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A Systematic Review on Mycotoxins in Food and Environment: Occurrence, distribution, Impact on human health and Prevention

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Abstract
Mycotoxins are naturally occurring secondary metabolites produced by fungi, molds, and saprophytes. These secondary metabolites are basically toxins found in various food items, such as preserved maize, cereals, nuts, among others. Upon consumption, they have the potential to induce diseases in living organisms, particularly in humans. Mycotoxin, commonly include aflatoxins, deoxynivalenol and patulin. The occurrence and distribution of these mycotoxins are shown to be dependent on environmental factors such as seasons and temperature variations. They posed a significant threat to both crops and living organisms. This paper compiles the data of mitigation of their adverse effects, numerous strategies proposed in past studies. The strategies included the implementation of innovative techniques like Cold Atmospheric Plasma (CAP) and the use of Natural Essential Oils (NEO). Advancements in technology had led to the development of novel methods aimed at combating the proliferation of mycotoxins.
Keywords: *Mycotoxins, Aflatoxin (AF), Cold Atmospheric, Plasma (CAP), Hazard Analysis Critical Control Point (HACCP)*

1. MYCOTOXINS: INTRODUCTION AND DISCOVERY

Mycotoxins were identified as hazardous secondary metabolites synthesized by fungi, posing significant threats to human and animal health, as well as agricultural productivity (Bennett and Klich, 2003). The term “mycotoxin” typically referred to the harmful chemical byproducts generated by fungi that readily colonize crops (Turner NW et al., 2009). Notable mycotoxins affecting humans and animals included aflatoxin, ergot alkaloids like ergotamine, patulin, trichothecenes, fumonisins, and ochratoxin A (Bennett and Klich, 2003).
The research on the mycotoxins emphasized on the multifaceted nature of mycotoxins, highlighting their production processes, contamination pathways, and evolving management strategies due to their severe impacts on food safety, agriculture, and public health (Wu & Groopman, 2014). Investigations underscored the prevalence of mycotoxin contamination in the food chain, causing economic losses and posing challenges to global food security (Marin et al., 2013).
Environmental factors such as humidity, temperature, and substrate composition influenced the biosynthesis of mycotoxins, contributing to their diverse array and necessitating comprehensive mitigation approaches (Bennett and Klich, 2003).
Historical perspectives traced the presence of mycotoxins and toxic fungi in the human food chain, highlighting significant outbreaks such as ergotism from Claviceps purpurea in rye and cardiac beriberi from moldy rice containing citreoviridin (John I. Pitt and J. David Miller, 2017). Studies explored the health impacts of mycotoxin exposure, including acute toxicity and chronic disorders, underscoring the importance of vigilance amidst declining crop diversity and climate change (John I. Pitt and J. David Miller, 2017).
In summary, the reviewed literature provided insights into the historical evolution of mycotoxin research, culminating in current understandings of their roles in human disease, agricultural challenges, and emerging threats in a changing environment.`

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2. MYCOTOXINS : OCCURRENCE AND DISTRIBUTION

Mycotoxins were identified across a diverse array of agricultural products, including cereal crops, legumes, animal feed, and their derivatives. Aflatoxin, a prominent mycotoxin, was found to have the potential to contaminate all grain crops. Pre-harvest infections of aflatoxin-producing fungi were documented, particularly in contexts of intensive cropping practices and diminished genetic diversity within cereal crops (Brown et al., 1999; Lillehoj et al., 1992). This preharvest contamination was prevalent in both temperate and tropical regions, often affecting plants stressed by factors such as insect damage, drought, and irregular watering schedules.

Post-harvest contamination was observed in storage facilities conducive to the growth of aflatoxigenic fungi, with feedlot waste serving as potential reservoirs for these pathogens (Hendrickson , 1972). The dispersal of aflatoxigenic fungi spores by insects to susceptible plant tissues facilitated colonization and subsequent contamination, as seen in maize through flowers and silks (Diener et al., 1987). Additionally, contamination caused by aflatoxin in cottonseed prior to harvest was noted to be influenced by factors such as, relative humidity, insect damage, timing of irrigation or rain, maturation stage, and varieties of cotton (Moule et al., 1976; Lillehoj et al., 1987). Moreover, mycotoxins were commonly found in peanut products, with seeds exhibiting the highest concentration of toxins (McKenzie et al., 1981; Cullen & Newberne, 1994). Conditions conducive to aflatoxigenic fungal growth, such as ambient temperatures exceeding 25°C and moisture content surpassing 8%, were associated with post-harvest aflatoxin contamination in peanuts. Notably, drought-stressed peanuts showed reduced innate resistance against fungal infections, impacting aflatoxin levels to be elevated (Wotton & Strange, 1987).

