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Mycotoxins and Mycotoxicoses, Detection and Analysis: A Review in Retrospect

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ABSTRACT

Mycotoxins are recognized as toxic compounds of great concern in the context of human health and economy. Mycotoxins are toxic chemical products formed as secondary metabolites by some fungi that readily colonise crops in the field or after harvest. The toxicity syndrome resulting from the intake of such contaminated material by animal and manis termed Mycotoxicosis.These compounds pose a potential threat to human and animal health through ingestion of food products prepared from these commodities.Mycotoxicoses affect various systems of the body according to the target organs of the mycotoxin. This review revealed the major mycotoxins of fungal origin and their mycotoxicoses. The study also reviewed the history of mycotoxin, methods of mycotoxin detection, analysis and the health implications of consuming mycotoxin-contaminated foods/products. In most developing countries, majority are ignorant of the inherent dangers of consuming mouldy produce or food contaminated with fungi and moulds with possible contamination by mycotoxigenic fungi. In view of this, there is need for general and public education to sensitise the people on the health hazards posed by mycotoxins. Proper washing and cooking practices of food commodities, good agricultural practices, fast and effective analyses and detection, good produce handling and storage are some of the control/regulatory measures that should be encouraged, as to assist in mitigating the side effects of mycotoxins in food and health particularly in the tropical and sub-tropical countries and in African where there is enabling environment that promotes fungal growth.

Keywords: Mycotoxin, Mycotoxicosis, Detection, Analysis, Health impact, Moulds.

Introduction

Mycotoxins are toxic secondary metabolites produced by toxigenic fungi that infest food and feed materials during pre-and post-harvest periods (Alshannaq, 2017). Mycotoxicology is the branch of mycology that focuses on analyzing and finding out these secondary metabolites produced by fungi, known as mycotoxins. The most commonly encountered dietary mycotoxins with worldwide occurrence are Aflatoxins, Ochratoxins, Zearalenone, Fumonisins, Trichothecenes, Patulin and Ergot Alkaloids, produced by the fungal genera *Aspergillus, Penicillium, Fusarium and Clavicep* (Pinotti *et al*., 2016). These are notably deleterious to animals and human beings. Most of the fungi can secrete more than a single mycotoxin, but a given mycotoxin can also be produced by some species that belong to distinct genera. There are certain mycotoxins which have demonstrated acute toxic effects, particularly when consumed at high concentrations, whereas others have toxic effects only after a long-term exposure to lower doses.Effects of chronic exposure include aggravation of disease pathogenesis in experimental animals and humans, reduced animal productivity, and impaired animal nutrition (Kibugu *et al.*, 2009). Mycotoxins can also be teratogenic, carcinogenic, mutagenic, estrogenic, nephrotoxic, hepatotoxic and immunosuppressive in humans and animals (Williams *et al*., 2004). Mycotoxicoses are the animal diseases caused by mycotoxins (Forgacs and Carll, 1962). While all mycotoxins are of fungal origin, not all toxic compounds produced by fungi are called mycotoxins. The target and the concentration of the metabolite are both important. Fungal products that are mainly toxic to bacteria (such as penicillin) are usually called antibiotics. The majority of mycotoxicoses, result from eating contaminated foods. Skin contact with mold- infested substrates and inhalation of spore-borne toxins are also important sources of exposure (El-Nezami *et al.*, 2002). Except for supportive therapy (e.g., diet,

hydration), there are almost no treatments for mycotoxin exposure, although Fink-Gremmels (1999), described a few methods for veterinary management of mycotoxicoses, and there is some evidence that some strains of *Lactobacillus* effectively bind dietary mycotoxins (El-Nezami *et al*., 1998). Oltipraz, a drug originally used to treat Schistosomiasis, has been tested in Chinese populations environmentally exposed to aflatoxin (Henry *et al.*, 2002). Some fungi are pathogenic to man and are disease causing organisms in humans, some of the diseases caused by them could be fatal if not treated. Such diseases include Aspergillosis Candidiasis, Coccidioidomycosis, Cryptococcosis, Histoplasmosis, Mycetomas, and Paracoccidioidomycosis. Furthermore, immune-compromised people are particularly susceptible to disease by genera such as *Aspergillus, Candida, Cryptoccocus* (Hube, 2004; Brakhage, 2005), *Histoplasma* and *Pneumocystis* (Kauffman, 2007). Many allergic reactions and allergies are caused by fungal spores and fungi from different taxonomic groups (Simon-Nobbe *et al*., 2008).

