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Managing Major Foodborne Mycotoxins: A Therapeutic Approach for Safety and Health

Azhar Abdullah Najjar[1*]

[1]*Department of Biological Sciences, King Abdulaziz University, Jeddah, KSA.*

ABSTRACT

Fungal mycotoxins from genera Aspergillus, Fusarium, and Penicillium contaminate feedstuff and food to induce serious health issues in humans and animals known as mycotoxicosis. Aspergillus, Penicillium, Alternaria, and Fusarium mycotoxins pose a serious threat to food quality and safety. Aflatoxins, zearalenone, ochratoxins, patulin, fumonisins, trichothecenes, deoxynivalenol have been documented to exert nephrotoxicity, immunotoxicity, hepatotoxicity, carcinogenicity, teratogenicity, and neurotoxicity in animals and humans. Implementation of HACCP-based procedures can mitigate mycotoxin-linked contamination whereas traditional methods (physical, biological, and chemical) could facilitate the decontamination process. However, the rising fungal resistance and conventional systems-associated challenges demand innovative strategies to rapidly eliminate mycotoxins without impacting the quality. The most important food-contaminating mycotoxins include liver-damaging aflatoxins; kidney-damaging ochratoxin A; cancer-causing, liver-damaging, and developmental defects-associated fumonisins; acute cardiac damage-related moniliformin; and gastroenteritis and immunotoxicity-associated zearalenone and deoxynivalenol. Therefore, mycotoxins can be categorized as teratogens, hepatotoxins, allergens, nephrotoxins, mutagens, neurotoxins, immunotoxins, and carcinogens. Mycotoxins are associated with various animal and human diseases including porcine pulmonary edema, Reye's disease, Balkan endemic nephropathy, equine leuko-encephalomalacia, and alimentary toxic aleukia of humans. This study discusses the individual and combined impacts of foodborne fungal mycotoxins along with the related biochemical mechanisms and pathologies.

Keywords: *Foodborne, Mycotoxins, Prevention, Fungi, Contamination*

Corresponding author: Azhar Abdullah Najjar
e-mail ✉ anajjar@kau.edu.sa
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INTRODUCTION

Mycotoxins are hazardous secondary metabolites of fungi, which mainly grow on food crops (They are low molecular weight fungal metabolites (*Aspergillus*, *Penicillium* spp., *Alternaria*, and *Fusarium*) contaminating feeds and foods during storage, and pre-and post-harvest practices (Gavahian *et al*., 2022). More than 400 mycotoxins are considered toxic causing hepatitis, necrosis, hemorrhage, testicular atrophy, gynecomastia, cancer, neurological disorders, and mortality in extreme conditions (Adebo *et al*., 2021). Socioeconomic, agronomic, and environmental aspects can enhance the risk of mycotoxin-related food contamination. Food safety has become an important concern for animal and human health. Developed countries have implemented quality standards and guidelines to monitor food quality whereas food safety and quality monitoring standards are still poor in developing countries. Animal and human food poisoning is a major detrimental aspect of mycotoxin-contaminated food consumption. Several aflatoxin outbreaks were reported in Russia during World War II, which led to the death of over five thousand Alimentary Toxic Aleukia patients. Mycotoxins' food contamination occurs in the field, storage, or during handling and processing and their presence drastically compromises the quality of food products (Awuchi *et al*., 2021).

Mycotoxin contaminations in date palm (Al-Sheikh, 2009), apple juice (patulin) (Bahati *et al*., 2021), coffee beans (ochratoxigenic Aspergillus) (Moslem *et al*., 2010), wheat flour (aflatoxin) (Gashgari *et al*., 2010), cheese (Floury *et al*., 2010), and raisins (Gashgari *et al*., 2011) have been reported in KSA. Aflatoxins, citreoviridin, alter toxins, citrinin, cyclopiazonic acid, fumonisins, cytochalasins, fusarochromanone, ergotamine, ergopeptine alkaloids, ergot alkaloids, fusaric acid, kojic acid, nivalenol, lolitrem alkaloids, moniliformin, oosporeine, 3-Nitropropionic acid, ochratoxins, patulin, sporidesmin A, phomopsins, sterigmatocystin, trichothecenes, tremorgenic, zearalenols, and zearalenone are common foodborne outbreaks-associated mycotoxins. The conventional methods (physical, chemical, and biological) can alleviate mycotoxin contaminations to safer levels. However, these approaches generate significant changes in the food substrate (texture, flavor, color), and nutritional content (lipid oxidation, vitamin breakdown, and polysaccharides re-polymerization and depolymerization). Mycotoxins remain thermally and chemically stable during traditional food processing (Mohsen *et al*., 2020). Therefore, innovative strategies without direct heat applications are being preferred, which are expected to significantly reduce mycotoxin concentrations in foods and enhance organoleptic quality.