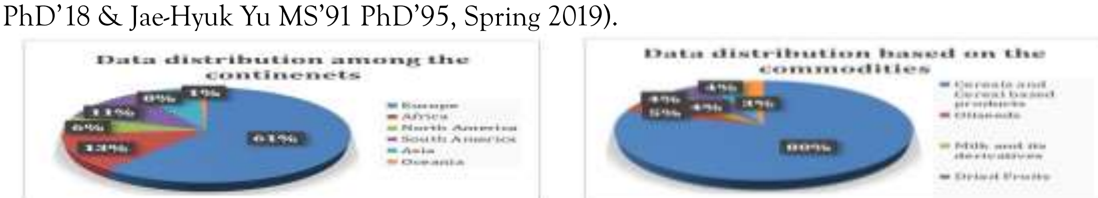
Furthermore, according to the studies, the production of mycotoxins, such as aflatoxins and zearalenone, in distillery byproducts highlighted potential risks in feed and food industries (Hesseltine, 1985). Despite fermenting processes, aflatoxins were not eliminated, raising concerns about their persistence in downstream products. Additionally, fumonisins, another group of mycotoxins, were commonly found in commercial cornbased human feedstuffs (Pittet et al., 1992; Stack & Eppley, 1992; Sydenham et al., 1991). These findings accentuated multifaceted challenges posed by mycotoxin contamination across various agricultural sectors. The Figure 1, shows or depicts the data distribution based on (a) the information gathered from different geographic regions and (b) the commodities from these geographic regions.

3. MYCOTOXINS : TYPES, SOURCES AND THEIR EFFECTS

Mycotoxin-producing fungi in food were broadly categorized into two groups: field fungi, which manifested before harvest (pre-harvest), and storage fungi, which emerged only after harvest (post-harvest).

Studies identified economically significant mycotoxins, including aflatoxin (AF), ochratoxins (OTA), patulin (PAT), fumonisins, citrinin (CIT), trichothecenes (TH), and zearalenone (ZEA). These mycotoxins posed challenges for both crop growers and consumers, impacting profitability and health. Millets, sorghum, maize, soybean, peanuts, and their derivatives, along with by-products derived from contaminated primary ingredients, were noted as particularly susceptible to mycotoxin contamination.

Various food sources, such as food waste, moldy bread, cottonseed, spices, grains, oilseeds, leguminous seeds, and industrial byproducts used in animal feed, were reported to harbor mycotoxins (Ahmad Alshannaq PhD'18 & Jae-Hyuk Yu MS'91 PhD'95, Spring 2019).



(a) (b)

Fig. 1: The data distribution based on (a)geographic regions and (b) commodities

Predominantly, saprophytic molds and fungi, including Aspergillus, Fusarium, Penicillium, Alternaria, and Claviceps, were cited as frequent contaminants affecting crops both pre-harvest and post-harvest.

Aflatoxins, particularly deadly mycotoxins, were associated with *Aspergillus flavus* and *Aspergillus parasiticus* molds, thriving in various crops such as tree nuts, oilseeds, spices, and cereals. Aflatoxin M1 was highlighted for its presence in the milk of animals fed contaminated feed, with excessive levels causing acute poisoning (aflatoxicosis) and potentially leading to liver damage and cancer.

Ochratoxin A, another common mycotoxin, was produced by numerous species of *Aspergillus* and *Penicillium*, contaminating a vast number of food commodities worldwide. While its link to kidney damage and cancer in animals was well-documented, evidence regarding its effects in humans remained ambiguous.

Patulin, produced by molds including *Aspergillus*, *Byssochlamys* and *Penicillium*, was commonly found in decaying apples and apple products, potentially causing liver, spleen, and kidney damage in animals, along with gastrointestinal symptoms in humans. Although not conclusively proven carcinogenic, patulin was believed to be genotoxic.

Fusarium species, common soil fungi, produced toxins such as fumonisins, zearalenone (ZEN), and trichothecenes like nivalenol (NIV) and deoxynivalenol (DON). These toxins affected various grain crops, with specific toxins associated with particular cereals. Trichothecenes were noted for their hazardous effects on humans, causing diarrhea and irritation of skin or intestinal mucosa, while ZEN exhibited estrogenic effects, potentially leading to infertility, particularly in pigs. Fumonisins were linked to liver and kidney toxicity in animals and human esophageal cancer. These findings, documented by the World Health Organization (WHO) in 2023, emphasized the complex and widespread impact of mycotoxins on human health and food safety.

4. IMPACT OF SEASONS ON MYCOTOXINS

The study aimed to investigate the potential impact of climatic conditions on the variability of mycotoxin contamination and fungal infection on a small geographic scale. The research conducted in 2014 focused on 51 maize fields in the Emilia Romagna area of northern Italy. The data regarding the presence of *Aspergillus species* and *Fusarium species*, along with their associated mycotoxins, was assessed. Additionally, data on cropping strategies were collected for each field. During harvest, samples were collected and examined for trichothecenes, aflatoxins, and fumonisins. Meteorological data from nine stations provided hourly readings, and the fields were grouped with the nearest stations based on the principle of least distance. The incidence of *Aspergillus* species and *Fusarium* species ranged from 0.6 to 6.3% and 17.6 to 46.0%, respectively.

