32

Different Molds and their Toxins: As Contaminants in one Health Perspective

AUTHORS DETAIL

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INTRODUCTION

Mycotoxins are fungal metabolites that are formed in cereal crops and pose substantial risks to both human and animal health. These are very dangerous and unavoidable food pollutants (Amaike and Keller 2011). Mycotoxicoses are acute and chronic toxic diseases caused by mycotoxins. Their clinical characteristics, target organs, and prognosis rely on the mycotoxins inherent toxic properties, the amount and period of exposure, as well as the exposed person's overall health.

Aflatoxin, deoxynivalenol, ochratoxins, zearalenone, and fumonisins are common in underdeveloped nations and are generated by a variety of fungal species including *Penicillium verrucosum, Aspergillus flavus, Aspergillus ochraceus, Aspergillus parasiticus, Aspergillus nomius,* and *Fusarium* spp (Vila-Donat et al., 2018). These fungi infect barley, wheat, corn, peanuts, cotton, and a variety of other commodities, causing immunotoxicity, hepatotoxicity, nephrotoxicity, and teratogenicity in animals and humans (Amaike and Keller 2011; Abdallah et al., 2017). When there is high ambient temperature and moisture, fungal growth and mycotoxins are produced. Other variables that contribute to production risk include incorrect storage, shipping, harvesting, and processing techniques (Uegaki and Tsunoda, 2018). It has attracted international attention due to economic costs in terms of animal production, commerce, and human health. The globe is now dealing with a food safety crisis, and a number of studies have been undertaken to address this issue by informing consumers about food safety issues (Rebouças et al., 2017; Kwol et al., 2020).

In 1985, the US Food and Drug Administration (USFDA) established a diagnostic laboratory to monitor feed contamination with mycotoxins and assure a toxin-free diet. The Food and Agriculture Organization (FAO) and the World Health Organization (WHO) play major roles to prevent contamination by providing consumer education. Mycotoxins cannot be destroyed via cooking. The only option to obtain mycotoxin-free food is to use modern food processing techniques such as Hazard Analysis Critical Control Points (HACCP) and good manufacturing processes (GMP) (Maldonado-Siman et al., 2014). When mycotoxins are formed in crops, they have a direct detrimental influence on farm animals and can cause major health problems in human beings (Yang et al., 2020).

Mycotoxicoses have historically been common in mild zones, and today they are mostly seen in tropical areas. The global danger of mycotoxicoses is increased by international trade in foods from tropical nations. Medical professionals should at least be aware of the clinical symptoms of the most widespread mycotoxicoses, even though it is unrealistic for them to be able to diagnose mycotoxicosis in a single patient. This chapter aims to provide background information on mycotoxicoses as well as a clinical overview of one health triad.

Mycotoxins' Effects on Animal Health

There are several forms of mycotoxins that have diverse pathogenic and immunological impacts on animal species. Listed below are the brief description of all pathogenic and immunological effects on human beings and all other animals.

Effects of Zearalenone on Animal Health

Fusarium (F.) molds (*Fusarium graminearum, F. culmorum, F. crookwellense*) cause damage to wheat, oat, sorghum, and barley and generate Zearalenone (ZEN). *F. graminearum* is the primary producer of ZEN. In agricultural animals (cattle and sheep), it possesses estrogenic action. Zearalenone and its metabolites (α-zearalenol) bind to the estrogen receptor and induce a range of reproductive issues due to their structural similarities to estradiol (McCauley et al., 2017). ZEN was related with feminization, decreased libido, lower blood testosterone levels, decreased testicular weight, and altered spermatogenesis in boars (Mirza Alizadeh et al., 2022). In pigs, ZEN poisoning caused vulvovaginitis, fetal mortality,

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anestrus, reduced LH and P4 production, delayed post-weaning estrus, and promoted germinal epithelial degeneration (Imran et al., 2020). Another study indicated that ZEN toxicity resulted in decreased conception rate and litter size, as well as hypertrophy of the vulva, uterus, and ovaries in piglets (Grenier et al., 2019). ZEN toxicity in cattle resulted in reduced milk output, infertility, elevated serum estrogen concentrations (Liu and Applegate 2020), and a lower conception rate. Reduced testosterone levels in blood and sperm counts were seen in rats (Sadeghi et al., 2020), but in mice, chronic estrous and sterility (Pócs 2019), genotoxicity, and hepatocellular cancer were discovered in ZEN toxicity (Ruan et al., 2022).