A major part of the universal population in all over the world depends on cereals as a main food, and therefore, there is a high risk of mycotoxin. Moreover, mycotoxin contamination can have a large health, financial and social impact, specifically when the incidence of mycotoxin in food commodities is beyond the regulation limits set up by national and transnational establishments. There are various techniques for mycotoxin analysis. These include mainly ELISA test, the lateral flow test, the screening cards, and immunoaffinity columns (Pandy and Arade, 2016). Lately, the emergence of nanotechnology in mycotoxicology is still in its primary stage. Currently, research has been focused on the development of new nanomaterials to inhibit pathogenic fungi and mycotoxins [Abd-Elsalam *et al.*, 2017).

History

The term mycotoxin was coined in 1962 in the aftermath of an unusual veterinary crisis near London, England, during which approximately 100,000 turkey poults died (Blout, 1961). When this mysterious turkey X disease was linked to a peanut (groundnut) meal contaminated with secondary metabolites from *Aspergillus flavus* (aflatoxins), it sensitized scientists to the possibility that other occult mold metabolites might be deadly (Forgacs, 1962).Soon, the mycotoxin rubric was extended to include a number of previously known fungal toxins (e.g., the ergot alkaloids), some compounds that had originally been isolated as antibiotics (e.g., patulin), and a number of new secondary metabolites revealed in screens targeted at mycotoxin discovery (e.g., Ochratoxin A). The period between 1960 and 1975 has been termed the **Mycotoxin gold rush** (Maggon, 1977), because so many scientists joined the well-funded search for these toxigenic agents. Depending on the definition used, and recognizing that most fungal toxins occur in families of chemically related metabolites, some 300 to 400 compounds are now recognized as mycotoxins, of which approximately a dozen groups regularly receive attention as threats to human and animal health (Cole, 1986). Molds (i.e., microfungi) make mycotoxins; mushrooms, other macroscopic fungi make mushroom poisons. The distinction between a mycotoxin and a mushroom poison is based not only on the size of the producing fungus, but also on human intention.

Mycotoxin exposure is almost always accidental. In contrast, with the exception of the victims of a few mycologically accomplished murderers, mushroom poisons are usually ingested by amateur mushroom hunters who have collected, cooked, and eaten what was misidentified as a delectable species (Moss, 1996).

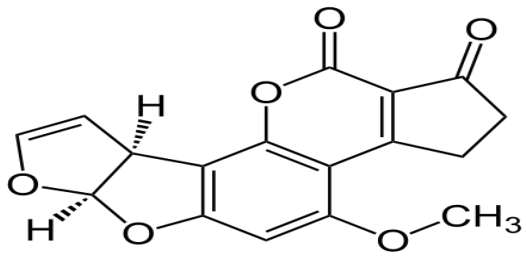
Major Mycotoxins and Mycotoxicoses

Mycotoxins are made by fungi and are toxic to vertebrates and other animal groups in low concentrations. Other low-molecular-weight fungal metabolites such as ethanol that are toxic only in high concentrations are not considered mycotoxins (Bennett, 1987). Mycotoxins are not only hard to define; but also challenging to classify due to their diverse chemical structures and biosynthetic origins, their myriad biological effects, and their production by a wide number of different fungal species. Clinicians often arrange them by the organ they affect. Thus, mycotoxins can be classified as hepatotoxins, nephrotoxins, neurotoxins, immunotoxins, and so forth. Cell biologists put them into generic groups such as teratogens, mutagens, carcinogens, and allergens. Organic chemists have attempted to classify them by their chemical structures (e.g., lactones, coumarins); biochemists according to their biosynthetic origins (polyketides, amino acid-derived, etc.); physicians by the illnesses they cause (e.g., St. Anthony's fire, stachybotryotoxicosis), and mycologists by the fungi that produce them (e.g., *Aspergillus* toxins, *Penicillium* toxins). None of these classifications is entirely satisfactory. Moreover, as our anthropomorphic focus shifts attention, the same compound may get placed in different cognitive cubbyholes. Aflatoxin, for example, is a hepatotoxic, mutagenic, carcinogenic, difuran-containing, polyketide-derived *Aspergillus* toxin. Of approximately 500 recognized mycotoxins, only a small variety is documented to motive mycotoxicoses in human and animals. The organs such as liver and kidneys are mostly affected as these are the ones in which mycotoxins are metabolized; however, they may also affect different systems of the body. Historically, acute mycotoxicoses have been common even in mild temperature zones, causing epidemics that devastated entire regions, from time to time influencing the direction of human documents (Bennett and Klich, 2003). Mycotoxicoses occur commonly in tropical regions due to high humidity and temperature required for fungal growth and secretion of mycotoxin (Peraica *et al*., 2016).