Significant heterogeneity was observed in aflatoxin B1 levels, ranging from below the limit of quantification to 93.8 μg/kg, and fumonisins, ranging from 1,718 to 106,054 μg/kg, even among fields in close proximity. While deoxynivalenol occurrence was notable (59%), there were only three samples that exceeded 1,750 μg/kg. The study concluded that the unfavorable conditions during storage and transportation, coupled with high temperatures, heavy precipitation, moisture content, contributed or aided to the formation of conducive environments for mycotoxin development.

Therefore, the unpredictability of climate and its associated uncertainties, often emphasized on a broad scale, posed concerns not only for the policymakers but also for the farmers dealing with the daily effects of mycotoxins and fungi incidence. Figure 2, shows the presence or positive rates of some of the main types of mycotoxins of maize of the new season in China during (a) 2020 and (b) 2021. It can be seen that the there was an increase in number among mycotoxins types such as Zearaleone and Fumonisins but decrease in number among Aflotoxins.

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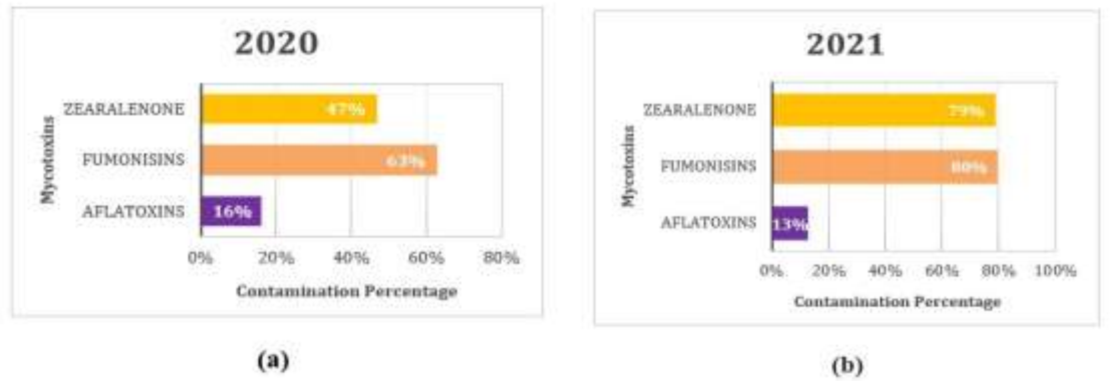

Fig. 2: Prevelance rates of some of the main mycotoxins of maize of the new season in China in (a) 2020 and (b) 2021

5. FACTORS AFFECTING MYCOTOXIN PRODUCTION AND THE CONTAMINATION OF FOOD AND FEED

Development and presence of mycotoxins in foods or feeds, which posed health risks to humans and animals, are influenced by various factors. Isolation and confirmation of mycotoxigenic fungal species alone do not necessarily indicate mycotoxin existence. Researchers have revealed that several factors influence fungal colonization and mycotoxin production, which are detected using precise and sensitive methods for mycotoxin analysis methods. These factors are typically categorized into three types: physical, chemical, and biological. Physical parameters such as relative humidity insect infestation and temperature favor fungal colonization and mycotoxin formation. Chemical factors include the application of fertilizers or fungicides. The interaction between toxic fungal species and substrates forms the basis of biological factors (D'Mello et al.,1997).

TABLE I: Diseases caused by Mycotoxins and their impact on humans

Mycotoxin	Fungi Type	Sources	Physiological Effects	References
Aflatoxins	*Aspergillus flavus* *Aspergillus parasiticus* *Aspergillus nomius*	Wheat, walnut, maize, peanuts, cotton, milk, egg, tree nuts, oilseeds, spices	Immunotoxicity, Neurotoxicity, DNA-adduct formation leads to mutation and cancer, poor growth	Edyta Janik-Karpinska et al., 2023
Ochratoxin A	*Aspergillus ochraceus* *Aspergillus carbonarius* *Penicillium verrucosum* *Penicillium nordicum*	Coffee beans, oats, wheat, maize, dried fruits, spices, wine, egg, meat	Nephrotoxicity, genotoxicity, ATP depletion, decreased gluconeogenesis	
T-2 toxin	*Fusarium sporotrichoides* *Fusarium poae* *Fusarium acuminatum* *Fusarium equiseti*	Barley, oats, wheat	Dermal toxicity, inhibition of cell proliferation, inhibition of protein synthesis, Vomiting	

