IJLS_28182_REV

INNOVARE JOURNAL OF LIFE SCIENCE

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 7, Issue 5, 2019

ISSN - 2321-550X

Review Article

HUMAN PATHOGENIC MYCOTOXINS: CURRENT RESEARCH AND EMERGING TRENDS

VIVEK CH[1], BHASKAR M[2], VEERAIAH K[1]

[1]Departwmnt of Zoology and Aquaculture, Acharya Nagarjuna University, Guntur, Andhra Pradesh, India. [2]Department of Zoology, Division of Animal Biotechnology, Sri Venkateswara University, Tirupati, Andhra Pradesh, India. E-mail: vivekchintada1@gmail.com

Received: 9 June 2019, Revised and Accepted: 12 August 2019

ABSTRACT

Fish utilization has been growing worldwide, primarily due to the availability, access, and price in relevance different style of meat consumption, such as grouse, pork, and poultry. Therefore, some problems begin to return back forward, primarily regarding the quality of fish on the market among the market. Fish health management is one all told the foremost vital problems among the assembly of cultivation species. Associate in nursing integer of studies has been conducted to acknowledge new procedures for reducing health problem of usually farmed species. Residues may be gift in any product of animal origin reason cost-effective losses and putt into a hazard human and animal welfare. Foodstuff contamination by mycotoxins may be a risk to human and animal health, and its in command of vital economic losses. Scenery phytotoxin laws are a flowery activity that involves interested parties and several other factors, each of a scientific and socio-economic nature might influence the institution of plant toxin limits and rules. The many countries had developed definite limits for mycotoxins in foodstuffs and feedstuffs, and therefore the number persists to grow, but the residual acceptable of mycotoxins within the fish remains nonexistent. Poison formation in agriculture foodstuffs happens in hot and wet weather, and inadequate or deficient storage facilities. In recent years, aflatoxins (AFs) and its environmental effects area unit mentioned in cultivation. This review is concentrated on effects of AFs in development.

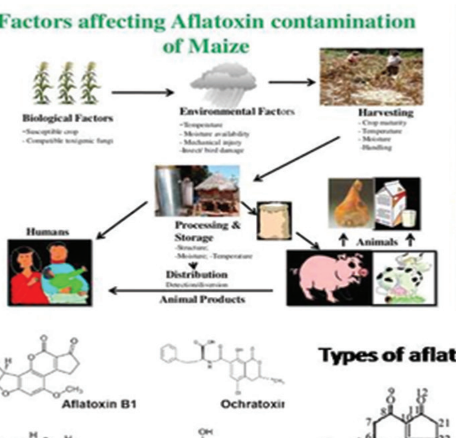
Keywords: Foodstuff, Mycotoxins, Human research.

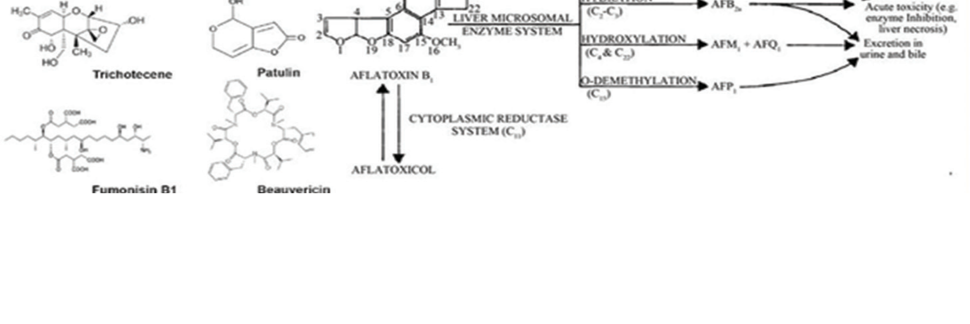
INTRODUCTION

Human being exposure to toxic chemicals may be allied with a wide array of human health disorders such as reproductive anarchy and birth scarcity, immune system inhibition, kidney and liver dysfunction, psychological health problems, and the endorsement of some types of cancer [103]. One of the main routes of human exposure to contaminants is the diet, with most foodstuff potentially hold natural or synthetic chemicals that could present toxic risk for the consumer. Victuals contagion by mycotoxins has been recognized as a public health hazard [42]. Mycotoxins can persist in organisms if the exposure is repeated or chronic [29]. Aflatoxins (AFs) include a stable and highly oxygenated structure of five fused rings and a lactone moiety [76]. Due to their diverse chemical structures and biosynthetic origins, mycotoxins have a myriad of biological effects with some being classified as carcinogenic, immunosuppressant or estrogenic, thus potentially causing severe metabolic disorders in humans [2,71].

SCOPE AND APPROACH

This review deals with the diversity of consequences of these mycotoxins and their metabolites including AFs, ochratoxin A (OTA), fumonisins (FNs), deoxynivalenol (DON), acetyl deoxynivalenols (AcDONs), and zearalenone (ZEA) when entered through the food chain to human body. The goal is risk assessment to estimate the impact on human health and prevent exposure to multiple chemicals. The US-based Center for Disease Control, recently carried out tests on blood samples and also isolated the most poisonous and cancer-causing substance known as Aflatoxin B_1 (AFB_1). Medical sources show this type of aflatoxin damages the liver (http://allafrica.com/stories/201608020624.html).





AFs

AFs are a group of the carcinogenic composite produced by *Aspergillus* fungi that can grow on different agricultural crops. Both acute and chronic disclosure to these mycotoxins can cause serious infirmity. Due to the high occurrence of AFs in crops worldwide fast and cost-effective analytical methods are required for the identification of contaminated agricultural commodities before they are processed into final products and placed on the market [62]. AFB_1, aflatoxin M1 (AFM_1) as well as OTA and DON are considered potentially toxic mycotoxins [21]. They occur in staple foods and highly consumed commodities such as cereals, milk and dairy products, dried fruits and legumes, coffee, and wine and beer [101]. This review summarizes advances in understanding the pathogenesis of necrotic enteritis of foodstuffs caused by AFs. In terms of toxicity, $AFB_1 > AFG_1 > AFB_2 > AFG_2$ and is usually explained by the presence of epoxidation of the 8,9-double bond as well as the greater potency accompanying the cyclopentenone ring of the B series, when compared with the six-membered lactone ring of the G series. $AFM_1$and AFM_2 are hydroxylated forms of AFB_1 and AFB_2. $AFM_1$and AFM_2 are major metabolites of AFB_1 and AFB_2 in humans and animals and may be present in milk from animals fed on AFB_1 and AFB_2 contaminated feed [14].

AFs M_1 and M_2 were first isolated from the milk of lactating animals (mammals) fed with aflatoxin contaminated feeds, hence, the M designation [27,32]. AFs are toxic, mutagenic, and carcinogenic compounds that can contaminate various types of agro-products, among which peanuts are one of the most susceptible foodstuffs [105]. Blankson and Mill-Robertson [14] illuminated the metabolism of AFB_1 predominantly occurs in the primary target organ (liver) which results in the formation of AFB_1-8, 9-exo-epoxide and 8, 9-endo-epoxide. The exo-epoxide which is more toxic than the endo-epoxide usually binds to DNA to form the predominant 8, 9-dihydro-8-(N7-58 guanyl)-9-hydroxy AFB_1 (AFB_1-N7-Gua) adduct. AFB_1-N7-Gua may later be converted to an apurinic site, and a more stable ring-opened AFB_1-formamidopyrimidine adducts (which happens to be more far more persistent *in vivo* than AFB_1-N7-Gua). During aflatoxin metabolism, human cytochrome P450 (CYP) enzymes such as CYP3A4, 3A5, 3A7, and 1A2 play a very key role [54].