Food industry-associated global mycotoxins

Mycotoxins such as aflatoxins, Ochratoxin A, *Fusarium* toxins, Fumonisin, Zearalenone, Trichothecenes, and

Deoxynivalenol/Nivalenol could be produced on a variety of different foodstuffs and cause adverse health effects. **Table 1** shows a list of major fungal mycotoxins and their toxicity effects on humans and animals.

Table 1. List of major fungal mycotoxins and their toxicity effects on humans and animals.

No	Mycotoxin	Description	References
1	Aflatoxins (M1, G1, G2, B1, B2,)	Produced by *Aspergillus flavus* and *Aspergillus parasiticus* and contaminates rice, maize, groundnuts, oats, nuts, milk, cottonseed, barley, copra, wheat, and spices. They damage the liver causing cirrhosis, necrosis, and cancer in some cases. Aflatoxin's presence in feed leads to reduced egg and milk production.	(Ameen & Al-Masri, 2023)
2	Citrinin	Produced by *Monascus, Aspergillus,* and *Penicillium* and contaminates groundnuts, rice, oats, wheat, maize, red rice, flour, fruit, barley, and rye. It damages the liver and kidneys in livestock and humans.	(Kamle *et al*., 2019)
3	Patulin	Produced by *Penicillium,* and *Aspergillus*. It is produced in rotting apples and affects fruit quality. Patulin is not considered a potent toxin, however, its genotoxic effect has been reported in multiple studies.	(Bahati *et al*., 2021)
4	Ochratoxin A	Produced by *Penicillium verrucosum* and *Aspergillus ochraceus* and contaminates sorghum, maize, oats, wheat, coffee, barley, cocoa, beer, dried vine fruits, and wine. It is known to cause cancer and kidney damage in rats.	(Lee *et al*., 2024)
5	Deoxynivalenol	Produced by *Fusarium graminearum* and contaminates oats, maize, malted barley wheat, and barley. It damages the reproductive organs, digestive tract, spleen, and bone marrow leading to feed refusal, vomiting, and weight loss.	(Kamle *et al*., 2019)
6	Fumonisin B1, B2, and B3	Produced by *Fusarium verticillioides* and contaminate cereal grains, particularly maize. They genetically damage human lymphocytes and cause horses' brain decay and rat cancer.	(Chen *et al*., 2021)
7	T-2 toxin	Produced by *Fusarium* and other mold species and contaminates sorghum, maize, rice, wheat, oats, barley, and other cereal grains. It causes alimentary toxic aleukia and oral and skin lesions in humans.	(Janik *et al*., 2021)
8	Zearalenone	Produced by *Fusarium graminearum* and contaminates sorghum, maize, grain, wheat, and barley. Zearalenone affects fetal development, reproduction, and newborns' health.	(Ropejko & Twarużek, 2021)

Aflatoxins (AF)

