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Mycotoxins in Foods and Indoor Air: Their Attendant Diseases and Modes of Injury on Biological and Human Systems

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ABSTRACT

Though some secondary metabolites from fungi have found application as antibiotics in modern medicine, majority of these compounds are however known to be hazardous to livestock and human systems. About 400 mycotoxins have been characterized in recent times with each potentially toxic to a biological or human system. Exposure of humans to airborne toxins-carrying spores produced by several species of fungi in water damaged buildings and damp indoor environments have been linked with allergies and sick building syndrome. Contamination of cereals, grains or tubers in the field, transit or store with a broad spectrum of noxious mycotoxins is well reported in literature. Scientific evidences have implicated consumption of such contaminated agricultural products with diseases such as nephropathy, immuno-deficiency, stunted growth, weight loss, onyalai, neural tube defect, CNS depression, kwashiorkor, hepatocellular carcinoma, jaundice, diarrhoea, beriberi and even death. Inhibition of protein synthesis and cell proliferation, inhibition of peptide chain elongation, binding to DNA and uncoupling oxidative phosphorylation, inactivation of ceramide synthase, transferases and other enzymes, and cell wall disruption etc are some of the mechanisms adduced for their toxic activity. With increasing incidence of mycotoxin-related diseases in the developing countries of Africa and other third world economies, concerns about their public health impacts are rife and heightening given that both chronic intermittent and acute exposures are deemed injurious. Therefore an understanding of their modes/mechanisms of injury in biological and human systems will help in tailoring their management in a broad scale.

INTRODUCTION

Besides the diseases caused by plant pathogenic fungi in several crops in the field, association of these mycobiota with agro-products during transit or storage could lead to their contamination with dangerous fungi-derived toxins (mycotoxins). Mycotoxins are a group of structurally diverse group of low molecular weight compounds produced mainly by filamentous fungi (and sometimes yeasts) which are toxic to biological systems including plants, livestock and humans (Gardiner *et al.*, 2005; Zain, 2011). Fungal infections leading to mycotoxin contamination of feed or foodstuff are predisposed by overcrowding crops in the field, insect infestation of crops in the field or store, and wounds on produce during threshing. Usually contaminations are exacerbated by poor tropical storage conditions characterized by high temperatures and moisture migration (Lacmelen, 2001).

Worldwide 25% of agricultural crops covering several cereals, legumes, nuts, and coffee are mycotoxin contaminated (Enyiukwu *et al.*, 2014). In the Czech Republic and Slovenia, Zain (2011) reported that 91% of raw milk in those countries was mycotoxin contaminated. In a survey in Nigeria up to 98-100% incidence of the nephrotoxic metabolite ochratoxin A (OTA) from *Aspergillus ochraceus* and *Penicillium verrucosum* were detected in cereals (maize, millet, sorghum, sesame and fonio) and red kola nuts obtained from Niger and Oyo states respectively (Adejumo and Adejumo, 2014). A similar survey in the Niger Delta region also recorded 100% incidence of aflatoxin B₁ in bread fruit, wheat, millet, and guinea corn. Analysis of semen and blood specimens of infertile men in the area at the University of Benin revealed that 37% were aflatoxin B₁ positive. In evaluations in Ogun state southwest Nigeria, the toxin was detected in 90% of blood and urine specimens, and 58% in autopsy samples of children with kwashiorkor, suggesting a correlation between the toxin and the debilitating disease (Adejumo and Adejumo, 2014).

Approximately 400 mycotoxins have been reported in literature and all are toxic to humans (Bryden, 2012). Some fungi can produce more than one mycotoxin while some mycotoxins are produced by more than one fungal species (Zain, 2011). *Alternaria* spp. for instance are known to produce about 70 mycotoxins which include alternatriol (AOH), alternatriol monomethyl ether (AME), alternuen (ALT), tenuzoic acid (TEA), and altertoxins I, II and III (ATX I, II & III). As high as 116-6432g/kg (72-89%) of these toxins have been isolated from a wide range of oils, cereals and cereal products such as bread contaminated with especially *A. alternata* (Nayyar *et al.*, 2014). Others such as aspergic acid, cyclopiozonc acid, kojic acid, naphtoquinones, fumonisins and fusaric acid have been isolated from cereal grains contaminated by *Aspergillus niger*, *Penicillium* spp., *Fusarium culmorum* and *Rhizoctonia solani* (Haikal, 2008). In addition, literature also shows

that *A. flavus*, *A. niger*, *A. oryzae*, and *A. teneus* produce aflatoxin B₁; *A. flavus* and *Penicillium italicum* produce fumonisin B₁ while several *Fusarium* spp. produce zearalenone (Amadi and Adeninyi, 2009). In Africa however, the mycotoxins considered of most agricultural importance include aflatoxins, ochratoxins, fumonisins, beauvaricin and the trichothecenes such as zearalenone, vomitoxin and T-2 toxins (Fig. 1). These toxins impair several biological systems in a variety of ways (Coulombe, 1993).

A plethora of harmful effects on plants, livestock and humans have been attributed to these toxins. In several plant families, toxic fungal metabolites have been reported to decrease growth, yield and yield parameters of crops. Metabolites from *F. equiseti* and *Drechslera rostrata* retarded root growth; while those from *A. teneus*, *A. alternata*, *A. flavus*, *F. solani*, *F. oxysporum* reduced the germination of soybean. Toxins screened from *F. moniliforme* retarded the shoot growth of sorghum, *Verticillium albo-atro* the viability of alfalfa, whereas those from *Pythium* spp. and *Rhizopus* sp. reduced the yield of potato (Haikal, 2008). Reduction of leaf length, width and area, leaf chlorophyll content, stomatal density and size on maize by toxic metabolites from *P. chrysogenum* have also been documented (Garuba *et al.*, 2014; Shirurkar and Wahegaonkar, 2014).

In humans, maladies such as allergies, reproductive dysfunction, birth defects, premature puberty in girls, haemorrhage, gene defects, cancers, jaundice, liver damage, kidney damage, immune dysfunction, kwashiorkor and even death have been reported due to fungi-derived toxins (Bankole, 2003; Enyiukwu *et al.*, 2014; Shirurkar and Wahegaonkar, 2014). For instance toxic dermatitis and conjunctivitis have been recorded due to improper handling of mycotoxin contaminated hay by farm-hands in Western Nigeria (Amadi and Adeninyi, 2009). According to Bryden (2012) epidemics and outburst of bizarre behavior, low reproductive fertility and high death rates have been linked to food poisoning from mycotoxins in cereal staples from around the world.

