07.022.

[98] S. Heinl, D. Hartinger, M. Thamhesl, E. Vekiru, R. Krska, G. Schatzmayr, R. Grabherr, Degradation of fumonisin B1 by the consecutive action of two bacterial enzymes, J. Biotechnol. 145 (2) (2010) 120–129, https://doi.org/10.1016/j.jbiotec.2009.11.004.

[99] L.H. Zhao, S. Guan, X. Gao, Q.G. Ma, Y.P. Lei, X.M. Bai, C. Ji, Preparation, purification and characteristics of an aflatoxin degradation enzyme from Myxococcus fulvus ANSM068, J. Appl. Microbiol. 110 (1) (2010) 147–155, https://doi.org/10.1111/j.1365-2672.2010.04867.x.

[100] G. Schatzmayr, F. Zehner, M. Täubel, D. Schatzmayr, A. Klimitsch, A.P. Loibner, E.M. Binder, Microbiologicals for deactivating mycotoxins, Mol. Nutr. Food Res. 50 (6) (2006) 543–551, https://doi.org/10.1002/mnfr.200500181.

[101] H.N. Hu, X. Jia, Y.P. Wang, Z.H. Liang, Removal of ochratoxin A by a carboxypeptidase and peptides present in liquid cultures of Bacillus subtilis CW14, World Mycotoxin J. 11 (4) (2018) 559–570, https://doi.org/10.3920/WMJ2017.2296.

[102] A.C. Mgbeahuruike, T.E. Ejioffor, O.C. Christian, V.C. Shoyinka, M. Karlsson, E. Nordkvist, Detoxification of aflatoxin-contaminated poultry feeds by 3 adsorbents, bentonite, activated charcoal, and fuller's earth, J. Appl. Poultry Res. 27 (2018) 461–471, https://doi.org/10.3382/japr/pfy054.

[103] M.E. Abd El-Hack, D.H. Samak, A.E. Noreldin, K. El-Naggar, M. Abdo, Probiotics and plant-derived compounds as eco-friendly agents to inhibit microbial toxins in poultry feed: a comprehensive review, Environ. Sci. Pollut. Control Ser. (2018), https://doi.org/10.1007/s11356-018-3197-2.

[104] M. Saeed, X. Yatao, F. Hassan, M. Arain, M. Abd El-Hack, A. Noreldin, C. Sun, Influence of graded levels of l-theanine dietary supplementation on growth