Aflatoxin

Aflatoxins are chemical metabolites and mycotoxins produced by *Aspergillus* species of fungi, like *A. flavus* and *A. parasiticus* (Adejumo & Adejoro, 2014; Ashiq, 2015; Martins*et al*., 2001; Adeyeye, 2016). The four major aflatoxins are called B1, B2, G1, and G2 based on their fluorescence under UV light (blue or green) and relative chromatographic mobility during thin-layer chromatography. Aflatoxin B1 is the most potent natural carcinogen known (Squire, 1981) and is usually the major aflatoxin produced by toxigenic strains. It is also the best studied: in a large percentage of the papers published, Aflatoxins are known as the most important fungal metabolites of a direct health hazard to humans. *Aspergillus flavus* is widely distributed in soil, air, and rotten plant residues. Aflatoxin production and contamination can take place in the field, in transit, or in storage. However, most infection takes place in the field while aflatoxin production takes place at any point under favourable conditions (Ashiq, 2015; Yin *et al*., 2008; Martins *et al*., 2001). Aflatoxins among all the mycotoxins were linked to human diseases such as liver cancer, Reye's syndrome, Indian childhood cirrhosis, chronic gastritis and kwashiorkor in many parts of the world, particularly in African and Asian countries where conditions for growth and storage encouraged fungi and mycotoxin production (Jelinek *et al.*, 1989; Palmgren & Hayes, 1987; Adeyeye, 2016). Kenya recorded a serious and largest and most acute out- breaks of aflatoxicosis ever documented (CAST, 2003) in

2004, with 125 dead cases and over 317 others hospitalized for consuming aflatoxin-contaminated maize (Adeyeye, 2016). The nature of the outbreak was due to the consumption of maize contaminated with extremely toxic AFB1 (Aflatoxin B1). The case-control studies carried out by Lewis *et al*., (2005) showed that the affected people in the area consumed home-grown maize stored under humid conditions. During the outbreak, AFB1 individual daily exposure was 50mg/day (Probst *et al*., 2007). The diseases caused by aflatoxin consumption are loosely called Aflatoxicoses. Acute aflatoxicosis results in death; chronic aflatoxicosis results in cancer, immune suppression, and other "slow" pathological conditions (Hsieh, 1988). The liver is the primary target organ, with liver damage occurring when poultry, fish, rodents, and nonhuman primates are fed aflatoxin B1. Cytochrome P450 enzymes convert aflatoxins to the reactive 8,9-epoxide form (also referred to as aflatoxin-2,3 epoxide in the older literature), which is capable of binding to both DNA andproteins (Eaton and Groopman, 1994).