Aflatoxins are noted to cause decrease in immunoglobulin A (IgA) in children and to impair human cellular immunity and resistance to diseases. In a study, it was observed that exposure of Dutch peasant processing workers to airborne peanut dusts laden with aflatoxins resulted to increases in the number of those that develop liver and lung cancers compared to their counterparts in a control group (Coulunba, 1993). In sub-Saharan Africa, and some parts of Asia; aflatoxins-related carcinomas resulted in greater than 600,000 deaths on annual basis (Wild and Gong, 2010; Zain, 2011). Scientific evidences suggest a strong correlation between aflatoxin B₁ on one hand and hepatitis B virus (HBV) and hepatitis C (HCV) in human hepatocellular carcinoma (HCC) in some parts of China, Malaysia, India and Kenya (Enyiukwu *et al.*, 2014). The fraction of HCC cases attributed to HBV and HCV has been

estimated to be about 23% and 20% in developed countries; and as high as 59% and 33% in developing countries respectively (Fig. 2). Also, association of aflatoxins with Reye syndrome -- a disease characterized by encephalopathy, visceral disintegration, and liver and kidney enlargement has been documented (Zain, 2011). Sterigmatocystin a mycotoxin (similar to

but less toxic to aflatoxin B₁) produced by *Bipolaris (Hemisthophorium) spp.*, *Aspergillus nidulans* and *A. vesicular* have been reported to damage the liver, kidney and DNA in human cells by impairing cell cycle, altering DNA, and inhibiting phosphorylation and ATP synthesis (Lillard, 2004).

Figure 1: Mycotoxins of most agricultural importance in Africa
Sources: Darwis *et al.* (2014); Shirurkar and Wahegaonkar (2014)

Figure 2: Mycotoxin-related human hepatocellular carcinoma and percent association with HBV and HCV

In Denmark, significant contamination of cereals with the ochratoxin A (OTA) have been correlated with high Balkan endemic nephropathy (BEN) -- a severe kidney damaging disease in the area (Bankole, 2003; Enyiukwu *et al.*, 2014). In affected human males, OTA is reported to be associated with testicular degeneration, seminiferous tubule atrophy and dissolution of germinative epithelium by interfering with gene transcription through the protagladins synthase route (Anon., 2017). It is also known to cause depletion of dopamine and related compounds in striated tissues (Hope, 2013). Similarly, high prevalence of oesophageal cancer in the republic of South Africa, China and Northeast Italy has been attributed to large scale consumption of cereal grains such as maize contaminated with fumonisins -- a toxin derived from *Fusarium spp.* (Enyiukwu *et al.*, 2014).

Exposure of humans to water damaged buildings or houses with defective architectural or structural designs; which make for poor indoor air circulation, poor indoor light quality, high degree of dampness and build up of toxin-laden fungal spores of mycotic organisms could lead to sick building syndrome (SBS). SBS has resulted to abandonment, burning and destruction of many houses in the USA and Canada (Peraica *et al.*, 1999; Hope, 2013). Satrotoxins A is one

of the mycotoxins implicated in SBS. It was reported to demonstrate neurological damage in individuals occupying water-damaged buildings at indoor air levels (Hope, 2013). According to this source, this macrocyclic trichothecene in addition to fumonisins, OTA and T-2 have been linked with neuronal degeneration and inflammation in the human brain cortex of fetuses and adults. Verucarins are another group of potent cytotoxic macrocyclic trichothecenes produced by species of *Fusarium*, *Trichoderma*, *Cephalosporium* and other fungi, their mode of injury on biological systems is suspected to border on damaging proliferating cells of the abdomen, bone marrow gastric mucosa and spleen by inhibiting protein and DNA synthesis in the affected organisms (Cudliffe *et al.*, 1974).

Gliotoxins are important aromatic amino acid class of epipolythiodioxopiperazine (ETP) toxins produced by *Trichoderma spp.*, *Penicillium spp.*, *A. fumigatus*, *Gliocladium fimbriatum*, and *Candida spp.* Gliotoxins are thought to be the virulence factor employed by these fungal organisms in macerating and colonizing tissues of immuno-compromised individuals during invasive mycoses (Gardiner *et al.*, 2005). Some of the public health problems due to mycotoxins in Africa are presented in Table 1.

Table1: Some mycotoxin-related public health problems in some African countries

Country	Mycotoxin	Disease Caused
East Africa, Uganda	Beauvericin	Nodding syndrome (childhood epilepsy)
Egypt	Aflatoxins	Primary hepatocellular carcinoma
Ghana	Aflatoxins	Anaemia
Ghana	Aflatoxins	Immuno-deficiency
Gambia	Aflatoxins	Liver cirrhosis
Gambia	Aflatoxins	Immunodeficiency
Cameroun	Aflatoxins	Primary hepatocellular carcinoma
Kenya	Aflatoxins	Aflatoxicosis
Nigeria	Aflatoxins	Infertility, Kwashiorkor
Tunisia	Ochratoxins	Nephropathy
Cote d'Ivoire	Ochratoxins	Nephropathy
Benin Republic	Aflatoxins	Stunted growth, under weight
Togo	Aflatoxins	Stunted growth, underweight
South Africa	Fumonisin	Oesophageal carcinoma

Sources: Zain (2013); Durringer *et al.* (2013); Dobranic *et al.* (2017)

Worldwide given the role of mycotoxins in human tissues degradation, kwashiorkor, immune dysfunction, cancers and invasive human mycoses, they are considered as major public health problems especially in developing tropical countries; where store hygiene is low, and storage conditions poor thereby, encouraging growth of toxic moulds on feed, foodstuffs and indoors (Eaton and Gallapher, 1994; Shephard, 2008). Also, with the increasing threat of climate change and its accompanying flooding (Salami and Salami, 2011), incidence of sick building syndrome is likely to increase in the near future. It becomes pertinent hence, to document and make handy the modes/mechanisms of action of mycotoxins in affected biological systems and human tissues.

Therefore, this work reviews available literature on some of the diseases caused by fungi-derived toxins from agriculturally and environmentally important mycotoxigenic flora and their modes of injury on biological and human systems.

Diseases caused by mycotoxins in livestock and humans

Though some studies have shown that gliotoxins has anticancer activity against mammary carcinomas and selectively kills activated hepatic stellate cells in rats without toxicity to the host, majority of the times fungal secondary metabolites are toxic, disrupting cellular responses to fungal infections involving the nicotinamide adenine dinucleotide phosphate oxidase (NADPH oxidase) enzyme complex. They are also reported to prevent viral RNA replication via inhibition of reverse transcriptase (Gardiner *et al.*, 2005). Also, antitumor, antiviral and antibacterial activities due to tenuazonic acid produced by species of *Phoma* and *Alternaria* have been documented (Blackmould, 2017). In medicine ergot alkaloids are used in the treatment of Parkinson's disease, migraine, cerebro-vascular insufficiency, and to

stimulate the uterus preparatory to parturition (Perraica *et al.*, 1999).

