Bulletin of Environment, Pharmacology and Life Sciences
Bull. Env. Pharmacol. Life Sci., Spl Issue [2] 2023: 202-208
©2023 Academy for Environment and Life Sciences, India
Online ISSN 2277-1808
Journal's URL:http://www.bepls.com
CODEN: BEPLAD

REVIEW ARTICLE **OPEN ACCESS**

Aflatoxin Toxicology: Unraveling the Comprehensive Overview of a Potent Mycotoxin

Yeole R. B., Bhutada S. A. and Dahikar S. B.
Department of Microbiology, Sanjivani Arts, Commerce and Science College, Kopargaon, Maharashtra (India)

ABSTRACT

Aflatoxins, a class of highly toxic and carcinogenic secondary metabolites produced by certain fungi, have received a lot of attention in toxicology because of their widespread occurrence, negative health effects, and potential economic impact.Aflatoxins are primarily produced by the fungi Aspergillus flavus and Aspergillus parasiticus, which commonly contaminate various food commodities such as cereals, nuts, and oilseeds, particularly in high temperature and humidity conditions.Aflatoxin toxicity mechanisms include a complex interaction of oxidative stress, inflammation, genotoxicity, and immune system impairment. Aflatoxin exposure has been linked to a variety of health problems, including acute hepatotoxicity, chronic liver diseases (such as cirrhosis), hepatocellular carcinoma (HCC), and immunosuppression. Mitigation of aflatoxin contamination in food and feedstuffs remains a critical challenge. Additionally, improvements in analytical techniques for aflatoxin detection and monitoring have improved standards for food safety legislation.This review provides an understanding of the sources, metabolism, toxicity mechanisms, health effects, and potential mitigation strategies of aflatoxins is crucial for safeguarding public health and ensuring food safety.
Key words: *Aflatoxin, Toxicity, Carcinogenic, Aspergillus, Oxidative stress.*

Received 28.05.2023 Revised 20.06.2023 Accepted 12.07. 2023

INTRODUCTION

The Food and Agricultural Organization (FAO) has reported that the economic losses of food and grains increasing as approximately 25% of the grains, nuts and cereals are contaminated by mycotoxins because of the mold and fungal growth [15, 18]. Mycotoxins are secondary metabolites produced by different types of fungi especially *Aspergillus, Fusarium and Penicillium* which are highly poisonous on animals and humans. The growth of fungi and the production of mycotoxins naturally increase due to environmental factors, particularly in tropical climates [18]. Mycotoxicosis describes the toxic impact of mycotoxins on both animal and human health. The effect of mycotoxin on health depends on the type of mycotoxin as well as the exposure time. The common mycotoxins produced by the fungal species include Aflatoxin (AF), Fumonisins (FBs), Ochratoxins (OTA), Zearalenone (ZEN), and Trichothecenes such deoxynivalenol (DON). Amongst these mycotoxins aflatoxins are considered the most toxic mycotoxins. Aflatoxins are a group of related fungal metabolites. Aflatoxin identification was related to a groundnut meal contaminated with *A. flavus*, which caused the strange ailment "Turkey X disease," which killed over a million turkey poultry birds in England in the 1960s [17].

Food is frequently contaminated with aflatoxins, which are secondary metabolites produced by fungi. Aflatoxins have the potential to harm human health, food security, and economic trade across much of different parts of the world. Mycotoxins are important in developing countries with poor infrastructure, harvesting, and food storage/storage methods because aflatoxins occur naturally in agricultural products. Aflatoxin contamination occurs at various stages of the food chain, including pre- and post-harvest in maize and peanuts, and may be excreted in hydroxylated form in milk or milk products. *Aspergillus flavus* and *Aspergillus parasiticus* can colonize maize, oilseeds, spices, groundnuts, tree nuts, milk, and dried fruit.

Aflatoxin B1 is the most dangerous aflatoxin to humans and animals because it causes hepatocellular carcinoma, which leads to liver cancer [26]. Aflatoxins suppress human and animal immune systems by interfering with the flexibility of the cells responsible for boosting immunity. Large doses of aflatoxins cause direct death and damage, while small long-term doses cause immunologic or nutritional effects, but both types of doses cause liver cancer due to aflatoxin accumulation. Children are more vulnerable to Aflatoxin toxicity because it increases the risk of early infections due to decreased immunization [16].