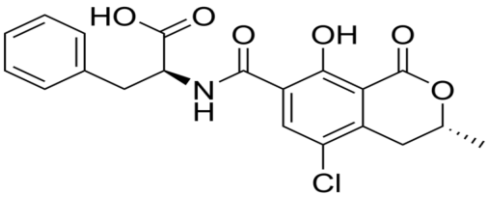


Structure of Aflatoxin B_1

Ochratoxins

Ochratoxin A (OTA) was the first mycotoxic compound isolated from *Aspergillus ochraceous*, and later it was found in other *Aspergillus* and *Penicillium* species such as *Penicillium verucosum*. There are several OTA analogues, ochratoxins B, C, and alkyl esters of ochratoxins that have similar structure but are less toxic. OTA is the main contaminant of cereals (corn, barley, wheat) and to some extent beans (coffee, soy, and cocoa). The levels of contamination are typically less than 200 ug/kg (Solfrizzo *et al.*, 2014). OTA is easily absorbed through the gastrointestinal tract mainly in the duodenum and jejunum based on animal studies (Heyndrick *et al*., 2015). There are no studies on skin or inhalational absorption of OTA. When absorbed, OTA has a high binding affinity for plasma protein. OTA was found in decreasing order of concentrations in kidney, liver, fat, and muscle tissues (Solfrizzo *et al.*, 2014). Excretion is mainly via renal elimination (Rushing and Selim, 2019). The toxicity of OTA involves several mechanisms. OTA inhibits protein synthesis by competing with the phenylalanine aminoacylation reaction catalyzed by Phe-tRNA synthase (Turner *et al.*, 2015). This results in inhibition of protein as well as DNA and RNA synthesis. OTA also disrupts hepatic microsomal calcium homeostasis by impairing the endoplasmic reticulum membrane via lipid peroxidation (Escrivá *et al.*, 2017). Ochratoxin A is the causative agent of kidney diseases (de-generation of proximal tubule cells resulting in interstitial nephritis and hyalinization of glomeruli) in pigs generally referred to as porcine nephropathy (Shephard, 2009**)**. OTA is the major ochratoxin component and is the most toxic among the analogues. However, it has been estimated that an infant could eat up to 10 kg of food contaminated with 20 ppb without significant adverse health effects (Shephard, 2009). OTA can be analyzed using TLC, HPLC, and ELISA. However, the possibility of cross-reactions cannot be fully ruled out. Other techniques should be used to confirm the levels of OTA (Malir *et al*., 2016). The tolerance levels for OTA have been

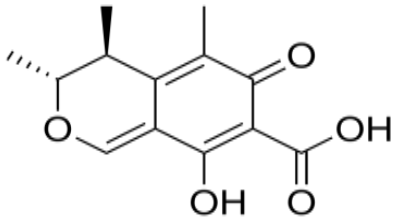
suggested as 1 ug/kg for infant foods and 5 ug/kg for cereals (Degen *et al*., 2018). Both the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO) Joint Expert Committee recommends a provisional tolerable weekly intake of 100 microgram/kg body weight of OTA (Soto *et al.,* 2015).



Structure of Ochratoxin

Citrinin

Citrinin was first isolated from *Penicillium citrinum* prior to World War II (Hetherington and Raistrick, 1931); subsequently, it was identified in over a dozen species of *Penicillium* and several species of *Aspergillus* (e.g., *Aspergillus terreus* and *Aspergillus niveus*), including certain strains of *Penicillium camemberti* (used to produce cheese) and *Aspergillus oryzae* (used to produce sake,miso, and soy sauce) (Manabe, 2001). More recently, citrinin has also been isolated from *Monascus ruber* and *Monascus purpureus*, industrial species used to produce red pigments (Blanc *et al*., 1995). Citrinin has been associated with yellow rice disease in Japan (Blanc *et al.,* 1971). It has also been implicated as a contributor to porcine nephropathy. Citrinin acts as a nephrotoxin in all animal species tested, but its acute toxicity varies in different species (Carlton, 1977).

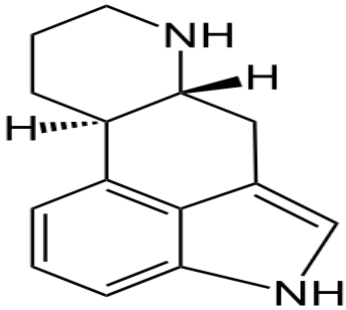


Structure of Citrinin

Ergot Alkaloids

The human disease acquired by eating cereals infected with ergot sclerotia, usually in the form of bread made from contaminated flour, is called ergotism or St. Anthony's fire. Two forms of ergotism are usually recognized, gangrenous and convulsive. The gangrenous form affects the blood supply to the extremities, while convulsive ergotism affects the central nervous system (Wu, (2013)). Ergotism is caused by *Clavicep pupurue*. Human ergotism was common in Europe in the middle Ages. For example, a three-volume work entitled Handbook of Geographical and Historical Pathology published in London by August Hirch between 1883 and 1886 recorded 132 epidemicsof European ergotism between the 6th and 18th centuries (Haller, 1993). Matossian (1981) has suggested that the "slow nervous fever" described by the 18th century English physician Jon Huxham may be another example of human ergotism. Slow nervous fever usually occurred in the summer and fall after a severe winter; Huxham suspected "bad food" as the source of the tror uble. Matossian (1989) has also postulated that ergot alkaloids may have had a strong influence on fertility trends in England and other European countries during the 17th and 18th centuries. Modern methods of grain cleaning have almost eliminated ergotism as a human disease.

