

# Impact Of Aflatoxins On Animal And Human Health

Mila Arapcheska<sup>1</sup>., Vangelica Jovanovska<sup>1</sup>., Zivko Jankuloski<sup>1</sup>, Zehra Hajruali –Musliu<sup>2</sup>, Rise Uzunov<sup>2</sup>

<sup>1</sup>Faculty of Biotechnical Sciences, University “St. Kliment Ohridski”, Bitola, Macedonia

<sup>2</sup>Faculty of Veterinary Medicine, University “Ss. Cyril and Methodius”, Skopje, Macedonia

## Abstract

The worldwide contamination of foods and feeds with aflatoxins is a significant problem. Occurrence of aflatoxins is influenced by certain environmental factors. The extent of feed and food contamination with aflatoxins vary with geographic location, agricultural and agronomic practices, and the susceptibility of commodities to fungal invasion during preharvest, storage, and/or processing periods

The high toxicity and carcinogenicity of these compounds and their ability to cause various pathological conditions in human and animals has led to widespread screening of foods and feeds potentially contaminated with them.

Crop contamination with aflatoxins causes significant economic loss for producers, marketers, and processors of diverse susceptible crops.

**Key words:** *aflatoxins, aflatoxicosis, animal health, human health*

## Introduction

Mycotoxins are a group of compounds which are products of secondary metabolism of molds. The name mycotoxin comes from Greek word “μυκησ” (fungus) and Latin word “*toxicum*” (poison). They are not essential to maintaining the life of the mold cell in a primary way (at least in a friendly world), such as obtaining energy or synthesizing structural components, informational molecules or enzymes. They are products whose function seems to be to give molds a competitive advantage over other mold species and bacteria (Durate-Vogel and Villamil-Jimenez, 2006)

Mycotoxins are nearly all cytotoxic, disrupting various cellular structures such as membranes, and interfering with vital cellular processes such as protein, RNA and DNA synthesis. They have adverse effects on humans, animals, and crops that result in illnesses and economic losses. Mycotoxins come in the organism of animal or human by contaminated food infested with spores, conidiospores and/or with fragments of mycelium. Alimentary ingestion of these fungal toxins in organism of animal or human cause intoxication called mycotoxicosis (Durate-Vogel and Villamil-Jimenez, 2006).

Because mycotoxicosis is food related it has great agro-economic importance. Economic impact of mycotoxins and mycotoxicosis include loss of animals reduced livestock production,

increased health care and veterinary care costs and disposal of contaminated foods and feeds (Husein and Brasel, 2001).

Between 300 and 400 different mycotoxins are known today, but not all of them are present in higher concentrations or have a significant health or economical impact (Cigić and Prosen 2009).

Due to their diverse chemical structures and biosynthetic origins, their myriad biological effects, and their production by a wide number of different fungal species, classification of mycotoxins is a challenge. Clinicians often arrange them by the organ they affect. Thus, mycotoxins can be classified as hepatotoxins, nephrotoxins, neurotoxins, immunotoxins, and so forth. Cell biologists put them into generic groups such as teratogens, mutagens, carcinogens, and allergens. Organic chemists have attempted to classify them by their chemical structures (e.g., lactones, coumarins); biochemists according to their biosynthetic origins (polyketides, amino acid-derived, etc.), and mycologists by the fungi that produce them (e.g., *Aspergillus* toxins, *Penicillium* toxins). None of these classifications is entirely satisfactory (Bennet and Klich, 2003).

Mycotoxins of greatest agro-economic importance are aflatoxins, ochratoxins, trichothecenes, zearalenone, fumonisins, tremorgenic toxins, and ergot alkaloids (Husein and Brasel, 2001).

## **Aflatoxins**

Aflatoxins were initially isolated and identified as the causative toxins in Turkey X disease (necrosis of the liver) in 1960 when over 100,000 turkeys died in England (Bennet and Klich, 2003).