Aflatoxins are secondary metabolites of *A. flavus* (AF), *A. parasiticus*, and *A. nomius*. They are the most important animal feed and human food-contaminating global mycotoxins. Aflatoxigenic properties of *A. pseudocaelatus*, *A. nomius*, *A. pseudotamari, A. sergii*, *A. ochraceoroseus*, *A. bombycis, A. parvisclerotigenus,* and *A. minisclerotigenes* have also been reported but their natural occurrence is low (Kumar *et al*., 2022). Fungal multiplication post-AF production is affected by environmental factors (high temperature, relative humidity, and moisture), plant genre, presence of oxygen and carbon dioxide, number of spores, insect infestation, mechanical damages, and fungicide and pesticide applications. Relative humidity and temperature are the most influential factors in AF production. Kumar *et al*. (2022) reported optimal temperatures of 29 to 35°C for AF growth whereas they noted maximum production at 24° C. Fungi were unable to produce AF above 42°C and below 13°C and at a relative humidity of below 70%. Aflatoxins remain resistant and stable to cold storage and heat processing (pasteurization, UHT (ultrahigh-temperature treatment), baking, and roasting) of foods (Chiozzi *et al*., 2022). Aflatoxin B_1 (AFB_1) is the most common and potent mycotoxin that has been classified as a class 1 carcinogen by WHO (World Health Organization). The mutagenicity, toxicity, and carcinogenicity of important mycotoxins could be arranged as $G_2 < B_2 < G_1 < B_1$ (Kumar *et al*., 2022). There are over 14 types of natural chemical AF but B1, B2, G1, and G2 are considered the most toxic mycotoxins. Aflatoxins' nomenclature is based on their color under ultraviolet radiation (G: green and B: blue). The products grown under humid and hot conditions (tree nuts, spices, maize, groundnuts, copra, rice, wheat, pistachio, and cottonseed) are more prone to fungal infection and aflatoxin generation. AFB1 metabolizes into AFM1, which is excreted in the milk of lactating animals and humans. The Codex Alimentarius Commission, European Commission, Switzerland, Germany, Belgium, Turkey, France, Iran, Sweden, Honduras, and Argentina have regulated 50 ng/L as the acceptable AFM1 limit for infant milk (UHT, pasteurized, and raw). Contrarily, the acceptable AFM1 limit in Kuwait, Bulgaria, the United States, the Czech Republic, Serbia Brazil, and China is 500 ng/L. Aflatoxins' toxicity poses significant economic and health impacts and aflatoxin-linked damage to the corn industry in the United States ranges from 52.1 million USD to 1.68 billion USD. Aflatoxins are teratogenic, carcinogenic, hepatotoxic, and, immunity-reducing toxins. They enter the body through respiration and cause direct structural alterations in DNA. Aflatoxin-associated liver cancer is the most pronounced impact of aflatoxins whereas synergism of aflatoxin and chronic HBV infection further enhances this risk as shown in **Figure 1** (Wu, 2015).

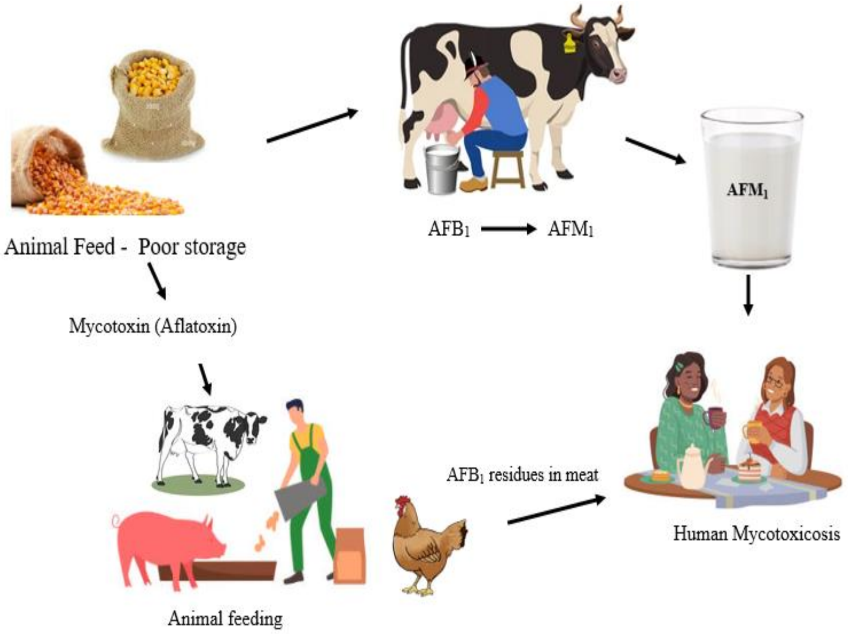

Figure 1. Schematic representation of mycotoxicosis infection cycle

Ochratoxin A (OTA)