AFs have been classified as carcinogenic to humans (Group 1) by the International Agency for Research on Cancer (IARC) [38-40]. AFM_1 is a metabolite of AFB_1 in humans and animals and can be transferred through the food chain due to its presence in milk from animals consuming contaminated feed [62]. AFs (B_1, B_2, G_1, and G_2) are metabolites produced by fungi (*Aspergillus flavus* and *Aspergillus parasiticus*) in crops, animal feed, and dairy products. AFs are highly toxic contaminants in food and feed, and their amounts increase under bad storage conditions favorite for fungal growth [17]. AFM_1 is a hydroxylated metabolite of AFB_1 found in milk of cow fed with a diet contaminated with AFB_1 [41]. AFB_1 is known the most carcinogenic among all the AFs, and hence its metabolite AFM_1 is given critical attention. Strict regulations for AFM_1 in milk and dairy products have been set. For example, European Union limits the level of AFM_1 to no more than 0.05 µg/kg in milk and dairy products and 0.025 µg/kg in infant food. AFs are mycotoxins produced mainly by *A. flavus*, *Aspergillus parasiticus,* and *Aspergillus nomius* fungi species; these substances are considered some of the most powerful and toxic existing in nature. When ingested by humans or animals, AFs have acute or chronic toxic effects with severe consequences [13].

Barani *et al*. [12] epitomized that incidence of AFs' contamination in red pepper in Iran was significantly higher than black pepper ($p<0.05$) and indicates a serious hazard for human health. AFs and OTA have been detected frequently in food, agricultural products, and traditional Chinese medicines, and their presence poses serious health and economic problems worldwide. Ginger can easily be polluted with mycotoxins [107,108]. Senerwa *et al*. [78] exemplified that the mycotoxin producing fungi contaminate feeds pre- or post-harvest and produce AFs B_1, B_2, G_1, and G_2. AFB_1 is a Class 1 human carcinogen and is converted to AFM_1 by cows and secreted in milk. AFM_1 is a Class 2B (possible) carcinogen and is associated with stunting in children. AFB_1 in feeds causes a decrease in milk production, reduced feed conversion efficiency, and reduced fertility. Shabani *et al*. [79] results suggest that nanozeolite (especially 0.75 and 1%) is able to reduce the adverse effects of AFs on meat quality, especially lipid oxidation. Asghar *et al*. [9] concluded that there is need to establish a strict and continuous national monitoring plan to improve safety and quality of spices in Pakistan. Somorin *et al*. [85] results highlighted the need for the development of strategies to reduce AFs contamination in "Egusi" for human consumption.

The investigation would benefit from the determination of the dynamic variation of AFs in infected herbs in preparation treatments, to further develop aflatoxin limits in herbal preparations [36]. Busia and Kisii Central districts have repeatedly reported high levels of AFs in foods [55]. The combination of AFB_1 with immobilized antibody introduces a barrier to electron transfer, resulting in current decrement [51]. In particular, high exposure to AFs may cause a fatal illness in people and animals, while chronic exposure can cause liver cancer in humans and, in domestic animals, growth depression, and immune suppression [45]. The study was conducted a qualitative, gendered study on awareness and perceptions of mycotoxins and how these influence risk of dietary exposure to mycotoxins among dairy farmers in Kenya [45]. Nikbakht *et al*. [61] concluded that high occurrence of AFM_1 in yogurt is a serious risk for public health. AFM_1 is a major carcinogenic compound that maybe existed in dairy products. Simao *et al*. [81] study describes a combination between hollow fiber membrane and dispersive liquid-liquid microextraction for determination of AFs in soybean juice by high-performance liquid chromatography (HPLC). The main advantage of this approach is the use of non-chlorinated solvent and small amounts of organic solvents.

TYPES OF AFS

According to Durolojkova *et al*. [22], AFs are potent toxic, carcinogenic, mutagenic, and immunosuppressive agents. Approximately 16 known types of AFs including AFB_1, aflatoxin B_2, aflatoxin B_3, aflatoxin G_1, aflatoxin G_2, aflatoxin G2a, AFM_1, aflatoxin M_2, aflatoxin P, and aflatoxin T2. The four major AFs that cause illness in humans and can be found in food are AFB_1, aflatoxin B_2, aflatoxin G_1, and aflatoxin G_2. The IARC has classified AFB_1 as a Group 1 carcinogen (carcinogenic to humans) and AFM_1 as a Group 2b carcinogen (carcinogenic to laboratory animals and possibly carcinogenic to humans, respectively).

AFs impact on fauna

Durolojkova *et al*. [22] enlighten that chronic exposure to sub-lethal doses of AFs can result in liver cancer, impaired protein formation, impaired blood coagulation, and toxic hepatitis. People who have aflatoxicosis might exhibit the following characteristics, namely, liver damage may be confirmed by jaundice and characteristic yellowing of tissues, Gall bladder may become swollen, immunosuppression may provide an opportunity for secondary infections, Vitamin K functions may decrease, and high level of AFB_1 – albumin adducts may be present in plasma.

OTA

Mycotoxins and their metabolites were estimated using the total diet study approach to assess the associated health risk to the people [109]. The OTA is a ubiquitous mycotoxin formed by fungi of offensively stored foodstuffs [66]. It is nephrotoxic and is alleged of being the main etiological driving force responsible for human Balkan endemic nephropathy (BEN) and associated urinary tract tumors. Outstanding relationship between OTA-induced porcine nephropathy in pigs and BEN in humans was observed. IARC has classified OTA as a possible human carcinogen (group 2B). At present, the mode of carcinogenic action by OTA is unknown. OTA is genotoxic following oxidative metabolism. This activity is thought to play a central role in OTA-mediated carcinogenesis and may be divided into direct (covalent DNA adduction) and indirect (oxidative DNA damage) mechanisms of action. Evidence for a direct mode of genotoxicity has been derived from the sensitive ^{32}P-post-labeling assay. OTA facilitates guanine-specific DNA adducts *in vitro* and rat and pig kidney orally dosed, one adduct comigrates with a synthetic carbon (C)-bonded C8-dG OTA adduct standard. The low molecular weight hapten, OTA, is a natural carcinogenic mycotoxin produced by *Aspergillus* and *Penicillium* fungi and so it commonly appears in wines, other foods, and in the environment [91].