Aflatoxins are difuranocoumarin derivatives produced by many strains of *Aspergillus flavus* and *Aspergillus parasiticus*; in particular. *Aspergillus flavus* is a common contaminant in agriculture. *Aspergillus bombycis*, *Aspergillus ochraceoroseus*, *Aspergillus nomius* and *Aspergillus pseudotamari* are also aflatoxin-producing species, but they are encountered less frequently.

There are four major aflatoxins designated on the basis of their fluorescence under UV light (blue or green) and relative chromatographic mobility during thin-layer chromatography as B1, B2, G1, and G2. B designation of aflatoxins B1 and B2 resulted from the exhibition of blue fluorescence under UV-light, while the G designation refers to the yellow-green fluorescence of the relevant structures under UV-light. M1 and M2 are metabolites found in milk of lactating animals fed with aflatoxin contaminated feed. Proportions of ingested aflatoxins B1 and B2 is hydroxylated and excreted in the milk as aflatoxins M1 and M2 (Bennet and Klich, 2003).

Aflatoxins are probably the best known and most intensively researched mycotoxins in the world. They have been associated with various diseases, such as aflatoxicosis in livestock, domestic animals and humans throughout the world. The occurrence of aflatoxins is influenced by certain environmental factors; hence the extent of contamination will vary with geographic location, agricultural and agronomic practices, and the susceptibility of commodities to fungal invasion during preharvest, storage, and/or processing periods. Aflatoxins have received greater attention than any other mycotoxins because of their demonstrated potent carcinogenic effect in susceptible laboratory animals and their acute toxicological effects in humans (De Lucca., 2007)

## Occurrence of aflatoxins

Aflatoxins can contaminate corn, cereals, sorghum, peanuts, and other oil-seed crops. Thus, food contamination by this group of mycotoxins has been implicated in both animal and human aflatoxicosis. Aflatoxins often occur in crops in the field prior to harvest. Postharvest contamination can occur if crop drying is delayed and during storage of the crop if water is allowed to exceed critical values for the mold growth. Insect or rodent infestations facilitate mold invasion of some stored commodities (Hedayati *et al.*, 2007).

Corn is probably the commodity of greatest worldwide concern, because it is grown in climates that are likely to have perennial contamination with aflatoxins and corn is the staple food of many countries (Li *et al.*, 2007)

Aflatoxin-contaminated corn in dairy rations have resulted in aflatoxin M1 contaminated milk and milk products, including non-fat dry milk, cheese, and yogurt (Fink-Gremmels., 1997).

Fungal growth and aflatoxin contamination are the consequence of interactions among the fungus, the host and the environment. The appropriate combination of these factors determines the infestation and colonization of the substrate, and the type and amount of aflatoxin produced. Water stress, high-temperature stress, and insect damage of the host plant are major determining factors in mold infestation and toxin production. Similarly, specific crop growth stages, poor fertility, high crop densities, and weed competition have been associated with increased mold growth and toxin production (Kozakiewicz 1989., De Lucca., 2007).

## Effects of aflatoxins on animal health

Aflatoxins have both acute and chronic toxicity in animals, and produce quite different effects: acute liver damage, liver cirrhosis, induction of tumours and teratogenic and other genetic effects (Benet and Klich., 2003).

Aflatoxicosis is primarily a hepatic disease. The susceptibility of individual animals to aflatoxins varies considerably depending on species, age, sex, and nutrition. In fact, aflatoxins cause liver damage, decreased milk and egg production, recurrent infection as a result of immunity suppression (Benet and Klich., 2003)..

While the young of a species are most susceptible, all ages are affected but in different degrees for different species. Clinical signs of aflatoxicosis in animals include gastrointestinal dysfunction, reduced reproductivity, reduced feed utilization and efficiency, anemia, and jaundice. Nursing animals may be affected as a result of the conversion of aflatoxin B1 to the metabolite aflatoxin M1 excreted in milk of dairy cattle (Pier *et al.*, 1980., Robens and Richard 1992).