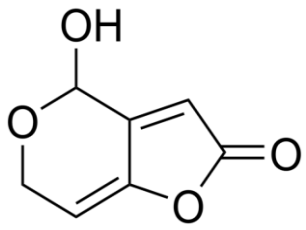
Nevertheless, purported ergot poisoning occurred in the French town of Pont-St.-Esprit in 1951 and was the subject of a full-length book treatment, The Day of St. Anthony's Fire (Fuler, 1968). Ergotism is still an important veterinarian problem. The principal animals at risk are cattle, sheep, pigs, and chickens. Clinical symptoms of ergotism in animals include gangrene, abortion, convulsions, suppression of lactation, hypersensitivity, and ataxia (Lorenz, 1979). Sometimes the line between toxin and drug is defined with the shift of a decimal point or a change in a small chemical moiety. The ergot alkaloids are a case in point. Their myriad actions have long engaged the interest of physicians and pharmacologists. Several ergot alkaloids induce smooth muscle contractions. For centuries it had been observed that grazing on grass infected with ergot caused abortion in pregnant farm animals, so it is not surprising that midwives and others adopted ergot as a folk medicine, using it as both an abortifacient and a drug to accelerate to uterine contractions for women in labor (Riddle, 1997).



Structure of Ergot Alkaloids

Patulin

Patulin is a polyketide lactone, produced by *Penicillium, Aspergillus*, and other mold species that grow on fruits such as apples, pears, and grapes. The LD50 of patulin ranges from 15 to 25 mg/kg and varies with animal species and route of exposure. Toxicity includes congestion and edema of pulmonary, hepatic, and intestinal blood vessels and tissues. Sarcomas were observed when large doses of patulin were injected into animals. As a result, there have been concerns over the possibility of carcinogenicity to children and adults who drink large amounts of fruit juice, especially apple juice, for many years (FDA, 2000). WHO Codex Alimentarius Commission recommends a limit of 50 ug/kg of patulin in apple juice and cider (International Agency for Research of Cancer 1984). Patulin is degraded by sulfur dioxide or sulfide, a common food preservative for dry fruits and juices.



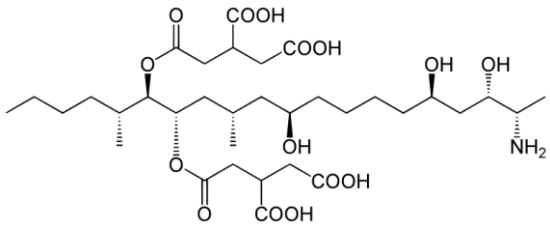
Structure of Patulin

Fumonisins

Fumonisins are group of 15 mycotoxins produced by Fusarium molds (mostly *Fusarium verticilloides* and *Fusarium moniliforme*) (IARC, 1993). The most frequently found member of this group is fumonisin B1 (FB1). It

interferes with the metabolism of sphingolipids (Voss *et al.*, 2007). In a single FB1-caused acute intoxication, only gastrointestinal symptoms (diarrhea, vomiting, e.t.c.) were reported. It has been implicated in sporadic animal diseases (Thiel *et al.*, 1992), especially equine leucoencephalomalacia (ELEM). They are common contaminants of corn and maize. Although they are not as potent as aflatoxins, their concentrations frequently reach hundreds of parts per million up to 300 mg/kg of maize.

There are more than 100 secondary metabolites produced by Fusarium species, a number of which can critically affect human and animal health (Bentley and Bennett, 1999). It has been reported severally epidemics of head blight and maize ear rot of Fusarium which are common in Asia, Africa and South America where cereals are predominantly grown. Chronic exposure to FB1 is connected to a high rate of neural tube defects (brain and spinal cord malformations). Several like Kashin Beck syndrome in the USSR, China and VietNam; Mseleni joint disease in southern Africa; endemic familial arthritis in India; alimentary toxic aleukia in the USSR; and oesophageal cancer in southern Africa were linked to Fusarium toxins. Most of these mycotoxins produced by moulds that are of importance to human health are produced under poor storage conditions (Desjardins and Proctor, 2007; Adeyeye, 2016).