However, majority of times fungal metabolites have been implicated in fatal diseases in livestock and humans. A study in southwest Nigeria found that Wister rats fed samples of paw paw (papaya) fruit contaminated with mycotoxigenic strains of *Aspergillus*, *Fusarium* and *Rhizopus* suffered varying levels of convulsion, paralysis and respiratory attacks (Oyeyipo *et al.*, 2012). Human exposure to water-damaged buildings, endemic with mycotoxin-carrying spores is reported to contribute up to 50% of human illnesses resulting from indoor air pollution (Hope, 2013).

In humans, fatigue is the primary symptom of the multisystem systemic toxicity that follow exposure to fungal toxins and therefore everyone exposed to mycotoxins will present fatigue and other symptoms such as hair loss, premature hair graying, and coughing up blood or black debris. Others are frequent and burning sensation after urination, nose bleeds, low grade fevers, cognitive dysfunction, joint stiffness, headaches, migraine and brain lesions etc. which may be unwittingly ascribed to other causes (Chronicles, 2014; Anon, 2017).

Gliotoxin (Source: ChemEssence.com)

In China, the toxin 3-nitropropionic acid (3-NPA) produced by *Arthrinium spp.* have been found associated with mouldy sugarcane poisoning in humans. This disease is characterized by dystonia, convulsion, staring to one side, capopedal spasms and coma. Indoors, moulds spores may not be visible to the human eye; however, they are highly dangerous and life threatening. There is a genetic undertone to indoor air mycotoxicosis. It is reported that at least a quarter of the human populations is unequipped to fight off mycotoxins; these have inherited mutant genes (HLA-DRBQ) which resulted in their immune systems not being able to produce antibodies against mycotoxins (Chronicles, 2014). In Canada and the USA, trichothecene toxins such as satratoxin H, verucanol, verucarins B and J, trichoverins A and B, T-2 toxin, diacetoxysripenol (DAS) and roridins from airborne spores of *Stachybotrys atra*,

Trichoderma spp., *Fusarium spp.*, *Trichothecum* and *Myrothecium spp.* are reported as major public health problems in water damaged environments being implicated in sick building syndrome (Table 1). These moulds hide behind water damaged walls, around showers and bathtubs, and above damp ceilings (Chronicles, 2014). In affected individuals, the disease presents with cold and flu-like symptoms, sore throat, diarrhoea, headache, fatigue, elevated body temperature, focal alopecia, dermatitis, oral lesions, swelling of the lips and lymph nodes, weak pulse, general malaise and death if allowed to progress (Peraica *et al.*, 1999; Volks and Zitomer, 2002). The disease is especially exacerbated by stressors such as work or psychological problems (Volks and Zitomer, 2002).

Table 1: Mycotoxins involved in Sick building syndrome

Fungus	Mycotoxins
<i>Alternaria alternate</i>	Tenuazonic acid, alternatiol, alternatiol monomethyl ether, alterotoxins
<i>Aspergillus fumigates</i>	Gliotoxin , verrucologen, fumitremorgceusins, fumitoxins, tryptoquivalins
<i>A. ustus</i>	Austamide, austdiol, austins, austocystins, kotanin
<i>A. versicolor</i>	Sterigmatocystin , 5-methoxysterimatocystin , versicolorins
<i>Chaetomium globosum</i>	Chaetoglobosins, chaetomin
<i>Memnoniella echinata</i>	Trichodermol, trichodermin, dechlorogriseofulvins, emnobotrins A and B, memnoconol, memnoconone
<i>Penicillium aurantiogriseum</i>	Auranthine, penicillic acid, verrucosidin, nephrotoxic glycopeptides
<i>P. brevicompactum</i>	Mycophenolic acid
<i>P. chrysogenum</i>	Roquefortine C, meleagrin, chrysogin
<i>Stachybotrys chartarum</i>	Satratoxins , verrucarins , roridins , atranones, dolabellanes, stachybotrylactones and lactams, stachybotrydialis
<i>Trichoderma harzianum</i>	Alamethicins , emodin, suzukacillin, trichodermin
<i>Wallemia sebi</i>	walleminols A and B

Source: Dobranic *et al.* (2017) *Toxins in bold are very harzardous

Human exposure to mycotoxins can occur by several ways, including ingestion, skin contact, and inhalation (Zain, 2011). In certain environments or occasions,

public health experts or environmental health professionals may suspect mould exposure, toxicity or sensitivity in an individual, if amongst other factors:

- ✚ Musty odours bother the patient?
- ✚ The patient have worked or lived in a building where the air vents were discoloured?
- ✚ He noticed water damage or discolorations on ceilings or elsewhere in his house or office?
- ✚ His home had been flooded
- ✚ He had leaks in the roof of his house?
- ✚ He experiences shortness of breath?
- ✚ He experiences recurring sinus infections?
- ✚ He experience recurring bronchial infections and coughing?
- ✚ He has flu-like symptoms?
- ✚ He notices an increase of symptoms on rainy days?
- ✚ He has frequent headaches?
- ✚ He is fatigued and has a skin rash? (<https://www.ehcd.com/mold-and-mycotoxins>)

Trichothecenes are immunosuppressive toxins and eminently compromise human immune systems exposing them to opportunistic bacterial or mycotic infections (Enyiukwu *et al.*, 2017). Due to the extreme degree of toxicity of trichothecenes they have been used as biological weapons. In mice, it was noted that the most acutely toxic trichothecene is verrucaric acid (0.5 mg/kg), followed by T-2 and nivanenol which are nearly equitoxic (Coulunba, 1993). This group of fungi-derived toxins exerts multi-organ effects on biological systems resulting in some forms of emesis, diarrhoea, cardiovascular alterations, bone marrow damage, and decreased reproduction. Neurological disorders such as cognitive disturbances, delirium, and dementia as well as balance dysfunction have also ensued from exposure to trichothecenes. In Poland, about 13 children exposed to trichothecenes in indoor air of water damaged buildings experienced cognitive disturbances (Hope, 2013). Ingestion of significant amounts of fumonisin toxins have been associated with alimentary toxic aleukia (ATA) a disease which resembles severe radiation injury. It is characterized by a burning sensation in the mouth, tongue, throat, gut, and stomach and other symptoms such as nausea, vomiting, diarrhoea, leukopenia, haemorrhaging, skin inflammation, vertigo, asphyxiation and death (Table 2). In sub-lethal doses the toxins could trigger tremogenic effects or cause irritable bowel or colitis (Zain, 2017; Anon., 2017). Association of kwashiorkor a disease whose symptoms include fatigue, edema of the stomach, feet and ankles, weight loss, diarrhoea, loss of muscle

mass and irritability with aflatoxin B₁ has been numerous reported (Eaton and Gallagher, 1994). According to Zain (2011) aflatoxin B₁ was also implicated in Reye's syndrome -- a debilitating disease which presents encephalopathy, visceral alteration and liver damage.