The most known mycotoxins are the AFs, patulin, citrinin, fumonisin B_1 (FB_1), ZEA, and the OTA [24]. In fact, OTA is produced by different species of *Aspergillus* and *Penicillium* such as *Aspergillus ochraceus*, *Aspergillus carbonarius*, *Penicillium verrucosum,* and *Penicillium nordicum*. However, *A. carbonarius* is considered to be the main producer of OTA on coffee and grapes [23]. Cabañes *et al*. [16] conducted that experiment only *A. carbonarius* isolates were detected as producers of OTA. The report is a strong evidenced by the contribution of *A. carbonarius* in the OTA contamination in wine. Sharma *et al*. [80] reported that the nephrotoxic food mutagen OTA produced DNA adducts in rat kidneys, the major lesion being the C8-linked-2′-deoxyguanosine adduct (OTB-dG). The ability of OA to move up the food chain is aided by its long half-life in certain edible animal species [47]. The filamentous fungus *Aspergillus niger* exhibits great diversity in its phenotype. It is found globally, both as marine and terrestrial strains, produces both organic acids and hydrolytic enzymes in high amounts, and some isolates exhibit pathogenicity [7]. Krogh *et al*. [46] first report which elucidates the association of OTA and citrinin and a naturally occurring disease in domestic animals. El Khoury [24] experimental results revealed that six essential oils reduced the expression of the five imperative genes. Mishra *et al*. [58] intend for the 1st time a sensitive OTA detection in cocoa beans using competitive aptasensor by differential pulse voltammetry. Arduini *et al*. [8] results demonstrated the possibility of employing a single clean-up and a cost-effective, and easy to use analytical system for both AFB_1 and OTA detection at µg/kg (ppb) level. It is generally Karczmarczyk *et al*. [44] assumed that fast and sensitive biosensor for detection of OTA in a red wine that utilizes gold nanoparticle-enhanced surface plasmon resonance. Consumption of OTA contaminated diets by broilers results in economic losses to the poultry industry. Supplementation of 1 mg OTA/kg diet caused time- dependent alterations in renal gene expression in chicks [110].
It was clearly depicted that sorbic acid under-dosing, in addition to not preventing fungal growth, can stimulate the production of OTA in isolates of *A. carbonarius* and *A. niger* [5]. Moreover, its expression profile was similar to the two biosynthetic genes previously identified, *AcOTApks* and *AcOTAnrps*, indicating a strong correlation of *AcOTAhal* gene with the kinetics of OTA accumulation in *A. carbonarius* [26].

FNs

FNs can cocontaminate foodstuffs and have been associated with hepatocellular and esophageal carcinomas in humans at high risk for exposure [59]. On the contrary, beauvericin is a mycotoxin produced by *Fusarium* species, frequently occurring in cereal grains in combination with FB_1 and DON [4]. The authors declare that the maize is the predominant food source contaminated by FNs, and this has particular health risks for communities consuming maize as a staple diet. The main biochemical effect of FNs is the inhibition of ceramide biosynthesis causing an increase in sphingoid bases and sphingoid base 1-phosphates and a depletion of the complex sphingolipids, thereby disrupting lipid metabolism and sphingolipid-mediated processes and signaling systems [94].

FNs are a family of naturally occurring mycotoxins mainly produced by *Fusarium verticillioides* and *Fusarium proliferatum* [95]. They are ubiquitous contaminants of cereal grains worldwide, with at least 15 variants isolated, including A, B, C, and P variants [15]. FB_1, the representative mycotoxin, causes several fatal animal diseases, including leukoencephalomalacia in horses, pulmonary edema in swine, neural tube defects in mice, nephrotoxicity in rodents, and hepatotoxicity in horses, swine, and rats [19,53,96-98]. In addition, FB_1 is a carcinogen and strong tumor promoter in animal and human cell models [6,30,36]

Necrotic enteritis in chickens develops as a result of infection with pathogenic strains of *Clostridium perfringens* and the presence of predisposing factors. Predisposing factors include elements that directly change the physical properties of the gut, damaging the epithelial surface, inducing mucus production, or changing gut transit times; factors that disrupt the gut microbiota; and factors that alter the immune status of birds [60]. The coexposure to AFB_1 and FB_1 in residents of rural China may contribute to the etiology of human chronic diseases in high-risk areas [87]. Future initiatives to better understand the relationship between FNs and human health should emphasize validation of biomarkers, such as urinary FB_1 concentration, as well as comparative studies to determine which animal models are most relevant to humans [99].

DON

DON, a trichothecene mycotoxin produced by *Fusarium graminearum*, is harmful to humans and animals [35]. Because different nitrogen sources are known to have opposite effects on DON production, in this review, we characterized the interactions and their mechanisms. The present review intended to help fill the gap on the scarcity of information concerning DON. The results strongly suggest that ingestion of DON naturally contaminated feed impaired intestinal barrier and immunological functions by modulating expression of genes coding for proteins involved in tight junctions, tissue remodeling, inflammatory reaction, oxidative stress reaction, and immune response [49]. Changes in DON and deoxynivalenol-3-glucoside (D3G) levels during noodle dough fermentation were opposite that for bread. Moreover, DON levels were increased after the noodle dough extrusion, whereas D3G levels were decreased [112].

The probabilistic assessment study indicated that high-end exposure to DON and its derivatives should be concerned, especially for children. Rigorous formulation of maximum limits for DON and its derivatives in the relevant foodstuffs combined with increased monitoring should be considered as an effective way to reduce risk [88]. Wolfarth *et al*. [104] concluded that nematodes and collembolans significantly contribute to the degradation of the mycotoxin DON in wheat straw and protect soil from DON contamination as an ecosystem service. The effects of DON and ZEA on reproduction in ruminants are unclear. In investigational conclusion, DON and ZEA metabolites may impair *in vitro* cell proliferation, steroid production, and gene expression in cattle [67].

Analysis of DON and its metabolites 3-acetyldeoxynivalenol (3-ADON) and 15-acetyldeoxynivalenol (15-ADON) in wheat flour samples by LC–tandem mass spectrometry (LC/MS/MS) during 2011–2013 was conducted [50]. Pralatnet *et al*. [68] results suggested that the risk of DON exposure through noodles and breads is very low in urban areas of Thailand. No risk can be attributable to AFB_1 exposure in the same food matrices, but further studies with a larger sample size are needed to confirm. Thanner *et al*. [90] concluded that the urinary DONe/creatinine ratio and the urinary ZEAe/creatinine ratio can be used as biomarkers for DON and ZEA intake in pigs.

DON naturally contaminated feed impairs the immune response induced by porcine reproductive and respiratory syndrome virus (PRRSV) live attenuated vaccine, and feeding pigs with DON-contaminated diet could inhibit vaccination efficiency of PRRSV modified live vaccine by severely impairing viral replication [72]. More recently, Ren *et al*. [70] culture-independent studies results indicate that an imbalance in calcium homeostasis and intracellular acidification are components of DON cytotoxicity in chicken lymphocytes. The variation pattern in DON content at the field scale is related to variations in soil texture, drainage conditions, crop density, and tillage strategy [84].

Wu *et al*. [106] results clearly showed that the feeds containing DON cause a wide range of effects in a dose-dependent manner. Such effects include weight loss, live injury and oxidation stress, and malabsorption of nutrients as a result of selective regulation of nutrient transporter genes such as EAAC-3, SGLT-1, PepT-1, CAT-1, and LAT-1. Collectively, Clark [18] findings suggest that sex and advanced life stage should be considered when formulating risk assessments for DON and other trichothecene mycotoxins. DON had no significant effect on clinical manifestation of PCVAD in PCV2b infected animals. DON has neither *in vitro* nor *in vivo* clear potentiating effects in the development of porcine circovirus infection despite slight increases in viral replication [73].