Effects of Ochratoxins on Animal Health

Molds of the *Aspergillus* and *Penicillium* species generated ochratoxin-A (OTA). The principal species that generated OTA were *Aspergillus (A.) ochraceous*, *A. sclerotiorum*, *A. melleus*, *A. sulphureus*, and *Penicillium (P.) verrucosum* (Han et al., 2018). Multiple foods are naturally contaminated with OTA, including cereals, almonds, cocoa beans, cassava flour, peanuts, dried fruits, chicken eggs, and milk (Kumar et al., 2018). In natural settings, 50% of cocoa beans and 22% of cocoa powder were found to be contaminated with OTA (Maciel et al., 2018). The toxicological effects of OTA varied amongst poultry species. However, it is nephrotoxic to all animals and it is most likely to be harmful to humans. OTA is also known to be hepatotoxic, neurotoxic, immunosuppressive, teratogen, and carcinogen (Zhu et al., 2017).

According to reports, OTA causes oxidative stress in human kidney-2 cells, which regulates the translocation of transcription factors such as the aryl hydrocarbon receptor (AhR) and the pregnant X receptor (PXR). By modulating cytochrome enzymes (CYP1A1 and CYP1A2), OTA activation of Ahr and PXR causes immunosuppression, renal damage, and malignancy (Zhang et al., 2022b). The first epidemics of ochratoxicosis were discovered in laying hens, broiler chickens, and turkey birds. Clinical symptoms reported in turkey include reduced feed intake, a low FCR, and a higher death rate. Nephritis and mild hepatitis were the pathological lesions. In broilers, there was a decrease in growth rate, a low FCR, nephrotoxicity, and air-sacculitis. Reduced egg production and nephritis were reported in laying chickens (Imran et al., 2020). In cases of ochratoxicosis, necropsy findings include swollen and pale-yellow kidneys, as well as a yellowish and friable liver. Vacuolar atrophy and megaleucocytosis of liver cells, biliary epithelial hyperplasia, and hypertrophy of proximal convoluted tubular epithelial cells of the kidney are among the microscopic abnormalities (Tahir et al., 2022). According to Kumar et al., (2020), OTA is more nephrotoxic than hepatotoxic in broilers. OTA also infects other organs, causing spleen, thymus, and bursa shrinkage as well as lymphocytic depletion. It has also been observed that OTA has a deleterious impact on bird performance, hematology, biochemistry, and the immune system in laying hens.

In poultry, OTA reduces the weight of immune organs (bursa and spleen), the quantity of antibodies (IgA, IgG, and IgM) carried by immune cells, and they react to phytohemagglutinin (PHAP) (Khan et al., 2017). It reduces hematological parameters (RBC count, WBC count, PCV, HB) and causes anemia in White Leghorn Cockerels. It lowers blood total proteins while increasing serum alanine transferase, urea, and creatinine (Orinya et al., 2016). There was no severe OTA health issues reported in cattle fed with naturally contaminated OTA feed. In one investigation, wheat contamination with OTA (390-540 g/kg) and AFB1 (12-13 g/kg) had no significant toxic-pathological impact in 12-week-old calves (Shida et al., 2022). Cattle may degrade up to 12 mg/kg body weight of OTA (Hashimoto et al., 2016). Calves die after being fed with 11-25 mg OTA/kg body weight orally. For cattle, the fatal dosage of OTA is greater than 13 mg/kg body weight when administered orally (Ricci et al., 2020). According to a study, it contaminated feed (48g/kg) causing feed refusal, reduced milk output, and retained fetal membrane in dairy cattle, however no signs or symptoms were detected in beef cattle. Ochratoxicosis is uncommon in small ruminants (sheep and goats). However, consuming an OTA-contaminated food over an extended period of time has negative health consequences (Malekinezhad et al., 2021). OTA typically affects the kidneys in dogs and cats. At the dose of 0.2 to 3 mg/kg, it can cause vomiting, anorexia, increased thirst, polyuria, ataxia, and death. Tubular epithelial degeneration, hemorrhagic enteritis of the large intestine, and necrosis of lymphoid organs (thymus, spleen, lymph nodes, and lymph nodes) are all pathological lesions (Gan et al., 2017).

Effects of Aflatoxins on Animal Health

Aflatoxins are poisonous substances produced by certain *Aspergillus (A.)* species (*A. flavus*, *A. parasiticus*, *A. nomius*, *A. arachidicola*, *A. bombycis*, *A. pseudotamarii*, *A. minisclerotigenes*, *A. rambellii*), which are found all over the world and pose serious health issues in animals (Pereyra et al., 2020). Aflatoxins are classified as B1, B2 (generates blue fluorescence) and G1, G2 (emits green fluorescence) (emits green fluorescence). The liver is the principal target of aflatoxin B1 (AFB1) vulnerable animal species. The metabolic activation of AFB1 is strongly correlated with Cytochrome p450, which are expressed in the liver. This CYP converts aflatoxin to a reactive 8, 9-epoxide that can bind to DNA and protein. AFB1-DNA adducts cause G to T trans version in the tumor suppressing gene p53, which is linked to liver cancer (Mungamuri and Mavuduru 2020). Pyrexia, anorexia, and malaise are early signs and symptoms of aflatoxicosis, and as the disease progresses, the animal has stomach discomfort, vomiting, and hepatomegaly. Acute aflatoxicosis is less common (Al-Ruwaili et al., 2018; Kyei et al., 2020), but it has

carcinogenic and immunosuppressive consequences in the chronic stage (Qian et al., 2016).