OTA is mainly produced by *Penicillium* and *Aspergillus* under storage and optimum environmental conditions. Tropical and subtropical regions (Southern and Eastern Europe, South America, and Canada) are the hotspots of OTA infection. Ochratoxins are of three types such as A, B, and C. OTA is important for animal and public health. Dermal contact and inhalation are the main entry routes of OTA, whereas foods also serve as a source of OTA exposure such as strawberries, maize, oranges, sorghum, mangoes, wheat, tomatoes, rice, watermelons, barley, sesame seeds, rye, soybeans, bread, peanuts, oats, apples, flour, rapeseed, pasta, coffee beans, grapes, cocoa, infant cereals, peaches, pears, figs, wine, nuts, spice, eggs, chickpeas, onions, milk, baby formulae of milk, dried beans, cheese, poultry, yam, pork, potatoes, fish, garlic, and jerky (Leitão, 2019). OTA has also been detected in bottled water, food coloring agents, and plant food supplements (Lee *et al*., 2024).

Fusarium toxins

Fusarium toxins are secondary metabolites of *Fusarium graminearum, F. oxysporum*, *F. roseum*, and *F. culmorum* (Ekwomadu *et al*., 2021). Fumonisins (FBs), nivalenol (NIV), zearalenone (ZEA), trichothecenes, and deoxynivalenol (DON) are common *Fusarium* mycotoxins. Other *Fusarium* mycotoxins such as moniliformin (MON), beauvericin (BEA), fusaproliferin (FUS), and enniatins (ENNs) have been recently discovered. *Fusarium* outbreaks in cereals (maize, wheat, and barley) have led to considerable economic losses worldwide due to poor grain quality and yield loss. The *Fusarium*-related losses in the United States generally range between 1–20 million USD during a normal year and 31–46 million USD during outbreaks (Wu, 2015). *Fusarium* mycotoxins exert chronic and acute toxicities in animals. Spontaneous *Fusarium* mycotoxicosis outbreaks have been documented in South America, Europe, New Zealand, Asia, and Africa. The global presence also leads to chronic and regular intake of these mycotoxins. The limits of *Fusarium* mycotoxins in cereal foods, milling products, and unprocessed cereals have been specified [DON (200–1750 μg/kg), ZEN (20–400 μg/kg), and FB1 + FB2 fumonisins (200–4000 μg/kg)] by the European Commission in 2006 (Ionel, 2018).

Fumonisin

Fusarium proliferatum, F. verticillioides, and *A. niger* are known to produce fumonisins, which were first reported in South Africa in 1988. 28 types of fumonisin have been identified that are categorized into four groups, fumonisins P (P3, P2, and P1), fumonisins A (A3, A2, and A1), fumonisins C (C4, C3, and C1), and fumonisins B (B3, B2, and B1). The B group contains the most important fumonisins (FB3, FB2, and FB1). The International Agency for Research on Cancer (IARC) recognizes FB1 as a potent human carcinogen (group 2B). The rise in FB1-associated liver and esophageal human cancers has been reported in recent studies (Chen *et al*., 2021). FB1 is toxic to multiple animal organs such as lungs, kidneys, liver, and cardiovascular and nervous systems. Fumonisins are commonly detected in corn foods whereas FB1 is found in sorghum, rice, triticale, beer, soybeans, cowpea seeds, beans, and asparagus (Kamle *et al*., 2019).

Zearalenone (ZEA)

Zearalenone (ZEA) or estrogenic mycotoxin is a secondary metabolite of *F. graminearum*, *F. culmorum*, *F. semitectum*, *F. cerealis*, *F. crookwellense*, and *F. equiseti*. ZEA mainly contaminates cereals including sesame, maize, nuts, sorghum, oats, wheat, barley, rice, and soybean (Ropejko & Twarużek, 2021). The natural resemblance of ZEA with estrogens leads to hormonal disruption and its high affinity to estrogen receptors causes fertility and reproduction disorders in mammals. Progressive exposure to ZEA (endocrine-modulatory compound) is associated with human carcinogenesis (Yu *et al*., 2022). The European Food Safety Authority (EFSA) report of 2014 reveals 80% bioavailability of this toxin in humans and animals (pigs, rats, and rabbits) (EFSA Panel on Contaminants in the Food Chain (CONTAM), 2014). Furthermore, animal tests have revealed that ZEA metabolism in the liver results in immunotoxicity, hepatotoxicity, nephrotoxicity, and carcinogenicity. Due to consumers' health risks, the European Union (EU) has specified the ZEA limit as 20–350 µg/kg for various types of unprocessed and processed cereals (EFSA Panel on Contaminants in the Food Chain (CONTAM), 2014).