AcDONs

The most predominant mycotoxins found in small-grain cereals are 8-ketotrichothecenes (type B trichothecenes) such as DON (also known as vomitoxin) and nivalenol and their acetylated derivatives including 3-ADON and 15-ADON, as well as an estrogenic mycotoxin, ZEA [100]. Stuper-Szablewska *et al*. [86] study showed a significant effect of the milling process on levels of mycotoxins in the final product. The results suggested the conversion of DON) and its derivatives may occur during wheat grain and flour storage [114].

ZEN

ZEAs are estrogenic fusarium mycotoxins consisting of a resorcinol moiety fused to a 14-member macrocyclic lactone. Substantial human estrogenicity was retained even in analogs lacking hydroxylation on the aromatic and macrocyclic rings [82]. At present, zearalenone-14-glucoside is in the pipeline, and its toxicological role is under a glowing scientific debate. In our work, it clearly showed high toxicological concerns as it is prone to conversion to well-known toxic compounds (i.e., ZEA and both zearalenol isomers) when exposed to breast cancer cells culture [20]. ZEA is a β-resorcylic acid macrolide with various biological activities. Herein, we report the synthesis and cytotoxic activities of 34 ZEA analogs against human oral epidermoid carcinoma (KB) and human breast adenocarcinoma (MCF-7) cells as well as noncancerous Vero cells [89]. The fact that β-ZEL was the predominant ZEN metabolite in horses not evidently exposed to mycotoxins along with its higher cytotoxicity raises the question of possible implications of this metabolite in interference with the equine immune system [75]. Sangsila *et al*. [74] results indicate that *Lactobacillus pentosus* strains are novel promising strains to reduce mycotoxin contamination in food products. ZEN and its reductive metabolite, α-zearalenol (α-ZEL), were present in pregnant women (11 out of 30 subjects) as conjugates at levels near the limit of quantification. The average total urinary concentration was 0.10 μg/L for ZEN and 0.11 μg/L for α-ZEL [28].

MANAGEMENT APPROACH ON THE REDUCTION OF AFS

Due to the toxicity of AFs post-harvest food, various studies for the reduction of AFs have been carried out across the world. In general, the removal of AFs is very difficult since they are stable and heat-resistant in dried materials [57]. Many researchers have tried to reduce AFs in foods and their materials through various methods. In general, the detoxification methods of removing AFs from contaminated foods and feeds are classified as physical, chemical, or biological treatments. For physical treatments, Hwang and Lee [37] reported that washing and heating processes were able to decrease the level of AFs in contaminated wheat by 50% and 90%, respectively. In the case of pressure-cooking in rice, it was able to reduce AFs by 80% [64]. The barrel temperature and material moisture have significant influences on the degradation rate of AFB_1, while the feed rate or screw speed has no significant influence [113]. In particular, Fan *et al*. [25] reported that alkaline-electrolyzed water (AIEW) influences the substantial degradation of AFs, depending on pH, the volume of AIEW, and the oil matrix in edible plant oils. In addition, *Rhodococcus erythropolis* decreased the level of AFs with high efficiency in lipid cultures [3]. Food irradiation as a technique to bring down the AFs contamination in foods was reported [33]. With gamma radiation of 25 kg, reduction rates of AFs were up to 40%.

The effects of chemical, physical, and cooking treatments on the reduction of AFB_1, B_2, G_1, and G_2 in soybean matrix were investigated. The reduction rate of AFB_1 after cooking was 97.9% for soybean milk and 33.6% for steamed soybeans [48]. Schwartzbord *et al*. [76] accomplished experiments testing laboratory-grade ethanol and clarin provide evidence that the latter can serve as a low-cost alternative to effectively reduce aflatoxin concentrations in oil pressed from high aflatoxin peanuts. The findings augur the need for interventions that will improve food safety in Haiti and limit exposure to AFs, particularly among rural communities [77]. Some studies have reported, the selection of transgenic hybrids will not replace integrated strategies of biocontrol, host plant resistance, or good crop management practices for achieving adequate mycotoxin control in corn [1].

OCCURRENCE OF MYCOTOXINS IN COMMERCIAL AQUA FEEDS: A REAL RISK TO AQUACULTURE?

There is increasing awareness of the negative effects of mycotoxins in aquatic species, which is highlighted in recent publications. Partly due to climate change associated with an overall increase of mycotoxins contamination in plant ingredients, and also due to the tendency to replace expensive animal-derived proteins, such as fish meal, by more economical plant proteins sources, which increases the probability of mycotoxin contamination in aquaculture feeds [34]. The risk of cooccurrence is high, and the knowledge on the effects of multimycotoxins contamination in aquatic species is basically none [31]. The mycotoxins concentrations used in the study, alkaline phosphatase (AP) from farmed *Litopenaeus vannamei* was sensitive to the presence of both mycotoxins; however, AP is more sensitive to the combination of AFB_1 and FB_1 suggesting a possible synergistic or potentiating inhibitory effect [65].

The T-2 toxin (T-2) is a trichothecene-A-type mycotoxin produced by the fungus *Fusarium* spp., which can contaminate animal feed. It is toxic to many living cells, especially the hepatocytes and bone marrow cells. The effects of dietary T-2 on growth, biochemical and immunity parameters, and histopathological changes in the hepatopancreas of white shrimp (*L. vannamei*). Collectively, these effects may have contributed to the inhibition of growth and decreased survival rate leading to a lower yield and quality of shrimp meat with resultant economic loss. Enlightenment of this challenge, this review identifies major research gaps and confers the way forward. *Yucca schidigera* extract (YSE) is composed of steroidal saponins, polysaccharides, and polyphenols, which have great absorption capacity for harmful volatile compounds, such as ammonia and hydrogen sulfide. Addition of 0.2% YSE in the diet was beneficial to the growth and non-specific immunity of white shrimp and water quality (Yand *et al*., 2015). Changes in both electrophoretic patterns and thermodynamic properties of myosin extracted from shrimp exposed to FB_1 were observed [56]. reduction in the levels of serum total protein, albumin, globulin, glucose, cholesterol, ALT, and elevation of AST and GGT and variable ALP levels observed in unsexed Japanese quail (*Coturnix japonica*) chicks to T_2-toxin treated groups [52]. Zeng *et al*. [111] concluded that the AFB_1 level in Pacific white shrimp (*L. vannamei*) diet should be <38.1 μg/kg.

MYCOTOXIN RESIDUES IN FISH AND RISKS FOR PUBLIC HEALTH

Global climate change is likely to change the degree of human exposure to pollutants and the response of human populations to these exposures, meaning that hazard of pollutants could revolutionize in the future. Changes in human behavior will also affect how humans come into contact with contaminated air, water, and food. Dietary changes, psychosocial stress, and coexposure to stressors such as high temperatures are likely to increase the vulnerability of humans to chemicals [11]. Fresh food products have a high-income elasticity of demand and few traditional trade barriers in high-income markets [93]. Mycotoxins have been integrated as precedence food contaminants by the Global Environment Monitoring System/Food Contamination Monitoring Assessment Programme of the WHO [102]. Mycotoxins are typically thermostable, tend to continue during the transformation and processing of infected plants and are usually not eradicated through cooking and sterilization [83,92]. The Food and Agriculture Organization's interest in emerging diseases caused by foodborne pathogens derives from its role as the leading United Nations agency with a mandate for food quality and safety matters [63]. The toxic effect of AFs and ZEA and their combination on laying performance, egg quality, and toxins residues in eggs [43].