AFB1 reduces the production of IL-4, which has anti-inflammatory properties, and promotes the release of IFN-κB p65 and TNF-α from natural killer (NK) cells, which speeds up the inflammatory process. AFB1's immunosuppressive function is due to a decrease in the ability of antigen presentation cells (APC) of dendritic cells (Mehrzad et al., 2017). AFB1 causes more cancer episodes than the others (Shahba et al., 2021).

Aflatoxin has a harmful and cancerous effect on both animals and humans. The acute poisoning results in mortality (Martins et al., 2018). Chronicity is characterized by immunosuppression, the development of neoplasms, and a variety of other clinical disorders. In birds, fish, nonhuman primates, and rodents, AFB1 causes necrosis and degeneration of the hepatic parenchyma. The frequency of aflatoxicosis is determined by a variety of factors, including the animal's breed, species, age, diet, and overall health (Alvarado et al., 2017). Broilers are much more resistant to aflatoxicosis than some other poultry birds (Kraieski et al., 2017). AFB1 is also known as the "silent killer" since it is an inevitable pollutant whose continuous pollution causes toxicopathological consequences. Acute aflatoxin poisoning results in decreased feed intake, decreased feed conversion ratio, changed natural behavior, immunodeficiency, hepatomegaly, nephritis, altered hematological parameters, and overall impaired performance. The chronic aflatoxicosis has been linked to increased blood urea nitrogen (BUN), reduced total protein and lipid levels in broiler bird serum (Rashidi et al., 2020). It exhibits toxicological effects in animals, causing a variety of outcomes such as acute liver injury, liver cirrhosis, tumor induction, teratogenicity, and other genetic abnormalities. Aflatoxicosis is mostly a liver disorder (Afum et al., 2016) causing gastrointestinal problems, reduced milk supply, immunosuppression, anemia, and liver damage. AFB1 conversion to its metabolite AFM1 secreted by dairy cows in milk makes nursing animals more susceptible to infection (Frazzoli et al., 2017). Many researches on the carcinogenic effects of AFB1, AFM1, and AFG1 in various animals have been undertaken (Yilmaz and Bag 2022).

Sheep have a higher resistance potential to aflatoxins (Cammilleri et al., 2019). According to a research, AF-contaminated feed (2.5 mg/kg) causes hepatotoxicity, nephritis, altered mineral metabolism, and a reduction in plasma mineral (Vila-Donat et al., 2018). Another research with the same dosage results in increased fibrinogen concentration (Rastogi et al., 2022). Alvarado et al., (2017) discovered that AFB1 contaminated feed (58.4 g/kg) caused hepatomegaly, nephritis, and bile duct hyperplasia in horses. Depression, jaundice, lameness, and mortality were the most common clinical indications of aflatoxicosis. Other symptoms of horse aflatoxicosis include subcutaneous bleeding, intestinal lesion, kidney problems, liver necrosis, and cardiac lesions (Kemboi et al., 2020).

Effects of Fumonisins on Animal Health

Fumonisin B1 and Fumonisin B2 are carcinogenic metabolites of *Fusarium (F.) verticillioides* and *F. proliferatum* (Nassif et al., 2018). Because of its neoplastic activity in rats, fumonisin B1 is more hazardous than fumonisin B2, and it also induces horse leukoencephalomalacia (Rehman et al., 2022). Fumonisin inhibits the enzyme sphinganine-N-acetyl transferase, which is involved in sphingolipid metabolism, causing an increase in sphinganine and sphingosine as well as a decrease in sphingolipid complex, which is a widely acknowledged explanation for fumonisin toxicity in most species (Abdel-Wahhab et al., 2018). Fumonisin toxin has been shown to impact several organs in chickens, calves, pigs and horses, including the intestines, brain, liver, and lungs (Chen et al., 2021).

It causes pathological lesions on the liver and other internal organs, swollen beaks, cerebral edema (Chen et al., 2016) and hemorrhages in the subcutaneous and hepatic parenchyma (Rodríguez-Bertos et al., 2020). Clinical signs that are dose-dependent in broiler chicks include slower weight gain (Saleemi et al., 2020), but in layer birds it causes diarrhea (Dadheech et al., 2016). In equines it causes leuko-encephalomalacia, malnutrition, incoordination, lungs and brain edema (Wangia 2020), liquefactive necrosis of white matter, cerebral cortical lesions, hypersensitivity, and death (Junker et al., 2020). Fumonisin caused liver and renal inflammation in ovine at doses ranging from 11.1-45.5 mg/kg body weight (Cimbalo et al., 2020). Fusarium mycotoxins impact cow reproductive activities by altering granulosa cell growth and steroid synthesis (Albonico et al., 2017).

