FEDERAL UNIVERSITY OF TECHNOLOGY MINNA

IMPROVING PUBLIC HEALTH AND INTERNATIONAL TRADE THROUGH MYCOTOXIN CONTROL

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Prof. Hussaini Anthony Makun (MMSN)
B.Sc., M.Sc. (ABU), PhD (Minna)
Professor of Biochemistry

INTRODUCTION

Fungi are ubiquitous plant pathogens and are major spoilage agents of foods and feedstuffs. They grow on many foods and feed. The optimal condition for growth differs for several fungi; nevertheless, it has been reported by Ominiski *et al* (1994) that most fungi that are toxigenic do better at temperature between 24 °C - 28 °C and moisture content of the substrate of above 17.5%. Their best substrates are those that provide oil and carbohydrate as an energy source, and proteins, minerals etc. The infection of plants by various fungi not only results in reduction in crop yield and quality, with significant economic losses, but also contamination of grains with poisonous fungal secondary metabolites called mycotoxins. The ingestion of such mycotoxin-contaminated grains by animals and human beings has enormous public health significance, because these toxins can cause diseases in man and animals (Bhat and Vasanthi 2003).

There are over three hundred mycotoxins found in foods, but those that have the most impact on agriculture and public health and consequently economy are aflatoxins (AFs), trichothecenes [e.g. deoxynivalenol (DON), T-2 toxin], fumonisins (FBs), zearalenone (ZEA), patulin (PAT) and ochratoxin A (OTA) (CAST, 2003). The AFs, especially, AFB_1, are potent hepatotoxins and hepatocarcinogens, which were implicated in the death of 215 people in Kenya who consumed highly AF-contaminated maize meals in 2004 (Makun *et al.,* 2012). Trichothecenes are a group of about 150 related compounds that are protein inhibitors with consequent immunosuppressive effects, causing severe damage to the digestive tract and death due to intestinal haemorrhage. The commonest trichothecenes are DON and T-2 toxin (CAST, 2003). Fumonisins, especially fumonisin B_1 (FB_1) cause liver and kidney cancer, and neural tube defects in rodents, leukoencephalomalacia in horses and pulmonary oedema in swine (Marasas *et al.*. 1988). Of major concern is the association

of FB_1 with elevated incidence of human oesphageal cancer in parts of South Africa, North Eastern Iran and China, upper gastrointestinal tract cancer in Northern Italy (Dutton, 1996) and neural tube defects in human babies (Hendricks, 1999). ZEA, an oestrogenic toxin that causes infertility in animals, is associated with outbreaks of precocious pubertal changes in children in Puerto Rico, and has been suggested to have a possible involvement in human cervical cancer (Zinedine *et al.*, 2007). OTA causes kidney and liver impairment in animals (especially pigs) and man (Stoev and Stefan, 2013).

Other emerging mycotoxins that are currently having global attention as reviewed by Njobeh *et al.* (2010) include patulin, moniliformin, penicillic acid, cyclopiazonic acid, ergot alkaloids, sterigmatocystin, ergot alkaloids, citrinin, *Alternaria* toxins and rubratoxins. The IARC (1987) classified sterigmatocystin as group 2B, which means it is carcinogenic in other species and is possibly carcinogenic to humans. Ergot alkaloids may cause strange hallucinations, the feeling of itchy and burning skin, gangrene, loss of hands and feet, and even death. Moniliformin causes cardiac permeability in young rats and ducklings, suggesting a mechanism for inducing Keshan disease in humans. Patulin elicits nausea, vomiting and gastrointestinal disturbances in human being and is classified by the International Agency for Research on Cancer in category 3 as a not classifiable toxic compound regarding its carcinogenicity to humans (IARC, 1993). Citrinin is a nephrotoxin while Cyclopiazonic acid (CPA) causes focal necrosis in most vertebrate inner organ in high concentrations and affects the ducts or organs originating from ducts (Huang *et al.*, 2014). Penicillic acid may cause hepatotoxicity, mutagenotoxicity, genotoxicity, in mice while alternaria mycotoxins affect adversely the liver and kidney and may be a factor in the aetiology of oesophageal cancer in Linxian, China (Liu *et al.* 1992). Rubratoxins are hepatotoxic

mycotoxin found in cereals they have been responsible for outbreak of toxicosis in the U.S (Farlex, 2012).

Historical Background

Although the involvement of fungi and their toxins in causing disease to man and animals dates to the period when the Dead Sea Scrolls were written (Richard, 2007), it seems the evidence for their historic occurrence and impact were not obvious until the Middle Ages, when ergot alkaloids poisoning outbreaks in Europe were responsible for the death of thousands of people. Ergotism, also known as Saint Anthony's Fire, a disease that had its origin in the ingestion of rye and other grains infested with the mould, *Claviceps purpurea* was the first known mycotoxicosis that killed tens of thousands of people in Europe for over 300 years between A.D 900 and 1300. The last epidemics of ergotism were in 1825. However, serious outbreaks did occur in Russia in 1926-7 and in England in 1928; in France in 1951 and Ethiopia in the 1970's resulting in nearly 50 deaths. The disease caused losing of extremities; fingers and limbs." Subsequently, between 1940s and 1950s a lethal human disease caused by *Fusarium* toxins and referred to as 'Alimentary Toxic Aleukia' was reported in Russia (Smith and Moss, 1985). Similarly, in 1938 Japan, *Penicillium* species were responsible for the colouring of rice that erratically led to the fatal human cardiac syndrome called 'yellow rice disease' (Uraguchi and Yamazaki, 1978). The livestock industry was also affected since 1822; the New Zealand sheep industry was devastated by facial eczema, a fungal infection caused by *Pithomyces chartarum.* Other deadly animal syndromes arising from fungal infections and termed differently as equine leukoencephalomalacia (1930s to 1970s in USA), stachybotryotoxicosis (1930s in USSR), red mould diseases (1945-1947 in Japan), and red clover disease, vulvovaginitis and mouldy corn toxicosis (1920s to 1950s in USA) plagued the world (Gbodi and Nwude, 1988). Despite these grave episodes, little attention was paid to fungal diseases. However, in 1960, when the Turkey X disease killed thousands of poultry animals in

Britain (Blount, 1965); the world became fully aware of the potential hazard of mycotoxins and responded to the disaster by a systematic and multidisciplinary approach which led to the discovery of aflatoxins. Following the discovery of aflatoxins, at least three hundred mycotoxins have been shown to occur in nature. But those that pose the greatest risk to human and animal health are aflatoxins (AFs), trichothecenes (deoxynivalenol and T-2 toxin), fumonisins, zearalenone, patulin and ochratoxin A (CAST, 2003) and of these AFs are the most notorious in the food trade because of their high prevalence and severity of health impact and are therefore the most studied.

Prevention and Control of Mycotoxins

The health hazards of mycotoxins translate to food insecurity and financial burden on the national health sector and this is complicated by rejection of export food commodities from international trade which further adversely affect national economy. For these reasons, there are recommended preharvest and postharvest mycotoxin intervention strategies. Preharvest measures include planting fungi resistant cultivars on appropriate soil types and tillage method that reduces fungi inoculum (Jouany *et al.*, 2007). Crop rotation with non-host crops like beets, vegetable interrupts the production of infectious crop debris and survival chance of *Fungi* inoculum for the next season crop. Sowing should be done on dates such that anthesis coincides with the time of release of spore (Eeckhout *et al.*, 2013). Biocontrol techniques which aim at outcompeting toxigenic strains and inhibiting mycotoxins synthesis are effective (IARC, 2015). Management strategies that improve plant nutrition, health and therefore resistance to diseases including fungal infestation such as appropriate use of fertilizer, irrigation, weed and other pesticide control are recommended. Harvesting should be done at maturity and in low moisture conditions (Jouany, 2007) using appropriate harvesting equipment that will result in minimal damage of grains as

damaged grains allow for increased fungal colonization and mycotoxin synthesis; is recommended (CAC, 2016).

Postharvest strategies like removing diseased and damaged kernels before and after storage is effective. Storage under constant low temperature 15°C and "safe" moisture level of <14% profoundly reduce fungi species in agricultural produce (Jouany, 2007). Thermal treatment, irradiation, chemical decontamination and bio-decontamination using microorganisms or enzymes and absorption of mycotoxins in gastrointestinal tract by absorbents are effective in removing mycotoxins from contaminated commodities (EFSA, 2009). The adoption of the principles of Hazard Analysis Critical Control Point (HACCP) into mycotoxin control scheme has led to an integrated approach. The integrated mycotoxin management system, which looks through the farm value chain and identifies all critical points where control can be implemented, has generated better results. While all these methods of prevention, reduction and detoxification of mycotoxins can significantly deplete mycotoxins in foods and feeds, it should be borne in mind that absolute elimination of these toxins from the value chain is impossible.

OUR CONTRIBUTIONS TO MYCOTOXIN MITIGATION

Our contribution to the prevention and control of these menaces to mankind is in identifying and measuring the extent of exposure and risks associated to the presence of mycotoxins in Nigerian food system, and invariably deriving intervention strategies against the food borne hazards.

Risk Assessment of Human Exposure to Mycotoxins in Nigeria

Risk assessment is a scientifically based process consisting of hazard identification, hazard characterization, exposure

assessment and risk characterization. The process requires that the hazard that is identified and whose nature of toxicity characterized on dose-response basis must have adverse health effect. Exposure assessment will therefore be the amount of the toxin taken via our foods while risk characterization on the other hand is the qualitative or quantitative estimation of the possibility of occurrence and severity of known or potential adverse health effects in a given population based on hazard identification and characterization and exposure assessment.

Hazard Identification

In accordance with risk assessment principles, we isolated and identified fungi from our crops (Table 1 and 2). The toxins secreted by representative isolates of the fungi were injected into mice to demonstrate their ability to be harmful to mice and therefore human beings. The mice were observed for signs of toxicity for 14 days. The toxicity of the extract was arbitrarily classified into four categories: very toxic (If all of the three extract treated mice died), moderately toxic (two of the three of the extract treated mice died), mildly toxic (If the one of the three mice was killed) and Non – toxic (If none of the three extract treated mice died) (Makun *et al*, 2010). Using this method, we identified the toxic fungi contaminating maize, rice or sorghum. Toxicity screening of fungi isolated from maize revealed that of the 30 isolates screened, 19 produced toxic metabolites (Makun *et al.*, 2010). Of these toxic nineteen isolates, 6 were very toxic, 4 were moderately toxic while 9 were mildly toxic. Of the nine isolates that produced mildly toxic metabolites, six were *Aspergillus* species and the other three were *Fusarium* spp. and *Mucor* spp. Two *Aspergillus* spp, one each of *Rhizopus* and *Fusarium* Species constituted the moderately toxic isolates. Of the six very toxic isolates, three were *Aspergillus* Species, two *Penicillium* spp and one *Fusarium* spp.

Toxicity screening results of fungal isolates from millet samples of the wet season showed that 15 of the 22 screened isolates produced toxic metabolites. The *Helminthosporium* spp. were highly toxic (4.5%) while the *A. niger, Penicillium spp* and *R. stolonifer* were moderately toxic (18.2%). The ten fungal isolates that produced mildly toxic metabolites were *Aspergillus flavus, A. fumigatus, A. glaucus, A. parasiticus, Fusarium* spp., *F. equiseti, F. trincintum* and *Syncephalastrum* spp. Seven isolates were found to be non-toxic (31.8%) and they include two isolates of *Mucor* and *Penicillium* spp., and one each of *Phoma* spp., *R. stolonifer* and *Syncephalastrum* spp (Makun *et al.*, 2010).

One hundred and forty-eight fungal isolates from both guinea corn (67) and rice (81) were tested for toxicity (Tables 1 and 2) (Makun *et al.*, 2009). Of all these, 95 were found to produce toxic metabolites that were lethal to mice and these were *Aspergillus* spp (41), *Fusarium* spp (14), *Penicillium* spp (10), *Trichoderma* spp (8), *Syncephalastrum* spp (4), three each of *Alternaria* spp, *Phoma* spp and *Curvularia lunata.* Others include two each of *Colletotrichum* spp, *Geotrichum candidum* and *Helminthosporium* spp, and one each of *Cladosporium werneckil, Cryptococcus neoformis* and *Mucor* spp. A few of the fungi which have not been known to produce mycotoxins were found to be toxigenic. For example, *Syncephalastrum* spp isolates from both guinea corn and rice were found to be moderately and mildly toxic.