CONCLUSIONS

There is, therefore, an urgent need for rigorous monitoring of the contamination levels of the local food supply to ensure that maximal limits in foods are not exceeded. The study's findings call for further larger-scale studies aiming at providing a comprehensive assessment of the dietary exposure of the Lebanese population to mycotoxins as well as to other food contaminants. Such studies are crucial to catalyze the development and adoption of proper management strategies to ensure the safety of the food supply in the country. Education of farmers, feed manufacturers and traders on good agricultural and feed storage practices could reduce the level of contamination and multiplication of aflatoxin producing fungi and increase profits for the dairy farmers [78]. Asghar *et al.* [10] suggested that the newly developed HPLC methods could be effectively functional for the routine analysis of the AFs in different cereals and grains. Several programs should continuously be developed by different health agencies to have a better understanding of the effect of these substances and to develop a unified strategy.

REFERENCES

1. Abbas HK, Bellaloui N, Bruns HA. Investigating transgenic corn hybrids as a method for mycotoxin control. Food and Nutr Sci 2016;7:44.
2. Fremy JM, AFSSA. Evaluation des Risques Lies a la Presence de Mycotoxines dans Leschaines Alimentaires Humaine et Animale. Rapport Final. Coordination Scientifique; 2009. p. 308.
3. Alberts JF, Engelbrecht Y, Steyn PS, Holzapfel WH, van Zyl WH. Biological degradation of aflatoxin B_1 by *Rhodococcus erythropolis* cultures. Int J Food Microbiol 2006;109:121-6.
4. Albonico M, Cortinovis C, Caloni F. *In vitro* toxicity of beauvericin alone and combined with fumonisin B1 or deoxynivalenol on Caco-2 cells. Int J Health Anim Science Food Safety, 2016;3:???
5. Alcano MD, Jahn RC, Scherer CD, Wigmann ÉF, Moraes VM, Garcia MV, *et al*. Susceptibility of *Aspergillus* spp. to acetic and sorbic acids based on pH and effect of sub-inhibitory doses of sorbic acid on ochratoxin a production. Food Res Int 2016;81:25-30.
6. Alizadeh AM, Rohandel G, Roudbarmohammadi S, Roudbary M, Sohanaki H, Ghiasian SA, *et al.* Fumonisin B_1 contamination of cereals and risk of esophageal cancer in a high risk area in Northeastern Iran. Asian Pac J Cancer Prev 2012;13:2625-8.
7. Andersen MR, Salazar MP, Schaap PJ, van de Vondervoort PJ, Culley D, Thykaer J, *et al.* Comparative genomics of citric-acid-producing *Aspergillus niger* ATCC 1015 versus enzyme-producing CBS 513.88. Genome Res 2011;21:885-97.
8. Arduini F, Neagu D, Pagliarini V, Scognamiglio V, Leonardis MA, Gatto E, *et al.* Rapid and label-free detection of ochratoxin A and aflatoxin B1 using an optical portable instrument. Talanta 2016;150:440-8.
9. Asghar MA, Iqbal J, Ahmed A, Khan MA, Shamsuddin ZA, Jamil K, *et al.* Development and validation of a high-performance liquid chromatography method with post-column derivatization for the detection of aflatoxins in cereals and grains. Toxicol Ind Health 2016;32:1122-34.
10. Asghar MA, Zahir E, Rantilal S, Ahmed A, Iqbal J. Aflatoxins in composite spices collected from local markets of Karachi, Pakistan. Food Addit Contam Part B Surveill 2016;9:113-9.
11. Balbus JM, Boxall AB, Fenske RA, McKone TE, Zeise L. Implications of global climate change for the assessment and management of human health risks of chemicals in the natural environment. Environ Toxicol Chem 2013;32:62-78.
12. Barani A, Nasiri Z, Jarrah N. Natural occurrence of aflatoxins in commercial pepper in Iran. Food Agric Immunol 2016;27:570-6.
13. Binder EM. Managing the risk of mycotoxins in modern feed production. Anim Feed Sci Technol 2007;133:149-66.
14. Blankson GK, Mill-Robertson FC. Aflatoxin contamination and exposure in processed cereal-based complementary foods for infants and young children in greater Accra, Ghana. Food Control 2016;64:212-7.
15. Bulder AS, *et al*. Safety Evaluation of Certain Food Additives and Contaminants. Geneva: World Health Organization; 2012.
16. Cabañes FJ, Accensi F, Bragulat MR, Abarca ML, Castellá G, Minguez S, *et al.* What is the source of ochratoxin a in wine? Int J Food Microbiol 2002;79:213-5.
17. Chew YL, Xing J, Lim LG, Zhan Z. A High Sensitivity LC/MS/MS Method with QuEChERS Sample Pre-treatment for Analysis of Aflatoxins in Milk Powder Samples; 2016.
18. Clark ES. Impact of Sex and Age on Deoxynivalenol-Induced Anorexia using a Murine Model. Michigan: Michigan State University; 2015.
19. Colvin BM, Harrison LR. Fumonisin-induced pulmonary edema and hydrothorax in swine. Mycopathologia 1992;117:79-82.
20. Dellafiora L, Perotti A, Galaverna G, Buschini A, Dall'Asta C. On the masked mycotoxin zearalenone-14-glucoside. Does the mask truly hide? Toxicon 2016;111:139-42.
21. Diaz DE. The Mycotoxin Blue Book. Nottingham: University Press; 2005.
22. Durolojkova E, Bajro MH, Panovska TK. The Toxicology of Aflatoxins and Public Awareness. Your Hosts Macedonian Pharmaceutical Association and Faculty of Pharmacy. Skopje: SS Cyril and Methodius University in Skopje; 2016. p. 657.
23. El Khoury A, Rizk T, Lteif R, Azouri H, Delia ML, Lebrihi A, *et al.* Occurrence of ochratoxin A and aflatoxin B1-producing fungi in Lebanese grapes and ochratoxin a content in musts and finished wines during 2004. J Agric Food Chem 2006;54:8977-82.
24. El Khoury R, Atoui A, Verheecke C, Maroun R, El Khoury A, Mathieu F, *et al.* Essential oils modulate gene expression and ochratoxin A production in *Aspergillus carbonarius*. Toxins (Basel) 2016;8:E242.
25. Fan S, Zhang F, Liu S, Yu C, Guan D, Pan C, *et al.* Removal of aflatoxin B(1) in edible plant oils by oscillating treatment with alkaline electrolysed water. Food Chem 2013;141:3118-23.
26. Ferrara M, Perrone G, Gambacorta L, Epifani F, Solfrizzo M, Gallo A, *et al.* Identification of a halogenase involved in the biosynthesis of ochratoxin A in *Aspergillus carbonarius*. Appl Environ Microbiol 2016;82:5631-41.
27. Filazi A, Ince S, Temamogullari F. Survey of the occurrence of aflatoxin M1 in cheeses produced by dairy ewe's milk in Urfa city, Turkey. Vet J Ankara Univ 2010;57:197-9.
28. Fleck SC, Churchwell MI, Doerge DR, Teeguarden JG. Urine and serum biomonitoring of exposure to environmental estrogens II: Soy isoflavones and zearalenone in pregnant women. Food Chem Toxicol 2016;95:19-27.
29. Galtier P, Loisaeu N, Oswald I, Puel OP. Toxicologie des mycotoxines: Dangers et risques en alimentation humaine et animale toxicology of mycotoxins: Hazards and risks in human and animal food. Bull Acad Vet Fr 2006;159:5-13.
30. Gelderblom WC, Marasas WF, Lebepe-Mazur S, Swanevelder S, Abel S. Cancer initiating properties of fumonisin B_1 in a short-term rat liver carcinogenesis assay. Toxicology 2008;250:89-95.
31. Gonçalves RA, Naehrer K, Santos GA. Occurrence of mycotoxins in commercial aquafeeds in Asia and Europe: A real risk to aquaculture. Rev Aquac 2016;10:263-80.
32. Gündinç U, Filazi A. Detection of aflatoxin M1 concentrations in UHT milk consumed in Turkey markets by ELISA. Pak J Biol Sci 2009;12:653-6.
33. Herzallah S, Alshawabkeh K, Fataftah AA. Aflatoxin decontamination of artificially contaminated feeds by sunlight, c-radiation, and microwave heating. J Appl Poult Res 2008;17:515-21.
34. Hooft JM, Elmor A, Ibraheem EH, Encarnacrao P, Bureau DP. Rainbow trout (*Oncorhynchus mykiss*) is extremely sensitive to the feed-borne *Fusarium* mycotoxin deoxynivalenol (DON). Aquaculture 2011;311:224-32.
35. Hou R, Jiang C, Zheng Q, Wang C, Xu JR. The areA transcription factor mediates the regulation of deoxynivalenol (DON) synthesis by ammonium and cyclic adenosine monophosphate (cAMP) signalling in *Fusarium graminearum*. Mol Plant Pathol 2015;16:987-99.
36. Hu Y, Kong W, Luo H, Zhao L, Yang M. Dynamic variation of bioactive compounds and aflatoxins in contaminated Radix Astragali during extraction process. J Sci Food Agric 2016;96:1571-9.
37. Hwang JH, Lee KG. Reduction of aflatoxin B_1 contamination in wheat by various cooking treatments. Food Chem 2006;98:71-5.
38. IARC. Monographs on the Evaluation FO Carcinogenic Risks to Humans. Lyon, France: IARC Press; 2002. p. 489-521.
39. International Agency for Research on Cancer. Some traditional herbal medicines, some mycotoxins, naphthalene and styrene. IARC Monogr Eval Carcinog Risks Hum 2002;82:171-300.
40. International Agency for Research on Cancer. Chemical agents and related occupations. A review of human carcinogens. IARC Monogr