Mycotoxins and Human Health

Mycotoxicosis occurs in humans as a result of eating fungal-contaminated food, and it can be acute or chronic, depending on the length of the condition (Anal et al., 2021). *Fusarium* species were implicated in multiple human epidemics of mycotoxicosis prior to the discovery and application of current milling procedures. Between 1932 and 1947, Russians suffered from alimentary toxic-alleluia, which was characterized by mucus membrane hyperemia, esophageal discomfort, inflamed larynx, trouble breathing, GIT inflammation, and ataxia. This was attributable to the consumption of infected cereal grains with *F. sporitrichoides* and *F. poae* (Milićević et al., 2016).

Aflatoxicosis mostly affects the liver, resulting in hepatitis and jaundice, which can lead to death. In Kenya, India, and Malaysia, several episodes of the same kind of aflatoxicosis (hepatitis) were detected in various years (Kamala et al., 2018). AFB1 has been related to liver cancer in conjunction with the hepatitis B virus and is a human carcinogen (Rindi et al., 2018). There have been several reports of AFB1 being linked to hepatocellular cancer in conjunction with HBV infection (Chu et al., 2017). This is because of the prolonged

exposure to a low dosage of AFB1. In China, around 250,000 individuals died from liver cancer, and further analysis found that the consumption of AFB1 was a contributing factor to HBV infection (Kumi et al., 2016). Ochratoxin-A causes nephropathy and renal carcinoma in animals, but its consequences on human health are not well understood. Research revealed that OTA contaminated feed was linked to human disorders such as chronic interstitial nephritis (CIN), Balkan endemic nephropathy (BEN), and other renal malformations, however the mechanism has not been thoroughly investigated (Stiborová et al., 2016).

Consumption of fumonisin-contaminated sorghum and maize in India caused food poisoning with stomach discomfort, borborygmi, and diarrhea (Achar and Sreenivasa 2021). In humans, IARC categorized fumonisin B1 as a Group 2B carcinogen (Organization 2018). Fumonisin poisoning has also been linked to lower folic acid absorption and neural tube developmental abnormalities in rural populations who fed contaminated maize in specific areas of North China and South Africa (van Gool et al., 2018). Fumonisin toxicity has also been connected to esophageal cancer in China as a result of fumonisin-contaminated feed intake (Chen et al., 2018). Trichothecenes have also been employed as a biological agent. T-2 toxin was employed as germ warfare in 'yellow rain' against the populace of the Democratic Republic of the Congo from 1975 to 1981 (Jung 2016). Similar biological warfare chemicals, such as DAS, nivalenol, DON, and ZEN, were identified from water sources and leaves in afflicted areas of Cambodia (Anal et al., 2021). Toxicity from zearalenone (ZEN) and deoxynivalenol (DON) have been recorded in the United States, Australia and Japan, leading to gastrointestinal symptoms such as nausea, vomiting, and diarrhea. Zearalenone has also been shown to be hazardous to human and animal gametogenesis and embryo development (Liu et al., 2018).

Occurrence and Toxicity of Zearalenone

Fusarium fungi produced zearalenone mycotoxins, which contaminates cereals and food stuff throughout the world. ZAE shows reproductive disorders in laboratory animals and also cause low acute toxicity. ZEA mostly occurred in cereal crops and foodstuffs around the world including Europe, Asia and Africa (Rai et al., 2020).

ZEA toxicity causes a limited effects on human health, but it can cause hyper estrogenic syndrome in humans. According to studies, high level of ZEA present in serum of children who were suffering in idiopathic puberty. ZEA could be the possible cause of early puberty in children as maize and their products are more prone to ZEA (Rai et al., 2020). It can also affect endometrium of women having reproductive disorders, leading to estrogenic effects. Occurrence of esophageal and breast cancer has also been reported from different parts of the world (Belhassen et al., 2015). Fig. 1 illustrates the absorption, metabolism and distribution of Zearalenone in different parts of the body.

Fumonisin

Fumonisin is produced from *Fusarium verticillioides*, and fumonisin B1 is mostly found in nature (Robert et al., 2017). According to human Epidemiological studies, esophageal cancer could be due to the consumption of corn grains which contains fumonisin in South Africa, Italy and China (Braun and Wink 2018).

Fumonisins are competitive inhibitors of sphinganine and sphingosine N-acyltransferase. It inhibits enzymes which produces a disruption of sphingolipid metabolism. It increases sphinganine and sphingosine and decreases complex sphingolipids in the serum and tissues of animals (Pierron et al., 2016). It can cause diarrhea and abdominal pain if the intoxication is acute and their chronic exposure can cause esophageal cancer (Smith 2018).