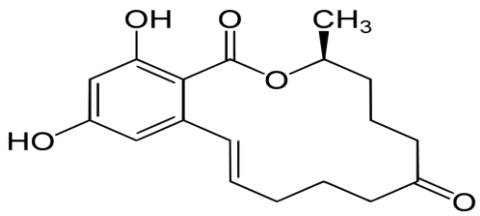


Structure of Fumonisin

Zearalenone

Zearalenone is a *Fusarium* metabolite with potent estrogenic activity; hence, in addition to being called (probably erroneously) a mycotoxin, it also has been labeled a phytoestrogen, a mycoestrogen, and a growth promotant. Zearalenone (ZEA) is produced by some Fusarium species (El-Nezami *et al*., 1998).

This is a myco toxin with low acute toxicity in experimental animals and there is no report of acute toxicity in humans. Symptoms of chronic exposure are caused by interactions of ZEA and its metabolites with estrogen receptors. Premature telarche (development of breasts in young girls) with precocious pseudopuberty has been seen in young girls in Costa Rica exposed to residues of ZEA in meat (used as a growth-promoting compound) (Solfrizzo *et al*., 2011). Premature telarche in girls and male gynecomastia were reported in Hungarian children consuming naturally ZEA- contaminated "healthy" food (El-Nezami *et al*., 2002)



Structure of Zearalenone

Table 1. Physiological Aspects of Mycotoxin Exposure

S/N	Mycotoxins	Strain, Main Producer	Occurrence	Symptoms, Signs, Toxicity (Mycotoxicosis)	Source
1.	Ochratoxin A	Aspergillus carbonarius, Penicillium verrucosum, Pichia verrucosum	Cereals, coffee, cocoa, wine, dried fruits, beer, grape juice, malt, beer, bread, bakery products, spices, beans, liver, kidney and blood of farm animals, food commodities of animal origin	Nephrotoxic, Nephrocarcinogenic, immunosuppressive, carcinogenic, teratogenic, the most toxic member of ochratoxins	Marin *et al*., 2013
2.	Aflatoxins	Aspergillus flavus, A. parasiticus, Aspergillus nomius	Maize, peanuts, tree nuts, dried fruits, milk, cereals, rice	Carcinogenicity, aflatoxicoses, immune suppression, hepatocarcinogens in animals and humans	Peraica *et al*., 1999
3.	Fumonisins (B1 and B2)	Fusarium moniliforme, F.proliferatu, F.verticillioides, Aspergillus niger	Maize and maize products	Cancer, neural tube defects, acute food-borne disease, cardiovascular effects	Zain, 2011
4.	Zearalenone	Fusarium graminearum, F. culmorum, F. heterosporum	Corn, wheat, barley, oats, sorghum, vegetable oil, silage, straw	Genotoxic, toxic to reproduction system, oestrogenic effects, haematological effects, haemolysis incidence in vitro, oxidative stress, endocrine disruptors	Capcarova *et al., 2014*
5.	T-2 toxin	Fusarium sporotrichioides,	Oat, barley, maize	Inhibition of RNA and DNA synthesis, oxidative stress, immunosuppressive and	Maruniakova *et al.*, 2014

		F. poae		cytotoxic effect, inhibition of steroidogenesis and proliferation in porcine granulosa cells, ATA	
6.	Deoxynivalenol	Fusarium culmorum, F.graminearum	Wheat, grains, maize, barley, silage	Mutagenic and carcinogenic properties, decreased nutritional efficiency	Rotter *et al.*, 1996
7.	Patulin	Penicillium, Aspergillus, Byssochlamys, Eupenicillium	Apple, apple juice and products	Inhibitory activity of many enzymes, alteration of immunity, macrophage function, gastrointestinal symptoms, kidney damage, changes in femoral bone structure, changes in sperm motility	Schneidgenova *et al*., 2014

Source: Marcela *et al*., (2016)

Methods of Detecting and Analysing Mycotoxins

There are many reasons for the presence or production of mycotoxins in our daily food or animal feed, and in many scenarios humans cannot avoid them (Peraica *et al*., 1999). With the development of detection technology, more than 300 mycotoxins have been isolated and studied for their chemical properties (Hao *et al.*, 2018).

Among the many mycotoxins studied, Aflatoxin, Ochratoxin, Zearalenone, Deoxynivalenol, and Fumonisin are the most toxic, having long plagued humanity and had enormous impacts on human health and the agricultural economy (Hussein and Brasel, 2001).