The economic impact of aflatoxin is directly attributed to crop and livestock losses, and indirectly to the cost of regulatory programs designed to reduce the risks to animal and human health. Aflatoxin contamination of food causes financial losses and economic damage to agriculture and animal husbandry, as well as significant pharmaceutical and medical costs for treating food poisoning.

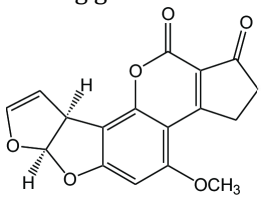
However, many recent advances in food processing, such as hazard analysis of critical control points (HACCP) and good manufacturing practices, have been developed to keep final food products safe and healthy. Furthermore, several physical, chemical, and biological methods can be used to partially or completely eliminate these toxins from food, ensuring consumer food safety and health concerns [14]. This research review aims to provide a comprehensive overview of aflatoxin's toxicology, with a focus on their sources, metabolism, toxicity mechanisms, health effects, and potential mitigation strategies.

Aflatoxin Occurrence and Synthesis

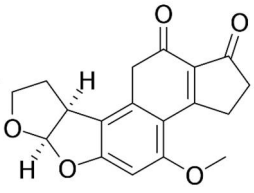
Aflatoxins are mostly produced by dangerous Aspergillus fungus, specifically, the secondary metabolites of *Aspergillus flavus* and *Aspergillus parasiticus*.In comparison to *A. flavus* and *A. parasitica*, other aflatoxin generating species include *A. bombycis, A. ochraceoroseus, A. pseudotamari, A. tamarii, Emericella astellata, and Emericella venezuelensis*, which are rare in nature and only infrequently detected in agriculture. Aspergillus species colonise one other and create aflatoxins, which contaminate grains and cereals at various stages of harvesting or storage [17]. Aflatoxin is produced through a series of 13 enzymatic events that begin with a fatty acid synthase-hexanoate reaction. Aflatoxins are produced by fungi via around 30 genes [33]. Fungal invasion, growth, and aflatoxin generation in crops are primarily determined by environmental conditions, crop type, and other ecological characteristics of a habitat. A wide range of physiological circumstances, such as pH and bioreactive agents, environmental influences, such as water activity and temperature, and biotic and abiotic environmental factors, nutritional factors like carbon and nitrogen sources, affect the production of aflatoxin. Simple sugars which promote aflatoxin production include glucose, sucrose, fructose, and maltose, but not peptone, sorbose, or lactose [24]. A useful carbon source for aflatoxin formation is lipid substrate [9]. LipA, a lipase gene, was cloned from *A. parasiticus* and *A. flavus*. A lipid substrate induces lipA expression and, as a result, aflatoxin formation. The addition of 0.5% soybean oil to non-aflatoxin-producing peptone medium causes lipase gene expression and the synthesis of aflatoxin [34].

Types of Aflatoxin

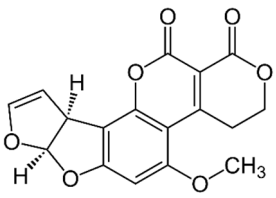
Over 20 varieties of aflatoxins are currently recognised, with the most well-known being B1, B2, G1, G2, M1, M2, aflatoxicol, and aflatoxin Q1. Some of these types are animal metabolic derivatives or metabolites. Aflatoxin M1 and aflatoxin M2 are metabolites of aflatoxin B1 and aflatoxin B2 discovered in the milk of nursing mammals fed aflatoxin-contaminated diet, respectively [21, 25]. These four primary aflatoxins are called from their blue (B) or green (G) fluorescence under UV light, as well as their relative mobility by thin-layer chromatography on silica gel [33]. The chemical structure of aflatoxins consists of a coumarin moiety connected to a difuran ring system. The key chemical feature of aflatoxins is the presence of a highly reactive and carcinogenic epoxide group. The epoxide ring is responsible for the toxic and mutagenic effects of these mycotoxins, as it readily binds to cellular macromolecules, such as DNA, forming covalent adducts and causing genetic mutations.



