Research Article



Occurrence and Toxicity of Mycotoxins from Food and Feed Resources

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Abstract | Mycotoxins are the secondary metabolites produced by different filamentous fungi. The significance of these low molecular weight compounds lies in the fact that they are the contributors of severe health issues in livestock and humans. Every year mycotoxins infect different crops and animal feedstock by accumulating in the food and feed crops in the field and during transportation, which leads to the huge economic losses. Presently about 300 types of mycotoxins have been identified, while, aflatoxins, fuminisons, ochratoxins, trichothecenes and zearalenone are the major mycotoxins infecting food and feed crops. Consumption of food contaminated with these mycotoxins can cause severe toxicity in human and animals. Members of these fungal genera *Fusarium spp.*, *Penicillium spp.*, and *Aspergillus spp.*, are major mycotoxins producers in food and feed crops. Mycotoxins thrive in high-temperature, humid environments, and they can enter the food chain either directly or indirectly by contaminating food and feed crops. They can cause infection before and after agricultural crop harvesting. Economically mycotoxins infection leads to loss of feedstock, reduced livestock production, human and animal life threatening diseases and major issues leading to global food security. All these factors demand for extensive research for early mycotoxins detection methods and making regularity bodies to contain the spread of mycotoxins. This review summarizes the occurrence and toxicity of five major types of mycotoxins associated with food and feed and their importance in human nutrition and animal health.

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Keywords | Mycotoxins, Aflatoxins, Ochratoxins, Crops, Secondary metabolites



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Introduction

Global food industry is facing serious challenges due to climate change, different plant diseases, water shortage and poor harvesting practices. Fungi are the larger contributor in incidence of different crops infections. Food and agricultural products contaminated by toxigenic molds (fungi) is a major global food security issue. Every year agro-industrial sector faces huge economic losses in billions of dollars due to fungal contamination of different crops. Improper handling, storage and poor harvesting strategies play its role in fungal infection which ultimately leads to mycotoxin contamination. Mycotoxins are secondary metabolites produced by different filamentous fungi (Bennett, 1987; Tola and Kebede, 2016). They are heterogeneous compounds of low molecular weight. Their notorious reputation is due to their ability to



cause serious diseases in humans and animals. Fungi produce different metabolites but not all of them are mycotoxins. Metabolites that are toxic towards bacteria and plants are known as antibiotics and phytotoxins respectively (Alshannaq and Yu, 2017). Mycotoxins enter the food chain through infected crops that can be consumed by either humans or animals. This leads to accumulation of mycotoxins in different organs and tissues in the human and animal bodies, which makes them conducive to deadly diseases. Mycotoxins first came into notice in 1962 when in England 100,000 turkey poults died due to peanuts feedstock poisoning with fungi Aspergillus flavus. Even though these metabolites are not required by fungi for their development and other function but they are detrimental to human health. They are established as mutagenic, carcinogenic and immunosuppressors agents (Kaushik, 2015).

These metabolites of fungal origin target different crops like wheat, barley, maize, sorghum, peanuts, pistachios etc. and their byproducts (Jard *et al.*, 2011). According to Food and Agricultural Organization (FAO) 25% of the cereals produced globally are contaminated with the mycotoxins. Mycotoxins can contaminate stored feedstock and food products. Different spices, fruits, nuts are also susceptible to the mycotoxins infection (Marin *et al.*, 2013). Mycotoxins can affect human health by consumption of fungal infected animal product like meat, eggs and milk. Most mycotoxins are chemically and thermally stable during food processing, including cooking, cooking, baking, frying, baking and pasteurizing. Some fungal toxins may have additional effects, such as phytotoxicity (Alshannaq and Yu, 2017). In general, all plants and plants that are stored inadequately for a long duration in elevated temperature and moisture conditions are at risk of fungal growth and contamination with fungal toxins (Bullerman, 1979).

Fungal species producing these toxins are knowns as toxigenic fungi. Currently 300 types of mycotoxins are reported as far. Out of these five categories of mycotoxins have enormous economic and health worth. They are aflatoxins (AF), ochratoxins (OT), trichothecenes, zearalenone (ZEN), fumonisins (F) and Patulin (P) (Figure 1) (Alshannaq and Yu, 2017). Each type is produced by diverse types of fungal species like plant pathogens such as Fusarium graminearum produces deoxynivalenol and nivalenol respectively, Fungi that grow on stressed plants such as Fusarium moniliform mostly produces fumonisin and Aspergillus flavus is associated with aflatoxin production (Marin et al., 2013; Sweeney and Dobson, 1998). Fungi that primarily colonize the plant before harvesting such as Penicillium verrucous produces ochratoxin