Among them, Aflatoxin B1 (AFB1) is the one that has been proven to be the most carcinogenic, being targeted to the liver and having genotoxicity (Murphy *et al*., 2006), while Ochratoxin A is a nephrotoxin and renal cancer compound, Zearalenone produces toxicity that attacks an animal's reproductive system (Yang *et al*., 2018).

Recently, research into the harm to human or animal health caused by mycotoxins has become a high-profile topic (Meena *et al*., 2017).

In determining mycotoxins, the samples need to be pre-treated with either of the following pre-treatment methods: Liquid-Liquid Extraction (LLE), Superficial Fluid Extraction (SFE), Solid Phase Extraction (SPE); afterwhich the sample can then be separated with any of the following analytical/separation methods; Thin Layer Chromatography (TLC), High Performance Liquid Chromatography (HPLC), Gas Chromatography (GC), Enzyme-Linked Immuno Sorbent Assay (ELISA), Near-Infrared Spectroscopy (NIR), and Liquid Chromatography-Mass Spectrometry (LC-MS) (Nacher-Mestre, 2013).

Pre-Treatment Methods

Liquid–Liquid Extraction (LLE)

This method involves exploiting the different solubility of the toxin in aqueous phase and in immiscible organic phase, to extract the compound into one solvent leaving the rest of the matrix in the other. Thus, solvents such as hexane and cyclo-hexane are used to remove non-polar contaminants, e.g. lipids and cholesterol. The procedure is effective for several toxins and works well in small-scale preparations (Bauer and Gareis, 1987). However, it is time consuming, and is dependent on which matrix is being used, and which compounds are been determined. Disadvantages lie with possible loss of sample by adsorption onto the glassware.

Supercritical Fluid Extraction (SFE)

This method uses a super critical fluid, such as CO_2 to extract the required compound from the matrix. This works well due to the high solvating power and density of the solvating liquid. Supercritical fluid chromatography on fused silica capillary columns have been applied previously for separating toxins (Young and Games, 1992), but it is not a successful technique owing to the problems related to SFE (Engelhardt and Hass, 1993). This technique is not suitable for routine analysis due to high costs and the need for specialised equipment (Holcomb *et al.,* 1996).

Solid Phase Extraction (SPE)

The basic principle of SPE technology is a variation of chromatographic techniques based around small disposable cartridges packed with silica gel, or bonded phases which are in the stationary phase. The sample is loaded in one solvent, generally under reduced pressure, rinsed, where most of the contaminants are removed, and eluted in another solvent (EMAN, 2003). These cartridges have a high capacity for binding of small molecules. The SPE systems have many advantages such as using a considerably less solvent, and their fastness in operation. Also, they can be used in pre-concentration of the samples for better detection.

Separation Techniques

Thin layer chromatography (TLC)

Thin-layer chromatography (TLC) is a technique that can be used for the separation, purity assessment, and identification of organic compounds (Betina, 1993).The most popular method used for mycotoxins analysis is TLC, which offers the ability to screen large numbers of samples economically. There are good reviews available on the applications of TLC for mycotoxin analysis (Holcomb *et al*., 1992). The use of TLC analysis for mycotoxins is still popular for both quantitative and semi-quantitative purposes. This is due to its high through- put of samples, low operating cost and ease of identification of target compounds. There have been uses of silica gel columns for purification of mycotoxins, example, ELISA for Aflatoxins in corn and peanuts. Silica gel layer seems to be one of the common layers used for TLC (Richardson *et al.,* 1985).

High performance liquid chromatography (HPLC)

This is a quantitative technique that is suited for online cleanup of sample extract and could be combined with different detectors (Li *et al.,* 2001). Most Modern analysis of mycotoxins relies heavily on HPLC employing

various adsorbents depending on the physical and chemical structure of the mycotoxin. Most of the protocols used for HPLC detection of mycotoxins are very similar. The most commonly found detection methods are UV or fluorescence detectors, which rely on the presence of a chromophore in the molecules (Razzazi-Fazeli *et al*., 2002). A number of toxins already have natural fluorescence (e.g. Ochratoxin A, Aflatoxin and Citrinin) and can be detected directly in HPLC; though some mycotoxins, such as Fuminisin, lack chromophore.