performance, carcass traits, meat quality, organs histomorphometry, blood chemistry and immune response of broiler chickens, Int. J. Mol. Sci. 19 (2) (2018) 462, https://doi.org/10.3390/ijms19020462.
[105] M.A. Abdelaziz, A.I. El-Faham, N.G. Ali, Using natural feed additives as alternative antimycotoxins in broiler diets, Egyptian Poultry Science Journal 35 (1) (2015) 291–310.
[106] N. Rangsaz, M.G. Ahangaran, Evaluation of turmeric extract on performance indices impressed by induced aflatoxicosis in broiler chickens, Toxicol. Ind. Health 27 (10) (2011) 956–960, https://doi.org/10.1177/0748233711401262.
[107] S.D. Stoev, P. Njobeh, I. Zarkov, T. Mircheva, D. Zapryanova, S. Denev, B. Dimitrova, Selected herbal feed additives showing protective effects against ochratoxin A toxicosis in broiler chicks, World Mycotoxin J. 12 (3) (2019) 257–268, https://doi.org/10.3920/WMJ2019.2432.
[108] P. Panda, A. Mehta, Aflatoxin detoxification potential of Ocimum tenuiflorum, J. Food Saf. 33 (3) (2013) 265–272, https://doi.org/10.1111/jfs.12048.
[109] R. Velazhahan, S. Vijayanandraj, A. Vijayasamundeeswari, V. Paranidharan, R. Samiyappan, T. Iwamoto, S. Muthukrishnan, Detoxification of aflatoxins by seed extracts of the medicinal plant, Trachyspermum ammi (L.) Sprague ex Turrill – structural analysis and biological toxicity of degradation product of aflatoxin G1, Food Contr. 21 (5) (2010) 719–725, https://doi.org/10.1016/j.foodcont.2009.10.014.
[110] I.A. Elsamra, S.M. Shama, A.S. Hamza, N.H. Youssef, M.S. Youssef, S.M. Alabd, Effect of some mould inhibitors and herbal plants on mycotoxins production byAspergillus flavusandFusarium verticilloidesin vitro and in stored corn grains, Arch. Phytopathol. Plant Protect. 45 (15) (2012) 1861–1878, https://doi.org/10.1080/03235408.2012.713799.
[111] B. Ponzilacqua, G.E. Rottinghaus, B.R. Landers, C.A.F. Oliveira, Effects of medicinal herb and Brazilian traditional plant extracts on in vitro mycotoxin decontamination, Food Contr. (2019), https://doi.org/10.1016/j.foodcont.2019.01.009.
[112] K.A. Abd-Elsalam, A.F. Hashim, M.A. Alghuthaymi, E. Said-Galiev, Nanobiotechnological strategies for toxigenic fungi and mycotoxin control, Food Preservation (2017) 337–364, https://doi.org/10.1016/b978-0-12-804303-5.00010-9.
[113] J.V. Gómez, A. Tarazona, F. Mateo, M. Jiménez, E.M. Mateo, Potential impact of engineered silver nanoparticles in the control of aflatoxins, ochratoxin A and the main aflatoxigenic and ochratoxigenic species affecting foods, Food Contr. 101 (2019) 58–68, https://doi.org/10.1016/j.foodcont.2019.02.019.
[114] D. Hu, S. Yu, D. Yu, N. Liu, Y. Tang, Y. Fan, A. Wu, Biogenic Trichoderma harzianum-derived selenium nanoparticles with control functionalities originating from diverse recognition metabolites against phytopathogens and mycotoxins, Food Contr. 106 (2019) 106748, , https://doi.org/10.1016/j.foodcont.2019.106748.
[115] A.A. Hassan, M.E. Howayda, H.H. Mahmoud, Effect of zinc Oxide nanoparticles on the growth of some mycotoxigenic mould, Studies in Chemical Process Technology (SCPT) 1 (4) (2013) 66–74.
[116] Y. Luo, X. Liu, J. Li, Updating techniques on controlling mycotoxins - a review, Food Contr. 89 (2018) 123–132, https://doi.org/10.1016/j.foodcont.2018.01.016.
[117] Y. Luo, Z. Zhou, T. Yue, Synthesis and characterization of nontoxic chitosan-coated Fe 3 O 4 particles for patulin adsorption in a juice-pH simulation aqueous, Food Chem. 221 (2017) 317–323, https://doi.org/10.1016/j.foodchem.2016.09.008.
[118] V.C. Thipe, M. Keyster, K.V. Katti, Sustainable Nanotechnology: Mycotoxin Detection and Protection, Nanobiotechnology Applications in Plant Protection, 2018, pp. 323–349, https://doi.org/10.1007/978-3-319-91161-8_12.
[119] C.M. Maragos, K.K. Sieve, M. Busman, Development of antibodies for N-(1-deoxy-D-fructos-1-yl) fumonisin B1 and cross-reaction with modified fumonisins, World Mycotoxin J. 11 (4) (2018) 493–502, https://doi.org/10.3920/WMJ2018.2308.