Contamination of food with fungal toxins is considered a plausible aetiological factor in Nodding Syndrome, a form of epilepsy affecting thousands of children in East Africa. The disease is said to be prevalent during periods of community displacement when food sources were unreliable and food quality was grossly compromised. Children that are affected with the disease developed eating- and cold-induced atonic seizures (with head nodding) and generalized seizures. According to Durringer *et al.* (2013) the mycotoxin beavericin associated with contaminating sorghum (a common East African staple) is regarded as the aetiological agent behind the disease. All 400 fungi-derived toxins are toxic affecting human health in one way or the other. Recently a large number of medical practitioners have admitted that mould-caused human illness is a pandemic, and that exposure to toxic moulds is responsible for 500,000 deaths per year in the US alone (Chronicals, 2014). Some human diseases in which analytic and/or epidemiological data suggest or implicate mycotoxin involvement from exposure to, contact with, and inhalation of spores of fungal pathogens or ingestion of substrates contaminated by them are presented in Table 2.

Table 2: Diseases caused by fungi-derived toxins in livestock and humans

Disease	Species Affected	Substrate	Aetiological agent
Akakabio-byo	Human	Wheat, barley, oats, rice	<i>Fusarium spp.</i>
ATA or septic angina	Human	Cereal grains (toxic bread)	<i>Fusarium spp.</i> ,
Balkan nephropathy	Human	Cereal grains	<i>Aspergillus spp. Penicillium spp.</i>
Cardiac beriberi	Human	Rice	<i>Penicillium spp. Aspergillus spp</i>
Celery harvester's disease	Human	Celery (pink rot)	<i>Sclerotinia spp.</i>
Dendrodochiotoxiosis	Human, horse	Fodder, fodder dust	<i>Dendrodochium toxicum</i>
Ergotism	Human	Rye, cereal grains	<i>Claviceps purpurea</i>
Oesophageal tumours	Human	Corn	<i>Fusarium verticillioides</i>
Hepatocellular carcinoma	Human	Cereal grains, peanuts	<i>A. flavus, A. parasiticus,</i>
Kashin Beck disease,	Human	Cereal grains	<i>Fusarium spp. Aspergillus flavus,</i>
Kwashiorkor	Human	Cereal grains	<i>A. parasiticus</i>
Onyalai	Human	Millet	<i>Phoma sorghina</i>
Reye's syndrome	Human	Cereal grains	<i>Aspergillus spp.</i>
Sick building syndrome	Livestock, human	Hay, cereal grains,	<i>Stachybotrys chartarum</i>

Source: Dobranic *et al.* (2017)

Structures of some of the mycotoxins implicated in human mycoses are shown in Figs. 3-5. However, besides knowledge of the biology of the aetiological agents and chemistry of their toxins that bring about the mycotoxicoses in livestock and humans, appropriate understanding of the mode/mechanism of the damage of the toxins in biological and human systems could contribute immensely towards tailoring effective control strategies and management of the affected individuals (Enyiukwu *et al.*, 2014).

Modes of action (MOA) of mycotoxins on biological and human systems

The mechanisms underpinning mycotoxin induced illnesses are suggested to involve oxidative stress,

allergic responses, irritant effects, inflammation and some forms of toxicity and infection (Hope, 2013). Gliotoxins are immunosuppressive toxins and the virulence factors which play roles in human tissue colonization during infective mycoses; being selectively antagonistic to macrophages and lymphocytes and causing apoptotic and necrotic cell death. Chemically, they contain disulphide bridge which imparts their toxicity by inactivating host proteins and macrophages through reaction with thiol groups and generation of reactive oxygen species following redox cycling (Bernette and Klich, 2003; Gardiner *et al.*, 2005; Enyiukwu *et al.*, 2017).

Fumonisin are neurotoxic, nephrotoxic and hepatotoxic compounds whose toxicity is thought to result from oxidative stress, apoptosis, cytotoxicity and

alteration in cytokine expression of cells (Stockmann-Juvana and Savolainen, 2008). Fumonisin is similar in structure to sphingolipids and in living cells and tissues their toxicity stems from binding to sphingolipid receptors and inhibiting the enzyme ceramid synthase leading to displacement and accumulation of sphingolipids in the systems. In nerve cells Zain (2011) noted also that they play roles in the inhibition of the uptake of folic acids via the folate receptors leading to neural tube defects.

Chemically aflatoxins (AFs) are a class of difuran-coumarins. They are of the naturally occurring potent carcinogenic fungal toxins which in mammals are reputed for being immunotoxic, genotoxic, hepatotoxic, mutagenic and to strongly damage kidney and liver tissues (Eaton and Gallanger, 1994; Hope, 2013). Besides *A. parasiticus*, *A. nominus* and related flora, species of *Rhizopus*, *Penicillium* and *Mucor* have been reported to produce AFs. Aflatoxin's toxicity is reasoned to stem from interference with the utilization of dietary protein by inhibiting synthesis of RNA, DNA and proteins. They are reported further to bind and destroy proteins of cell membranes, gap junctions and the intercellular matrix, disturbing cell to cell communication and thus causing tumorigenesis (Anon, 2017). The modes or mechanisms of action (MOA) of some mycotoxins in biological or human systems are summarized in Table 3.

In mammalian and eukaryotic cells, trichothecenes and other 12, 13-epoxytrichothecenes (sesquiterpenoids) toxins inhibit protein and DNA synthesis. T-2 is an amphipathic trichothecene molecule.

It is reported to interfere with membrane function by binding to lipid or protein moieties of cell plasma membranes. In a study with mammalian tissues, 10 minutes after exposure to T-2 toxin, it was found to reduce the uptake of calcium, glucose, leucine and tyrosine (Coulumba, 1993). Others such as nivanelol, T-2 toxins and verrucar A also, caused rapid breakdown of polyribosomes in H-Hella cells and potently retarded polypeptide chain initiation in mammalian tissues. Similarly, inhibition of polypeptide chain elongation or termination is reported as the mode of injury of trichodermin (Cundliffe *et al.*, 1974).