Fumonisin B1	*Fusarium moniliforme Fusarium proliferatum Fusarium verticillioides*	Corn, Sorghum, Barley, Wheat, Rice, Oats, Rye	Disruption of sphingolipid metabolism, gene expression changes, Fluid in lungs	Peter Surai & Miklos Mezes, 2005
Zearalenone	*Fusarium culmorum Fusarium sporotrichioides Fusarium graminearum*	Tomato, eggplant, pepper, cereals, grains	Competition for oestrogen receptors, imitation of oestrogen effects, lipid peroxidation, Infertility, early embryo mortality	

6. MYCOTOXINS AND FUTURE CHALLENGES IN THE FOOD MARKET

Mycotoxins can induce toxic ailments, including cancer, in emerging nations, rendering them unsuitable for a healthy lifestyle. Due to their resilience to heat across a wide range of cooking temperatures, it is understood that mycotoxins cannot be removed from food once it is contaminated. Thus, promoting preventive measures to regulate harmful elements in agricultural products at the field level becomes crucial for mitigating mycotoxin-related diseases (Omotayo et al., 2019).

7. CONTROL STRATEGIES AGAINST MYCOTOXINS

Prevention and control of mycotoxins would improve national economies and public health. Various approaches to decrease and manage mycotoxins have been explored globally, including in African nations.
In Africa, mycotoxin management involves:

1) Preventing mold or fungi growth in crops and other feed materials.
2) Decontaminating feeds and foods tainted with mycotoxins as a backup plan.
3) Continuous monitoring of the mycotoxins in food for humans, animals, and agricultural crops. Recent innovative methods for reducing mycotoxin levels in food include cold atmospheric plasma (CAP), polyphenols and flavonoids, magnetic materials and nanoparticles, and natural essential oils (NEOs). Long-term intervention approaches supported by James (2005) and the World Health Organization (2006) include strengthening national surveillance, intensifying food and feed inspections to ensure safety, and providing local assistance and education to ensure appropriate
harvesting, thorough drying, and pr`oper storage of food grains and animal feeds.

Hazard Analysis and Critical Control Points (HACCP) Implementation for Mycotoxin Control

Enhanced implementation of preventive strategies is essential to regulate or lower the mycotoxin levels in food items. It should be integrated into the food safety management system and form the cornerstone of HACCP (hazard analysis and critical control points). Under the HACCP system, physical, chemical, and biological hazards are identified, controlled, and monitored from farm to fork to ensure food safety. To reduce the health risks associated with mycotoxins, individuals should:

- Check for signs of mold on whole grains, dried fruits, and nuts, and discard any contaminated items.
- Prevent or remove damaged grains before, during, and after drying, as they are likely more prone to mold growth and mycotoxin contamination.
- Whenever possible, opt for purchasing fresh grains and nuts.
- Also ensure proper storage conditions, including dry, cool, and insect-free environments.
- Avoid prolonged storage of food items.
- Maintain a varied diet to enhance nutrition and minimize exposure to mycotoxins.

8. CONCLUSIONS, IMPLICATIONS AND OUTLOOK

Over 400 known toxic mycotoxins were found to be existing. Necrosis, hepatitis, hemorrhage, gynecomastia with testicular atrophy, neurological disorders, cancer, and death were among the negative consequences of mycotoxicosis resulting from mycotoxin contamination in humans (Adebo, 2021; Atanda, 2011; Milicevic, etal., 2015). Toxic substances known as mycotoxins were generated by specific types of fungi. Five mycotoxins, or families of mycotoxins, were frequently found in food: aflatoxins, fumonisins, ochratoxin, zearalenone, and deoxynivalenol/nivalenol.

Because of their toxicity, the risk they posed to human's and other living organism's health, the resulting financial losses, mycotoxin incidence, contamination along the agricultural produce, food, and animal feedstuff management chain were of global concern. Mycotoxin pollution was a major health hazard for a large portion of the world's population. They mostly impacted human health through the development of illnesses, including cancer and liver damage. Conventional techniques were used to remove mycotoxin because they lowered the level of toxins by adversely altering the climate and grain characteristics.

In conclusion, food contamination caused by mycotoxins was critical to global health. The reaction that happened or followed when the farm animal's feed got contaminated and subsequently their products, like meat, milk, and eggs, got affected, was another serious problem. In order to safeguard humans, the level of exposure to mycotoxins had to be minimized. Mycotoxins not only represented a risk to both human's and living organism's health but also impaired food security and nutrition by lowering people's access to good food. WHO recommended national authorities to monitor and ensure that the levels of mycotoxins in food products sold in their country were as low as possible and adhered to all applicable laws, regulations, and maximum levels both domestically and internationally.

Ensuring rigorous monitoring and adherence to safety standards was crucial in mitigating the harmful impact of mycotoxins on global health and food security.

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