Gas chromatography (GC)

Gas Chromatography is regularly used to identify and quantify the presence of mycotoxins in food samples (Scott, 1989). Most mycotoxins are not volatile and therefore have to be derivatised for analysis using GC. Several techniques have been developed for the derivatisation of mycotoxins. Chemical reactions such as silylation or polyfluoroacylation are employed in order to obtain a volatile material. As with other mycotoxins, Ochratoxin A cannot be directly determined by GC as it is not volatile (Scott, 1981).

Capillary electrophoresis (CE)

The individual detection ofclosely related toxins requires sophisticated separation technique in addition to high sensitivity. The effective separation of components can be based upon charge and mass dependent migration in an electrical field. The fast separations can be accomplished by capillary electrophoresis in aqueous buffer solutions, excluding the need for organic solvents (Wilkes *et al*., 1998).

Enzyme-Linked Imuno Sorbent Assay (ELISA)

Other separation techniques exist which are capable of running alongside or in place of chromatographic methods. Among these is ELISA which became very popular recently due to their relatively low cost and easy application (Goryacheva *et al.,* 2007b). Commercially available ELISA kits for detection of mycotoxins are normally based on a competitive assay form that uses either a primary antibody specific for the target molecule or a conjugate of an enzyme and the required target. The complex formed will then interact with a chromogenic substrate to give a measurable result. They can be portable, rapid and are highly specific as well as simple to use (Goryacheva *et al.,* 2007a).

Health Implications of Consuming Mycotoxins-Contaminated Foods

Mycotoxins are metabolites secreted by fungi growing on organic substrates of diverse nature which could produce fatal or side effects when ingested or consumed by humans or animals. Mycotoxins are chemical metabolites of great economic importance and health implication to both animals and humans. Aflatoxin ingestion has been implicated in hepatocellular carcinoma (liver cancer) (Adejumo and Adejoro, 2014, Williams *et al*., 2004), reported to be the third-leading cause of cancer worldwide according to WHO (2008), with about 600,000 fresh cases each year. Adejumo and Adejoro, 2014, Hussein and Brussel, 2001 and Zain, 2011 have reported that aflatoxin contamination reduces feed intake, increase liver and kidney weights of farm animals, as well as induce immune-suppression and hepatitis as well as high mortality in farm animals. Mycotoxins have been implicated in several countries for the outbreak of diseases. In India and Kenya mycotoxins have been implicated in the outbreak of aflatoxic hepatitis, in the outbreak of enteric ergotism in India; in the outbreak of vascular ergotism in Ethiopia;

and in the outbreak of deoxynivalenol mycotoxicosis in India and China. The out- breaks have been linked to consumption of cereals that were grown and stored under drought and humid conditions during either the growing season or harvest or storage (Jelinek *et al*., 1989). Fatal effects could be vomiting, weight loss, tumors growth, and death. Several toxics secreted by fungi are well known, and majority of them occur in grain crops. Most mycotoxins affect organs in the body and could be fatal to blood, kidneys, skin, or central nervous system, and some are known carcinogens (Ashiq, 2015; Yin, *et al.*, 2008; Martins *et al*., 2001). Fungi are the major source of mycotoxins in foods. Aspergillus, Penicillium, and Fusarium are the fungi of greatest importance to humans with respect to food poison by mycotoxins.

The extent of detrimental consequences of mycotoxins on the health of people or animals depend on dose and length of exposure, type of mycotoxin, physiological and dietary status, and possible synergistic outcomes of different chemical compounds to which the human beings are exposed (Gajecka *et al.,* 2013). The study concerning the evolution of mycotoxins and mycotoxicoses is receiving considerable attention with the overall thrust for prevention of mycotoxin production and to save our food/feed products from contamination and fungi-causing mycotoxicoses.

Conclusion and Recommendation

Fungi are very important organisms and their usefulness and economic importance cannot be overstated. However, many of them produced metabolites that are poisonous or dangerous to humans and animals. These metabolites called mycotoxins are important because their implications in animal and human health are substantial and the economic importance widely studied. Unfortunately, majority of the populace in developing countries do not know the inherent dangers of consuming mouldy produce with possible contamination by mycotoxigenic fungi because of lack of awareness about the danger involved. Therefore, there is need for general and public education to sensitise the people on the economic and health hazards posed by mycotoxins.

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The authors declare no competing financial, professional and personal interests.

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Ethical approval for this research was given based on institutional guidelines.

Consent for publication

Authors declare that they consented for the publication of this research work.

Availability of data and material

Authors are willing to share the data and material according to relevant needs.

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