Following the demonstration that these fungi contaminating Nigerian crops produce toxic metabolites, we attempted to identify the mycotoxins they produce. Makun *et al.* (2011) showed that all strains of *A. flavus* (aflatoxins B_1 and B_2), *A. parasiticus* (aflatoxins B_1, B_2, G_1 and G_2), *A. ochraceus* (ochratoxin A), *F. proliferatum* and *F. verticillioides* (fumonisins B_1 and B_2) isolated from rice, were excellent producers of their respective mycotoxins. Patulin was produced by *A. terreus*, whereas

deoxynivalenol, zearalenone and T-2 toxin were produced by *F. chlamydosporum* and other *Fusarium* spp. Garba, (2017) will subsequently prove that aflatoxins B_1, B_2, G_1 and G_2 are elaborated by *A. flavus* and *A. parasiticus,* ochratoxins by *A. ochraceus, A. niger, A. carbonarius, A. oryzae, Neosartorya fischeri, Sterocleista ornate, Emericella quadrilineate* and *Pencillium verrucosum,* fumonisin B_1 by *F. oxysporum, F. verticillioides, F. proliferatum, F. chlamydosporum, F. poae, F.acuminatum,* zearalenone by *F. oxysporum, F. verticillioides, F. proliferatum,* and *F. graminearum* and deoxynivalenol by *F. verticillioides, F. graminearum* and *F. poae.*

In summary, the hazards we identified in Nigerian foods and feeds are fungi some of which secrete toxins that are lethal to mice, and the five agriculturally significant mycotoxins, aflatoxins, fumonisins, ochratoxins, zearalenones and deoxynivalenol are major toxins secreted by these fungi in our foods as shown below.

Screening of Foods and Feeds for Toxigenic fungi and Mycotoxins

1. Sorghum

Sorghum (guinea corn) a staple grain for over 750 million people in Africa, Asia and Latin America is the crop extensively studied for my PhD, rice been the other. We analyzed 168 mouldy sorghum samples from the 25 local government areas of Niger State during the three seasons; dry harmattan, dry hot and rainy seasons for their fungal, aflatoxin B_1 (AFB_1) ochratoxin A (OTA) and zearalenone (ZEN) contamination using conventional fungi identification methods and thin layer chromatography respectively. Eight hundred and eighty-four (884) fungi were isolated from one hundred and the mouldy sorghum samples. The three major fungal contaminants of sorghum in the state were *A. niger, Rhizopus oryzae* and *A. flavus.* AFB^1 was found in 91

out of the 168 samples analyzed while ZEN was detected in 60 out of the 168 samples examined. Twenty-three of the 112 that were analyzed for ochratoxin A, contained the toxin. The levels were quite high mostly above safe levels and this is because the study was biased as only visibly mouldy samples were analyzed. This does not still negate the results as such samples are usually cleaned up and consumed by human beings and animals fed directly. However, when we conducted an unbiased ochratoxin A survey with 18 representative samples from Minna using more sensitive method (HPLC), we found low contamination of sorghum at mean level of 8.28µg/kg (Makun *et al.*, 2013). In a third work, where we surveyed sorghum grains and traditional alcoholic beverages (burukutu and pito) in Minna and Bida for toxigenic fungi and aflatoxins, nine genera of fungi were isolated (table 1) and the presence of *Macrophomena spp* was demonstrated in sorghum for the first time (Apeh *et al.* 2016). *Fusarium* and *Penicillium* species were found to be resistant to fermentation and tannin and *Aspergillus niger* was also resistant to tannin. The grains were contaminated with the toxins of up to a total aflatoxin level of 21.74µg/kg while the burukutu and pito had lesser concentration of maximum levels of 8.98 and 2.00µg/kg, indicating a carryover of 47% and 25% aflatoxins from grain to the alcoholic beverages respectively. The study also proved that daily aflatoxin intake from the products was above the provisional maximum tolerable daily intake, making sorghum an important source of toxin for which control should be established.

The most profound and comprehensive work conducted on fungi and mycotoxins in sorghum in Nigeria was carried out by our PhD student Garba, (2017) who is yet to publish his works. He elucidated the fungi, aflatoxin B_1, B_2, G_1 and G_2, ochratoxin A, fumonisin B_1, and B_2, zearalenone and deoxynivalenol profile across all areas where sorghum is grown in the country using polymerase chain reaction based methods and HPLC

respectively. From over 400 samples, 87 composite samples were obtained from 29 districts in six of the seven agroecological zones of the country, a total of 348 fungi belonging to 11 genera and 63 species were isolated. *Aspergillus* and *Fusarium* spp were the most dominant species in Nigerian grown sorghum (Table 1). The occurrence of the mycotoxins was climate dependent with the Fusarium toxins (FB, DON and ZEA) predominating in cooler zones, DS, SGS MA and NGS while the Aspergillus toxin (AF and OTA) dominated the hot humid climate (NGS, SDS and SS). The exception to the rule is the occurrence of aflatoxins and zearalenone in highest concentrations in the Sahel savannah and the reason is, the zone has extreme dry and hot condition (44 °C) which serves as stress factor that diminishes the resistance of plants to fungal invasion and consequently mycotoxin contamination. Considering the mean values obtained for total aflatoxins, ochratoxin A and zearalenone, most if not all the samples were unfit for human consumption as the safe limits by Codex Alimentarius Commission of 4, 5and 100 µg/kg respectively were exceeded. While most samples contain fumonisin B_1 and deoxynivalenol below legislated levels of 1000µg/kg and 500 µg/kg respectively, the simultaneous occurrence with other mycotoxins made virtually all the samples studied unsafe for human foods.

2. Rice

We screened 196 mouldy field (28), market (84) and stored (84) rice samples collected during the three seasons from the four microclimatic zones comprising of all the local government areas of Niger state for aflatoxin B_1, ochratoxin A and zearalenone and fungi for my PhD project (Makun 2007). The toxins were detected in 97, 56 and 93 samples respectively at incriminating concentrations of over a 1100 µg/kg. The three toxins simultaneously occurred in 22 samples. One thousand and sixty-two fungal isolates belonging to 17 genera were identified and of these, *Penicillium* spp., *A. flavus, A. parasiticus, A. niger, Mucor* spp,

Rhizopus spp. and *Alternaria* spp were dominant. Others were *Fusarium* spp., *Trichoderma* spp., *Curvularia lunata, Helminthosporium* spp., *F. oxysporium and A. ochraceus.*

During my postdoctoral fellowship with the Food Environment and Health Research Group of the University of Johannesburg, South Africa, we isolated a total of 357 fungal isolates of nine genera including *Aspergillus, Fusarium, Sarocladium, Acremonium, Curvularia Botryosphaeria, Penicillium Alternaria* and *Ascomycota* in decreasing order of predominance from 21 field, store and market rice samples. The most frequent fungal contaminants of the rice samples were *A. flavus, A. fumigates, A. niger, A. parasiticus* and *F. proliferatum.* Fungal isolates were primarily identified based on morphological characteristics, while representative isolates were characterized genetically (Makun *et al.,* 2011). An evolutionary tree was constructed from the resulting sequences of the isolated fungi. Mycotoxin screening of same samples using thin layer and high performance liquid chromatography methods was done (Makun *et al.*, 2011a) T-2 toxin was detected using TLC only. AFs were detected in all samples, at total AF concentrations of 28– 372 µg/kg. OTA was found in 14 of the 21 samples, also at high concentrations (134–341 µg/kg) that are considered as critical levels in aspects of kidney damage while ZEA (53.4%), DON (23.8), FB_1 (14.3%) and FB_2 (4.8%) were also found in rice, although at relatively low levels. The simultaneous occurrence of the toxins which could have synergistic effects raises further public health concern.

With the realization that Kaduna State is the largest rice producer in the country accounting for 22% of national production followed by Niger State, Olorunmowaju (2012), screened 86 samples of field, stored and marketed rice from 22 local government areas of Kaduna State for fungi, aflatoxins and

ochratoxin A. She isolated 288 fungi isolates of 5 genera namely *Aspergillus, Fusarium, Mucor, Penicillium* and *Rhizopus* in decreasing order of predominance. The commonest fungi contaminating rice from the state were, *A. niger, A. ochraceus, A. parasiticus, A. flavus, Fusarium spp* and *Mucor spp*. Using HPLC, it was proven by the work that all the samples contained aflatoxins at total aflatoxin concentration of up to 432µg/kg and ochratoxin A was found at higher prevalence but low concentrations of maximum of 35.6µg/kg. All the samples were unsafe for human consumption as 100% and 58.02% of the samples had aflatoxin and ochratoxin A levels above regulated limits. Multi-occurrence of mycotoxins was a common phenomenon in over 80% of the samples. We also analyzed 15 samples each of rice and Madidi (rice dough) from various locations of Nasarawa State for aflatoxins which were detected at unsafe total aflatoxin concentrations of maximum of 113.2 and 144 µg/kg in 5 and 8 samples respectively. It is worthy of note that the processed product has lower mycotoxin content (Makun *et al.*, 2014).

Maize

We have three major works on this crop. The first being screening of fungi and their toxin producing potentials in 93 samples from Niger and Kogi States (Makun *et al.*, 2010). *Fusarium spp, Aspergillus fumigatus* and *A. flavus* were the most common contaminants of maize from the two states. The second was conducted by Muhammad, (2012). She analyzed 95 maize kernel samples from all the four microclimatic zones of Niger State for their fungal, aflatoxin (B_1, B_2 and G_1) and ochratoxin A contamination. Nine fungi genera were isolated from the samples collected; the major fungal contaminants of maize in the state were *Aspergillus niger, A. flavus, A. parasiticus, Mucor spp,* and *Rhizopus spp*. Aflatoxins and ochratoxin A occurred in 80% and 88% of the samples at unacceptable concentrations of up to

139μg/kg and 10μg/kg respectively. The third work was by Makun *et al.* (2013) who found ochratoxin in 16 out of 17 samples of maize at concentration of up to 139μg/kg and 14 of the 17 were not safe for human consumption. None of the sample tested was safe for human consumption as adjudged by European Union and Standard Organization of Nigeria. From these works, maize is second to groundnut in susceptibility to mycotoxin contamination.

Wheat

Makun *et al.* (2010) found extremely high AFB_1 contaminations of wheat marketed in Minna, Nigeria at unacceptable levels (range: 40-275 μg/kg) in 27 of the 50 tested samples. The severe contamination levels of this crop in Nigeria making it a principal source of mycotoxins has raised public health concern which underscores the need for the regulation of mycotoxins in Nigeria.

Bean

In spite of the hard seed coat of this crop which ensures limited access to microbes and low mycotoxin contamination about 59% of bean samples from markets in Minna were found to be contaminated with aflatoxin B_1 at levels of above a 130μg/kg (Makun *et al.*, 2010).

Roots and Tuber

Makun *et al.* (2010) isolated and identified *Fusarium* spp, *Aspergillus* spp, *Aspergillus niger, Penicillium* spp, *Mucor* spp and *Geotrichum candidum* from 17 out of 50 marketed dried yam flour from Minna. Also, Makun *et al.* (2013) analyzed fermented cassava (Manihot esculenta) flakes (garri) (18) from markets located in Minna and its environs for ochratoxin A (OTA) by High Pressure Liquid Chromatography (HPLC). OTA was detected in garri in all the 18 samples tested at moderate concentration but 10 of the samples were not safe for human consumption as it had

toxin levels above the regulated limit of 5µg/kg. This is the first report of ochratoxin A in garri.

Millet

Makun *et al.* (2007) analyzed 83 dry harmattan (34) and rainy (49) season samples of millet from all the 25 local government areas of Niger State for their mycological and aflatoxin contaminations. A total of 158 fungal isolates were cultured and identified from the samples studied. While 87 isolates were identified from rainy season samples, 71 fungal isolates were found in samples of the dry harmattan season. Ten genera of fungi namely *Aspergillus* (70), *Penicillium* (43), *Fusarium* (23), *Rhizopus* (6), *Mucor* (5), *Syncephalastrum* (4), *Phoma* (4), *Cladosporium* (1), *Arthroconidia* (1) and *Helminthosporium* (1) in order of decreasing predominance were the identified fungal contaminants of millet in the State in 2000. *Penicillium spp, Aspergillus flavus* and *Aspergillus niger* were the most dominant fungal contaminants of millet in the state. The field samples were the most polluted by fungi. Of the 49 rainy season samples that were tested for aflatoxin B_1 using thin layer chromatography, 12 were found to be positive for the toxins at alarming concentrations of between 1370.28 and 3495.10 µg/kg. Marketed samples had the highest number of aflatoxin contaminated samples (10/12) while samples stored in "rumbu" and sacks had a contaminated sample each. Subsequently, Makun *et al.* (2014) using a more sensitive tool, HPLC did not detect any of the four aflatoxins in millet seed (15) and millet dough (*Fura*-15) samples from Minna, indicating resistance to aflatoxin contamination. Our third work determined the mycological and aflatoxin contents of 30 millet seed and 20 millet dough samples (Ochai, 2014). Fewer fungi isolates than in previous work were found namely *Aspergillus flavus S, Aspergillus flavus L, Aspergillus parasiticus Aspergillus tamari, Fusarium* spp *Cercospora* spp *Coryospora* sp *Curvularia* spp *Macrophomena* spp *Penicillium*

spp *Rhizopus* spp The high tannin content of millet was advanced as the reason for the low fungi load however, it was shown in the work that *Aspergillus niger, Fusarium* spp and *Penicillium* spp were resistant to tannin as they possess tannase, an enzyme that degrades the compound. In this work, low concentration of aflatoxin B_1 (1.38 ± 0.33µg/kg) and AFB_2 (1.00 ± 1.00 µg/kg) was detected with only one market sample having level above Nigerian permissible limit, an indication of resistance of the grain to mycotoxin contamination. It was also shown that processing the grain to fura reduces the aflatoxin B_1 and B_2 levels by 23% and 39% respectively. Our fourth study on millet found 100% prevalence of ochratoxin A in 18 samples at moderate concentrations of between 10µg/kg and 46µg/kg with all the samples been unsafe for human consumptions because they had toxin concentration of above 5µg/kg, the regulated limit (Makun *et al.*, 2013).