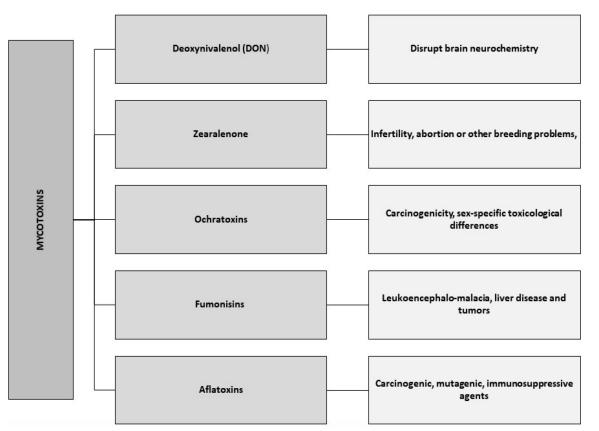


Figure 1: Main types of mycotoxins and their toxity.



(Tola and Kebede, 2016). Many national and international public health and governmental authorities such as the US Food and Drug Administration (FDA), World Health Organization (WHO), Food Agriculture Organization (FAO) and the European Food Safety Authority (EFSA), are taking strict measures to contain the spread of mycotoxin infected foodstocks and animal feeds (Alshannaq and Yu, 2017). Occurence and toxicity of major food and mycotoxins and their implications on health are summarized in Table 1.

Resources of mycotoxins

Mycotoxins occurrence is fairly common in cereal crops, legumes, animal feedstocks and various animal products. Plants are susceptible to toxigenic fungi attack during both pre harvest and post- harvest conditions. There are two groups of fungi that yield mycotoxins in food; that attack earlier harvest, commonly known as field fungi, and mycotoxins which affects crops after harvesting in storage known as storage fungi. Temperature and rainfall amendment in temperate and tropical regions makes these areas more prone to mycotoxins attack in different plant products during pre-harvest duration. Different plant growth stressors like drought, insect attack and timing of irrigation makes plants vulnerable to fungal contamination. Different storage conditions promote growth of toxigenic fungi in post-harvest duration worldwide. Seeds harbor the most amounts of mycotoxins. Increased moisture and temperature conditions heightened production of aflatoxins in stored peanut seeds. Also, drought stressed seeds showed reduced resistance to fungal infection respectively (Alshannaq and Yu, 2017). These environmental conditions varies in different regions leading to formation of different mycotoxins in each region for example aflatoxins are mostly common in African and Asian subcontinent regions, fumonisins and aflatoxins commonly occur in Australia, chratoxin, zearalenone (ZEN) and vomitoxin incidence is high in North America region; in South America aflatoxins, fumonisins, ochratoxin, vomitoxin (DON) are fairly common and in Eastern European countries, ZEN and vomitoxin occur in high quantities and in Western European regions ochratoxin, ZEN, and vomitoxin contamination is reported (Tola and Kebede, 2016).

Main Types of Mycotoxins

Aflatoxins: Aflatoxins belong to one of the main class of aflatoxins. They are mostly produced by fungal species like *Aspergillus parasiticus* and *Aspergillus flavus*. Fungal species *A. nomius* and *A. pseudotamarri* are also

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known to produce them. They are considered as the most potent form of mycotoxins among others. They are reported as potential carcinogens causing liver cancer in many animal species (Ashiq, 2015). Almost 20 types of aflatoxins are present out of which isoforms B1, B2, G1 and G2 hold significant position. Aflatoxin AFB1 and AFB2 are produced by A. flavus. These aflatoxins infect milk, milk products and meat products. Other forms are mainly produced by A. parasiticus (Prandini et al., 2009). These toxins mostly infect crops in tropical and sub-tropical regions where they colonize wide range of crops and crop products including maize, rice, pistachios, oilseeds, groundnuts, tree nuts, cottonseed, pepper and various dried organic products. Production of aflatoxin by fungi depends upon season especially dry season pressure, rainfall, suitability of crop genotype for its climate, agricultural practices, insect damage and postharvest conditions. Higher temperature (27°C to 30°C) and high humidity provides ideal growing condition to Aspergillus spp.

Aflatoxins have wide ranging effects on food security and disease incidence (Pereira et al., 2014). Studies suggested that aflatoxicosis is linked to liver cancer, immunosuppression, susceptibility to diseases for example HIV and intestinal disorders and complication in pregnancy due to reduced immunity (Gustafsson et al., 2016). Aflatoxicosis outbreaks were reported in India where both dogs and humans suffered from hepatitis associated with consumption of contaminated maize (Krishnamachari et al., 1975; Reddy and Raghavender, 2007). In 2010 Kenya, consumption of contaminated maize caused death of a child (Mutiga et al., 2015). Clinical signs of animal intoxication include gastrointestinal dysfunction, anemia, jaundice, hemorrhage, and an overall decrease in productive parameters. Aflatoxin contamination was reported in medicinal herbs AFG2, AFB1 and AFGB2 were found in different types of herbal medicines (Nian et al., 2018). Aspergillus niger and A. flavus, A. fumigatus were found in a yerba mate infusion, a favorite drink from South America (Alvarenga et al., 2016).