Fumonisin is a dangerous mycotoxin. Coulumba (1993) noted that a link exists probably between short term dietary intake of fumonisin B₁ and hepatocellular carcinomas (HCC). Their mechanism of injury in several biological systems is thought to involve inhibition of protein synthesis and inactivation of critical enzymes (Table 3). Scabby grain disease, a disease affecting populations in Australia, China, Japan and USA symptomized by nausea, vomiting and diarrhea has been ascribed to the fusaria-derived toxins deoxynivalenol (DON) and Zearalenone (ZEN) (Zain, 2011). ZEN is an estrogen agonist. In biological systems zearalenone has been known to increase certain yeast and fungal infections and therefore could predispose or exacerbate certain opportunistic mycotic infections especially in people living with some forms of immunosuppressive diseases including cancers, HIV or undergoing chemotherapy such as prolonged prednisolone or dialysis therapy (Anon., 2017; Enyiukwu *et al.*, 2017).

Figure 3: Structures of some common mycotoxins contaminating agro-products and causing indoor air pollution
Key: a = Diacetylscripenol (DAS), b = nivanelol, c = Sterigmatocystin, d = Ochratoxin A, e = Deoxynivalenol, f = T-2 toxin

Sources: Mycotoxin Info; PubChem; ChemSpider.com; en.wikipedia.org

Figure 4: Structures of some common mycotoxins contaminating agro-products and causing indoor air pollution

Key: **g** = Cyclopiazonic acid (CPA), **h** = zearalenone (ZER), **i** = Fumonisin, **j** = Citrinin, **k** = Palutin, **l** = Ergot alkaloid

Sources: Mycotoxin Info; PubChem; ChemSpider.com; en.wikipedia.org

Figure 5: Structures of some common mycotoxins contaminating agro-products and causing indoor air pollution

Key: **m** = Aflatoxin B₁, **n** = 5-methyl Sterigmatocystin, **o** = Penicillic acid, **p** = Roridin, **q** = verrucarin J, **r** = satratoxin H

Sources: Mycotoxin Info; PubChem; ChemSpider.com; en.wikipedia.org

Zearalenone is thought to increase permeability of molecules across cell membranes and to promote

synthesis of RNA, DNA and protein in the uterus (Anon., 2017).

According to Mycotoxin Info (2016) T-2 toxin has a broad array of toxic effects on animals. The mechanism of its toxicity is common to other trichothecenes involving inhibition of protein synthesis followed by disruption of the synthesis of DNA and RNA which ultimately interferes with the metabolism of membrane phospholipids. This condition specifically affects rapidly dividing cells such as the ones of the intestinal mucosa, skin and lymph nodes, bone marrow, spleen, and thymus cells. Common symptoms in animals include feed refusal, weight loss, vomiting and inhibition of immunity. Other symptoms are diarrhea, gastritis, and emaciation, necrosis of cartilaginous tissues, apoptosis and death. Furthermore, alteration of hematic values like reduction of serum proteins and cholesterol levels has also been observed. Poultry is particularly sensitive to type A trichothecenes compared to other species and exhibit peculiar symptoms like mouth and tongue lesions (Cardwel, 2000; Mycotoxin Info, 2016).

The Ochratoxins (A, B, C) are usually chlorinated (unchlorinated) dihydro-isocoumarin derivatives bonded to phenylalanine through an amide. They affect several organs in the body including the liver, kidney, brain, heart, testicles, spleen and urinary bladder, immune system, and genes. Ochratoxin A (OTA) for instance have been implicated in Balkan endemic nephropathy and focal segmental glomerulosclerosis. Species of *Penicillium*, *Petromyces*, *Neopetromyces*, *A. niger* and *A. ochraceus* significantly produce these toxins (Hope, 2013). The toxicity of ochratoxins is pivoted on oxidative stress due partly to infringement of the activities of antioxidant enzymes such as catalases, superoxide dismutase, glutathione peroxidase, glutathione reductase, phenylalanine tRNA complex on the one hand, and inhibition of mitochondrial ATP (energy) production and increased lipid peroxidation in the kidney, liver and serum on the other hand (Anon., 2017).

Tenuazonic acid is a potent fungal toxin which has been linked to esophageal cancer and onychomycosis (a haematological disorder) in some populations. Studies showed that birds and other test animals exposed to tenuazonic acid developed gizzard lesions, precancerous lesions and haemorrhaging. The mechanism of action of this toxin is thought to involve inhibition of synthesis of proteins by suppressing the release of newly formed proteins from ribosomes into the cell cytoplasm. (Blackmold, 2017).

Penitrem A is a powerful neurotoxin, and tremogenic GABA agonist produced by *P. crustosum*. The toxin is capable of crossing the blood-brain barrier causing neurological diseases characterized by sustained limb weakness, ataxia, and convulsion which in most cases are under-diagnosed due partly to similarity of its symptoms to other such diseases. In the brain it attaches to GABA receptors disrupting electrical coordination which presents as cramp-like induction and oxidative stress (Moldes-Anaya, 2015). Exposure of persons to fungi in buildings that have microbial growth

could result to several nervous system effects, rheumatoid diseases, loss of appetite, in addition to haemorrhaging of the mucous membrane of the intestinal and respiratory tracts. *S. chartarum* was suspected to be connected with pulmonary haemorrhaging in human infants in Cleveland, Ohio, USA. This organism secretes an enzyme stachyase which in concert with other toxins is thought to aid the pathogen to extract iron from susceptible host cells (NCBI, 2004).

Cyclopiasonic acid (CPA) exerts its toxic effects by impairment of the calcium metabolism that usually leads to damages to smooth muscles and the neural system (Suzuki et al., 1992; Mycotoxin.Info, 2016). Animal studies with rats revealed that CPA has an inhibitory effect on the endoplasmic and sarcoplasmic reticulum Ca^{2+} -dependent ATPase which mediates the cellular Ca^{2+} pools (Suzuki et al., 1992; Uyama et al., 1993). This effect is thought by Uyama et al. (1993) to be consistent with the hypothesis that CPA induced decrease in stored Ca due to Ca-pump inhibition, reduced the Ca^{2+} -dependent K^{+} current and indirectly enhances Ca^{2+} -influx through membrane activity resulting from the increased excitability in smooth muscles. In addition to neurotoxic effects, this metabolic disruption leads to immunomodulatory and immunosuppressive effects (Mycotoxin.Info, 2016). Furthermore this source reported that necrosis of liver, gastrointestinal tissue, kidneys and skeletal muscles have also been reported. CPA has implications in the promotion of carcinogenic effects in birds, specifically pathological changes in spleen and bursa fabricii.