[120] D. Peschen, H.-P. Li, R. Fischer, F. Kreuzaler, Y.-C. Liao, Fusion proteins comprising a Fusarium-specific antibody linked to antifungal peptides protect plants against a fungal pathogen, Nat. Biotechnol. 22 (6) (2004) 732–738, https://doi.org/10.1038/nbt970.
[121] H.-P. Li, J.-B. Zhang, R.-P. Shi, T. Huang, R. Fischer, Y.-C. Liao, Engineering Fusarium head blight resistance in wheat by expression of a fusion protein containing aFusarium-specific antibody and an antifungal peptide, Mol. Plant Microbe Interact. 21 (9) (2008) 1242–1248, https://doi.org/10.1094/mpmi-21-9-1242.
[122] Z.-Q. Hu, H.-P. Li, J.-B. Zhang, E. Glinka, Y.-C. Liao, Antibody-mediated prevention of Fusarium mycotoxins in the field, Int. J. Mol. Sci. 9 (10) (2008) 1915–1926, https://doi.org/10.3390/ijms9101915.
[123] A. Temesgen, G. Teshome, Major mycotoxins occurrence, prevention and control approaches, Biotechnol. Mol. Biol. Rev. 12 (1) (2018) 1–11, https://doi.org/10.5897/bmbr2018.0274.
[124] M. Tinoco, B.B. Dias, R.C. Dall'Astta, J.A. Pamphile, F.J. Aragão, In vivo trans-specific gene silencing in fungal cells by in planta expression of a double-stranded RNA, BMC Biol. 8 (1) (2010) 27, https://doi.org/10.1186/1741-7007-8-27.
[125] M. Wang, A. Weiberg, F.-M. Lin, B.P.H.J. Thomma, H.-D. Huang, H. Jin, Bidirectional cross-kingdom RNAi and fungal uptake of external RNAs confer plant protection, Nature Plants 2 (10) (2016), https://doi.org/10.1038/nplants.2016.151.
[126] R.S. Arias, P.M. Dang, V.S. Sobolev, RNAi-mediated control of aflatoxins in peanut: method to analyze mycotoxin production and transgene expression in the peanut/Aspergillus pathosystem, JoVE 106 (2015), https://doi.org/10.3791/53398.
[127] S. Campo, C. Peris-Peris, C. Siré, A.B. Moreno, L. Donaire, M. Zytnicki, B. San Segundo, Identification of a novel microRNA (miRNA) from rice that targets an alternatively spliced transcript of theNramp6(Natural resistance-associated macrophage protein 6) gene involved in pathogen resistance, New Phytol. 199 (1) (2013) 212–227, https://doi.org/10.1111/nph.12292.
[128] H. Puchta, Applying CRISPR/Cas for genome engineering in plants: the best is yet to come, Curr. Opin. Plant Biol. 36 (2017) 1–8, https://doi.org/10.1016/j.pbi.2016.11.011.
[129] B. Bakan, D. Melcion, D. Richard-Molard, B. Cahagnier, Fungal growth and Fusarium mycotoxin content in isogenic traditional maize and genetically modified maize grown in France and Spain, J. Agric. Food Chem. 50 (4) (2002) 728–731, https://doi.org/10.1021/jf0108258.
[130] R.J. Wall, A.M. Powell, M.J. Paape, D.E. Kerr, D.D. Bannerman, V.G. Pursel, H.W. Hawk, Genetically enhanced cows resist intramammary Staphylococcus aureus infection, Nat. Biotechnol. 23 (4) (2005) 445–451, https://doi.org/10.1038/nbt1078.
[131] S.G. Lillico, C. Proudfoot, T.J. King, W. Tan, L. Zhang, R. Mardjuki, C.B.A. Whitelaw, Mammalian interspecies substitution of immune modulatory alleles by genome editing, Sci. Rep. 6 (1) (2016), https://doi.org/10.1038/srep21645.
[132] F. Forabosco, M. Löhmus, L. Rydhmer, L.F. Sundström, Genetically modified farm animals and fish in agriculture: a review, Livest. Sci. 153 (1–3) (2013) 1–9, https://doi.org/10.1016/j.livsci.2013.01.002.
[133] M. Plotan, R. Devlin, J. Porter, M.E.O. Benchikh, M.L. Rodríguez, R.I. McConnell, S.P. FitzGerald, The use of biochip array technology for rapid multimycotoxin screening, J. AOAC Int. 99 (4) (2016) 878–889, https://doi.org/10.5740/jaoacint.16-0115.
[134] J. He, T. Zhou, J.C. Young, G.J. Boland, P.M. Scott, Chemical and biological transformations for detoxification of trichothecene mycotoxins in human and animal food chains: a review, Trends Food Sci. Technol. 21 (2) (2010) 67–76, https://doi.org/10.1016/j.tifs.2009.08.002.