Deoxynivalenol (DON): Fusarium species are chiefly responsible for the production of a metabolite called deoxynivalenol (DON) which is also known as trichothecene and it is a vomitoxin. Mainly it is produced by *Fusarium* species including *F. culmorum* and *F. graminearum*, one of plant pathogens that infect crops like wheat, grains, and oats by causing most damage in the fields. These toxins have more than



Mycotoxin	Causative Fungi	Sources	Health Implications	References
Deoxynivalenol (DON)	Fusarium spp.,	Wheat and barley	Diarrhea, dysentery, ataxia, mu- cosal hemorrhages, and sudden death.	Adesso <i>et al.</i> (2017)
Zearalenone	Fusarium spp.,	Corn, wheat, barley, sorghum and oats		Tola and Kebede (2016)
Ochratoxins	Aspergillus ochraceus and Penicil verrucosum, Penicillium citrinum	Peanuts, corn, and stored grains	Hepatotoxicity, immunotoxicity, neurotoxicity, teratogenicity, and carcinogenicity	Gupta <i>et al</i> . (2018)
Fumonisins	Fusarium verticillioides, Fusar- ium proliferatum, Aspergillus niger	Cereals, cowpeas and aspar- agus	Leukoencephalo-malacia, liver disease and tumors	Smith <i>et al</i> . (1996)
Aflatoxins	Aspergillus flavus and Aspergil- lus parasiticus	Maize, oilseeds, spices, groundnuts, tree nuts, milk, peanut and dried fruits.	liver cancer, immune-suppression, HIV and malaria	Ogodo <i>et al.</i> (2016)

Table 1: Occurrence and toxicity of major food and feed mycotoxins

150 related compounds which are divided into four groups (A-D) (Ashiq, 2015). These fungi mostly grow at a temperature of 30°C after 2 months of infection. Despite its heat stable nature, study suggested that the incidence of fungi was suppressed by boiling at higher temperatures in noodles and spaghetti (Avantaggiato *et al.*, 2005).

DON is hazardous to the pigs, sheep and cows, horses substantially. These toxins are related with intense acute diarrhea, mucosal hemorrhages, dysentery, ataxia and sudden death in these animals. They hinder the synthesis of protein by binding to the 60S ribosomal subunit. They decrease overall health and increase the susceptibility to bacterial infections in horses due to consumption. Also, they instigate apoptosis of cells in the immune system, and invigorate the generation of inflammatory cytokines in animals (Adesso *et al.*,2017).

Zearalenone: Zearalenone is a mycotoxin mainly produced by *Fusarium graminearuma*. Zearalenone is classified as mycoestrogen often called a phytoes-trogen because it has structural similarity to a female hormone called estradiol (Bennett and Klich, 2003; Bhatnagar *et al.*, 2002). This feature helps the toxin to bind estrogen receptors in humans and in breeding animal causing various reproductive disorders (Marin *et al.*, 2013). These mycotoxins mostly affect cereal crops like corn, wheat, sorghum, barley and oats. These substrates particularly corn are contaminated by zearalenone producing fungi.

Contamination of the grains of oat by zearalenone has been reported around the world, essentially in

mild atmospheric conditions. Normally, concentrations of zearalenone are low in grain polluted in the fields, but increased occurrence up to 30% and 40% were observed in damp environment (Tola and Kebede, 2016). Despite its disadvantages reduced form of zearalenone, zearalenolit is used for its estrogenic activity. Both of these compounds are used as oral contraceptives. Post menuposal women are often treated with zearalenolit (Bennett *et al.*, 1987).

Ochratoxins: Ochratoxin are commonly produced by *Penicillium verrucosum*, *Aspergillus ochraceus* and *Penicillium citrinum*. Orchtoxins have further three types named OTA, OTB and OTC. Between different ochratoxins, ochratoxin (OTA) occurs with highest frequency and it is the most lethal (Duarte *et al.*, 2010). OTA is a strong nephrotoxin produced by *A. niger, Petromyces spp, A. ochraceus, A. carbonarius* (Frisvad *et al.*, 2007). OTA usually infects commodities like peanuts, wine, rice, spices, coffee, corn, beans and cereal grains (Magnoli *et al.*, 2007). OTA is a probable carcinogen, teratogenic and a immunotxic agent (Beardall and Miller, 1994).