Penitrem A (Source: en.wikipedia.org)

Citrinin is nephrotoxic (Boudless, 2016), while citreoviridin, verrucosidin caused progressive paralysis of the limbs by impairing interneurons, and motor neurons of spinal cord and brain medulla. These toxins have been linked to CNS depression as well as respiratory and cardiovascular failures (Nishie et al., 1988; Viera et al., 1996). Some mechanisms of injury of mycotoxins on human and biological systems are summarized in Table 3. Patulin and its closely relative penicillic acid exert nephrotoxic (kidney) and immunotoxic effects. Patulin produces gastrointestinal symptoms like gastric ulcers, intestinal hemorrhages,

lesions in the duodenum and alteration of intestinal barrier function (Mycotoxin Info, 2016).

Human health effects of inhaling mycotoxins are grossly poorly documented despite presence of their large amounts in aerosols. According to Jean-Mark *et al.* (2010) amongst airborne mycotoxins sterigmatocystin is prevalent. Sterigmatocystin is a xanthone produced by strains of *Aspergillus*, *Bipolaris* and *Emericella* which occur in cereals, cheese, nuts coffee, bread cereal-based products. It is a genotoxic teratogen, mutagen, hepatogen and a possible human carcinogen. Animal studies using cattle suggested that symptoms of exposure to the toxin include loss of milk production, diarrhoea, renal lesions, hepatomas, and pulmonary tumours (Pubmed, 2017a; Blackmould, 2017b). Like aflatoxins and sterigmatocystin, their close derivative 5-methoxysterigmatocystin a genotoxic carcinogen also contains furo-furan ring which is thought responsible for their biological activity (Jaksic *et al.*, 2012). The mechanism of action (MOA) of sterigmatocystin is reported to be by binding to DNA, and uncoupling oxidative phosphorylation without causing swelling of the mitochondria. It inhibits acylCoAcholesterol acyltransferase (ACAT) with selectivity for ACAT-2 isoenzyme (www.toku-e.com).

Strains of the fungal saprophyte *Trichoderma spp.* (especially *T. viride* and *T. hazianum*) produce a class of antibiotic and toxic secondary metabolites generally called peptaibols. Alamethicin is member of this class of membrane acting toxins others are emodin, suzukacillin, and trichodermin. They are suspected to play roles in sick building syndromes which accompany water damage buildings (Table 1.). Alamethicins impair voltage-gated ion channels in the lipid bilayers of cells (www.caymanchem.com/alamethicin/cas27061-7B-5). Fringeli *et al.* (1979) suggested that its injury on affected tissues is as a result of binding and incorporating itself into cell membranes and creating pores in the matrix; which could lead to loss of radicals (Nasery *et al.*, 1979).

Penicillic acid is another important airborne mycotoxin produced by *A. flavus* and *P. roqueforti* through acid degradation of penicillins in water damaged environments. It is also known to contaminate corn and cereal grains. Penicillic acid exhibits a broad spectrum of activity including cytotoxic, mutagenic, genotoxic and tumorigenic carcinogenic activities. Its heart attacking activity has also been reported (Blackmould, 2017c). According to Kang and kim (2004) penicillic acid is strongly fungitoxic; it induced abnormal hyphal branching and apical swelling in *Phytophthora spp.* The mechanism of its injury on susceptible organisms is reported to involve inducing single stranded DNA breaks, inhibiting DNA synthesis in Chinese hamster ovary (CHO) cells, irreversibly inactivating GDP-mannose dehydrogenase and interrupting alginate biosynthesis (PubChem, 2017: www.scbt.com/penicillic-acid/AKR1A1...).

Alamethicin (Source: <http://www.mpbio.com/>.)

Nephrotoxic glycopeptides are another class of fungi-derived toxins. Some such as vancomycin has found medical importance as broad-spectrum antibiotic (<https://pubchem.ncbi.nlm.nih.gov/compound/vancomycin#section>). This class of substances however, could cause nephrotoxicity which usually results in increased serum creatinine levels. They are produced by *Penicillium aurantiogriseum* and have been implicated as one of the mycotoxins responsible for sick building syndrome (Table 1). Affected individuals may present headache, dizziness and taste disturbances (www.medweb.tulane.edu>doku.php>glycopeptides). Nephrotoxic glycopeptides are large molecules and are noted to have very complex structures. In Yugoslavian *P. aurantiogriseum* isolates from a village in which the idiopathic human Balkan nephropathy disease is hyper-endemic, showed a similar nephropathology in mice and were acutely cytotoxic, hence reinforcing a need to regarding this novel *Penicillium* nephrotoxin as a potential factor in human nephropathy (Yeullet *et al.*, 1988). Tests with bacteria showed that nephrotoxic glycopeptides inhibit the synthesis of cell walls and peptidoglycan synthesis by infringing the addition of new amino acid units to it. The mechanism of this action is reported to involve binding to acyl-D-alanyl-D-alanine terminals of growing peptide chain, inactivating the enzyme transpeptidase and thus prevents further elongation and cross linking of peptidoglycan matrix in bacteria (www.medweb.tulane.edu>doku.php>glycopeptides)*

Vancomycin (A nephrotoxic Antibiotic)
(Source:chem257.pbworks.com)

Beavericin (BEA) is a lipophilic hexadepsipeptide mycotoxin. It is produced by the entomophagous fungi *Beauveria basiana*, *F. semitectum*, *F. sablotirans* and *Fusarium spp.* Also, strains of *Polyporus spp.*, *Plaeceiomyces spp.* and *Isaria spp.* are known to produce the toxin alongside other toxins such as dextuxins, bassianolide, efrapeptins, tenellin and oosporecin. Beavericin is associated with the contamination of sorghum, corn, corn products and cereals. It has good insecticidal and herbicidal properties. It also exhibited antimicrobial, cytotoxic, and potent anticancer activities; and induced apoptosis in mammalian cancer lines due to inhibition of calcium ion (Ca^{2+}) flux in cells (Logrieco *et al.*, 1998; Sood *et al.*, 2017). Beavericin closely resembles the eniatin antibiotics, however, they seem to differ in target (Wang and Xu, 2012). Unlike penicillins and nephrotoxic glycopeptides (eniatin antibiotics) which are cell membrane or cell wall inhibitors, beavericin targets cell organelles, nucleus and enzymes (Sood *et al.*, 2017). This compound is a specific cholesterol acyltransferase inhibitor. It has been reported to be toxic to several human cell lines and to induce programmed cell death through cytolysis followed by internucleosomal DNA fragmentation (Logrieco *et al.*, 1998). Furthermore, Düringer *et al.* (2013) was of the opinion that BEA formed ionophores in membranes, disturbed intracellular calcium ion homeostasis, disrupts cellular metabolism and induces apoptosis. Besides toxicity to mammalian cells, beavericin due to its antimicrobial, insecticidal and herbicidal properties is considered a potential and novel agent for pesticides and medicines and hence requires further scientific studies (Wang and Xu, 2012).