Sesame

Despite its natural resistance to mycotoxin contamination because of its inherent composition of sesamin, a constituent of sesame oil which inhibits the growth of Aspergillus species (Lee *et al.* 2007), Makun *et al.* (2014) have found aflatoxins in 8 of the 30 samples tested at unsafe concentrations of up to 140.90µg/kg. Apeh *et al.* (2016) using scanning densitometer, CAMAG TLC Scanner 3 with winCATS 1.4.2 software demonstrated aflatoxin contamination in 25 of 50 samples from Nasarawa, Niger and Jigawa States at levels of up to 60.05µg/kg. The workers also identified *Aspergillus flavus, Fusarium* spp, *Penicillium* and *Phoma* spp as the dominant fungal contaminants of sesame in Nigeria. With regards to the nephrotoxin, ochratoxin A, Makun *et al.* (2013) using HPLC with UV detector gave the first Nigerian report of ochratoxin A in sesame, showing a 100% contamination in 19 samples from Niger State at moderate concentrations of between 1.90 µg/kg and 15.66µg/kg.

Groundnut

In a mycological and mycotoxin assessment of 81 samples of raw and roasted groundnut from farm, store and market across the four microclimatic zones of Niger State, Ifeji, (2012) and Ifeji *et al.* (2014) found that the genera of fungi contaminating groundnut in Niger State in order of frequency were *Aspergillus, Rhizopus, Mucor, Penicillium,* and *Fusarium* with *A.niger, A.ochraeus, A.flavus, Rhizopus spp* and *Mucor spp* being the most predominant fungi contaminants of the commodities. The three mycotoxins (AFB_1, AFB_2 and OTA) evaluated occurred in 88.9, 75.3 and 90.1% of the samples respectively at concentrations above the Nigerian and European Union (2 µg/kg) action limits. All the aflatoxin positive samples were above the safe limits for AFB1 while 55% of the samples had OTA concentrations exceeding the 5 µg/kg regulatory limit of Nigeria.

Acha

Using HPLC with ultraviolet detector, all 30 samples of Fonio tested for aflatoxins were negative (Makun *et al.*, 2014). However, in the previous year, another set of 20 samples were all found to be contaminated by ochratoxin A at relatively low concentrations (Makun *et al.*, 2013), making it the first report of ochratoxin A in the grain. Its high nutritional values and natural resistance to aflatoxins and to some extent ochratoxin A suggest acha as one of our healthy foods. Although less than 10% of the samples tested for aflatoxin had levels above the Codex safe limit, 13 of the 19 samples tested for ochratoxin A were unsafe for human consumption.

Vegetables

With the heighten global interest particularly by Codex Alimentarius Commission, Makun *et al.* (2012a) investigated the aflatoxin B_1, B_2, G_1 and G_2 content of fresh and dried samples of baobab leaves (*Adansonia digitata*) (20), okra (*Abelmoschus*

esculentus) (20) and red hot chili pepper (RCP) (*Capsicum annuum*) (20) from Minna, Nigeria. A total of sixty samples; (baobab (20), (okra (20) and (chili (20) were collected. For each vegetable, ten fresh and ten dried were analyzed for the four aflatoxins. The mycotoxins were not found in baobab leaves and okra but detected in 60% of the hot chili pepper samples at mean concentration of 5.8μg/kg. In a more elaborate work, we determined the mycoflora and aflatoxin content of 200 samples of fresh and dried vegetable, which are widely used because of their nutritional and medicinal principles (Suleiman *et al.* 2017). Fifty (50) fresh pumpkin (*Curcurbita spp*), fresh spinach (*Spinancia oleracea*), bitter leaf (*Vernonia amygdalina*) comprising of (25 dried and 25 fresh) and 50 samples of tomato (Solanum lycopersicum) (25 dried and 25 fresh) were collected from local vegetable vendors in Minna metropolis, Nigeria. A total of 165 isolates mainly of species of *Aspergillus, Penicillum, Fusarium* and *Mucor* were identified. Aflatoxins were detected in all the vegetables at low concentration except for dried bitter leaf that had up to 56μg/kg. Aflatoxin G_1 was the most predominant type found in the products. In the two studies, aflatoxins were found at mean values far below regulated levels in baobab (kuka), okra, spinach, pumpkin, tomatoes, dried red chili indicating that they are safest foods in Nigeria.

Meat

Liver as the organ of metabolism of toxins was our interest and we analyzed one hundred and twenty-two (72 cow livers and 50 goat livers) 24 hour fresh liver samples from abattoirs in Minna for aflatoxin M_1, a hydroxylated metabolite of B_1 (Makun *et al.*, 2017). AFM_1 contamination in the present investigation of livestock liver samples is alarmingly high and may pose a serious public health problem to animal and human health. Goat liver (52%) and cow liver (62.5%) samples were contaminated beyond the safe limit (0.05μg/kg). Also, cow liver samples had

significantly higher concentrations of AFM_1 (0.000-21.730 µg/kg) than goat liver (0.000-4.321 µg/kg) samples. Livestock liver samples in Minna are therefore a major source of aflatoxin to human beings.

3. Milk and Milk Products

We determined the levels of this toxin in powdered milk, raw cow milk, human breast milk and other milk products in the country with a view to ascertaining whether aflatoxin M_1 is problematic in our dietary system. 19 of the 100 powdered milk sampled from market stores in Lagos and analyzed using automated thin layer chromatography had levels above the safe level of 0.05µg/kg (Makun *et al.* 2010). Okeke *et al.* (2012) found 100% prevalence of aflatoxin M_1 in 30 samples (10 each) of fresh milk, fermented defatted skimmed milk (*nono)* and full fat or partially skimmed milk (*kindirmo)* from two dairy farm settlements in Bida Local and all were at unacceptable levels of above the safe limit. Pathogenic microbes namely *Bacillus subtilis, Enterococcus faecalis, Staphylococcus aureus, Aspergillus flavus* and *Aspergillus niger* were isolated from the same sample at unacceptable counts (Okeke *et al.* 2014). Aflatoxins M_1 was found in 69 0f 140 milk products from Minna (Makun *et al.*, 2016). The findings reveal; incidence of 77.5% in human milk, nomadic cow milk samples had the highest incidence of 80%, cheese had 40% incidence, nono had 35% incidence, commercial cow milk had 25% incidence and yoghurt had 10% incidence. 51 of the samples had toxin levels above (0.05 µg/L) the EU and Nigerian legislated limit. Poor women that sustain on cereals had higher aflatoxins content than women that feed on tuber and richer ones that have variety of diets. Exposure to AFM_1 from milk and milk products at concentrations demonstrated in these investigation is of great concern as infants in the country are encouraged to be exclusively breast fed for six months after which alternative milk intake sometimes from animal origin can be sourced.

4. Animal Feeds

In a survey of fungi and ochratoxin A in 100 privately milled poultry feeds (52) and commercial feeds in Niger State, nine fungi genera were isolated. The most frequently isolated fungi genera in both privately milled and commercial feed was *Aspergillus spp* which was about 40% of mould isolate. *Penicillium spp* was 20% in private feed and 13% in commercial feed. A total of 874 fungi were isolated consisting of 458 fungi species in privately milled feed and 416 fungi species found in commercial feed (Adeniran, 2013). Thirty-seven percent of the commercial poultry feed brands was contaminated with OTA at a range 0-236.73µg/kg while 100% of privately milled feed were contaminated with OTA at a range of 22.76-226.51µg/kg. The finding of this investigation showed that 71% of the sampled poultry feed had OTA contaminations which were far in excess of the maximum permissible level of 5µg/kg established in Nigeria.

Iheanacho *et al.* (2014) evaluated the aflatoxin content of 92 animal feed samples comprising of poultry, cattle, horse and pig feeds from South Africa and found low levels of the toxins. Only four poultry feeds had aflatoxins level above the South Africa regulated limit for feeds (10µg/kg). The low contamination rate is evidence of effective regulatory system. Even the low levels are considered unsafe when consumed on a continuous basis because they may pose some health related problems especially when AFs are found together with other significant mycotoxins such as ochratoxins and/or fumonisin.

Hazard Characterization

The next logical step in risk assessment is to evaluate the dose response nature of the adverse effects of the fungi and their mycotoxins. Therefore 13 of the very toxic fungi isolated from guinea corn and rice (Makun 2009a) were further subjected to acute toxicity testing at doses of 40, 160, 640, 2560 mg/kg body weight. At 40 mg/kg body weight four isolates (*A.niger,*

Trichoderma spp, Fusarium verticillioides and *Penicillium verrucosum*) killed a mouse each out of the three used for the test. Four fungal isolates (*A.niger, A.parasiticus, F.verticillioides* and *Penicillium verrucosum*) caused death at 160 mg/kg body weight. All the thirteen fungal isolates except *Helminthosporium* and *Trichoderma spp* were lethal to mice at 640 mg/kg body weight. Except for *A. parasiticus* and *Helminthosporium spp*, all other extracts caused 100% mortality at 2560 mg/kg body weight. From this result, *A. niger* and *F. verticillioides* caused the highest lethality in mice even at low concentration and therefore were the two most toxic fungi found in guinea corn and rice. *F. verticillioides* was selected as the novel most toxic fungi contaminating guinea corn and rice in Niger State because less information about its toxicity was available in literature as compared to *A. niger.*

The culture material of *Fusarium verticillioides* was therefore subjected to acute toxicity studies in chicks and mice (Makun *et al.* 2010a). Oral administration of the fungal extract to mice and chicks caused mortality at 833.33mg/kg and 2500mg/kg body weight respectively. The intraperitoneal LD_{50} values of the extract in both animals were between 45.40–87.90 mg/kg body weight with the mice being more susceptible. The total fumonisin content of the fungal residue as analyzed using veratox competitive direct enzyme linked immunosorbent assay (CD-ELISA) was 8.233ppm. The crude extract invariably fumonisins are harmful to the liver, kidney and gastrointestinal tract. Haemorrhage and degenerative necrosis of the liver cell, mucous layer of the digestive tract and the digestive tract in its entirety were histopathological changes observed in the chicks. Kidney of the mice show wide spread intra renal tubular necrosis with micro thrombi formation while there was wide spread fatty degeneration of mice liver as evidence by empty clear vacuoles and broad fibrosis appearing as septae signifying early cirrhosis (plates 5, 6, 7 and 8).

Using more accurate equipment, flow cytometry, TLC and HPLC, the culture material of same *Fusarium verticillioides* was tested for its *in vitro* cytoxic effect to human lymphocytes in comparison with those of aflatoxin B_1, fumonisin B_1 and ochratoxin A (Makun *et al.* 2011a). The mycotoxin profile of the extract was elucidated using TLC, column chromatography and HPLC. Figure 2 show dose-dependent cytotoxic effects of the toxins to human lymphocytes. At concentrations of 25, 50 and 100 µg/ml, OTA was more toxic than AFB_1 followed by the extract which was comparatively as toxic as FB_1. Cytotoxicity data also revealed that, apoptosis and necrosis were the major form of cell death induced by the tested mycotoxins and extract. The extract was found to contain fumonisins B_1 (FB_1), B_2 (FB_2) and B_3 (FB_3) at concentrations of 16.302, 6.423 and 2.456 ppm, respectively. The two studies therefore reveal that *F. verticillioides* produces the three major fumonisins and that these toxins can damage the liver, kidney and digestive tracts of animals and possibly human beings and elicit immunodeficiency in human beings. Aflatoxins and ochratoxin were also shown to be immunotoxic to man in the studies.

Iheanacho *et al.* (2014a) would also prove the cytotoxicity of aflatoxin B_1 to human lymphocytes using the same methyl tetrazolium bromide (MTT) method. The AFB_1 standard (80 µl/ml) used as a point of reference exhibited the greatest cytotoxic effect in causing cell mortality (73% cell viability recorded after 24 hrs of exposure), which increased over time (59% cell viability recorded after 72 hrs of exposure). Garba (2017), also tested the cytotoxic potentials of aflatoxins, fumonisins, ochratoxin A, zearalenone and deoxynivalenol on human mononuclear lymphocytes for 24 and 72 hours respectively in various concentrations of 2, 4 and 8µl and found that these toxins at concentrations detected in our sorghum and

sorghum based foods reduce the viability of human immune cells by between 50 and 97%.

The conclusion here is that culture material of *Fusarium verticillioides* from rice which contains fumonisins are lethal to chicks and mice causing damage to the liver, kidney and gastrointestinal tract. We have also shown that the five major mycotoxins found in our foods are injurious to human lymphocytes.

