



Food Microbial Contamination by Toxigenic Molds-Threat for Human and Animal Health

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Abstract

The food is necessity for keeping in life humans and animals, but it can also be a threat for their health and wellbeing. Food can be contaminated by a range of microorganisms and their toxins causing foodborne illnesses. Among them the mycotoxigenic molds produce mycotoxins as metabolic products. Most of them are carcinogenic causing acute damage to human and animal organs. The most important genera in the spoilage of foods and animal feeds are *Aspergillus* and *Penicillium* species which produce a variety of aflatoxins having deleterious effects on human and animal health.

Keywords: Mycotoxins; Aflatoxins; Occurance; Detection; Control

Introduction

Mycotoxins-aflatoxins

Mycotoxins are chemical compounds, metabolic products of the mold group Michofite, so named mold secondary metabolites. *Aspergillus* species are one of the most important genera of toxigenic molds in the spoilage of foods and animal feeds that produce a variety of aflatoxins (AFTs), that cause severe health problems to humans and animals [1-3]. Among them, the aflatoxin B₁ is the most potent liver carcinogen producing acute liver damage, liver cirrhosis, tumor induction, and terarogenesis. From the harmful impact of the aflatoxins especially are affected the third world countries. There is evidence that acute aflatoxicosis outbreaks in Asia and India caused symptoms such as vomiting, abdominal pain, pulmonary edema, and fatty infiltration and necrosis of the liver, as well as fatalities [4,5].

Many other mycotoxins produced by *Aspergillus* are of great significance from the point of view of human health in cancer induction and immunosuppression. The immunosuppression caused by AFTs can increase susceptibility to infectious diseases, particularly in populations where AFT ingestion is chronic, and it can be developed by either alone or in combination with other mycotoxins. Aflatoxin B₁ is an immunosuppressor [6].

Organs that are mainly attacked by aflatoxins resulting in acute toxicity and carcinogenicity are the liver and the lungs [4]. Human liver cancer has a high incidence in central Africa and parts of Southeast Asia, and studies in several African countries and Thailand have shown a correlation between aflatoxin intake and the occurrence of primary liver cancer. It was found very strong correlation between the daily dietary intake of AFB₁ and the incidence of primary liver cancer in humans [7]. Suppression of phagocytosis by alveolar macrophages that persisted for 2 weeks was caused by exposure of lungs to aerosolic AFTs [8,9]. The main target organ of Ochratoxin A (OTA) is kidney. Animal studies showed that OTA is a potent renal carcinogen [10], also being carcinogenic to humans, as well as an immunosuppressive, teratogenic, and nephrotoxic compound [11]. High dosage of mycotoxins' contamination causes chronic mycotoxicosis, such as HCC, involving formation of DNA adducts, regulation of DNA methylation, and alteration of gene expression [12,13].

The purpose of this article is to draw attention to the danger of food contamination with mycotoxins, especially with

Aspergillus species, as well as for the possible prevention and control of this food natural contamination threatening the health of humans and animals.

Varieties of Aflatoxins

Significant mycotoxins produced by *Aspergillus species* and their toxic effects are presented in Table 1.

Mycotoxin(s)	Toxicity	Species
Aflatoxin B ₁ and B ₂	Acute liver damage, cirrhosis, carcinogenic (liver), teratogenic, and immunosuppressive	<i>A. flavus</i> , <i>A. Parasiticus</i> ,
Aflatoxin G ₁ and G ₂	Effects similar to those of B aflatoxins, G ₁ toxicity less than that of B ₁ but greater than that of B ₂	<i>A. Parasiticus</i> , <i>A. nomius</i>
Cyklopiazonic acid	Degeneration and necrosis of various organs, tremorgenic, low oral toxicity	<i>A. flavus</i> , <i>A. tamaritii</i>
Ochratoxin A	Kidney necrosis (especially in pigs), terato-genic, immunosuppressive, probably carcinogenic	<i>A. ochraceus</i> , and related species, <i>A. carbonarius</i> , <i>A. niger</i> (occasional)
Sterigmatocystin spp	Acute liver and kidney damage,	<i>A. versicolor</i> , <i>Emericella</i>
Fumitremorgens	carcinogenic (liver) Tremorgenic (rats and mice)	<i>A. fumigatus</i>
Territrems	Tremorgenic (rats and mice) Tremorgenic	<i>A. terreus</i> <i>A. clavatus</i>
Cytochalasins	Cytotoxic	<i>A.clavatus</i>
Echinulins	Feed refusals (pigs)	Tryptoquivalines

^aAdapted from Table 24.1 in *Food Microbiology*, 24. *Toxigenic Aspergillus species*, pp.539