Beavericin (Source: www.chemSpider.com)

Management of mycotoxicosis in humans

Though contamination of agricultural products with fungi-derived toxic metabolites is not entirely avoidable, good agronomic and farm practices are surely the starting point of their control (Coulombe, 1993). Surveys suggest lower incidence of mycotoxin contamination of agro-products and mycotoxicoses occurred in developed economies of the world than the developing nations

(Shephard, 2008; Darwish *et al.*, 2010). According to Shephard (2008) good agronomic, manufacturing and marketing practices as well as strict legislative controls in Europe and America are seen as the reasons behind this development.

Management of mycotoxins and mycotoxicosis especially in the African context however, will require holistic approach, beginning from the farm through the value chain lines and many of the control approaches may be used in integrated systems (Enyiukwu *et al.*, 2014). Management methods involving field and store hygiene, good value chain protocols and use of plant-derived extracts for the reduction of mycotoxin contamination on agro-products and their attendant health burden of consumers have been reviewed by Enyiukwu *et al.* (2014). Early identification and segregation of contaminated kernels of corn, peanuts and other grains is a welcome strategy. This for example could be done by use of electronic equipment (e-equipment) that identify and reject grains that exhibit fluorescence due to aflatoxins (Coulunba, 1993). In feed processing factories, ammoniation of cotton seed and cotton; as well as addition of binders such as sodium calcium aluminosilicate (anticaking agent) has been found to significantly reduce the bioavailability of AF_1 (Coulunba, 1993; Enyiukwu *et al.*, 2014). Such measures could contribute to reducing to a large extent biological magnification of these noxious toxins in the food chain (Enyiukwu, 2002).

In endemic areas proper physical exercising (or exposure to 'sauna') is imperative for offsetting the adverse effects of some mycotoxins in the body. It is reported that activities involving sweat induction reduces the burden of nephrotoxic carcinogenic OTA since it is excreted from sweat. And therefore may prove valuable in the management of chronic intermittent exposures. Also, nutritional fortification, amendment and improvement of cereals and tubers and commonly consumed tropical staples during processing along value-chain lines with vitamins A, C, D and E and whey proteins are reported to significantly reduce the effects of mycotoxins on consumers by providing co-enzymes, reducing lipid peroxidation and acting as oxidative stress breakers. Korean ginseng, curcumin, chlorophyll, extracts of *Glyrrhizia glabra* and Licorice plant have also been shown to protect vulnerable body organs or to reasonably reverse and eliminate the biochemical changes that took place in mycotoxin-affected organs or tissues possibly by antioxidant activity, or strengthening some enzymatic pathways. Breeding for mycotoxins resistant cultivars and/or biotechnologically modifying commonly consumed staples such as orange flesh sweet potato, tubers and cereals with ability to produce significant amounts of vitamins A, C, D and E and certain flavonoids which will not be lost during processing will undoubtedly contribute to ameliorating mycotoxicosis in livestock and humans.

Other interventions involve chemotherapy using melatonin, glutathione and related antioxidants. In acute attacks, sequestering agents such as charcoal

Table 3: Modes of action (MOA) of some mycotoxins in biological and humans systems

Mycobiota	Mycotoxin Produced	Disease(s) caused	Symptoms	MOA	Sources
<i>Fusarium spp.</i>	Fumonisin	Akakabio-byo		Inhibits ceramide synthase and disrupts sphingolipid metabolism	Voss <i>et al.</i> (2007)
<i>F. sporotrichioides</i> , <i>F. Poae</i>	Trichothecenes (T-2, Diacetoxyscirpenol)	Alimentary aleukia (ATA)	toxic Oesophal pains, gastroenteritis, laryngitis, mucus membrane hyperaemia, leukopenia, skin inflammation and death	Bind to ribosomes and mitochondria, inhibits peptidyl transferase activity; protein and DNA synthesis. Immunosuppressive agents, decreasing immunoglobins and the formation of coagulation factors and hence opens up the host to opportunistic infections.	Zain (2011); Enyiukwu et al. <i>et al.</i> (2014); Anon (2017)
<i>Penicillium spp.</i>	Ochratoxin A	Balkan nephropathy	Tubule interstitial nephritis; kidney, pelvis, ureter, and urinary bladder tumors	Genotoxic interfering with gene transcription due to activation via co-oxidation through the prostaglandin synthase (P-H) route. Stimulates lipid peroxidation, inhibits enzymes involved in synthesis of phenylamine tRNA complex, and mitochondrial ATP production). Toxicity is thought to result from oxidative stress	Enyiukwu <i>et al.</i> (2014) Anon. (2017); Surai <i>et al.</i> (2010)
<i>Aspergillus spp.</i> , <i>Penicillium spp.</i>	Citreoviridin	Cardiac beriberi (Yellow rice disease)	Causes CNS depression, respiratory and cardiovascular failure, shortness of breath, and leg swelling, numbness of the hands and feet, confusion, trouble moving the legs, and pain, loss of appetite and constipation, dyspnea, gaspin, coma and death	In affected individuals, it inhibits protein synthesis	Nishie <i>et al.</i> (1988); Vieta <i>et al.</i> (1996); Voss <i>et al.</i> (2007) Ency. of Food Mycotoxins 2017