Exposure Assessment

The question to answer at this point is, are we exposed and ingest aflatoxins, fumonisins, ochratoxin A, zearalenone and deoxynivalenol at unsafe levels? The maximum tolerable limits for aflatoxins in human foods is 4 μg/kg while for animal feeds is 20 ppb with infant foods having the least regulated levels (0 – 4 μg/kg). The maximum allowable concentrations by countries that legislate against mycotoxin as recorded by CAST, (2003) are 5 μg/kg for OTA, 100 μg/kg for ZEA, 1000 μg/kg for FB and 500 μg/kg for DON. The regulated limit for aflatoxin M_1 in milk and milk products for infants is 0.05μg/l. Considering the mean values obtained during our screening of foods and feeds for the five mycotoxins in animal feeds, bean, groundnut, garri, maize, meat, millet, milk and milk products, sesame, sorghum, bitter leaf, red pepper and wheat and *burukutu*, Nigerians are exposed to mycotoxins especially aflatoxins and ochratoxins at very unsafe levels. However, the aflatoxin levels found in South African animal feeds were all below legislated levels and therefore safe for consumption. Similarly, baobab (kuka), okra, pumpkin, spinach, tomatoes, dairy products from commercial farms, powdered milk and to lesser extent Fonio (*acha*) and millet are safe foods with regard to mycotoxin contamination.

Estimation of the amount of toxins ingested from our processed

food per kilogram body weight per day, week, month or year was carried out after obtaining the levels of mycotoxins in three commonly consumed sorghum based foods, weight of processed food taken daily and body weight of four categories of Nigerians subsisting on sorghum in Northern Nigeria (Garba, 2017). We calculated the dietary intake of the five mycotoxins in infants (0-3 years), children (4-17years), adults (18-49years) and 50 and above years for sorghum as follows total aflatoxins (0.59-3.33, 0.35-2.06, 0.29-1.29 and 0.28-1.62), fumonisins (2.18-11.15, 1.24-5.80, 0.79-5.47 and 1.08-5.03), ochratoxin A (0.08-0.85, 0.14-5.01, 0.04-0.42, 0.04-1.12), zearalenone (10.45-19.12, 6.58-11.29, 5.51-9.60, 2.29-8.09) and deoxynivalenol (4.62-17.26, 2.73-10.47, 2.32-8.86 and 2.29-8.15) µg/kg respectively. In a separate work, aflatoxin B_1 and total aflatoxin exposure from sorghum in Niger State was also calculated to be 1.75 and 2.04µg/kg bw/day (Apeh, 2014). Additionally, he estimated the daily intake of B_1 from traditional alcoholic beverage marketed in Niger State to be 3.42µg/L. Bandyopadhyay *et al.* (2007) had earlier reported an average daily aflatoxin exposure per person from sorghum in Nigeria as 3.3µg.

On Codex scale, provisional maximum tolerably daily intake-PMTDI is to be as low as reasonably possible for aflatoxins because they carcinogenic (formerly 0.0004µg/kg bw/day), 2µg/kg for fumonisins, 0.1µg/kg for ochratoxin A, 0.2µg/kg for zearalenone and 1µg/kg for deoxynivalenol. It is obvious that all the determined dietary daily intake levels for aflatoxins, zearalenone and deoxynivalenol from sorghum food products in Northern Nigeria have exceeded the allowable limits. Except for very few persons, the intake levels of fumonisins and ochratoxin A have generally exceeded permitted levels also. Considering that sorghum is resistant to mycotoxin contamination than most crops, it is very reasonable to conclude that Nigerians ingest the five major mycotoxins at alarming levels daily from their meals.

Only about 19.3% (411) of the total samples of Nigerian foods and feeds tested (2133) in all our works were found to be fit for human consumption.

Risk Characterization

Based on the above three risk evaluation findings, it is possible to estimate the severity or otherwise of the health and economic implications of the studied mycotoxins in Nigerian populace. The unacceptable levels of mycotoxin contamination and consequent intake from our foods and feeds have grievous public health and economic implications.

Aflatoxins are potent carcinogens of the liver which we have shown in our works to also be immunotoxic to human beings. If at 350 µg/kg of aflatoxins death can result (Azziz-Baumgartner *et al.,* 2005), the toxin likely accounts for the deaths of some primary school children in Ibadan, Nigeria who ingested incriminating levels of AF in groundnut cake *'kulikuli'* in 1988 (Fapohunda, 2011) and 125 death of persons who consumed maize 355µg/kg of the toxin in Kenya. Apart from death, chronic ingestion of aflatoxins above 0.001µg/kg bw/day by persons with hepatitis B virus exacerbate liver cancer incidence. This level has been exceeded in most of our foods. Based on the exposure level determined and the 13.2% presence of Hepatitis B virus in Nigerian populace, using the model of Liu and Wu, (2010), we estimated 33,453 liver cancer cases due to aflatoxin B1 in sorghum in Nigeria annually which culminates to a financial health loss of $1,637 million. No wonder aflatoxin ingestion from maize and groundnut only is the cause of 7761 liver cancer cases in Nigeria annually and the monetized total aflatoxin liver cancer burden from these two crops is between $380 and $3, 174 million (Meridian Institute, 2013). Its immuno suppressive ability as shown in our works could aggravate malaria and HIV/AIDS, kwashiorkor, growth stunting in children, genetic defects at neonatal stages and other liver diseases

(Makun *et al.*, 2012).

Ochratoxins are potent nephrotoxins, immunosuppressants, teratogens and carcinogens that cause kidney and liver impairments in man and animals especially pigs. It is the causative agent of endemic nephropathy in 20,000 people in Croatia, Bosnia and Herzegovina, Yugoslavia, Bulgaria, and Romania, and urothelial tumours of pelvis and ureter in Egypt, Croatia, Bulgaria and Yugoslavia and chronic interstitial nephropathy in Tunisia (Peraica *et al.* 1999). The presence of the toxin which are within the lower limits of OTA concentrations (200–1,000 μg/kg) that caused mycotoxic porcine nephropathy in Bulgaria (Stoev *et al.*, 2002), could with other factors, such as malaria, hypertension and diabetes, cause the rising incidences of chronic renal diseases experienced presently in Nigeria as well as animal nephropathy. Chronic renal failure (CRF) accounts for about 10% of medical admissions in Nigeria and an extrapolation of this puts the frequency figure between 200 and 300 patients per million of population (NAN, 2008)

Fumonisins have been classified by the International Agency for Research on Cancer (IARC, 1993) as possible human carcinogens in category IIB. They are associated with increased incidence of human oesphageal cancer in parts of South Africa, North Eastern Iran and China, upper gastrointestinal tract cancer in Northern Italy and neural tube defects in human babes, and leukoencephalomalacia in equine and pulmonary oedema in pigs (Marasas, 2001). Zearalenone, on the other hand is an oestrogenic toxin that causes infertility in animals and is associated with outbreaks of precocious pubertal changes in children in Puerto Rico and has been suggested to have a possible involvement in human cervical cancer (JECFA, 2000). Deoxynivalenol is RNA, DNA and protein inhibitor with consequent immunosuppressive effects, causing severe damage

to the digestive tract and death due to intestinal haemorrhage. We are therefore vulnerable to these diseases as the toxins are present in foods.

Simultaneous occurrence of the five studied mycotoxins in twos, threes, fours and fives in same sample was a common observation in the course of our works. The interactions of these toxins could be synergistic, additive or antagonistic (Miller, 1995). Aflatoxin B_1 and fumonisin B_1 synergistic interaction in exacerbating liver cancer in human population in China and experimental animals (Uena *et al.*, 1997) has drawn global attention. While aflatoxin aggravates the nephrotoxigenicity of ochratoxin with increased growth inhibition and mortality of chicks, ochratoxin A also aggravates the mutagenicity of aflatoxins in some other experimental animals (Speijer and Speijer, 2004). Other combinations reviewed by same authors that exhibit synergistic interactions include AFB_1 and the trichothecenes, FB_1 and OTA, and FB_1 and ZEA. Synergistic and additive growth depression effects of DON and FB_1 in pigs and broiler chicks respectively was also reported.

Economic losses due to mycotoxins arise from reduction in crop and livestock production, and human health. FAO statistics estimates that 25% of world's food crops are lost to mycotoxin yearly and a substantial part of the wastage is in Africa. African countries including Nigeria lose $670 million annually in order to meet European Union regulation on aflatoxins (Otuki *et al.* 2001). National Agency for Food and Drug Administration Control destroyed aflatoxin-contaminated food worth more than US$200,000 (SFI, 2005). Between 2007 and 2016 there were rejections of Nigerian produces at EU borders due to aflatoxin level which culminated to the imposition of import ban restricting export of five major agricultural produce from Nigeria to any European Union member country. This ban caused *a*

decline of ₦671.1 billion or 34.6% non-crude component of trade including processed and unprocessed food items (National Bureau of Statistics). Africa loses 40% labour productivity in Africa due to diseases and deaths exacerbated by AFs (Miller, 1995). But how does one assess the economic losses following increased pre-five mortality rates, and the death of the primary school pupils in Ibadan, and people in an Indian village and two districts in Kenya after eating moulded food contaminated with aflatoxin?

The presence of these toxins at unacceptable levels particularly in simultaneous occurrence in our foods are not only associated to the increased severity and incidence of liver, kidney, malnutrition, infertility, HIV/AIDS, cancer and other infectious diseases but have adverse implications on international trade and consequently our nation's economy which necessitates their elimination from our food and trade systems.

Plate 1: Micrograph of chick intestine after oral administration of 5000 mg/kg body weight of extract. (x 400 H & E). Mucosal denudation of intestine

Plate 2: Micrograph of mice kidney at X 100 H & E magnification after dosing interperitoneally with 66.36mg/kg body weight of extract of *F. verticillioides*. Showing wide spread intra renal tubular necrosis with micro thrombi formation

Plate 3: Micrograph of mice liver at X 100 H % E magnification after administration of a single oral dose (1438.80 mg/kg body weight) of extract. Showing massive eosinophillic leucocytes infiltration and aggregation in the mucosa. This implies eosinopillic graniloma resulting from intense inflammation caused by injury.

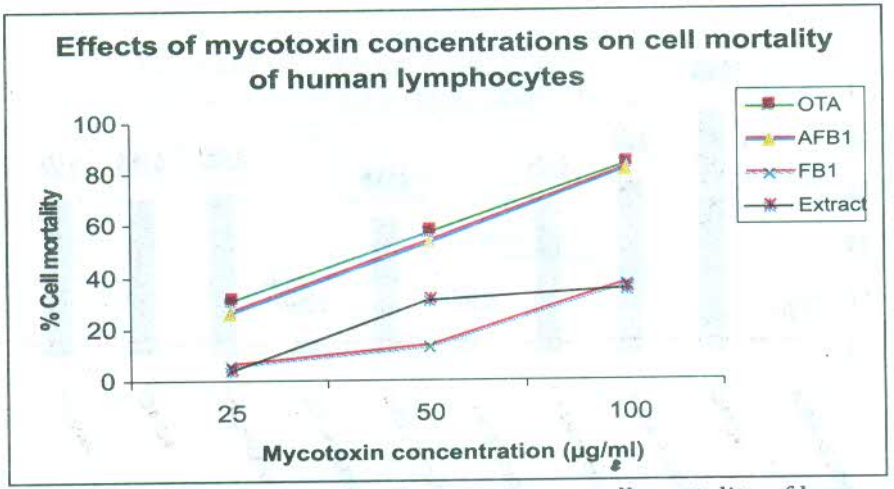

Fig. 1: Effects of mycotoxin concentration on cell mortality of human

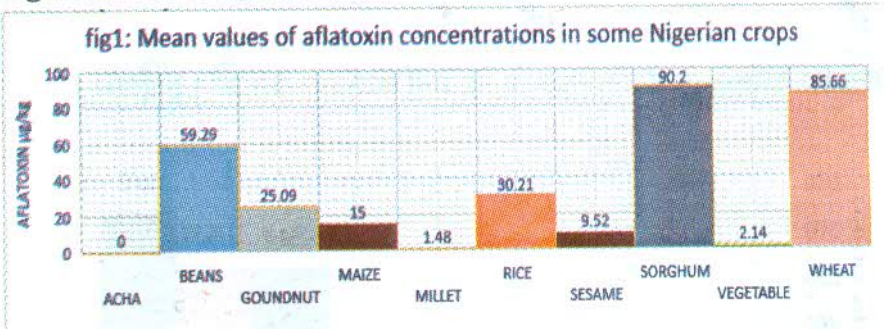

Fig. 2: Mean values of ochratoxin A concentrations in some Nigerian crops

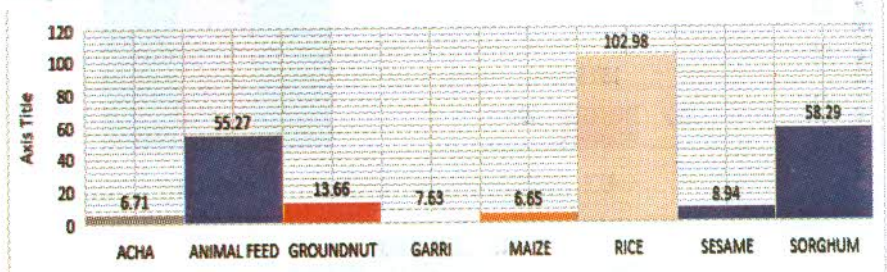

Fig. 3: Mean ocharatoxin A concentrations values of some feeds and foods in Nigerian