The exposure of fumonisin has also been linked with neural tube defect in many species including humans. Due to the inhibition of the fumonisin enzyme, this action is strongly related (Jin et al., 2021).

Aflatoxin

Aspergillus flavus, *A. parasiticus* and *A. nomius* produce secondary metabolites called aflatoxin which is highly toxic. Mostly wheat, walnut, peanuts and tree nuts are infected by these fungi. It can cause serious issues to human and animal health by causing various complications like hepatotoxicity, teratogenicity and immunotoxicity (Kumar et al., 2017).

Aflatoxins can cause damage at molecular level such as DNA mutation, posttranslational peptide chains modification, proteins and nucleic acids methylation and formation of free radicals. Aflatoxins have cancerous effects and occur frequently in food, that's why these are continuously examined in some groceries and agricultural products (Kowalska et al., 2017).

According to recent evidence, aflatoxins can be determinant of stunted child growth and lower cell mediated immunity, that's why increases disease susceptibility. However, since this is only a temporary relationship, more research is needed (Gong et al., 2016).

Ochratoxin

Ochratoxin is produced by different fungi including *Aspergillus Ochraceus*, *A. carbonarius*, *A. Niger* and *Pencillium verrucosum*. It is found in large variety of agricultural products such as cereal grains, dried fruits, wine and coffee (Ropejko and Twarużek 2019). OTA involve in the pathogenesis of some renal diseases like Balkan endemic nephropathy, kidney tumors occurring in Balkan Peninsula. Chronic interstitial nephropathy occurs in Tunisia and other countries in North Africa (Malir et al., 2016).

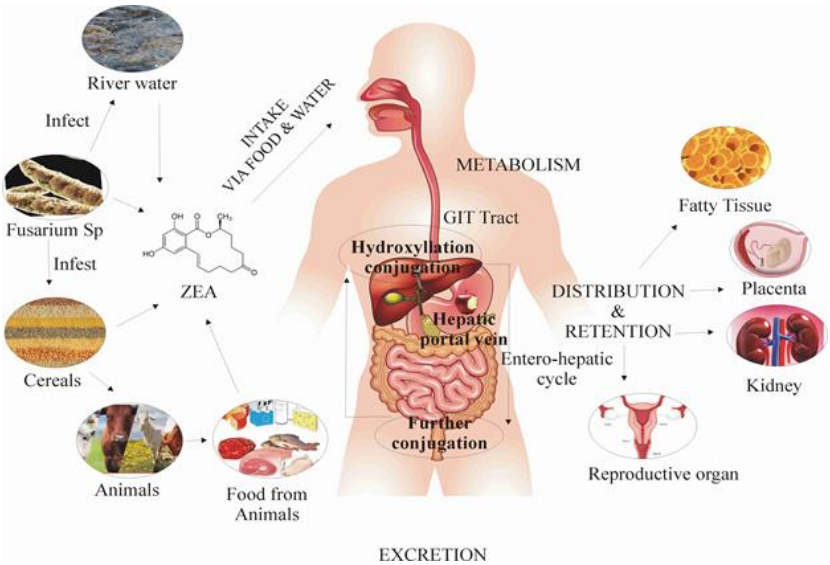

Fig. 1: Toxico-kinetics of Zearalenone (ZEA): absorption, metabolism and distribution in different body parts.

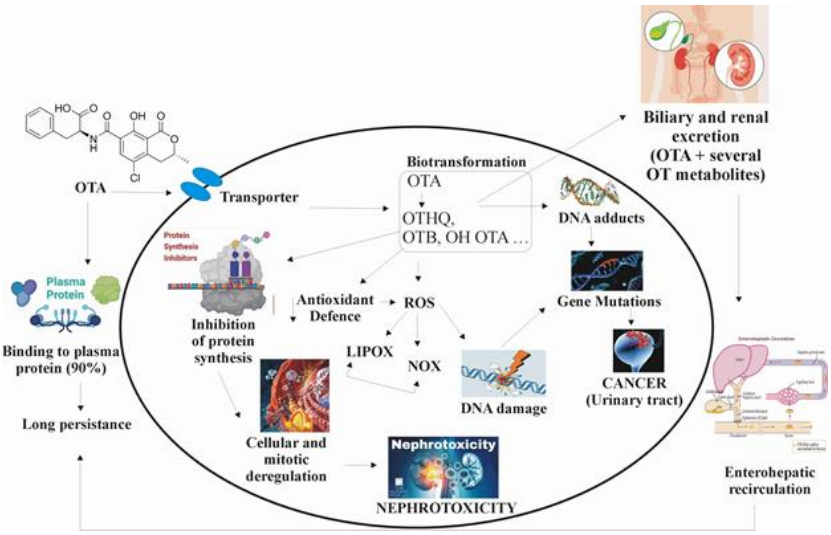

Fig. 2: Diagrammatic representations of Ochratoxin A (OTA) pathway and intracellular pathological effects. OTHQ: Hydroxyl Quinone Ochratoxin OTB: Dechlorinated ochratoxin LIPOX: Lipoperoxidation OH: *hydroxyl* free radical ROS: Reactive oxygen species, NOX: Nitrogen oxide.