<i>Sclerotinia sclerotiorum</i>	Psoralens (Xanthotoxin, begapten)	Celery harvester's disease	Photodermatitis, vesicular and bullous lesions on human skin irradiated by natural sunlight, erythematous, edematous, and pigmentary lesions can be produced on human and animal skins	cell surface membrane alterations, probably disrupts the phosphorylation epidermal growth factor (EGF) (transmembrane glycoprotein) with tyrosine kinase activity	Laskin (1989), Horsfall (2012) www.accessdata.fda.gov/scripts/plantox/detail.cfm
<i>Claviceps purpurea</i>	Ergot alkaloids	Ergotism	Necrotic or gangrenous symptoms – colds, prickling sensation in limbs, muscular pains, intense heat in limbs, loss of limbs, acute convulsion or drowsiness, death or mental impairment	Binds to α -adrenoreceptors, inhibits β -adrenoreceptors, cause convulsions, gangrenous and serotonin syndromes. Vaso-constriction, uterine constriction and inhibition of prolactin secretion.	Horsfall (2012), Anon. (2017)
<i>Aspergillus flavus</i> , <i>A. Parasiticus</i>	Aflatoxin B ₁	Hepatocarcinoma (HCC) ((Fig. 6))	Pain in the upper right part of the belly, a lump or feeling of heaviness or swelling in the belly, loss of appetite and feelings of fullness, weight loss, weakness or deep fatigue, nausea, vomiting, yellow skin and eyes, dark urine and pale, chalky bowel movements, and fever	Inhibits activity of P ₅₃ tumour suppressor gene at codon 299	Kew <i>et al.</i> (2013). www.webmd.com/cancer/hepa...
<i>Aspergillus flavus</i> , <i>A. Parasiticus</i>	Aflatoxin B ₁	Kwashiorkor (Fig. 6)	Severe protein–energy malnutrition characterized by edema, irritability, ulcerating dermatoses, and an enlarged liver	Perturbs protein-calorie metabolism, promotes immune toxicity resulting from inhibition of T-cell and macrophages	Enyiukwu <i>et al.</i> (2014) en.wikipedia.org
<i>Fusarium verticillioides</i> , <i>Proliferatum</i>	F. Fumonisin B ₁	Neural tube defects (Fig. 6)	Defects of the brain, spine, or spinal cord. Usually in the first month of pregnancy	Inhibits cytokines and ceramide synthase in sphingolipid-dependent functions	Missmer <i>et al.</i> (2006); Riley <i>et al.</i> (2006)

<i>Fusarium verticilloides</i> , <i>Proliferatum</i>	F.	Fumonisin B ₁	Oesophageal tumors	Dysphagia, weight loss, bleeding and vomiting of blood, passing melana, low blood count, abdominal or chest pain, and hoarse voice.	Inhibits ability of cells to proliferate (Pitt, 2000), induces loss of electrolyte in affected cells	Enyiukwu <i>et al.</i> (2014). www.medicinenet.com/esophageal_cancer/...
<i>Phoma sorghina</i> , <i>Alternaria spp.</i>		*Tenuazonic moliniformin	acid, Onyala, oesophageal cancer (Fig. 6)	Hemorrhagic lesions on oral, nasal, and subconjunctival mucous membranes, skin, and soles of feet, hematuria, melena and menorrhagi, chronic thrombocytopenia.	Inhibits fibroblasts, cell proliferation and protein synthesis	Rabbie <i>et al.</i> , (1975); Zhou and Quang, 2008; Blackmold, 2017) en.wikipedia.org
<i>Aspergillus spp.</i>		Aflatoxin B ₁	Reye's syndrome	Encephalopathy, visceral deterioration, kidney/liver enlargement	Inhibition of protein synthesis	Ryan <i>et al.</i> (1979); Zain (2011); Sura <i>et al.</i> (2010).
<i>Stachybotrys atra</i>		Roridin E, Verrucaric acid, satratoxin H	Sick building syndrome	Headache, eye, nose and throat irritation, fatigue, dizziness and nausea.	Inhibition of protein synthesis	Volk and Zitomer (2002)
<i>A. fumigatus</i> ; <i>C. Albicans</i>	C.	Gliotoxins	Participates in host tissue maceration during invasive mycoses	NA	Inhibits macrophages, T-cells activation and proliferation	Voss <i>et al.</i> (2007)
<i>P. .palutin</i> , <i>custosum</i> , <i>Expansum</i>	P. P.	Palutin,	Kidney damage	gastrointestinal symptoms like gastric ulcers, intestinal hemorrhages, lesions in the duodenum and alteration of intestinal barrier function	Palutin binds to sulfhydryl groups in proteins and amino acids in the plasma membrane	Mycotoxin Info, 2017; Surai <i>et al.</i> (2010)
<i>P. cyclopium</i> , <i>A. tamari</i> , <i>A. flavus</i> , <i>P. Viricatum</i>	A.	Cyclopiazonic acid (CPA)	Liver necrosis; nerve cells damage	Necrosis of liver, gastrointestinal tissue, kidneys and skeletal muscles	Impairs calcium metabolism, damages to neural system, inhibits cellular ATPase in the endoplasmic reticulum (ER), and impairs neural systems.	Mycotoxin Info, 2017

<i>F. culmorum</i> , <i>graminaerum</i>	<i>F.</i> Deoxynivalenol (DON)	Mitochondrial dysfunction	gastroenteritis impaired gut integrity, diarrhea; intestinal bleeding; anorexia; increased liver size, reduced weight gain and severe immunosuppression	Immunodysfunction and suppression of rapidly growing cells.	Mycotoxin Info (2017)
<i>F.graminaerum</i> , <i>culmorum</i> , <i>Euiseti</i> , <i>verticillioides</i>	<i>F.</i> Zearalinone (ZEN)	Estrogen agonists	Early puberty in girls, sexual disorders, alteration in development of sexual apparatus	Influences transcription in cellular nuclei; increases membrane permeability of protein and promotes synthesis of proteins , RNA and DNA by the uterus	Anon. (2017)

*Suspected mycotoxin. NA = Not available

A (Kwashiorkor)

B (Neural Tube Defect)

C (Liver with HCC)

D (bleeding heart due to onychomycosis)

Figure 6: Some serious diseases in which mycotoxins have been implicated in humans around the world

Source: en.wikipedia.org

which bind, absorb or adsorb the fungi-derived toxins may be administered by health professionals in standard clinics and hospitals (Hope, 2013). So far however, there is no cure for mycotoxicosis. Antibiotics and drugs have little effects on the toxins. Blackmold (2017) holds the opinion that the best management approach is to avoid or stop the exposure to mycotoxins especially indoors through:

- Proper home hygiene. Fix leaking roof as soon as possible to avoid saprophytes from colonizing your roof racks and ceiling. Ensure you also repaint kitchen and bathroom walls regularly to avoid build up of mycotoxigenic saprophytes on them. For this reason also wash bathtubs regularly with sodium hypochlorite (bleach).
- Do not store agro-produce for too long before consuming them especially fruits, nuts such as peas and vegetables except where refrigerated.
- If you perceive musty odours in your home or office quickly report this to appropriate environmental professional to screen your house.
- If you feel uncomfortable after ingesting a particular agro-produce, consult a clinicians to examine you and possibly samples of the ingested food material for signs and symptoms of mycotoxins or toxic moulds.
- Service your air conditioners regularly as these could be havens for *Aspergillus spp.* and other toxic moulds.

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