Eval Carcinog Risks Hum 2012;100F:225-44.
41. Iqbal SZ, Jinap S, Pirouz AA, Faizal AR. Aflatoxin M_1 in milk and dairy products, occurrence and recent challenges: A review. Trends Food Sci Technol 2015;46:110-9.
42. JECFA. Evaluation of Certain Mycotoxins in Food: 56th Report of the Joint FAO/WHO Expert Committee on Food Additives. WHO Technical Report Series, No. 906. Geneva, Switzerland: World Health Organization; 2002. Available from: http://www. whqlibdoc.who.int/trs/WHO_TRS_906.pdf?ua=1. [Last accessed on 2013 Jun].
43. Jia R, Ma Q, Fan Y, Ji C, Zhang J, Liu T, *et al.* The toxic effects of combined aflatoxins and zearalenone in naturally contaminated diets on laying performance, egg quality and mycotoxins residues in eggs of layers and the protective effect of *Bacillus subtilis* biodegradation product. Food Chem Toxicol 2016;90:142-50.
44. Karczmarczyk A, Reiner-Rozman C, Hageneder S, Dubiak-Szepietowska M, Dostálek J, Feller KH, *et al.* Fast and sensitive detection of ochratoxin A in red wine by nanoparticle-enhanced SPR. Anal Chim Acta 2016;937:143-50.
45. Kiama TN, Lindahl JF, Sirma AJ, Senerwa DM, Waithanji EM, Ochungo PA, *et al*. Kenya dairy farmer perception of moulds and mycotoxins and implications for exposure to aflatoxins: A gendered analysis. Afr J Food Agric Nutr Dev 2016;16:11106-25.
46. Krogh P, Hald B, Pedersen EJ. Occurrence of ochratoxin A and citrinin in cereals associated with mycotoxic porcine nephropathy. Acta Pathol Microbiol Scand B Microbiol Immunol 1973;81:689-95.
47. Kuiper-Goodman T, Scott PM. Risk assessment of the mycotoxin ochratoxin A. Biomed Environ Sci 1989;2:179-248.
48. Lee J, Her JY, Lee KG. Reduction of aflatoxins (B_1, B_2, G_1, and G_2) in soybean-based model systems. Food Chem 2015;189:45-51.
49. Lessard M, Savard C, Deschene K, Lauzon K, Pinilla VA, Gagnon CA, *et al.* Impact of deoxynivalenol (DON) contaminated feed on intestinal integrity and immune response in swine. Food Chem Toxicol 2015;80:7-16.
50. Liu Y, Lu Y, Wang L, Chang F, Yang L. Occurrence of deoxynivalenol in wheat, Hebei province, China. Food Chem 2016;197 Pt B:1271-4.
51. Ma H, Sun J, Zhang Y, Bian C, Xia S, Zhen T, *et al.* Label-free immunosensor based on one-step electrodeposition of chitosan-gold nanoparticles biocompatible film on au microelectrode for determination of aflatoxin B1 in maize. Biosens Bioelectron 2016;80:222-9.
52. Madheswaran R, Balachandran C, Murali Manohar B. Influence of dietary culture material containing aflatoxin and T(2) toxin on certain serum biochemical constituents in Japanese quail. Mycopathologia 2004;158:337-41.
53. Marasas WF, Kellerman TS, Gelderblom WC, Coetzer JA, Thiel PG, van der Lugt JJ, *et al.* Leukoencephalomalacia in a horse induced by fumonisin B1 isolated from *Fusarium moniliforme*. Onderstepoort J Vet Res 1988;55:197-203.
54. Marin S, Ramos AJ, Cano-Sancho G, Sanchis V. Mycotoxins: Occurrence, toxicology, and exposure assessment. Food Chem Toxicol 2013;60:218-37.
55. Menza NC, Muturi MW, Kamau LM. Oil contents and aflatoxin levels in peanuts varieties produced in Busia and Kisii central districts Kenya. Trop Med Surg 2016;4:1.
56. Mexía-Salazar AL, Hernández-López J, Burgos-Hernández A, Cortez-Rocha MO, Castro-Longoria R, Ezquerra-Brauer JM, *et al.* Role of fumonisin B_1 on the immune system, histopathology, and muscle proteins of white shrimp (*Litopenaeus vannamei*). Food Chem 2008;110:471-9.
57. Ministry of Food and Drug Safety. Aflatoxin Risk Profile; 2010. Available from: http://www.foodnara.go.kr /foodnara/boardread.do?boardNo=1309162875941andcommand =READ&mid=S07_05_03&boardId=series. [Last accessed on 2014 Mar 16].
58. Mishra RK, Hayat A, Catanante G, Istamboulie G, Marty JL. Sensitive quantitation of ochratoxin A in cocoa beans using differential pulse voltammetry based aptasensor. Food Chem 2016;192:799-804.
59. Mitchell NJ, Xue KS, Lin S, Marroquin-Cardona A, Brown KA, Elmore SE, *et al.* Calcium montmorillonite clay reduces AFB1 and FB1 biomarkers in rats exposed to single and co-exposures of aflatoxin and fumonisin. J Appl Toxicol 2014;34:795-804.
60. Moore RJ. Necrotic enteritis predisposing factors in broiler chickens. Avian Pathol 2016;45:275-81.
61. Nikbakht MR, Lachiniyan S, Rahbar S, Oubari F, Rostami Z, Tajehmiri A. Aflatoxin M_1 contamination in traditional yoghurts produced in Guilan province Iran. Asian J Pharm Res Health Care 2016;8:1-3.