Trichothecenes (TCT)

TCT is predominantly a *Fusarium*-produced large group of mycotoxins. *Verticimonosporium*, *Trichoderma*, *Myrothecium*, *Trichothecium*, *Cylindrocarpon* spp., *Stachybotrys*, and *Cephalosporium* genera are also known to produce trichothecenes. Over 200 types of trichothecenes and their derivatives have been reported, which are categorized into four types (A–D). Types A and B are commonly prevalent in cereals (Villafana *et al*., 2019). Type A trichothecenes (neosolaniol (NEO), mono acetoxyscirpenol (MAS), diacetoxyscirpenol (DAS), and T-2 and HT-2 toxins) are mainly produced by *F. langsethiae* and *F. sporotrichioides*. The production of type B (deoxynivalenol (DON fusarenon-X (FUS-X; synonym 4-acetylnivalenol), and co-contaminants 3- and 15-acetyl DON (3A-DON or 15A-DON)) is associated with *F. culmorum* and *F. graminearum*. However, an important type B trichothecene, nivalenol (NIV), is often produced by *F. poae* in cereals (Sliwinska & Paszczyk, 2021). Trichothecenes inhibit protein synthesis in eukaryotes by affecting the 60S ribosomal subunit-binding peptidyl transferase enzyme leading to ribotoxic stress. Trichothecenes can also affect leucocytes to cause immune stimulation or immunosuppression. Trichothecenes significantly impact grain and cereal production because of the risks associated with human consumption, malting, and livestock feed. FDA reports revealing that mycotoxin-associated economic losses could range from 0.5 million USD to over 1.5 billion USD in the United States including deoxynivalenol (wheat), fumonisin (corn), and aflatoxin (peanuts and corn) (Villafana *et al*., 2019). Therefore, management of these mycotoxins is necessary to avoid economic and health (animal and human) issues.

Deoxynivalenol/Nivalenol

Deoxynivalenol (DON) or vomitoxin is commonly detected in rye, wheat, oats, barley, corn, and oats whereas its presence is comparatively lesser in triticale, rice, and sorghum. Generally, the presence of NIV in cereals is lower than in DON (However, an equivalent presence of NIV and DON has been reported in barley and wheat in Japan. Animal toxicity investigations have revealed higher NIV toxicity than DON. NIV and DON LD_{50} values in mice were noted as 39 and 78 mg/kg, respectively. Both NIV and DON inhibit cell metabolism by affecting protein, RNA, and DNA synthesis. They also affect mitochondrial functions and cell division. NIV and DON toxicity-related major symptoms include vomiting, abdominal discomfort, weight loss, diarrhea, anorexia, and throat inflammation (Lee *et al*., 2020).

Mycotoxin production-related important factors

Multiple factors determine the mycotoxins' infection capability, which includes biotic factors, storage, harvesting, processing, and climate. Mycotoxin production depends on climate, plants, storage- conditions, and noninfectious factors (nutrient bioavailability and pest damage). Kernels, nuts, fruits, and pulses are the active sites for fungal growth whereas the amount of fungus propagules directly correlates to the mycotoxin concentration. Mycotoxins affect the crop during pre and post-harvesting procedures and storage. Different toxic species of *Fusarium, Penicillium*, and *Mucor* have been detected in overwintered grains. Temperate temperatures (22-30°C), high relative humidity (70%-90%), and high moisture content (20%-25%) enhance the fungal growth and mycotoxin production. Mites and insects physically injure the kernel, which facilitates mold invasion leading to toxin production. Molds' presence in air and soil is mostly natural, which complicates preventing their feed/food contaminations. However, fungal growth and mycotoxin production-associated factors can be controlled (Nji *et al*., 2022). Mycotoxins' ubiquitous presence and ability to grow in various habitats (psychrophilic and thermophilic) significantly enhance their survivability.