Domestic animals (pets and agricultural), monkeys and laboratory rats and mice have been the subject of a large body of research on the adverse effects of aflatoxins (particularly B1). These effects include adducts and mutations, cancer, immunosuppression, lung injury and birth defects. Also, aflatoxins have been shown to interact with DNA (nuclear and mitochondrial adducts) and polymerases responsible for DNA and RNA synthesis (Bennet and Klich, 2003).

Among other domestic animals aflatoxicosis in cows is also described. As a result of acute toxicity, calves develop a disease that features blindness, circling and falling down, twitching of ears and grinding of teeth. Spasm of the rectum is seen in most cases. Death usually

follows within two days of onset of severe clinical signs. Postmortem findings revealed pale, firm and fibrosed liver. The kidneys are yellow and surrounded by wet fat (Diekman and Green 1992., Pier *et al.*, 1980)

Other pathological features in cattle are blood coagulation defects, which may involve impairment of prothrombin, factors VII and X and possibly factor IX. A single dose of aflatoxin causes increases in plasma enzymes (aspartate aminotransferase, lactate dehydrogenase, glutamate dehydrogenase, gamma-glutamyltransferase and alkaline phosphatase) and in bilirubin, probably reflecting liver damage. Other abnormal clinical findings are proteinuria, ketouria, glycosuria and hematuria (Hussein and Brasel, 2001)

The induction of cancer by aflatoxins has been extensively studied. Aflatoxin B<sub>1</sub>, aflatoxin M<sub>1</sub>, and aflatoxin G<sub>1</sub> have been shown to cause various types of cancer in different animal species. However, only aflatoxin B<sub>1</sub> is considered as having produced sufficient evidence of carcinogenicity in experimental animals to be identified as a carcinogen (Benet and Klich., 2003)..

### **Effects of aflatoxins on human health**

Humans are exposed to aflatoxins by consuming foods contaminated with products of fungal growth. Evidence of acute aflatoxicosis in humans has been reported from many parts of the world, namely the Third World Countries. Conditions increasing the likelihood of acute aflatoxicosis in humans include limited availability of food, environmental conditions that favor fungal development in crops, and lack of regulatory systems for aflatoxin monitoring and control. The expression of aflatoxin-related diseases in humans may be influenced by factors such as age, sex, nutritional status, and/or concurrent exposure to other causative agents such as viral hepatitis (HBV) or parasite infestation (Benet and Klich., 2003., Berek *et al.*, 2001., [Duarte-Vogel and Villamil-Jiménez 2006](#)).

In the studies reported in the medical literature aflatoxin B<sub>1</sub> has been linked to hepatocellular carcinoma in humans. Exposure to aflatoxins been implicated in hepatocellular carcinoma, hepatic failure, encephalopathy and Reye's syndrome, such exposure may also be important in the health and well being of the fetus and neonates (Hayes 1980., Benet and Klich., 2003).

### **Methods for analysis of aflatoxins in food, feed and techniques for assessing human exposure**

Mainly used methods for analysis of aflatoxins in food and feed are the thin layer chromatography (TLC), liquid chromatography (LC), and immunochemical methods. TLC is one of the most widely used separation techniques in aflatoxin analysis. Since 1990, it has been considered the AOAC official method and the method of choice to identify and quantitate aflatoxins at levels as low as 1 ng/g. Similar in many respects with TLC is LC. Usually TLC is used as a preliminary work for optimization of LC separation conditions (Cigić and Prosen 2009).

TLC and LC methods for determining aflatoxins in food are laborious and time consuming. Often, these techniques require knowledge and experience of chromatographic

techniques to solve separation and interference problems. Through advances in biotechnology, highly specific antibody-based tests are now commercially available that can identify and measure aflatoxins in food in less than 10 minutes. These tests are based on the affinities of the monoclonal or polyclonal antibodies for aflatoxins (Cigić and Prosen 2009).

In the last few years, new technologies have been developed that more accurately monitor individual exposures to aflatoxins. Particular attention has been paid to the analysis of aflatoxin DNA adducts and albumin adducts as surrogates for genotoxicity in people (Sinovec *et al.*, 2009).