62. Oplatowska-Stachowiak M, Sajic N, Xu Y, Haughey SA, Mooney MH, Gong YY, *et al*. Fast and sensitive aflatoxin B_1 and total aflatoxins ELISAs for analysis of peanuts, maize and feed ingredients. Food Control 2016;63:239-45.
63. Orriss GD. Animal diseases of public health importance. Emerg Infect Dis 1997;3:497.
64. Park JW, Kim YB. Effect of pressure cooking on aflatoxin B_1 in rice. J Agric Food Chem 2006;54:2431-5.
65. Pérez-Acosta JA, Burgos-Hernandez A, Velázquez-Contreras CA, Márquez-Ríos E, Torres-Arreola W, Arvizu-Flores AA, *et al.* An *in vitro* study of alkaline phosphatase sensitivity to mixture of aflatoxin B1 and fumonisin B_1 in the hepatopancreas of coastal lagoon wild and farmed shrimp *Litopenaeus Vannamei*. Mycotoxin Res 2016;32:117-25.
66. Pfohl-Leszkowicz A, Manderville RA. Ochratoxin A: An overview on toxicity and carcinogenicity in animals and humans. Mol Nutr Food Res 2007;51:61-99.
67. Pizzo F, Caloni F, Schreiber NB, Cortinovis C, Spicer LJ. *In vitro* effects of deoxynivalenol and zearalenone major metabolites alone and combined, on cell proliferation, steroid production and gene expression in bovine small-follicle granulosa cells. Toxicon 2016;109:70-83.
68. Pralatnet S, Poapolathep S, Giorgi M, Imsilp K, Kumagai S, Poapolathep A, *et al.* Survey of deoxynivalenol and aflatoxin B_1 in instant noodles and bread consumed in Thailand by using liquid chromatography-tandem mass spectrometry. J Food Prot 2016;79:1269-72.
69. Qiu M, Wang Y, Wang X, Sun L, Ye R, Xu D, *et al*. Effects of T-2 toxin on growth, immune function and hepatopancreas microstructure of shrimp (*Litopenaeus vannamei*). Aquaculture 2016;462:35-9.
70. Ren Z, Wang Y, Deng H, Deng Y, Deng J, Zuo Z, *et al.* Effects of deoxynivalenol on calcium homeostasis of concanavalin A stimulated splenic lymphocytes of chickens *in vitro*. Exp Toxicol Pathol 2016;68:241-5.
71. Richard JL, Payne GA, Desjardin AE, Maragos C, Norred WP, Pestka JJ, *et al*. Mycotoxins Risks in Plant, Animal and Human Systems. CAST Task Force Report. Ames, Iowa, USA: Council for Agricultural Science and Technology; 2003. p. 1-217.
72. Savard C, Gagnon CA, Chorfi Y. Deoxynivalenol (DON) naturally contaminated feed impairs the immune response induced by porcine reproductive and respiratory syndrome virus (PRRSV) live attenuated vaccine. Vaccine 2015;33:3881-6.
73. Savard C, Provost C, Alvarez F, Pinilla V, Music N, Jacques M, *et al.* Effect of deoxynivalenol (DON) mycotoxin on *in vivo* and *in vitro* porcine circovirus Type 2 infections. Vet Microbiol 2015;176:257-67.
74. Sangsila A, Faucet-Marquis V, Pfohl-Leszkowicz A, Itsaranuwat P. Detoxification of zearalenone by *Lactobacillus pentosus* strains. Food Control 2016;62:187-92.
75. Schumann B, Winkler J, Mickenautsch N, Warnken T, Dänicke S. Effects of deoxynivalenol (DON), zearalenone (ZEN), and related metabolites on equine peripheral blood mononuclear cells (PBMC) *in vitro* and background occurrence of these toxins in horses. Mycotoxin Res 2016;32:153-61.
76. Schwartzbord JR, Brown DL. Aflatoxin contamination in Haitian peanut products and maize and the safety of oil processed from contaminated peanuts. Food Control 2015;56:114-8.
77. Schwartzbord JR, Leroy JL, Severe L, Brown DL. Urinary aflatoxin M_1 in Port-au-Prince and a rural community in North-East Haiti. Food Addit Contam Part A Chem Anal Control Expo Risk Assess 2016;33:1036-42.
78. Senerwa DM, Mtimet N, Sirma AJ, Nzuma J, Kang'ethe EK, Lindahl JF, *et al*. Direct Market Costs of Aflatoxins in Kenyan Dairy Value Chain; 2016.
79. Shabani A, Dastar B, Hassani S, Khomeiri M, Shabanpour B. Decreasing the effects of aflatoxins on color and oxidative stability of broiler meats using nanozeolite. J Agric Sci Technol 2016;18:109-21.
80. Sharma P, Manderville RA, Wetmore SD. Structural and energetic characterization of the major DNA adduct formed from the food mutagen ochratoxin A in the narI hotspot sequence: Influence of adduct ionization on the conformational preferences and implications for the NER propensity. Nucleic Acids Res 2014;42:11831-45.
81. Simão V, Merib J, Dias AN, Carasek E. Novel analytical procedure using a combination of hollow fiber supported liquid membrane and dispersive liquid-liquid microextraction for the determination of aflatoxins in soybean juice by high performance liquid chromatography - fluorescence detector. Food Chem 2016;196:292-300.
82. Shier WT, Shier AC, Xie W, Mirocha CJ. Structure-activity relationships for human estrogenic activity in zearalenone mycotoxins. Toxicon 2001;39:1435-8.