Mycotoxin management

Food safety is crucial for public health whereas mycotoxins pose significant food safety risks in developing countries. Food safety can be ensured through the reduction of fungal growth by mycotoxin prevention. Mycotoxin prevention and control practices include GAP (good agricultural practices), physical methods (milling and cleaning), control measures during harvesting and storage, degradation/detoxification, biotechnological applications, fermentation methods, and a controlled atmosphere for biological control during storage. Pre-harvesting is the key stage where mold growth and mycotoxin production can be prevented. Safe pre-harvesting strategies include the selection of insect and fungi-resistant plants, choosing a plant variety according to soil structure, proper irrigation and fertilization timing, and insecticide applications to avoid insect damage. Appropriate harvesting time (full maturity and low moisture) reduces the risk of mycotoxin contamination as over-maturity enhances mold growth susceptibility. The use of suitable harvesting equipment and methods, and drying of crops after maturity to reduce grain moisture to a safe level help in preventing mold growth and toxin production (Kępińska-Pacelik & Biel, 2021).

The recent advances have prompted novel mycotoxin control strategies including the application of a controlled atmosphere with protective and inhibitory effects, and the use of natural antioxidant compounds and essential oils to mitigate mold growth and toxin production in grains during storage. Furthermore, the use of clean transport vehicles to avoid cross contaminations; periodic monitoring of aeration, temperature, humidity, and pest infestation during storage; use of fungi inhibitors (propionic acid) to contaminated feed and food; and disinfectant (sodium hypochlorite) application in the storage area are useful in preventing mycotoxin production. Physical methods (sorting, dehulling, cleaning, and washing of moldy seeds) have been reported to reduce various mycotoxins in food products regardless of the grain genre. Milling considerably reduces *Fusarium* mycotoxins in grains, particularly the wet milling of maize has been reported to degrade mycotoxins (Kumar *et al*., 2022).

The cultivation of fungi-resistant plants with improved genetic composition can effectively suppress mycotoxin production.

Aflasafe (a blend of four fungi) has revealed the beneficial aspects of biotechnological applications in mycotoxin prevention. Aflasafe application covers the grains to reduce the growth of AF-producing aflatoxigenic fungi in groundnuts and maize (https://aflasafe.com/). Mycotoxins are heat resistant and remain viable during normal cooking. Contrarily, Lee *et al*. (2024) have reported a 66% to 83% reduction of ZEN in response to heat treatment at 120°C–160°C. Scott and Lawrence (1994) have also reported a 60–100% reduction of fumonisins after a heat treatment at 220°C (25 min) and 190°C (60 min). These reductions might be due to structural changes in response to heat treatments at high temperatures.

Degradation/detoxification-based biological mycotoxin control is an efficient alternative method (Liu *et al*., 2022). The fermentation efficacy in eliminating and reducing mycotoxins has been recently established. Mycotoxins are generally neutralized through detoxification, conversion, binding, decontamination, and degradation after the fermentation of food. The structural modification of mycotoxin molecule, inactivation, removal, detoxification, and adhesion to bacterial cell walls leads to reduced toxicity during the fermentation process. However, these preventive methods remain unable to solely solve the mycotoxin problem. Therefore, these practices should be added to the integrated food safety management system based on the hazard analysis and critical control point (HACCP).

Novel therapeutic strategies for controlling mycotoxins' food contamination

Improved food safety awareness among consumers has urged researchers to look for novel mycotoxin-controlling techniques without impacting food quality and toxic residues. In this regard, innovative methods of cold atmospheric plasma (CAP), flavonoids, polyphenols, nanoparticles, magnetic materials, and natural essential oils (NEOs) are rapidly emerging (Ahmed *et al*., 2022; Cai *et al*., 2022).

Natural essential oils (NEOs)

NEOs and their bioactive molecules are highly effective, eco-friendly with low drug resistance, and green anti-fungal additives against food-contaminating toxins. Anti-fungal and anti-mycotoxin NEO mechanisms involve the inhibition of key enzymes associated with carbohydrate breakdown, mycotoxin generation, and fungal cell disruption. These actions are possible by (I) altering fungal gene expressions, (II) polyphenols-based disruption of microorganisms' cell membrane and cell, and (III) structural damage to cell walls and cell membrane (Cai *et al*., 2022). Nanoemulsion-encapsulated *Origanum majorana* L. essential oil has demonstrated (*in situ* and *in vitro*) promising antioxidant and inhibitory efficacy against AFB_1 mycotoxin to serve as a novel food preservative for better food safety (Chaudhari *et al*., 2020). Kollia *et al*. (2019) have reported capsaicin-based *A. carbonarius* and *Aspergillus* section *Nigri* OTA inhibition in grapes by 61.5% and 78.1%, respectively. Mint and sage essential oils also significantly decreased the OTA synthesis whereas its production was completely restricted against wild oregano and garlic essential oils. The anti-fungal potential of turmeric oil has been documented against maize-contaminating *A. flavus* and aflatoxins whereas *Mentha spicata* essential oil effectively inhibited the *A. flavus* toxin production in chickpeas for up to one year, which was associated with the plasma membrane. NEOs are highly efficient in ZEN inhibition. Lemon, grapefruit, eucalyptus, and palmarosa successfully alleviated the ZEN levels whereas *Curcuma longa* essential oil completely stunted *Fusarium graminearum* growth and zearalenone formation to lower levels of 3 and 3.5 mg/L, respectively.