Citrinin and OTA cause nephropathy in birds. They are chiefly responsible for the incidence of the disease Balkan Endemic Nephropathy in humans. OTA directly affect mitochondrial efficiency. It increases peroxidation of lipid and arrangement of free radicals. OTA and citrinin both are developmental toxicants (Gupta *et al.*, 2018). In Asia, Africa, Europe, the Middle East and South America beverages produced from the fermentation of cereals, milk and sugarcane subjected to mycotoxin infection. The soy and almond



in vegetarian diets also carries OTA toxin (Marsh *et al.*, 2014). Many countries like Spain, China, Germany, and India have reported the natural occurrence of mycotoxins in medicinal plants including herbal infusions. Evidence showed that between 4.1-34.8% of OTA might be present in herbal medicines (Malir *et al.*, 2014).

Fumonisins: Fumonisins are mycotoxins produced by various fungal species including *Fusarium verticillioides*, *Fusarium proliferatum* and *Aspergillus niger*. More than 30 homologs have been recognized so far out of which Fumonisin B1 (FB1) is the most abundant and toxicologically significant. Fumonisins are commonly reported as contaminants of asparagus, rice, beer, figs, maize and maize products. Fumonisins are fairly heat stable compounds and grow over a temperature range of 15°C to 30°C.

Fumonisin B1 (FB1) is a possible human carcinogen (2B group) it affects the sphingolipids metabolism in the body due to structural similarity to sphingolipids precursors (Murugesan et al., 2015). Feed contaminated with this toxin can lead to incidence of diseases in horses, swine and rabbits (Mycotoxins, 2003). Leukoencephalomalacia syndrome incidence was reported in horses with symptoms like blindness, lethargy, convulsions and death (Marin et al., 2013). Toxic products produced from Fusarium sp. can have severe effect on banana qulaity. The tomato plant (Lycopersicum esculentum) require high humidity, warmer temperature that increases the risk of contamination with mycotoxgineic molds. They have soft epidermis more exposed to the fungal infestation and mycotoxin production (Van de Perre et al., 2014).

Mycotoxicosis and Economy

Mycotoxins contamination contributes towards huge economic losses each year in food and feed industry globally. Consumption of infected feed stock by animals leads to the poor development, reproductive issues and decreased immunity. These hazards possess serious threats to livestock and dairy industry (Pinotti *et al.*, 2016). There is a huge gap between harvesting of crop and transportation of the crops to the market from where crops get exported. The long timeframe between packaging and usage, altered environmental conditions in the storage in different spots can lead to mycotoxins contamination (Bhat and Miller, 1991). Mycotoxins infection not only affects the quality and yield of the crops but also leads to disposal of contaminated crops. Ultimately huge economic investment is required to find control strategies, maintaining toxin free environment during storage, additional health care and searching alternative feed sources (Richard *et al.*, 2003). Apart from aforementioned factors, different regularity bodies need to function to maintain International trade standards (Alkadri *et al.*, 2014).

Mycotoxins Control Strategies

A control program for mycotoxins should provide information about the interaction and toxic effects of fungi with the crops, best harvesting methods that include maximum yield by preventing the exposure of mycotoxins to the crops. Each program should also include the information that how mycotoxicosis can be prevented and diagnosed and how crops can be best harvested for the consumption of humans that are beneficial to them (Jard et al., 2011). Different biological control methods can be employed for containing spread of mycotoxins. Numerous bacterial species, yeasts and non-toxigenic strains of fungi like A. flavus and A. parasiticus can help in controlling mycotoxin spread. Scientists were successful in their attempts for preventing spread of mycotoxins using non toxigenic strains of A. flavus and A. parasiticus in the fields of maize, cotton, peanuts and pistachios. Evidences have also shown that some endophytic bacteria can control the growth of fungi that is producing fumonisins by specific mechanism (Van der et al., 1965). Moreover, fungal strains of Trichoderma have been reported to control pathogenic molds by mechanisms such as competition for nutrients and space, rhizosphere modification, mycoparasitism, biofertilization and the stimulation of plant-defense mechanisms (Bhat et al., 2010).

Conclusions and Recommendations

Mycotoxins have a wide range implication in world food security. Despite their abundance and potent nature different methods need to be adopted for their early detection, managing their levels in the crops, and effective control in the stored crops. These methods will not only enhance crop and crop products quality but also ensure the safety of food and feed products.

Novelty Statement

The present study can provide significant insight to food safety and related issues.

Author's Contribution

Shomaila Sikandar: Designed and conducted the study.

Imran Afzal and Sadaf Sarfraz: Helped in writing, formatting and proof reading of the manuscript.

Conflict of interest

The authors have declared no conflict of interest.

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