### **Economic impact of aflatoxins**

The economic impact of aflatoxins derive directly from crop and livestock losses as well as indirectly from the cost of regulatory programs designed to reduce risks to animal and human health (Benet and Klich., 2003).

Other adverse economic effects of aflatoxins include lower yields for crops. The high toxicity and carcinogenicity of these compounds and their ability to cause various pathological conditions has led to widespread screening of foods and feeds potentially contaminated with them (Sinovec *et al.*, 2009).

### **Conclusions**

The occurrence of aflatoxins is influenced by certain environmental factors; hence the extent of contamination will vary with geographic location, agricultural and agronomic practices, and the susceptibility of commodities to fungal invasion during preharvest, storage, and/or processing periods.

Aflatoxins have both acute and chronic toxicity in animals, and produce quite different effects: acute liver damage, liver cirrhosis, induction of tumours and teratogenic and other genetic effects.

Exposure of humans to aflatoxins been implicated in hepatocellular carcinoma, hepatic failure, encephalopathy and Reye's syndrome, such exposure may also be important in the health and well being of the fetus and neonates.

Aflatoxins and the associated health disorders in humans and animals have been recognized as a major health and economical problem which dictates measures to minimize the exposure by applying proper agricultural practice, storage of products and control of the products intended for human or animal consumption.

The high toxicity and carcinogenicity of these compounds and their ability to cause various pathological conditions has led to widespread screening of foods and feeds potentially contaminated with them

## References

1. Bennett J.W., Klich M. Mycotoxins. *Clinical Microbiology Reviews*. Vol. 16, No. 3. (2003) pp: 497-516.
2. Berek L, Petri IB, Mesterházy Á, Téren J, Molnár J. Effects of mycotoxins on human immune functions *in vitro*. *Toxicol in Vitro*. Vol.15. (2001) pp:25-30.
3. Cigić K.I., Prosen H. An Overview of Conventional and Emerging Analytical Methods for the Determination of Mycotoxins. *Int. J. Mol. Sci.* Vol. 10. (2009) pp: 62-115.
4. De Lucca A.J. Harmful fungi in both Agriculture and Medicine. *Rev Iberoam Micol* Vol. 24. (2007) pp: 3-13.
5. Diekman MA, Green ML. Mycotoxins and reproduction in domestic livestock. *J Anim Sci* Vol.70. pp: (1992) 1615-1627.
6. Duarte-Vogel S, Villamil-Jiménez LC. Micotoxins in public health. *Rev Salud Publica (Bogota)*. Suppl 1. pp: (2006) 129-35.
7. Fink-Gremmels, J. Mycotoxins: their implications for human and animal health. *Vet. Q.* Vol.21. (1999) pp:115–120.
8. Hayes, A. W. Mycotoxins: a review of biological effects and their role in human diseases. *Clin. Toxicol.* Vol.17. (1980) pp:45–83.
9. Hussein S.H., Brasel J.M. Toxicity, metabolism, and impact of mycotoxins on humans and animals. *Toxicology*. Vol. 167 (2). (2001) pp: 101-134.
10. Hedayati M.T., Pasqualotto A.C., Warn P.A., Bowyer P. Denning D.W. *Aspergillus flavus*: human pathogen, allergen and mycotoxin producer. *Microbiology* Vol.153. pp: (2007) 1677–1692.
11. Kozakiewicz, Z. *Aspergillus Species on Stored Products*. (1989) Wallingford: CAB International.
12. Li FQ, Yoshizawa T, Kawamura O, Luo X-Y, Li Y-W. Aflatoxins and fumonisins in corn from the highincidence area for human hepatocellular carcinoma in Guangxi, China. *J Agric Food Chem* Vol.49: (2001) pp:4122-426.
13. Pier, A. C., Richard J. L., Cysewski S. J. Implications of mycotoxins in animal disease. *J. Am. Vet. Med. Assoc.* Vol.176 (1980) pp: 719–724.
14. Robens, J. F., and J. L. Richard. Aflatoxins in animal and human health. *Rev. Environ. Contam. Toxicol.* Vol.127. (1992) pp:69–94.