Table 1: Mycotoxins with their toxic effects produced by *Aspergillus species*^a

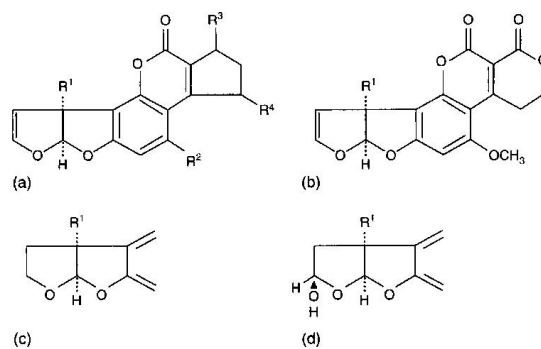
The letters B and G refer to the fluorescent colors (blue and green, respectively) observed under long-wave UV light, and the subscripts 1 and 2 refer to the toxins's separation patterns on thin-layer-chromatography plates.

Occurrence of AFs

The first data for *Aspergillus* associated with food date back to 300 years ago. They commonly occur in stored food such as grains, nuts, and spices and more frequently in tropical and subtropical climates [14,15]. *A. flavus* is one of the most commonly occurring *Aspergillus* molds in nuts and oilseeds, soybeans, mung beans and sorghum. *A. Nomius* was detected most often in peanuts and corn. The most important crops invaded by these molds are corn, peanuts and cottonseed [15]. Cereals and spices are also common crops invaded for *A. flavus*, as a result of poor drying, handling, or storage [16]. The invasion of AFTs in these commodities can take place before harvest while still in the ground, during the storage and processing. Food contaminated with AFTs is the most important risk factor in South East Africa and South East Asia [17]. AFTs are also frequent at high levels in airborne, respirable grain dust particles during cereal processing and in indoor air, because of what they represent potential threat for the environment [18-20]. There is evidence for a significant increasing in fatality from cancer and respiratory cancer in peanut-processing workers exposed to AFT-contaminated dust. There are data for co-occurrence on various mycotoxins such as AFTs with ochratoxin A in spices and processed cereal-based foods [21,22].

Chemical Structure of Aflatoxins

AFTs are difuranocoumarin derivatives (Figure 1) and they are synthesized through the polyketide pathway. The B-type AFTs are characterized by a cyclopentane E-ring. These compounds have a blue fluorescence under long-wavelength UV light, while the G-type AFTs have a xanthone ring in place of the cyclopentane and fluoresce green under UV light. AFTs of the B₂ and G₂ type have a saturated bis-furanyl ring. In Figure 1 only the bis-furan is shown. AFTs of the B_{1a} and G_{1a} type have a hydrated bis-furanyl structure.



Aflatoxins	Structure	R ¹	R ²	R ³	R ⁴
B ₁	A	H	OCH ₃	=O	H
M ₁	A	OH	OCH ₃	=O	H
P ₁	A	H	OH	=O	H
Q ₁	A	H	OCH ₃	=O	OH
R ₀	A	H	OCH ₃	OH	H
R ₀ H ₁	A	H	OCH ₃	OH	OH
B ₂	AC	H	OCH ₃	=O	H
B _{2a}	AD	H	OCH ₃	=O	H
M ₂	AC	OH	OCH ₃	=O	H
G ₁	B	H	-	-	-
G ₂	BC	H	-	-	-
G _{2a}	BD	H	-	-	-
GM	BC	OH	-	-	-

Source: *Microbial Food Contamination*, Charles L. Wilson, ed., 2nd ed., Section I, part 6, pp.127

Figure 1: Chemical structure of aflatoxins

Biochemical Activation and Molecular Mechanism of Aflatoxin Action

AFTs are converted into acutely toxic and carcinogenic reactive species by undergoing the process of oxidative metabolism. Their toxicity and carcinogenicity are exerted by covalent binding of reactive AFT metabolites to cellular macromolecules proteins, DNA and RNA. Carcinogenicity and mutagenicity by transformation with DNA modified by the carcinogen-mutagen, aflatoxin B₁, of AFTs are associated with their DNA binding properties [7].

Factors Affecting Aflatoxin's Growth and Toxin Production

Environmental factors have an influence on the production of mycotoxins [23]. AFTs are produced at optimum temperature and water activity (a_w). The temperature ranges from 12 to 40 °C. The optimum temperatures for *A. flavus* and *A. parasiticus* are from 30 to 33 °C. The optimum water activity for growth is near 0.996. The optimum water activity for growth of AFTs is of 0.80 to 0.83, but they are produced in greater quantity at higher a_w (0.98 to 0.99). pH is another important factor for growth of AFTs, with a range from above 2.0 up to 10.5 [17]. The final mycotoxin concentrations observed in food may be due to complex interactions between species and the environmental factors of the samples analyzed [24].