In animals, ochratoxins involved in detrimental effects, such as renal, neuronal, immuno and embryonic toxicity. There may be unexplored fungus species where the occurrence of OTA may be attributed (Kortei et al., 2021). Fig. 2 shows the diagrammatic representations of Ochratoxin A (OTA) pathway and its intracellular pathological effects.

Impact of Mycotoxins in the Environment

Globally, there is a greater focus on air pollution. Mold is one such contaminant that may be found not just outside but also inside environments with excessive dampness. Mycotoxicosis is a multidisciplinary problem that requires the participation of environmentalists, medical and veterinary professionals, agricultural engineers, plant pathologists, analytical chemists, and agronomists. It occurs in both developed and developing nations when social, environmental, and economic factors combine with climatic conditions (temperature and humidity) that encourage mold development (Dragan et al., 2019).

Mycotoxins and agricultural product contamination fluctuate from year to year, based on the environment and handling circumstances. Multiple research projects have been conducted to investigate the negative effects of fungus-contaminated environments, particularly *fusarium*, on the respiratory and cutaneous systems. Ochratoxins (A, B, and C)

and trichothecenes (T-2) are two significant classes of mycotoxins that have been detected in food and water-damaged structures and have been linked to substantial health problems in humans (Ratnaseelan et al., 2018). It has been claimed that trichothecenes can be produced at 300-fold the concentration of spores normally seen in the air of polluted buildings (Awuchi et al., 2021), causing multisystem effects in those who are exposed (Ratnaseelan et al., 2018).

Climate change has a substantial impact on food security, such as toxigenic fungus infection and contamination with mycotoxins. Acclimatization of mycotoxigenic fungus and synthesis of mycotoxins, particularly AFB1, appears unaffected by climate change, leading to ongoing contamination of animal feed and human food, culminating in major health problems in animals and humans (Sadiq et al., 2019).

Major Environmental Mycotoxin Sources

Climate change is mostly responsible for the AFB1 or ZEN contamination of maize and wheat harvests (Gruber-Dorninger et al., 2019). The amount of mycotoxins in the soil is determined, how they get there, whether directly or through contaminated straw (Zhang et al., 2022a). Additionally, after runoff or rainfall, mycotoxins will move from agricultural areas to surface waters (Juraschek et al., 2022).

Crops that are contaminated by mycotoxins are turned into feed, which is subsequently consumed by animals or humans and discharged into the environment after digestion. Its contamination persists in animal and human excreta, resulting in a substantial source of secondary environmental pollution (Zhang et al., 2022a).

About 50% of Aflatoxin B1, 20% of ZEN and 37% of DON will be expelled in feces, according to sampling evidence studies done to determine the level of mycotoxins in animal feces (Zhang et al., 2022a).

Aflatoxin

In nature, there are more than 20 different forms of aflatoxins including their derivatives, but only four, types namely B1, B2, G1, and G2, have been shown to be harmful to both humans and animals. The main Aspergillus strains that generate AFs, or furanocoumarins, are *A. flavus*, *A. parasiticus*, *A. nomius*, and *A. pseudotamarii* (Ráduly et al., 2020).The most cancer-causing and thoroughly researched AF is aflatoxin B1 (Benkerroum 2020).

AFM1 is a 4-hydroxy derivative of AFB1 that is produced in the liver and secreted into milk by human and nursing animal mammary glands that have consumed AFB1-contaminated food. AFB1 is converted into aflatoxin B1-8,9-epoxide (AFB0), which has both exo and endo isomer, in the liver via the cytochrome P450 enzyme system (CYPs) (Cao et al., 2022).

Acute aflatoxicosis causes mortality, however chronic exposure causes cancer, immunosuppression and pathological problems that take time to show. Chronic aflatoxin exposure reduces DNA replication in the bone marrow, which results in low cell counts (Benkerroum 2020).

Ochratoxin

Mycotoxins are toxic secondary metabolites produced by some fungal species. As per reports, more than hundreds of mycotoxins have been discovered so far (Gizachew et al., 2019).