Cold plasma

Plasma is a fully or partially ionized gas and is known as the fourth state of matter. The passing of electric current through neutral gas dissociates gaseous molecules to generate plasma. The discharge of Plasma occurs when the voltage exceeds the breakdown voltage to generate reactive oxygen and nitrogen species (RONS). Non-thermal cold plasma generation relatively requires low energy at ambient temperature and atmospheric pressure. Cold atmospheric plasma (CAP) can be indirectly or directly exposed to water, buffers, and acids to discharge plasma for the preparation of broad-spectrum sanitizers (Esua *et al*., 2020; Ali *et al*., 2022). Antimicrobial properties and capability of degrading complex biochemical molecules are linked to the unique blend of reactive chemistries (O_3, O_2^-, $\bullet OH$, H_2O_2, $ONOO^-$, NO_3^-, and NO_2^-), electric field, and UV photons. They exhibit non-thermal features by remaining close to ambient temperature (Hojnik *et al*., 2021). Non-thermal CAP is a fast and low-cost innovative strategy for the decontamination of food and agricultural pathogens without affecting product quality (Esua *et al*., 2020).

Flavonoids and polyphenols

The biological properties (anti-inflammatory, antiviral, antioxidant, and antibacterial) of Phytonutrients (flavonoids and polyphenols) favor their applications in different food systems (Mehany *et al*., 2021). The anti-mycotoxin mechanisms of flavonoids and polyphenols are multidimensional such as (I) lipophilicity and antioxidant properties are important for their bioactivity, (II) structural modifications in fungal membrane to inhibit mycotoxin production, (III) mycotoxin production-related genes down-regulation, and (IV) enzyme activity inhibition (Ahmed *et al*., 2022). Hamad *et al*. (2021) have recommended plant extracts and polyphenol applications to inhibit fungal growth and mycotoxins production. Polyphenols can restrict patulin accumulation by quercetin and umbelliferone-based down-regulation of genes involved in the patulin biosynthetic pathway. AFB1 inhibitory effects of gallic and chlorogenic acids in edible beans have also confirmed the anti-mycotoxin efficiency of phenolic compounds. Flavanones extracted from citrus byproducts (neohesperidin, hesperidin, naringin, and hesperetin glycoside) have reduced patulin accumulation by 95%. Makhuvele *et al*. (2020) have revealed that the combination of bioactive phenols and β-cyclodextrin (nanosponge method) efficiently inhibited the fungal attack and detoxified mycotoxins. Natural dietary complexes having various nonnutritive active compounds exhibit antioxidant and medicinal properties. Natural herbal extracts and these bioactive molecules are known to effectively reverse the hazardous impacts of mycotoxins. Therefore, dietary fiber and polyphenol interventions could be promising strategies against fungal and mycotoxin hazards.