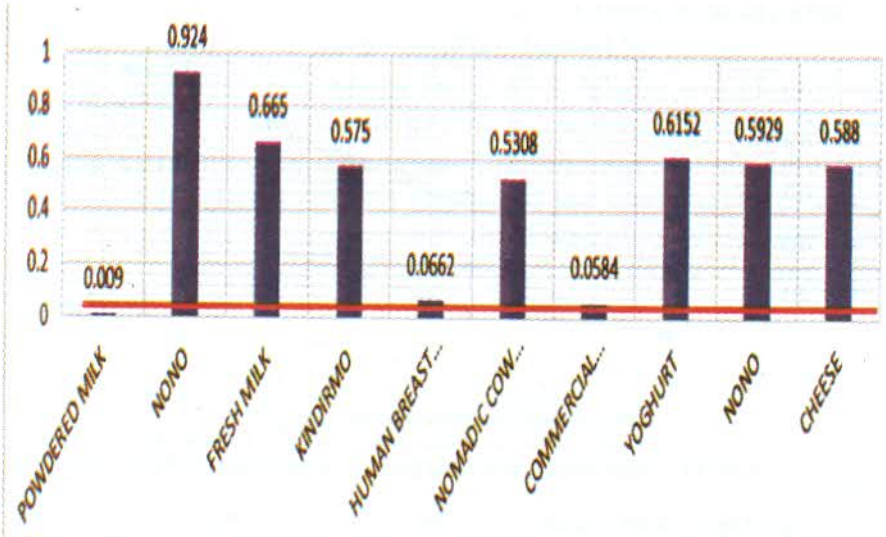

Fig. 4: Aflatoxin M_1 levels in milk and milk products in Nigeria

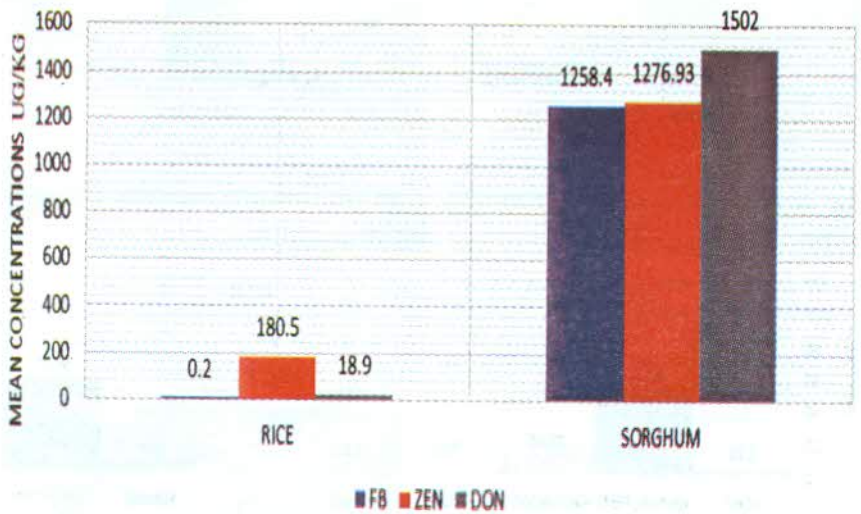

Fig. 5: Mean concentrations of fumonisin, zearalenone and deoxynivalenol in Nigerian grown rice and sorghum

Table 1: **Fungi contaminating foods and feeds in Nigeria and South Africa established by Makun *et al.* from 2007 - 2017**

Animal feed	Groundnut	Maize	Milk products	Millet	Rice
Alternaria spp	*A. niger*	*Aspergillus flavus*	*Fusarium spp.*	*Aspergillus*	*Aspergillus.*
A flavus	*A. flayus*	*Aspergillus fumigatus*	*Aspergillus flavus*	*flavus*	*aculeatus*
A.fumigatus	*A. fumigates*	*Aspergillus glaucus*	*Mucor spp.*	*Aspergillus*	*A. candidus*
A.malleus	*A. ochraeus*	*Aspergillus nidulan*	*Penicillium spp.*	*nidulans*	*A. flavus*
A. nidulans	*A.parasiticus*	*Aspergillus niger*	*Rhizopus spp.*	*Aspergillus*	*A .fumigatus*
A. niger	*Fusarium*	*Aspergillus parasiticus*	*Aspergillus niger*	*niger*	*A. niger*
A.ochraceus	*Mucor spp.*	*Aspergillus terreus*		*Aspergillus*	*A. niveus*
A. parasiticus	*Penicillium*	*Aspergillus versicolor*		*glaucus*	*A. ochraceus*
A. flaviceps	*Rhizopus spp.*	*Fusarium* spp		*Aspergillus*	*A. oryzae*
Cladosporum		*Mucor* spp		*parasiticus*	*A. parasiticus*
spp		*Rhizopus* spp		*Aspergillus*	*A. penicillioides*
Curvularia spp		*Syncephalastrum* spp		*versicolor*	*A. sclerotiorum*
Fusarium spp		*Penicillium* spp		*Arthroconidia*	*A. terreus*
F. oxysporum		*Fusarium oxysporum*		spp.	*A. tubingensis*
F.semitectum		*Fusanum* spp		*Cladosporium*	*A. unguis*
F.solani		*Penicillium notatum*		spp.	*Eurotium*
Mucor spp		*Pithomyces chartanum*		*Fusarium nwale*	*amstelodami*
Penicillium		*A.ochraceus*		*Penicillium* spp.	*Penicillium*
spp		*Yeast spp*		*Mucor* spp.	*.oxalicum*
P. citrinum				*Penicillium*	*Fusarium*
P. notatum				*rubrum*	*.chlamydosporum*
P. rubrum				*Rhizopus* spp.	*F. proliferatum*
P.verrucosum				*Phoma* spp.	*F. pseudonygamai*
Rhizopus spp				*Syncephalastru*	*F.verticilli oides*
Torula spp				*m* spp.	*Fusaruim spp.*
Yeast				*Fusarium*	*Pseudofusarium*
				verticillioides	*purpureum*
				Fusarium spp	*Acremonium* sp
				Aspergillus	*Alternaria azukiae*
				fumigatus	*Alternaria* sp
				Fusarium	*Ascomycota*. sp
				equiseti	*Botryosphaeria.dot*
				Fusarium spp	*hidea*
				Fusarium	*Curvularia affinis*
				trincintum	*Curvularia* sp.
				Helminthospori	*Sarocladium*
				um spp	*attenuatum*
				Penicillium	*Sarocladium*
				verrucosum	*oryzae*
				Rhizopus	
				stolonifer	
				Syncephalastru	
				m spp	
				Aspergillus	
				tamari	
				Cercospora spp	
				Coryospora sp	
				Curvularia spp	
				Macrophomena	
				spp	

PREVENTION AND CONTROL

With regards to mycotoxin intervention strategies, we have (a) established the reducing effects of local processing methods on mycotoxin levels (b) derived botanicals with fungicidal effects,

(c) obtained indigenous atoxigenic fungi that bioexcluded and suppress mycotoxin production by the toxigenic ones of same species and (d) provided code of practice for the prevention and reduction of aflatoxins and ochratoxin A in sorghum and sorghum based products.

Table 2: **Fungi contaminating foods in Nigeria and South Africa established by Makun *et al.* from 2007 - 2017**

Sesame	Sorghum and Sorghum Products		Vegetables	Yam flour
Aspergillus flavus,	*Aspergillus flavus*	*Fusarium moniliforme*	*Aspergillus flavus,*	*Fusarium spp*
A. parasiticus,	*Aspergillus fumigatus*	*Fusarium poae*	*Aspergillus parasiticus,*	*Aspergillus spp*
Aspergillus niger,	*Aspergillus carbonarius*	*Fusarium acuminatum*	*Aspergillus niger,*	*Aspergillus niger*
A. tamari,	*Aspergillus parasiticus*	*Fusarium hlamydosporum*	*Mucor spp*	*Penicillium spp*
Alternaria spp,	*Aspergillus oryzae*	*Fusarium proliferatum*	*Penicillium. brevicopactum*	*Mucor spp*
Fusarium spp,	*Aspergillus unguis*	*Fusarium subglutinans*	*Fusarium culmorum*	*Geotrichum candidum*
Cercospora spp	*Aspergillus niger*	*Fusarium avenaceum*	*Penicillium Brevicopactum*	
Coryospora spp	*Apergillus ustus*	*Fusarium sambucinum*	*Penicillum chrysogenium*	
Macrophomena spp	*Aspergillus versicolor*	*Fusarium trincinctum*		
Penicillium spp	*Neosartorya fischeri*	*Fusarium equiseti*		
Phoma spp	*Aspergillus melleus*	*Fusarium decemcellulare*		
Rhizopus spp,	*Aspergillus ochraceus*	*Fusarium dimerium*		
	Emericella nidulans	*Fusarium longipes*		
	Aspergillus japonicum	*Fusarium lateritium*		
	Sclerocleista ornata	*Alternaria alternata*		
	Aspergillus paradoxus	*Alternaria infectoria*		
	Emericella quadrilineata	*Curvularia lunata*		
	Penicillium citreonigrum	*Curvularia pallescens*		
	Penicillium restrictum	*Endomyces fibuliger*		
	Penicillium crustosum	*Phoma sorghina*		
	Penicillium implicatum	*Absidia cocorymbifera*		
	Penicillium malodoratum	*Rhizomucor pussillus*		
	Penicillium rogulosum	*Rhizomucor stolonifer*		
	Penicillium expansum	*Candida krusei*		
	Penicillium janczewski	*Schizosaccharomyces pombe*		
	Penicillium fellatum	*Rhodontonila mucilaginosa*		
	Penicillium paxillii	*Rhizomucor vuil*		
	Penicillium aurentiogresum	*A. tamari,*		
	Penicillium glabrum	*Cercospora spp*		
	Penicillium nalgiovense	*Coryospora spp*		
	Paecilomyces variotii	*Macrophomena spp*		
	Penicillium decumbens	*Phoma spp*		
	Fusarium verticilloides	*Rhizopus spp,*		
	Fusarium solani			
	Fusarium oxysporum			

Deriving New Analytical Methods

It is essential for analytical methods to accurately generate valid results that can be used in assessing risks in order to apply appropriate intervention strategies. This is particularly important when dealing with health related hazards like fungi and mycotoxins in foods and feeds. One of the biggest challenges in the field of mycology is to differentiate fungal species from same genus and determine concentrations of mycotoxins which occur most times at picogram levels. A false result could lead to fatality of people and animals. In addressing these difficulties, we derived a simple easy, to use and rapid molecular method for analysis of morphological form of species of *Aspergillus*. It was employed in accurate identification and differentiation of *Aspergillus flavus* and *A. parasiticus* (Iheneacho *et al.* 2014). The DNA was extracted and amplified using commercial kits but the gel electrophoresis used which was a modified method of Saghai-Maroof *et al.* (1984) allowed for the easy, rapid separation and visualization of DNA fragments of *A flavus* and *A. parasiticus* for routine use (Figure 1).

An attempt to correlate expression of Nor~1 (aflD) gene which is the main factor responsible for AFs production with levels of AFs in South African compound feeds to obtain a predictive model for aflatoxins in compound foods was carried out (Iheneacho *et al.* 2014a). To achieve this, compound feeds (n = 30) were analyzed for Nor~1 gene using real time polymerase chain reaction (RT-PCR), while AFs levels in same samples were analyzed using high-performance liquid chromatography (HPLC) after an immune-affinity clean-up extraction procedure. Results indicated that AFs levels in positive samples ranged from 0.7 to 33.0 ppb. These levels generally did not statistically correlate (R2 = 0.093) with those of Nor~1 gene in similar samples, the reason being that even if the gene is present it may or may not have been expressed to produce aflatoxins. Consequently, Nor~1 gene

levels established via RT-PCR cannot be used as a predicting model for AFs in compound feeds.

Effects of Processing

Gbodi *et al.* (2001) examined the effects of local processing methods on aflatoxin levels of some common Nigerian maize, rice and sorghum based foods. Of all the procedure tested, cooking of rice with oil, salt, pepper and other seasonings to prepare jollof rice and the preparation of fried rice by frying and boiling with salts and other seasonings eliminated aflatoxins from the foods. Other cooking methods reduced aflatoxins by between 49.8 and 98.1% (Table 3). Processing contaminated guinea corn to boiled corn starch (pap) has no effect on aflatoxin content. Wet cooking, use of salt and frying with oil were most effective in aflatoxin reduction. Moist heat opens the lactone ring of aflatoxin forming carboxylic acid which then undergoes decarboxylation, and salts also destroys aflatoxins.

Garba (2017) has also evaluated the effectiveness of seven of our traditional sorghum food processing methods which end products are *fura*, dough (Tuwo), alcoholic beverage (*pito*), waina, Chichion (*Dambu*), pap (*Kamu*) and *ogi*. He proved that the processing methods involved significantly reduce the levels of aflatoxin B_1 (59.4-95.2%), ochratoxin A (74.0-96.1%), fumonisin B_1 (73.5-94.8%), zearalenone (39.4-82.3%) and deoxynivalenol (60.8-95.3%) in the end products. Dehulling, grinding, boiling in water into thick paste, being the procedure for preparation of tuwo was the most effective in reduction of aflatoxin B_1, fumonisin B_1, ochratoxin A and deoxynivalenol while processing to waina was most effective for reduction of zearalenone. In all the samples, only a tuwo sample from Southern Guinea Savannah showed 272.3% increase in ZEA concentration while there was 66.7% increase in the concentration of OTA in Masa/Waina sample from the Sahel

Savannah. Such increase could be because of concentration or introduction of toxin during processing.