Ochratoxin A, Ochratoxin B, and Ochratoxin C are the three varieties of ochratoxins that are classified based on their chemical makeup (Wang et al., 2022). It is hard to avoid ochratoxin because it is present in many dietary products. Studies show that ochratoxins do not pose a serious harm to the general public's health. The most common species in food are *A. ochraceus*, mesophilic xerophile species *A. styenii*, and *A. westerdijkiae*, which can be dangerous before and after harvest in cereals, fruits, coffee, cocoa beans, and nuts. Ochratoxin is primarily produced by *A. chraceus*, which can grow in environments with temperatures between 8 and 40 degrees Celsius, high water activity (aw) values between 0.9 and 99 and pH levels between 3 and 10 (Gizachew et al., 2019).

A. ochraceus can also produce toxic metabolites like penicillic acid, viomellein, vioxanthin and xanthomegnin. Ochratoxin found in many tropic and sub-tropic foods such as fresh fruits, dried fruit wine and some vegetables (Wang et al., 2022).

Animals can be infected through feed and humans through beverages and food. Ochratoxin enters in the circulatory system through gastrointestinal system. It has higher affinity with serum albumin and proteins so it accumulate in organs of human and animal (Yang et al., 2022).

Fumonosins

Aflatoxin, ochratoxin, zearalenone, and trichothecene mycotoxins are of lesser concern than fumonisin because of their frequent presence and possible harm to human and animal health (Wangia-Dixon and Nishimwe 2020).

Abalone fed with fumonisin-contaminated feed demonstrated that the toxin leached into the saltwater and affected the aquatic ecosystem. Fumonosins are formed on relatively common seaweed abalone (Greeff-Laubscher et al., 2020).

The major source of fumonisin production is the gene cluster fumonisin biosynthetic gene (FUM) in Fusarium and Aspergillus. The expression of these genes is co-regulated, and the expression of the FUM genes is connected to them as well (Pierron et al., 2016).

Not only the crops, but many popular ornamental plants e.g., aster begonia, carnation, chrysanthemum, gladiolus, etc. are mostly attacked by different *Fusarium* species, viz., *F. oxysporum*, *F. foetens*, *F. hostae*, and *F. redolens* at different stages of production (Sokolovic et al., 2022).

Table 1: Toxic effect different toxin on one health triad

Type of Toxin	Study Model/ Animal Type	Dose	Results	Overall effect	Reference
AFB1	Kunming mice	450 µg/kg BW	↑Gene expression for oxidative stress and apoptosis	Oxidative damage Apoptosis	(Li et al., 2021a)
AF	Animals		↓ Feed intake	Milk production Egg production	(Sarma et al., 2017)
AF	broiler chicks	50 and 100 ppb	↑ ALT ↑ ALP ↑ AST	bile-duct hyperplasia periportal fibrosis hydropic degeneration fatty change	(Ortatatli et al., 2005)
ZEN	E. coli	23.0 U/mg, 64.7 U/mg, 119.8 U/mg and 66.5 U/mg	↓ Enzymes activity ↓ Bacterial growth	Detoxifying agent in food and feed industry	(Wang et al., 2018)
ZE	In Vitro and In Vivo Studies	40 µM	PI3K/Akt-Mediated Nrf2 Signaling Pathway	Oxidative Stress and Apoptosis	(Rajendran et al., 2021)
AF	Rats	2 mg/kg body wt.	↓ Mortality, body weights, feed intake, and litter weights ↓ Embryonic resorptions and fetal body weights	maternal and Developmental toxicity	(Mayura et al., 1998)
AF	Broiler	211.88 µg / kg	↑ Vacuolar degeneration of hepatocytes, ↑ thickening in the wall of bile duct associated with leucocytic cells infiltration in the portal triad ↑ Necrobiotic changes of renal tubular epithelium with pyknosis of their nuclei and hypercllularity of glomerular tufts. ↑ necrosis of neurons ↑ neuronophagia of necrotic neurons and necrosis of purkinje cells of the cerebellum		(Shebl et al., 2010)
Fumonisin	Escherichia coli	10 µg/ml	↓ detoxification enzymes		(Li et al., 2021b)
ZEN, OTA, FB1, AFB1	Experimental animal	0.5 µg/kg bw/day 100–120 ng/kgbw/day 2 µg/kg bw/day -	↑ Changes Microbiota composition ↑ Changes metabolic activity ↓ Growth ↑ Immunotoxicity		(Robert et al., 2017)
OTA	broiler chicken	50 µg/kg	↓ Immune response ↑ Depression in phagocytosis		(Casafranca Loayza 2018)
OTA	Lab animals	100–120 ng/kg bw/day	↑ Nephrotoxic (renal tumors) ↑ Carcinogenic		(Robert et al., 2017)
OTA	albino rats	50 ppb OTA and 25 ppb ZnONPs	degeneration, ↑ sinusoidal spaces ↑ infiltration of lymphocytes ↑ vascular congestion and necrosis.		(Hassan et al., 2021)
ZEN	Bacillus	1.20 ± 0.11, 0.47 ± 0.22 mgkg1	Degrade ZEN in feed and alleviate the adverse effect of ZEN for piglets.		(Wu et al., 2021)
ZEN	Pigs	1.0 ppm	hyperererestrogenic syndromes		(Rogowska et al., 2019)

↑: increase ↓: decrease AFB: Aflatoxins B ZEN: Zearalenone OTA: Ochratoxin A FB1: fumonisin B1 ALT: alanine transaminase ALP: *alkaline phosphatase* AST: Aspartate Aminotransferase

Zearalenone

When zearalenone (ZEN) (a substantial family of mycotoxins that is classified as a xenoestrogen) binds to estrogen receptors in a manner similar to that of natural estrogens, it causes a variety of reproductive problems, including hormonal imbalance (Sohrabi et al., 2022).