Magnetic materials and nanoparticles

Eco-friendly, effective, and low-cost mycotoxin control with nanoparticles and magnetic materials is becoming a preferred choice. Chitosan-coated magnetic particles (Fe_3O_4) could effectively adsorb patulin from the fruit juice. Depending on the pH and concentration, nanocellulose and retinoic acid conjugation could efficiently adsorb AFB_1 from various food items without any toxicity (Fuad & Abeer, 2023). Magnetic nanoparticles (nano-clay, surface-active maghemite, and nano-gel) and nanomaterials (selenium nanoparticles (SEN), zinc oxide nanoparticles (ZON), copper nanoparticles, and silver nanoparticles (SLN)) are known to effectively bind and remove mycotoxins from agricultural foods and feedstuff (Padrilah *et al*., 2024). Hu *et al*. (2017) have reported DON and FB_1 reduction by 76% and 63%, respectively by *Trichoderma harzianum* JF309-produced SEN. SLN prevented aflatoxigenic and ochratoxigenic fungal growth and aflatoxin and OTA accumulation in a maize-based medium. Similarly, ZON effectively inhibited the growth of *Penicillium* spp., *Fusarium* spp., and *Aspergillus* spp., and the production of OTA, AFB1, and FB1 in food model systems (Gómez *et al*., 2019). Maize byproducts-made magnetic carbon nanocomposites have also exhibited significant AFB_1 detoxification potential in poultry with up to 90% adsorption at pH 7 within 180 min. The cross-linked chitosan-glutaraldehyde complex demonstrated significantly high multi-toxin adsorption capability among various tested adsorbent materials. Nano-fungicides from essential oils and phytochemicals (thymol, eugenol, phloretin, caffeic acid, tannins, and catechols) also depicted antibacterial and antifungal activities to inhibit toxigenic fungal growth and mycotoxin contamination without risking the humans and animals (Hamad *et al*., 2021).

Mycotoxins eliminating nanoparticles' molecular mechanism is linked to their inflammatory and oxidative stress-inducing roles in addition to the interaction with nucleic acids for microorganism destruction in animals and higher plants (Horky *et al*., 2018). Their interactions with the cell membrane specifically induce apoptosis, ROS generation, mitochondrial function inhibition, autophagy, and lipid peroxidation. ZON damages the fungal hyphae's lipid bilayer cell membrane through ROS production leading to a complete breakdown of affected cells. Scanning electron microscopy confirmed this phenomenon by revealing unusual bulge formation or deformation of fungal hyphae after ZON (12 mmol/L) treatment (Pietrzak *et al*., 2015). During a study, a relaxed chitosan polysaccharide structure in quercetin (Q)-loaded chitosan (CS) nanoparticle was cross-linked with tripolyphosphate (TPP), which triggered a hepato-protective cascade leading to antioxidant protection by stimulating nuclear factor E2-related factor 2 (Nrf2)-induced heme-oxygenase-1 (HO-1) production. Quercetin inhibits lipopolysaccharide (LPS) induced nitric oxide synthase (iNOS) and NO generation through p38 mitogen-activated protein kinases (p38MAPK) and IκB kinase (IKK). The transcriptional response was mediated by the acting antioxidant response element (ARE) of the enzyme detoxication promoters-encoding gene Horky *et al*. (2018) have investigated the key characteristics of carbon nanoparticles [carbon nanotubes, fullerenes, and graphene (graphene oxide (GO), reduced graphene (rGO), and native graphene (G)], and their binding interactions with mycotoxins. Mycotoxins can follow various binding interactions to bind at grooves, bundles, Horkysurfaces, and channels between nanoparticles. However, a thorough understanding of NPs' interactions with the individual components of fungal cells remains unclear and requires further in-depth investigations.

CONCLUSION

The associated health hazards make mycotoxins an important public concern. Mycotoxins generally act in combinations that complicate the prediction of their toxicity. The damage to livestock feed by mycotoxins poses a direct risk to animal health and indirectly impacts humans. Mycotoxins-based feed, food, and livestock contamination makes them unfit for consumption, export, and import and thus leads to economic losses. Their excessive levels are commonly detected in feed and food in developing and developed countries. Developed nations follow strict rules to ensure the supply of quality food, however, developing nations are still far behind. Therefore, mycotoxin toxicity reduction is necessary in developing countries if complete eradication is not possible. Mycotoxin contamination of agricultural products, animal feed, and human food has become a global concern because of the associated health risks, and economic losses. Rapid and early mycotoxin detection is crucial for the elimination, overall food safety, and prevention of health issues. The enhanced consumer awareness about regulatory issues, food safety, limited efficiency, potential carcinogenic by-products, and reduced quality discourage the use of traditional (physical, chemical, and biological) detoxification methods. The rising resistance, particularly in new strains, has further geared the research towards novel rapid strategies for mycotoxin management in foods with short processing time without considerably affecting textural, morphological, physicochemical, and structural features.

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