83. Sirot V, Fremy JM, Leblanc JC. Dietary exposure to mycotoxins and health risk assessment in the second French total diet study. Food Chem Toxicol 2013;52:1-1.
84. Soderström M, Börjesson T, Roland B, Stadig H. Modelling within-field variations in deoxynivalenol (DON) content in oats using proximal and remote sensing. Precis Agric 2015;16:1-14.
85. Somorin Y, Akinyemi A, Bertuzzi T, Pietri A. Co-occurrence of aflatoxins, ochratoxin A and citrinin in "egusi" melon (*Colocynthis citrullus* L.) seeds consumed in Ireland and the United Kingdom. Food Addit Contam Part B 2016;9:230-5.
86. Stuper-Szablewska K, Szablewski T, Buśko M, Perkowski J. Changes in contents of trichothecenes during commercial grain milling. LWT Food Sci Technol 2016;69:55-8.
87. Sun G, Wang S, Hu X, Su J, Zhang Y, Xie Y, *et al.* Co-contamination of aflatoxin B_1 and fumonisin B_1 in food and human dietary exposure in three areas of China. Food Addit Contam Part A Chem Anal Control Expo Risk Assess 2011;28:461-70.
88. Sun J, Wu Y. Evaluation of dietary exposure to deoxynivalenol (DON) and its derivatives from cereals in China. Food Control 2016;69:90-9.
89. Tadpetch K, Kaewmee B, Chantakaew K, Kantee K, Rukachaisirikul V, Phongpaichit S, *et al.* Synthesis and cytotoxic activities of semisynthetic zearalenone analogues. Bioorg Med Chem Lett 2016;26:3612-6.
90. Thanner S, Czeglédi L, Schwartz-Zimmermann HE, Berthiller F, Gutzwiller A. Urinary deoxynivalenol (DON) and zearalenone (ZEA) as biomarkers of DON and ZEA exposure of pigs. Mycotoxin Res 2016;32:69-75.
91. Tria SA, Lopez-Ferber D, Gonzalez C, Bazin I, Guiseppi-Elie A. Microfabricated biosensor for the simultaneous amperometric and luminescence detection and monitoring of ochratoxin A. Biosens Bioelectron 2016;79:835-42.
92. Turner NW, Subrahmanyam S, Piletsky SA. Analytical methods for determination of mycotoxins: A review. Anal Chim Acta 2009;632:168-80.
93. Unnevehr LJ. Food safety issues and fresh food product exports from LDCs. Agric Econ 2000;23:231-40.
94. Van Der Westhuizen L, Shephard GS, Gelderblom WC, Torres O, Riley RT. Fumonisin biomarkers in maize eaters and implications for human disease. World Mycotoxin J 2013;6:223-32.
95. Vesonder R, Peterson R, Plattner R, Weisleder D. Fumonisin B_1: Isolation from corn culture, and purification by high performance liquid chromatography. Mycotoxin Res 1990;6:85-8.
96. Voss KA, Plattner RD, Bacon CW, Norred WP. Comparative studies of hepatotoxicity and fumonisin B_1 and B_2 content of water and chloroform/methanol extracts of *Fusarium moniliforme* strain MRC 826 culture material. Mycopathologia 1990;112:81-92.
97. Voss KA, Plattner RD, Riley RT, Meredith FI, Norred WP. *In vivo* effects of fumonisin B_1-producing and fumonisin B_1-nonproducing *Fusarium moniliforme* isolates are similar: Fumonisins B_2 and B_3 cause hepato and nephrotoxicity in rats. Mycopathologia 1998;141:45-58.
98. Voss KA, Riley RT, Snook ME, Waes JG. Reproductive and sphingolipid metabolic effects of fumonisin B(1) and its alkaline hydrolysis product in LM/Bc mice: Hydrolyzed fumonisin B(1) did not cause neural tube defects. Toxicol Sci 2009;112:459-67.
99. Voss KA, Riley RT. Fumonisin toxicity and mechanism of action: Overview and current perspectives. Food Saf 2013;1:2013006.
100. Waalwijk C, Kastelein P, Vries I, Kerényi Z, van der Lee T, Hesselink T, *et al*. Major changes in *Fusarium* spp. in wheat in the Netherlands. Eur J Plant Pathol 2003;109:743-54.
101. Weidenborner M. Mycotoxins in Foodstuffs. New York: Springer; 2008. p. 1-503.
102. World Health Organization. List of Priority Contaminants and Commodity Combinations; 2002. http://www.who.int/foodsafety/publications/chem/en/tds_feb2002.pdf.
103. World Health Organization. Total Diet Studies: A Recipe for Safer Food; 2005. Available from: http://www.who.int/foodsafety/chem/TDS_recipe_2005_en.pdf?ua=1. [Last accessed on 2013 Oct].
104. Wolfarth F, Wedekind S, Schrader S, Oldenburg E, Brunotte J. Regulation of the mycotoxin deoxynivalenol by *Folsomia candida* (*Collembola*) and *Aphelenchoides saprophilus* (*Nematoda*) in an on-farm experiment. Pedobiologia 2015;58:41-7.
105. Wu LX, Ding XX, Li PW, Du XH, Zhou HY, Bai YZ, *et al*. Aflatoxin contamination of peanuts at harvest in China from 2010 to 2013 and its relationship with climatic conditions. Food Control 2016;60:117-23.
106. Wu L, Liao P, He L, Ren W, Yin J, Duan J, *et al.* Growth performance, serum biochemical profile, jejunal morphology, and the expression of nutrients transporter genes in deoxynivalenol (DON) challenged growing pigs. BMC Vet Res 2015;11:144.
107. Yang QH, Tan BP, Dong XH, Chi SY, Liu HY. Effects of different levels of *Yucca schidigera* extract on the growth and nonspecific immunity of Pacific white shrimp (*Litopenaeus vannamei*) and on culture water quality. Aquaculture 2015;439:39-44.
108. Yang Y, Wen J, Kong W, Liu Q, Luo H, Wang J, *et al.* Simultaneous determination of four aflatoxins and ochratoxin A in ginger after inoculation with fungi by ultra-fast liquid chromatography-tandem mass spectrometry. J Sci Food Agric 2016;96:4160-7.
109. Yau AT, Chen MY, Lam CH, Ho YY, Xiao Y, Chung SW, *et al.* Dietary exposure to mycotoxins of the Hong Kong adult population from a total diet study. Food Addit Contam Part A Chem Anal Control Expo Risk Assess 2016;33:1026-35.
110. Zeferino CP, Wells KD, Moura AS, Murarolli RA, Rottinghaus GE, Ledoux DR. Gene expression in the kidneys of broilers fed ochratoxin a for different time periods. World Mycotoxin J 2016;9:257-68.
111. Zeng SL, Long WQ, Tian LX, Xie SW, Chen YJ, Yang HJ, *et al*. Effects of dietary aflatoxin B_1 on growth performance, body composition, haematological parameters and histopathology of juvenile Pacific white shrimp (*Litopenaeus vannamei*). Aquac Nutr 2015;22:
112. Zhang H, Wang B. Fates of deoxynivalenol and deoxynivalenol-3-glucoside during bread and noodle processing. Food Control 2015;50:754-7.
113. Zheng H, Wei S, Xu Y, Fan M. Reduction of aflatoxin B_1 in peanut meal by extrusion cooking. LWT Food Sci Technol 2015;64:515-9.
114. Zhang H, Sun J, Zhang Y, Lu M, Sun L, Li W, *et al*. Retention of deoxynivalenol and its derivatives during storage of wheat grain and flour. Food Control 2016;65:177-81.