Zearalenone, a mycotoxin produced by fungi of the genus *Fusarium*, widely exists in animal and human food (Han et al., 2022). Because of its toxicity and estrogenic action, zearalenone can grow in fresh flowing water, disrupting the aquatic ecology and endangering both human and aquatic biota (Kortei et al., 2021).

Zearalenone mycotoxins, which inflict catastrophic effects on the organs and remain in the tissues of animals, will be produced in animal feed because of the inadequate storage conditions. Humans will ultimately ingest these wastes causing serious complications (Zhang et al., 2022a). Zearalenone is highly toxic and can affect the health of animal and humans. It also provides insight to its harmful effects on human health and agriculture along with its effective detection, management, and control strategies (Mahato et al., 2021). Fig. 3 shows the schematic diagram illustrating the effects of different toxins on one health triad. Table 1 shows the effects of different toxins on human, animal, and environmental health.

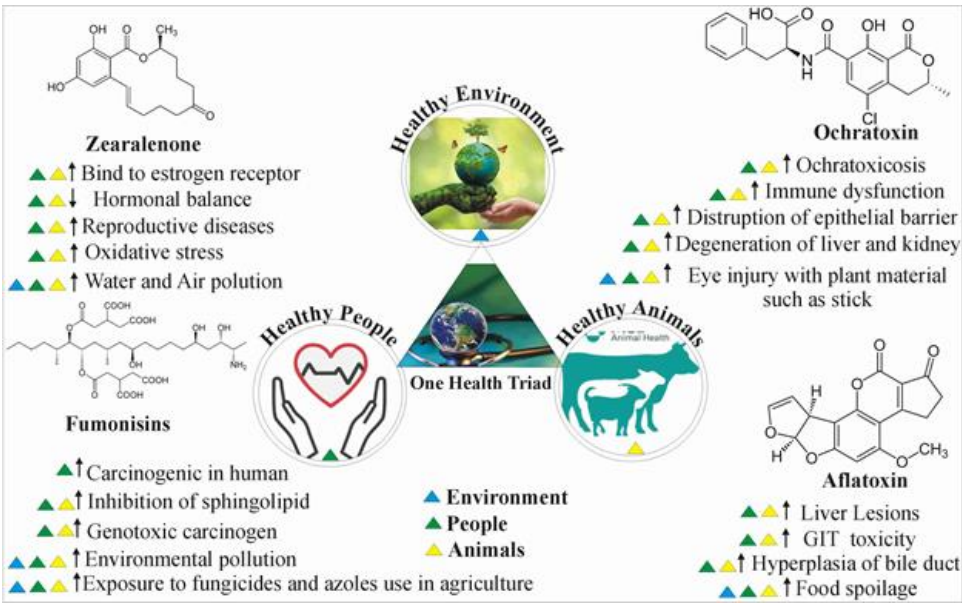

Fig. 3: Schematic diagram illustrating the effects of different toxins on one health triad i.e. Effect of ochratoxin (Hassan et al., 2021), zearalenone (Gao et al., 2022), Fumonisin (Pierron et al., 2016) and Aflatoxin (Qazi and Fayyaz, 2006) on humans, animals and environment.

Conclusion

Mycotoxicosis is a worldwide food safety concern. The FAO and WHO expert committees examined the risk analysis of mycotoxins toxicity and concluded that it is a major concern in developing countries since they can cause serious and irreversible health problems in animals and humans. Meanwhile, the possibility cannot be ruled out that environmental and biological variables influence the presence and prevalence of fungal pathogens in stored agricultural products (Sarwar et al., 2018).

It is well understood that once mycotoxins have contaminated feed or food, nearly nothing can be done to eliminate them. The most fundamental and effective method for reducing fungal infection at sensitive agricultural storage facilities is to manipulate environmental conditions. This will reduce the entry of fungal-derived mycotoxins into the feed and food chain, ultimately reducing their negative impacts on animal and human health. We can address the shortcomings of this global one-health issue by enlisting multidisciplinary professionals and relevant authorities to play critical roles in risk factor assessment and mitigation, research gap identification, basic and applied research promotion, public awareness, and capacity building.

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