Phytofungicides

Application of synthetic seed dressing fungicides is effective measure of control of seed borne fungi and consequently mycotoxin contamination. However, the toxicity of synthetic fungicide to animals and human beings has led to the quest for non toxic, environment friendly phytofungicides. Accordingly, after showing that *Fusarium verticillioides* and its metabolites are harmful to germinating maize seedling, we proved that application of the ethanolic extract of neem reversed the adverse effect of the fungus and its metabolities by improving on germination percentage and seedling vigour with a concomitant reduction in rot index (Anjorin *et al.,* 2008). Similarly, the ethanolic extract of the leaf of *Lippia multiflora* (L) Modenke Family Verbanaceae (commonly called lemon-scented verbena) did not only improve on the germination rate and seedling vigour of sorghum seed but reversed the damage caused by *Aspergillus flavus* and its metabolites on infected sorghum seed (Anjorin *et al.,* 2008a). The *in-vitro* and *in-vivo* investigation of the antifungal properties of *Jatropha curcas* and *Ricinus cumunis* seed extracts in the control of mycelia growth and rot development of yam caused by *Fusarium verticilliodes* and *Aspergillus flavus* by Makun *et al.,* 2011b) indicates the promising potentials of *J. curcas* and *R. cumunis* seeds in management of plant fungal diseases caused by the studied fungi. Makun *et al.* (2012b) also subsequently demonstrated the *in-vitro* fungistatic efficacy of crude leaf extracts of *Azadirachta indica, Blumea perotitiana* and *Lippia multiflora* against *A. niger* and *F. verticilloides* which were the predominant fungi contaminating cowpea (bean) marketed in Minna. While the neem leaf extract had the least efficacy against the fungi, combination of *Lippa* and *Blumea* inhibited the mycelial growth of the fungi at 65% and 48.75% respectively.

Berkheya setifera and *Carissa bispinosa* are promising candidates for phytofungicides. Garba (2017), using two methods, food poisoning and Agar well diffusion method has demonstrated the effective antifungal properties of these plants against 18 common toxic fungal contaminants of food and feed namely *Aspergillus. versicolor, A. carbonaris, A. flavus, A. parasiticus, A. ochraceus, A. niger, A. fumigatus, Penicillium verrucosum, Fusarium verticillioides, F. solani, F. oxysporum, F. chamydosporum, F. subglittinans, F. acuminatum, F. avenaecem, F. poae, F. proliferatum* and *F. graminearum.* Using the food poisoning method, the extract of *Berkheya setifera* when aseptically diluted into 20ml of molten agar media, at different concentrations showed "Regular" (60 – 69%) and "Good" (70 – 79%) antifungal activity. The unique feature of the extract at all concentration is that, there is no significant difference ($P > 0.05$) between the 80, 100, 120, 140 and 160µg/20ml of the extract. Employing same technique, the extract, of *Carissa bispinosa* at concentrations of 80, 100, 120, 140 and 160µg/20ml demonstrated a good antifungal activity. All the concentrations tested showed test scores of "Regular" (60 – 69%) and "Good" (70 – 79%) and on two occasions "Very good" (80 – 90%) antifungal activity. The unique feature of the extract at all concentration is that, there is no significant difference ($P > 0.05$) between the levels of the extract tested.

Berkheya setifera extract using Agar well diffusion method clearly showed a low activity even at high concentration. The effective inhibition limit of **6.00mm** was attained in few cases and a significant difference ($P = 0.05$) existed between the standard drug (AmphotericinB) and the extract in all concentrations with regards to the zone of inhibition. The antifungal activity of *Carissa bispinosa* extract using Agar well diffusion method clearly revealed a higher activity when compared with the *Berkheya setifera* extract. The effective

inhibition limit of **6.00mm** has been attained in most cases and across all the concentrations. There is no significant difference (P = 0.05) between the standard drug (Amphotericin B) and the extract in all concentrations with regards to the zone of inhibition. Microscopic examination (plates 1, 2, 3, 4) showed dose dependent disintegration of fungal mycelium, vesicles, verticillates and macronidia of treated fungi. Thin layer chromatography of the extracts of the morphologically transformed fungi reveals suppression of ability to elaborate aflatoxin and ochratoxin A. Further purification of the extracts of the two plants will yield higher efficacy at lower dose with regards to inhibition of fungal growth and mycotoxin production.

Biocontrol

One of the newest most successful preharvest biocontrol method against aflatoxin contamination deployed in USA and Africa is the use of non toxigenic *Aspergillus flavus* and *A. parasiticus* to competitively exclude the aflatoxin producing ones of same species from maize farms. The technology has been developed into products referred to as *aflaguard* and *aflasafe* in USA and Africa respectively. In line with such technology, we have obtained indigenous atoxigenic strains of *Aspergillus flavus, A. parasiticus, A. carbonarius* and *A. niger* that suppress both the growth and, aflatoxin and ochratoxin A producing potentials of fungal isolates of same species found in Nigerian sorghum. These are bio resources that can progress into an industry that will control mycotoxins in sorghum and sorghum based products.

Participation in Prevention and Control of Mycotoxins by Codex Alimentarius Commission

Codex Alimentarius Commission (CAC) is the world body that proposes, promote coordination of all works on food standards, determine priorities and initiates and guide the preparation of draft standards, finalize standards and publish them, and amend

published standards as appropriate in the light of development. The Food and Agriculture Organization and World Health Organization consults CAC in matters pertaining to implementation of Joint FAO/WHO food standards programme. The Committee that provides CAC with technical advice is the Joint FAO/WHO Expert Committee on Food Additives (JECFA). Standards protect the health of consumers and ensure fair practices in the food trade. We prepared the first official document on sorghum for CAC in 2012 (**CX/CF 12/6/14)** after Algeria, Tunisia and Sudan had failed in the previous years to produce a document with sufficient data to initiate discussion towards setting mycotoxin standards for sorghum. This was the first assignment Nigeria did for CAC. The discussion paper on sorghum led WHO to conduct extensive multi-mycotoxin screening of sorghum in Burkina Faso, Mali, Ethiopia and Sudan where it was discovered that sterigmatocystin and diacetoxyscirpenol occurred more than the dreaded aflatoxins.

Under our expert advice and leadership, in 2013 Nigeria subsequently prepared the proposed draft annex for the prevention and reduction of aflatoxins and ochratoxin A contamination in sorghum (code of practice for the prevention and reduction of mycotoxin contamination in cereals (CAC/RCP 51-2003). The document (**CX/CF 13/7/8**) provides good agricultural, hygienic, and manufacturing practices that prevent and control aflatoxins and ochratoxin A in guinea corn. It gives the codes on when, how, and what techniques to employ in planting, harvesting, transport, storage, processing, packaging and marketing of sorghum to ensure grains and products meet the international and safe limits of 4µg/kg and 5µg/kg for aflatoxin and ochratoxin A.

Following the outcome of the WHO sorghum survey, the expert advice of JECFA was sought on sterigmatocystin and

diacetoxyscirpenol. Being one of two experts representing Nigeria on JECFA since 2012, I wrote on the prevention and control of sterigmatocystin and diacetoxyscirpenol for the 83rd meeting of JECFA held in November 2016 in Rome (**WHO Technical Report Series; No. 1002, 2017**). We observed that diacetoxyscirpenol has reproductive and developmental toxicity and therefore recommend the development of new sensitive analytical techniques and markers for its analysis and the modified forms and encourage screening of food commodities for the toxin. Same recommendations were given for sterigmatocystin.

Another indirect contribution in the work of CAC that I participate in, is as a member of the African Union Codex Expert Committee on Contaminants in Food. The Strategic Plan for the FAO/WHO Coordinating Committee for Africa (CCAFRICA) was developed with the overall objective to strengthen the role and enhance the participation and effectiveness of CCAFRICA within the Codex Alimentarius Commission and the Codex African region. In support of this objective, the African Union's Interafrican Bureau for Animal Resources (AU/IBAR) has been organizing Expert meetings since 2009. Since then AU/IBAR has convened the meeting of experts to develop science based regional positions on various Codex issues of relevance to the region before sessions of Codex Committees and Task Forces. Expert meetings have been organized in preparation for sessions of various Codex Committees. I am one of the four African Union experts taking the science based decisions on contaminants in foods for Africa since 2011 which has greatly improved Africa's participations in CAC meetings.

Providing Resource information on Mycotoxins

In addressing paucity of information on mycotoxins particularly for students, educators, researchers, regulatory officers and

policy makers in the African continent, we have shared our mycotoxin research experience in three books and two book chapters that are open access and are used by scientists all over the world as specialized references and textbooks. The first book chapter, Njobeh *et al.* (2010) provides incidence data, exposure, health impact and control of toxic fungi and mycotoxins, the second which is on aflatoxin contamination in foods and feeds in Africa (Makun *et al.* 2012) has cumulative download of 7000 as at 23rd May 2017. The compendium of abstracts of Mycotoxicology in West Africa: 1980-2015, captures 295 research efforts in various aspects of mycotoxin research in the region (Edema *et al.* 2015). The second book dwells on the epidemiology, prevention and control of food related diseases, cholera, staphylococcal food poisoning and *Toxoplasma gondii* and prion diseases in the food value chain (Makun, 2016). The book which has 10 chapters has contributors from Brazil, Mexico, Saudi Arabia, South Africa, Spain, Turkey and USA. It had a cumulative download of 5000 as at 24th May 2017. The third which was the first book I edited had a download of 45000 as at 24th July 2017 and is titled "Mycotoxin and food safety in developing countries" (Makun 2013). It captures the mycotoxin research experience of scientists from Africa, Asia and Middle East.

RECOMMENDATIONS

1. Cereals dependent diets system should be abolished. Diversifying our dietary system to include mycotoxin resistant crops like acha, millet, fresh root and tuber and vegetables to form a substantial part of our meals is recommended.

2. Good agricultural, hygienic and manufacturing practices as enshrined in the Code of practice for the prevention and reduction of mycotoxin contamination in cereals (CAC/RCP 51-2003) be adhered to by our farmers.

3. Federal Ministry of Agriculture and Rural Development whose mandate it is to regulate contaminants in food commodities within the country needs to establish regional laboratories that will conduct annual surveillance to identify contaminants to regulate, communicate risks of mycotoxin contamination and train farmers on how to eliminate them before enforcing legislated limits.

4. Standards Organization of Nigeria to conduct national toxicological and risk analysis of mycotoxins and other contaminants in Nigerian dietary system and use the generated data to set national standards that fit our agricultural and cultural systems instead of just adopting international standards.

5. Mycotoxicology Society of Nigeria is advised to formulate a national mycotoxin policy on mycotoxin management for inclusion in the national food policy which is expected to give policy directions to government, food regulatory agencies and stakeholders in the food value chain.

6. Practitioners in the public health, agriculture and food sectors are expected to be very knowledgably in the impact and control of carcinogenic food toxins, mycotoxins, and therefore we recommend the training on mycotoxins as taught courses to undergraduate and postgraduate students of medicine, veterinary medicine, agriculture and food science and other related fields.

7. One of the major challenges faced in mycotoxin research in Nigerian universities is the lack of analytical equipment. In most cases, the equipment is available but cannot be operated or maintained. The solution to this is contracting out the maintenance of these costly, sophisticated machines to qualified

technical companies along global practice. The initial rise in cost of analysis will come down with increased patronage guaranteed by efficient and endurable service.

8. Mycotoxin research like in other laboratory based sciences is capital intensive that requires research grants. This undergoes the need for the Federal Government to invigorate the national research and innovation system by implementing the National Research and Innovation Council (Establishment etc.) Bill of 2016 sponsored by Senator David Umaru of Niger East Senatorial District. It is also a call for TETFund to resuscitate the National Research Grant.

9. The fate of Nigeria lies in the hands of the academic and military institutions. While the soldiers keep it united, the academics are expected to innovate and convert it a wealthy knowledge based nation. These institutions and other instruments of governance cannot achieve these goals without merit being their guiding principle and so must be insulated from obnoxious partisan politics, ethnic and religious influence.

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REFERENCES

Adeniran, L.A. (2013). Mycobiota and concentration of ochratoxin A in poultry feeds in Minna, Nigeria. M.Tech Dissertation of Federal University of Technology, Minna.

Adeniran L.A, **Makun, H.A.** and Muhammed H.L. (2013). Survey of mycotoxigenic fungi in concentrated poultry feed in Niger State, Nigeria. *Journal of Food Research* 2 (2): 128-135

Apeh D.O. (2014). Mycoflora and aflatoxins of *Sorghum Bicolor* and traditional alcoholic beverages in Minna and Bida, Niger State, Nigeria.