Control and Inactivation of Aflatoxins

Prevention of the plants from becoming infected with aflatoxigenic molds is the primary method of control of AFTs in agricultural commodities. Controls are carried out with screening techniques which are based on separation of affected grains, nuts or seeds. Screening for AFTs in corn, cottonseed and figs usually is performed by examination under UV light. Infected commodities with AFTs are segregated by electronic color-sorting machines which detect discolored kernels.

Management practices were also applied for reduction of pre-harvest [25,26] and post-harvest [27] contamination of agricultural commodities with AFTs. Sensitive and accurate analytical methods were developed for separate and simultaneous determination of the frequent mycotoxins, including aflatoxin B₁ [28-31].

Various treatments can be used for destroying AFTs in various agricultural products [32,33]. So, ozone and hydrogen peroxide have been demonstrated to remove AFTs from contaminated peanut meals. Anhydrous ammonia gas that was used at elevated temperatures and pressures was effective with a 95 to 98% reduction in total AFTs in peanut meal. With these techniques detoxification of animal feeds in several countries (Senegal, France and the USA) was applied. The surfaces of baked products may be contaminated with airborne mold spores during the relatively long product cooling period between baking and packaging. The baking of dough products reduces the microflora and moisture content, so enabling the mycotoxins that could cause spoilage to be reduced. Reduction of available oxygen

by modified-atmosphere packaging of foods in barrier film or with oxygen scavengers can inhibit AFTs formation by *A. flavus* and *A. parasiticus*.

Conclusion

Aspergillus is one of the most important genera in the spoilage of foods and animal feeds, containing a number of highly mycotoxigenic molds. The aflatoxigenic and ochratoxigenic species are the most important for human health. Other mycotoxins produced by many other mycotoxigenic molds are also of great importance for animal health than those products by *Aspergillus* species.

Because food mycotoxin contamination may occur at any stage of the food chain from the primary production, processing and storage to distribution and consumption, it is necessary to introduce a proper control as a prevention, a preventive quality systems according to the accepted standards for safety food, as well as application of the quality managing.