Apeh Daniel Ojochenemi, Ochai Daniel Ochai, Adejumo Aderemi, Muhammad Hadiza Lami, Saidu Abubakar Ndaman, Atehnkeng Joseph, Adeyemi Rinde Henry, Mailafiya Simeon Chidawa and **Makun Hussaini Anthony** (2016). Mycotoxicological Concerns with Sorghum, Millet and Sesame in Northern Nigeria, *Journal of Analytical & Bioanalytical Techniques*; 7: 336.

Alexandra H. Heussner, Lewis E.H. Bingle. (2015). Comparative **Ochratoxin** Toxicity: A Review of the Available Data. *Toxins* (Basel) 2015 Oct; 7(10): 4253–4282.

Angela Filannino, Tom A.E. Stout, Bart M. Gadella, Edita Sostaric, Flavia Pizzi, Ben Colenbrander, Maria Elena Dell'Aquila, Fiorenza Minervini (2011). Dose-response effects of estrogenic mycotoxins (**zearalenone**, alpha-and beta-zearalenol) on motility, hyperactivation and the acrosome reaction of stallion sperm. *Reprod Biol Endocrinol.* 2011; 9: 134.

Anjorin, S.T, **Makun, H.A**, and Iheneacho, H.E. (2008). Effect of *Lippia Multiflora* leaf extract and *Aspergillus flavus* on germination and vigour indices of *Sorghum Bicolor* [L] (Moench). *International Journal of Tropical Agriculture and Food System*, 2 (1): 130 – 134.

Anjorin, S.T., **Makun, H.A**., Adesina, T and Kudu, I. (2008). Effects of *Fusarium verticilloides*, its metabolites and neem leaf extract on germination and vigour indices of maize (*Zea mays* L.). *African Journal of Biotechnology*: 7 (14): 2402-2406.

Audebert, M., Theumeur, M., Henneb, Y., Payros, D., Borin, C., Tadrist, S., Beltz, S., Puel, O., Oswald, I. (2014). Genotoxicity of aflatoxin precursors. Abstracts of Lectures and Posters of the World Mycotoxin Forum 8th Conference, Wien, Austria, 10–12 November 2014; 2014. P43: 102.

Bandyopadhyay, R., Kumar, M., and Leslie, J.F. (2007). Relative severity of aflatoxin contamination of cereal crops in West Africa. *Food Additives and Contaminants* 24(10) 1109-1114.

Bankole S.A., Adebanjo A. (2003) Mycotoxins in food in West Africa: current situation and possibilities of controlling it. *African Journal of Biotechnology* 2:254–263

Bhat R.V., Vasanthi S. (2003) Mycotoxin food safety risks in developing countries. Food Safety in Food Security and Food Trade. Vision 2020 for Food, Agriculture and Environment, Focus 10, Brief 3, pp 1–2 http://ideas.repec.org/p/fpr/2020br/1003.html

Bhatnagar, D., Yu, J and Ehrlich, K.C. (2001) Toxins of filamentous fungi. *Chemical Immunology* **81**:167-206.

Blount, W.P. (1961). Turkey "X" disease. A paper presented at the 10th Annual Conference of the British Turkey Federation Ltd. Hanogate held on 31st January 1961.

Codex Alimentarius Commission (2012). Discussion paper on fungi and mycotoxins in Sorghum. Joint FAO/WHO CCCF document CX/CF 12/6/14

Codex Alimentarius Commission (2013). Draft annex for the prevention and reduction of aflatoxin and ochratoxin A in Sorghum (CX/CF 13/7/8) to Code of Practice for the prevention and reduction of mycotoxin contamination in cereals (CAC/RCP 51-2003).

CAST (2003). Council for Agricultural Science and Technology, "Potential economics costs of mycotoxin in the United States" in Mycotoxins: Risks in Plant, Animal and Human System, Task force Report No. 139, pp136-142.

David, G.S. and Gary, P.M. (2017) Mycotoxins in Crops: A Threat to Human and Domestic Animal Health. *The American Phytopathological Society.* APSNet Feature article, March 2017

Edema Mojisola, Somorin Yinka, Atanda Olusegun, Irurhe Olubukola, **Makun Hussaini**, Areola Foluke, Ewuola Emmanuel, Ezekiel Chibundu, Oyebanji Adeola and Ogara Isaac (2015). Compendium of Abstracts of Mycotoxicology in West Africa: 1980-2015. Sara Book Publication, Ahmedabad: 1-140

Eeckhout, M., Landschoot, S., Deschuyffeleer, N., De Laethauwer,

S. and Haesaert, G. (2013). Guidelines for prevention and control of mould growth and mycotoxin production in cereals Mycohunt Annex 1 to D8.1. Report guidelines on prevention measures. Accessed on 1st October, 2016 at http://en.mytox.be/wp-content/uploads/ 2013/09/ Guidelines-for-prevention-and-control-of-mould-growth-and-mycotoxin-production-in-cereals.pdf

EFSA-European Food Safety Agency (2009). Review of mycotoxin-detoxifying agents used as feed additives: mode of action, efficacy and feed/food safety

Farlex (2012) Saunders Comprehensive Veterinary Dictionary, 3 ed. © 2007 Elsevier, Inc.

Feng Chen, Yulin Ma, Chunyi Xue, Jingyun Ma, Qingmei Xie, Genhu Wang, Yingzuo Bi, Yongchang Cao (2008). The combination of deoxynivalenol and **zearalenone** at permitted feed concentrations causes serious physiological effects in young pigs; *Journal of Veterinary Sciences.* 2008 Mar; 9(1): 39–44. Published online 2008 Mar 31. doi: 10.4142/jvs.2008.9.1.39 PMCID: PMC2839111

Gbodi, T.A., **Makun, H.A.**, Kabiru, Y.A., Ogbadoyi, E., Tijani, A.S., Lawal, S.A. and Bayero, A. (2001) Effect of local processing methods on aflatoxins contents of some common Nigerian foods prepared from artificially contaminated maize, rice and sorghum *Journal of Agricultural Sciences. Mansoura University* 26 (6): 3759-3770.

Gbodi T.A. and Nwude, N. (1988). Mycotoxicosis in Domestic Animals. A Review. *Vet. Hum. Toxicol* 30(3): 235-245.

Gong, Y.Y., Cardwell, K.K., Hounsa, A., Eggal, S., Turner, P. C., Hall,

A.J., & Wild, C.P. (2002). Dietary aflatoxin exposure and impaired growth in young children from Benin and Togo: A cross sectional study. *British Medical Journal*, 325, 20–21.

Hueza, Isis; Raspantini, Paulo; Raspantini, Leonila; Latorre, Andreia; Górniak, Silvana (2014). "Zearalenone, an Estrogenic Mycotoxin, Is an Immunotoxic Compound". *Toxins.* **6** (3): 1080–1095

IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Summaries and Evaluations, Sterigmatocystin; Monographs; IARC: Lyon, France, 1987; Volume 10, p. 72.

International Agency for Research on Cancer (IARC), Some Naturally Occurring Substances: IARC (International Agency for Research on Cancer (1993) Toxins derived from *Fusarium graminearum, F. culmorum* and *F. crookwellense*: zearalenone, deoxynivalenol, nivalenol and fusarenone X. In: *IARC monographs on the evaluation of carcinogenic risks to humans: some naturally occurring substances; food items and constituents, hetercyclic aromatic amines and mycotoxins,* Vol **56:**445-466.

IARC. (2015). In C.P. Wild, J.D. Miller, & J.D. Groopman (Eds.), Working Group Publication. Mycotoxin control in low- and middle income countries. Geneva, Switzerland: WHO Press, World Health Organisation. Report No. 9 http://www.iarc.fr/en/ publications/pdfs online/wrk/wrk9/IARC_WGR9_Coverpages.pdf.

Ifeji, E.I., **Makun, H.A.**, Mohammed, H.L., Adeyemi, R.Y.H., Mailafiya, S.C., Muhammad K.H and Olurunmowaju, Y.B. (2014). Natural occurrence of aflatoxins and ochratoxin A

in raw and roasted groundnut from Niger State, Nigeria *Mycotoxicology*, 1: 35-45

Iheanacho, H.E., Dutton, M.F., Steenkamp, P.A., Steenkamp, L. Mthombeni, J.Q, Swart, A. and **Makun, H.A.** (2014) Cytotoxic effects of aflatoxin B_1 standard in relation to aflatoxin extracts from South African compound feeds on human lymphocytes. *Mycotoxicology*, 1: 1-8

Iheanacho, H.A., Dutton, M.F., Steenkamp, P.A., Steenkamp, L. **Makun, H.A.**, Swart, A and Mthombeni, J.Q. (2014), Real time PCR of Nor~1 (aflD) gene of aflatoxin producing fungi and its correlative quantization to aflatoxin levels in South African compound feeds. *Journal of Microbiological Methods*. 97 (2014) 63–67

Iheanacho, Henry, Patrick B. Njobeh, Francis M. Dutton, Paul A. Steenkamp, Lucia Steenkamp, Julian Q. Mthombeni, Barnabas H. Daru, **Anthony H. Makun** (2014). Morphological and molecular identification of filamentous *Aspergillus flavus* and *A. parasiticus* isolated from compound feeds in South Africa. *Food Microbiology* 44:180-184

JECFA, (2000). WHO Food additives series: 44 safety evaluation of certain food additives and contaminants: Zearalenone. Joint FAO/WHO Expert Committee on Food Additives

Jouany, J.P. (2007). Methods for preventing, decontaminating and minimizing the toxicity of mycotoxins in feeds, *Animal Feed Science and Technology* 137:342–362

Lane KS (2005). New support for FDA regulation of tobacco. Available at www.Tobacco.org

Liu, G., Qian, Y., Zhang, P., Dong, W., Qi, Y. and Guo, H.T. (1992). Etiological role of *Alternaria alternata* in human esophageal cancer, *Journal of Chinese Medicine* **105**: 394–400.

Makun Hussaini Anthony (Ed) (2016). Significance, Prevention and Control of Food Related Diseases. ISBN 978-953-51-2277-7. In Tech Publisher. Croatia 1-312

Makun Hussaini Anthony (Ed) (2013). Mycotoxin and Food Safety in Developing Countries. ISBN 978-953-51-1096-5. In Tech Publisher. Croatia. 1-268

Makun H.A., Dutton M.F., Njobeh P.B., Mwanza M., Kabiru A.Y. (2011). Natural multi-occurrence of mycotoxins in rice from Niger State, Nigeria. *Mycotoxin Research* 27: 97–104.

Makun Hussaini Anthony, Apeh Daniel Ojochenemi, Adeyemi Henry Rinde Yemi, Nagogo Tahir, Okeke Johnbosco Okechukwu, Mustapha Amina Saidu and Oyinloye Bukunmi Ayobami (2014): Determination of aflatoxins in sesame, rice, millet and acha from Nigeria using HPLC. *Chemical Science Transactions* 3 (4): 1516-1524

Makun Hussaini Anthony, Apeh Daniel Ojochenemi, Mwanza Mulunda, Shittu Taofiq Oriyomi, Nneji Fortunate Jideofor, Omotosho Tunde, Egbe Ogheneruno Seun, Yusuf Ohunene Umuhani, Oshotse Bernardine Robertson, Abdulrahim Isah, Yusuf Olajumoke Halima, Eneche Benedict, Abdulrahman Umar, Ochai Daniel Ochai and Adejumo Aderemi (2016). Aflatoxin M_1 in Breast Milk, Cow Milk and Milk Products in Minna, Nigeria and their Predisposing Factors, *Biochemistry & Analytical Biochemistry*, 5 (4): 1-6.

Makun, H.A., Gbodi, T.A., Akanya, H.O., Salako, E.A., and Ogbadu, G.H., (2009a). Fungi and some mycotoxins found in mouldy Sorghum in Niger State, Nigeria. *World Journal of Agricultural Sciences*. 5 (1): 05–17.Available at www.idosi.org.

Makun, H.A., Gbodi, T.A., Akanya, H.O., Salako, E.A., and Ogbadu, G.H., (2009b). Health implications of toxigenic fungi found in two Nigerian staples: Sorghum and rice. *African Journal of Food Sciences*. 3 (9): 250–256. Available online at www.academicjournals.org/AJFS

Makun, H.A., Anjorin, S.T., Abidoye, A.S., Rufai, A.R., and Kabiru, Y.A. (2012). Incidence and botanical control of seed-borne fungi of cowpea in Niger State, Nigeria. *ARPN Journal of Agricultural and Biological Sciences* 7 (8): 654-658.

Makun Hussaini, Dutton Michael, Njobeh Patrick, Phoku Judith, Yah Clarence (2011). Incidence, phylogeny and mycotoxigenic potentials of fungi isolated from rice in Niger State, Nigeria. *Journal of Food Safety* 31, 334-349

Makun Hussaini Anthony, Dutton Michael Francis, Njobeh Patrick Berka, Gbodi Timothy Ayinla and Ogbadu Godwin Haruna (2012). Aflatoxin Contamination in Foods and Feeds: A Special Focus on Africa In: Prof. Ayman Amer Eissa (Ed.) 'Trends in Vital Food and Control Engineering' ISBN: 978-953-51-0449-0, InTech,

Makun Hussaini, Dutton Michael, Mwanza Mulunda and Njobeh Patrick (2011). Mycotoxins profiling of the culture material of *Fusarium verticillioides* (Sacc.) Nirenberg culture (CABI-IMI 392668) isolated from rice in Niger

State, Nigeria and its cytotoxic effects on human lymphocytes comparatively to those of some mycotoxin standards *African Journal of Biotechnology.* 10(56):12031-12038

Makun, H.A., Anjorin, S.T., Adeniran, L.A., Onakpa, M.M., Muhammad, H.L., Obu, O.R. and Agbofode, Y.V. (2011). Antifungal activities of *Jatropha curcas* and *Ricinus cumunis* seeds of *Fusarium verticillioides* and *Aspergillus flavus* in yam. *ARPN Journal of Agricultural and Biological Sciences* 6 (6):22-27

Makun H.A., Anjorin S.T., Moronfoye B., Adejo F.O., Afolabi O.A., Fagbayibo G., Balogun B.O. and Surajudeen A.A. (2010). Fungal and aflatoxin contaminations of some human food commodities in Nigeria. *African Journal of Food Sciences.* 4 (4): 127 – 135

Makun H.A., Gbodi T.A., Akanya H.O., Sakalo A.E., Ogbadu H.G., Tifin U.I. (2010). Acute toxicity and total fumonisin content of culture material of *Fusarium verticillioides* (Sacc.) Nirenberg (CABI-IMI392668) isolated from rice in Nigeria. *Agriculture and Biology Journal of North America* 1 (2): 103-112.

Makun, Hussaini A. Timothy, A. Gbodi, Olufunmilayo, H. Akanya, Ezekiel, A. Salako and Godwin, H. Ogbadu. (2007). Fungi and some mycotoxins contaminating rice *(Oryza sativa)* in Niger State, Nigeria. *African Journal of Biotechnology* 6 (2): 99 – 108.

Makun, H.A., Gbodi, T.A., Tijani, A.S., Abai, A. and Kadiri, G.U. (2007). Toxicologic screening of fungi isolated from millet (*Pennisetum* spp) during the rainy and dry harmattan

seasons in Niger State, Nigeria, *African Journal of Biotechnology* 6 (1): 34 – 40.

Makun Hussaini Anthony, Mulunda Mwanza, Henry Iheanacho, Daniel Ojochenemi Apeh, Sani Abdulrahim, Shaibu Jamiu, Oloso Shamsudin, Chiamaka Njeakor and Yusuf Mohammed (2017). Comparative Study of Aflatoxin M1 in Livestock Livers from Minna, Nigeria, *Journal of liver* 6 (1): 1-5.

Makun H.A., Adeniran, A.L., Mailafiya, S.C., Ayanda I.S., Mudashiru A.T., Ojukwu, U.J., Jagaba, A.S., Usman Z. and Salihu, D.A. (2013). Natural occurrence of ochratoxin A in some marketed Nigerian foods. *Food Control* 31: 566-571

Makun, H.A., Mailafiya, S.C., Saidi, A.A., Onwuike, B.C. and Onwubiko, M.U. (2012). A preliminary survey of aflatoxin in fresh and dried vegetables in Minna, Nigeria. *African Journal of Food Science and Technology* 3 (10): 268-272.

Marasas, W.F.O (1995). Fumonisins: their implications for human and animal health. *National Toxins* **3**: 193-198.

Marasas, W.F.O. (2001). Discovery and occurrence of the fumonisins: A historical perspective. *Environmental Health Perspectives Supplements Volume 109, Number S2.*

Marasas, W.F.O., Jaskiewics, K., Venter, F.S. and van Schalkwyk, D.J. (1988). *Fusarium moniliforme* contamination of maize in oesophageal cancer areas in Transkei. *South African Medical Journal* **74**: 110-114.

Miller, J.D. (1995). Fungi and mycotoxins in grains: Implications for stored product research. *J. Stored. Prod. Res.* 31 (1): 1-16

Muhammad K.H. (2012). Mycoflora and mycotoxin contamination of maize (Zea mays) during raining season in Niger State, Nigeria. M.Tech dissertation of Federal University of Technology, Minna

National Toxicology Program (NTP) (1999). Toxicology and carcinogenesis studies on fumonisin B1 in F344/N Rats and B6CF1 mice (Feed Studies). Technical Report Series 496; NIH Publication 99-3955; U.S. Department of Health and Human Services, National Institute of Health: Research Triangle Park, NC.

Njobeh B.P., Dutton F.M., **Makun, H.A**. (2010). Mycotoxins and human health: Significance, prevention and control In: Ajay K. Mishra, Ashutosh Tiwari, and Shivani B. Mishra (Eds) 'Smart Biomolecules in Medicine' VBRI Press, India 132-177

Ochai, D.O (2014). Evaluation of fungal and aflatoxins contamination of Pennisetum species (millet) and millet based products from Niger State, Nigeria. M.Tech Dissertation of Federal University of Technology, Minna.

Okeke Kingsley Susan, Abdullahi Isa Obansa and **Makun Hussaini Anthony** (2014). Microbiological quality of dairy cattle products. *British Microbiology Research Journal* 4(12): 1409-1417.

Okeke, K.S., Abdullahi, I.O., **Makun, H.A**. and Mailafiya, S.C. (2012). A preliminary survey of aflatoxin M_1 in dairy cattle products in Bida, Niger State, Nigeria. *African Journal of Food Science and Technology* 3 (10): 273-276.

Olorunmowaju, B.Y. (2012). Incidence of fungi and mycotoxins in rice (Oryza sativa) samples collected from Kaduna State, Nigeria. M.Tech Dissertation of Federal University of Technology, Minna.

Ominski, K.H. (1994). Ecological aspects of growth and toxin production by storage fungi. In: Miller, J.D., Trenholm, H.S. (Eds.). Mycotoxin in grains: Compounds other than aflatoxin. Eagan press, USA. pp. 287-305.

Otsuki, T., Wilson, J.S. and Sewadeh, M., (2001). What price precaution? European harmonization of aflatoxin regulations and African groundnut exports. *European Review of Agricultural Economics* 28: 263-283.

Peraica, M., Radic, B., Lucic, A., Pavlovic, M., 1999. Toxic effects of mycotoxins in humans. Bull. W. H. O. 77, 754–766.

Peterson, S.W., Ito, Y., Horn, B.W., Goto, T., 2001. Aspergillus bombycis, a new aflatoxigenic species and genetic variation in its sibling species, A. nomius. *Mycologia* 93, 689–703

Ramljak, D., Calvert, R.J., Wiesenfeld, P.W., Diwan, B.A., Catipovic, B., Marasas, W.F., Victor, T.C., Anderson, L.M., and Gelderblom, W.C. (2000). A potential mechanism for fumonisin B1-mediated hepatocarcinogenesis: Cyclin D1 stabilization associated with activation of Akt and inhibition of GSK-3â activity. *Carcinogenesis* 21, 1537–1546.

Richard, J.L. (2007). Some major mycotoxins and their mycotoxicoses - An overview. *Int. J. Food. Microbiol.* 119:3-10

SFI, (2005). Report on food safety problems and issues in different regions of the world. Safe Food International Available at http://www.safefoodinternational.org/african_region_international_report.doc.

Smith, J.E, Moss, M.O. (1985). Mycotoxins: formation, analysis and significance. Wiley, Chichester, pp 1–143

Speijers, GJ. and Speijers, M.H. (2004) Combined toxic effects of mycotoxins *Toxicology Letters 153*, 91-98.

Stoev, Stoycho D. and Stefan A. Denev. (2013). **Porcine**/Chicken or Human **Nephropathy** as the Result of Joint Mycotoxins Interaction. *Toxins* (Basel) 2013 Sep; 5(9): 1503–1530.

Suleiman M.S., Nuntah L.C., Muhammad H.L., Mailafiya S.C., **Makun H.A.**, Saidu, A.N., Apeh, D. and Iheanacho H.E. (2017). Fungi and Aflatoxin Occurrence in Fresh and Dried Vegetables Marketed in Minna, Niger State, Nigeria, *Journal of J Plant Biochemistry & Physiology*, 5 (1): 176-180

Su-Mi Kim, Jong-Hyeon Park, Kwang-Nyeong Lee, Se-Kyung Kim, Su-Hwa You, Taeseong Kim, Dongseob Tark, Hyang-Sim Lee, Min-Goo Seo, Byounghan Kim (2015). Robust Protection against Highly Virulent Foot-and-Mouth Disease Virus in **Swine** by Combination Treatment with Recombinant Adenoviruses Expressing **Porcine** Alpha and Gamma Interferons and Multiple Small Interfering RNAs. *J Virol.* 2015 Aug 15; 89(16): 8267–8279.

Tanaka, T., Hasegawa, A., Yamamoto, S., Lee, U.S., Sugiura, Y.; Ueno, Y. (1988). "Worldwide Contamination of Cereals by the Fusarium Mycotoxins Nivalenol, Deoxynivalenol, and

Zearalenone. 1. Survey of 19 Countries". *Journal of Agricultural and Food Chemistry. American Chemical Society.* **36** (5): 979–983.

Travis R. Bui-Klimke, Felicia Wu. (2015). **Ochratoxin** A and human health risk: A review of the evidence. *Crit Rev Food Sci Nutr.* 2015 Nov 10; 55(13): 1860–1869.

Uraguchi, K. and Yamazaki, M. (1978). Toxicology: biochemistry and pathology of mycotoxins. Halsted press, Japan. 1-278.

Wagacha J.M., Muthomi J.W., (2008). Mycotoxin problem in Africa: current status, implications to food safety and health and possible management strategies. *International Journal of Food Microbiology* 124: 1-12.

World Health Organization (WHO) (2001). Food Additives Series 47, FAO Food and Nutrition Paper 74, Presented at the 56th Meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA), WHO, Geneva. p. 557.

World Health Organization (2017). **Evaluation of Certain Contaminants in Food.** Eighty-third report of the Joint FAO/WHO Expert Committee on Food additives. WHO Technical Report Series; No. 1002, 2017 (182 Pages) **Note: 46, 115 were written by Makun, H.A.)**

Zhang, H. and Li , J.L. (1989). Study on toxicological mechanism of moniliformin. *Wei Sheng Wu XueBao* **29**: 93–100.

PROFILE OF THE INAUGURAL LECTURER

Born on 23rd May 1966 in Minna, Nigeria to the family of Mr. Peter Ojongbede and Mrs. Lami Roseleen Makun at Minna General Hospital. I had my primary and secondary education in Bosso and Waziri Primary Schools (1977), and Government Secondary School, Minna (1981). After which I obtained my Bachelor and Master of Science degrees in Biochemistry from Ahmadu Bello University, Zaria in 1985 and 1991 respectively. My PhD degree in Biochemistry was obtained from Federal University of Technology, Minna in 2007.

I started work as a secondary school teacher in 1987 at Day Secondary School, Minna and then FUT, Minna on 9th October 1992. I have twenty-five years' experience as a university academic staff and a researcher in areas relating to environmental health monitoring, mycotoxicology and mycology. My doctoral thesis was titled "Studies on Mycoflora and Mycotoxins Contaminating Guinea Corn and Rice in Niger State, Nigeria." The novelty of finding *Fusarium verticillioides* in Nigerian rice during my PhD work which is the fungi associated with oesophageal cancer (EC) in South Africa, earned me a National Research Foundation Postdoctoral Fellowship (PDF) with Food Environment and Health Research Group of the University of Johannesburg (UJ), South Africa. Being a university teaching staff for over two decades, I have taught many biochemistry and environmental toxicology related courses at both undergraduate and postgraduate levels. Have supervised and graduated over seventy-four (74) B-Tech, ten (10) M-Tech students and three (3) PhDs. The graduate students all worked on mycotoxins. Have won national and international research grants to the cumulative sum of $981,879.97.

Am a member of Mycotoxicology Society of Nigeria, Pan African

Environmental Mutagen Society and International Society o Mycotoxicology. Am currently a member of Experts o Mycotoxins in Food, Food Hygiene, Food Import/Expo Inspections and Certification System of the National Agency fo Food and Drug Administration and Control (NAFDAC) of Nigeri National Codex Committee of Nigeria, African Union Expe Committee on Contaminants in Food (2011 to date) and Joi FAO/WHO Expert Committee on Contaminants in Food (JECFA (2012-2020).

I coordinated the writing of the "Discussion Paper on Fungi an Mycotoxins in Sorghum" which was adopted as a document of th Joint FAO/WHO Experts Committee on Food Additives (JECFA) i 2012 and participated in the writing of "Proposed Draft Anne for "Prevention and Reduction of Aflatoxins and Ochratoxin A i Sorghum" in the existing code of practice for the prevention an reduction of mycotoxin contamination in cereals (CAC/RCP 51 2003)". I have 62 publications, mostly on mycotoxins in pee review journals, technical papers and books. I wrote on th Prevention and Control of Sterigmatocystin an Diacetoxyscirpenol for the 83rd Meeting of JECFA held i November, 2016 in Rome.

I have held several administrative positions in the University an am currently the Director of Research, Innovation an Development, Federal University of Technology, Minna, and Lea Researcher of the Food and Toxicology Research Group of th same University.

I am married to Barrister Evelyn Pambelo Hussaini and blesse with four children (21, 18, 16 and 11 years). I have passion fo election monitoring, jogging and reading.

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