References

1. Monson MS, Settlage RE, Mendoza KM, Rawal S, El-Nezami HS, et al. (2015) Modulation of the spleen transcriptome in domestic turkey (*Meleagris gallopavo*) in response to aflatoxin B₁ and probiotics. *Immunogenetics* 67: 163-78.
2. Capcarova M, Zbynovska K, Kalafova A, Bulla J, Bielik P (2016) Environment contamination by mycotoxins and their occurrence in food and feed: Physiological aspects and economical approach. *J Environ Sci Health B*. 51:236-44.
3. Yang X, Liu L, Chen J, Xiao A (2017) Response of Intestinal Bacterial Flora to the Long-term Feeding of Aflatoxin B1 (AFB1) in Mice *Toxins* 9: 317.
4. Reed KM, Mendoza KM, Abrahante JE, Coulombe RA (2018) Comparative Response of the Hepatic Transcriptomes of Domesticated and Wild Turkey to Aflatoxin B1. *Toxins* 10: 42.
5. Muhammad I, Sun X, Wang H, Li W, Wang X, et al. (2017) Curcumin successfully inhibited the computationally identified CYP2A6 enzyme-mediated bioactivation of aflatoxin B1 in arbor acres broiler. *Front Pharmacol* 8:143.
6. Pierron A, Alassane-Kpembé I, Oswald IP (2016) Impact of mycotoxin on immune response and consequences for pig health. *Animal Nutr* 2:63-8.
7. Wilson CL (2008) *Microbial Food Contamination*. Taylor & Francis Group, LLC, CRC Press, USA.
8. *Damp Indoor Spaces and Health* (2004) Institute of Medicine (US) Committee on Damp Indoor Spaces and Health. National Academies Press, Washington (DC), USA.
9. Bbosa GS, Kitya D, Lubega A, Ogwal-Okeng J, Anokbonggo WW, et al. (2013) Review of the Biological and Health Effects of Aflatoxins on Body Organs and Body Systems. *Aflatoxins Mehdi Razzaghi-Abyaneh, IntechOpen*.
10. Russo P, Capozzi V, Spano G, Corbo MR, Sinigaglia M, et al. (2016) Metabolites of microbial origin with an impact on health: ochratoxin A and biogenic amines. *Front Microbiol* 7: 482.
11. Ladeira C, Frazzoli C, Orisakwe OE (2017) Engaging one health for non-communicable diseases in Africa: perspective for mycotoxins. *Front Public Health* 5: 266.
12. Dai Y, Huang K, Zhang B, Zhu L, Xu W (2017) Aflatoxin B1-induced epigenetic alterations: an overview. *Food Chem Toxicol* 109: 683-9.
13. Zhu L, Zhang B, Dai Y, Li H, and Xu W (2017) A review: epigenetic mechanism in ochratoxin a toxicity studies. *Toxins* 9: 113.
14. Pandya JP, Arade PC (2016) Mycotoxin: a devil of human, animal and crop health. *Adv Life Sci* 5: 3937-41.
15. Alshannaq A, Jae-Hyuk Y (2017) Occurrence, Toxicity, and Analysis of Major Mycotoxins in Food. *Int J Environ Res Public Health* 14: 632.
16. Thathana MG, Murage H, Abia ALK, Pillay M (2017) Morphological Characterization and Determination of Aflatoxin-Production Potentials of *Aspergillus flavus* Isolated from Maize and Soil in Kenya. *Agriculture* 7: 80.
17. Doyle MP, Beuchat LR (2007) *Food Microbiology: Fundamentals and Frontiers*, (4th Edn.) American Society for Microbiology, ASM Press, USA.
18. Schaarschmidt S, Fahl-Hassek C (2018) The Fate of Mycotoxins During the Processing of Wheat for Human Consumption. *Compr Rev Food Sci Food Safet* 556-93.
19. Viegas S, Paula LV, Almeida FA, Caroletino E, Viegas C (2015) Assessment of Workers' Exposure to Aflatoxin B1 in a Portuguese Waste Industry. *Ann Occupa Hyg* 59: 173-81.
20. Aleksic B, Draghi M, Ritoux S, Bailly S, Lacroix M, et al. (2017) Aerosolization of Mycotoxins after Growth of Toxinogenic Fungi on Wallpaper. *App Environ Microbiol* 83: PMC5541226
21. Ozbey F, Kabak B (2012) Natural Co-Occurrence of Aflatoxins and Ochratoxin A in Spices. *Food Control* 28: 354-361.
22. Assunção R, Martins C, Dupont D and Alvito P (2016) Patulin and ochratoxin a co-occurrence and their bioaccessibility in processed cereal-based foods: a contribution for Portuguese children risk assessment. *Food Chem Toxicol* 96: 205-14.
23. Kalinina SA, Jagels A, Cramer B, Geisen R, Humpf-HU (2017) Influence of Environmental Factors on the Production of Penitrem A-F by *Penicillium crustosum*. *Toxins* 9: 210.
24. Magan N, Aldred D, Hope R, Mitchell D (2010) Environmental Factors and Interactions with Mycobiota of Grain and Grapes: Effects on Growth, Deoxynivalenol and Ochratoxin Production by *Fusarium culmorum* and *Aspergillus carbonarius*. *Toxins* 2: 353-66.
25. *Critical Reviews in Food Science and Nutrition* (2013) Aflatoxins: Biosynthesis, Occurrence, Toxicity, and Remedies. 53: 862-74.

26. Gebrelassie R, Dereje A, Solomon H (2014) On Farm Pre Harvest Agronomic Management Practices of Aspergillus Infection on Groundnut in Abergelle, Tigray. *J Plant PatholMicrobiol* 5:228.
27. Abdu Selim Hamid, Isaias Goitom Tesfamariam, Yucheng Zhang, Zhen Gui Zhang (2013) Aflatoxin B1-induced hepatocellular carcinoma in developing countries: Geographical distribution, mechanism of action and prevention (Review). *Oncol Lett* 5: 1087-92.
28. Laganà A (2017) Introduction to the Toxins Special Issue on LC-MS/MS Methods for Mycotoxin Analysis. *Toxins* 9: 325.
29. Li H, Yang D, Li P, Zhang Q, Zhang W, et al. (2017) Palladium Nanoparticles-Based Fluorescence Resonance Energy Transfer Aptasensor for Highly Sensitive Detection of Aflatoxin M₁ in Milk. *Toxins* 9: 318.
30. Ren G, Hu Y, Zhang J, Zou L, Zhao G (2018) Determination of Multi-Class Mycotoxins in Tartary Buckwheat by Ultra-Fast Liquid Chromatography Coupled with Triple Quadrupole Mass Spectrometry. *Toxins* 1: 28.
31. Levasseur-Garcia C (2018) Updated Overview of Infrared Spectroscopy Methods for Detecting Mycotoxins on Cereals (Corn, Wheat, and Barley). *Toxins* 10: 38.
32. Karlovsky P, Suman M, Berthiller F, Meester JD, Eisenbrand G, et al. (2016) Impact of food processing and detoxification treatments on mycotoxin contamination. *Mycotoxin Res* 32: 179-205.
33. Mauro A, Garcia-Cela E, Pietri A, Cotty PJ, Battilani P (2018) Biological Control Products for Aflatoxin Prevention in Italy: Commercial Field Evaluation of Atoxigenic *Aspergillus flavus* Active Ingredients. *Toxins* 10: 30.