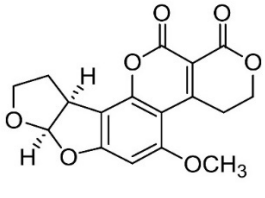
Aflatoxin B1



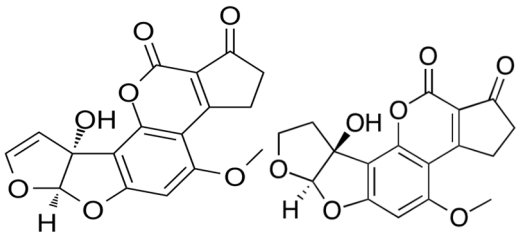
Aflatoxin B2



Aflatoxin G1



Aflatoxin G2



Aflatoxin M1 Aflatoxin M2

Fig. 1. Structure of Aflatoxin

The most powerful naturally occurring carcinogen produced by Aspergillus species is called AFB1. In fact, AFB1 is a Group 1 carcinogen according to the IARC. This substance is unquestionably acutely harmful to people, is likely to cause liver necrosis after repeated exposure, and may play a role in the occurrence of human liver cancer in specific regions of the world by working in concert with the hepatitis B virus [21, 8]

Absorption, Distribution, Metabolism, and Excretion (ADME)

After consuming contaminated food or feed, aflatoxins are primarily absorbed through the digestive system. The process of absorption is influenced by a number of variables, including the chemical structure of aflatoxin, the type of food matrix, and the presence of additional dietary components. Because aflatoxins are lipid-soluble, the intestines can easily absorb them.Due to its function in detoxification and metabolism, the liver is the first significant organ to come into contact with absorbed aflatoxins. Once ingested, aflatoxins have the ability to bind to plasma proteins and travel more easily to different tissues and organs. The fraction of the administered dose that reaches systemic circulation is referred to as bioavailability. Aflatoxins have variable bioavailability, which can be influenced by other compounds in the diet that may interact with aflatoxins, affecting absorption and metabolism [20].

Once in the bloodstream, aflatoxins can spread throughout the body, with a preference for specific organs, particularly the liver, due to its role in metabolizing these toxins. Aflatoxins have been shown to bind to plasma proteins, influencing their distribution and accumulation in various tissues. Aflatoxin's primary target organ is the liver, where they are extensively metabolized. However, aflatoxins can build up in other tissues as well, such as the kidneys, lungs, and adipose tissue. Understanding the toxic effects of aflatoxins on various organs and systems requires an understanding of how they are distributed within the body (Bbosa et al, 2013).

When aflatoxins reach the liver, they are biotransformed by phase I and phase II enzymes. The primary metabolic pathway involves the transformation of aflatoxins into less toxic or more water-soluble metabolites that can be eliminated from the body. The phase I metabolism involves cytochrome P450 enzyme-mediated oxidation and reduction reactions. As a result of these reactions, aflatoxins are converted into intermediate metabolites, including the highly reactive and carcinogenic epoxide forms[10]. Metabolism in phase II involves conjugation reactions in which reactive intermediates produced in phase I are conjugated with endogenous molecules such as glutathione. This conjugation makes the metabolites more water-soluble, allowing for easier excretion.

Bile secretion into the intestines is the main method by which metabolized aflatoxins and their conjugates are eliminated. Some of the metabolites can be deconjugated and reabsorbed in the intestines, which results in enterohepatic circulation and prolongs their survival in the body. Feces can directly excrete some of the metabolized aflatoxins and their conjugates. However, some metabolites may be subjected to additional digestion by the gut microbiota, creating secondary metabolites that can be reabsorbed. Some metabolites are filtered by the kidneys and eliminated in the urine, so this is another method of excretion.

Understanding aflatoxins' ADME processes is critical for assessing their toxicological effects, establishing safe exposure limits, and developing prevention and mitigation strategies.

MECHANISMS OF TOXICITY

Aflatoxin-Induced DNA Damage and Mutagenicity

Aflatoxins are highly toxic genotoxic compounds that can cause direct DNA damage. Aflatoxin epoxides, which are highly reactive and carcinogenic, can bind covalently to DNA molecules, forming adducts. These DNA adducts have the potential to cause mutations in critical genes, resulting in genetic changes and disruptions in normal cellular processes. Aflatoxin-induced DNA damage and mutagenicity are thought to be important factors in cancer development[25].

Formation of Aflatoxin-DNA Adducts

When the epoxide form of aflatoxins reacts with specific DNA bases, primarily guanine (G), aflatoxins-DNA adducts form. The AFB1-N7-guanine adduct is the most common and well-studied adduct. These covalent modifications can cause DNA helix distortions and disrupt normal DNA replication and repair

processes. If these adducts are not repaired, they can cause permanent mutations in critical genes such as tumor suppressor genes and oncogenes, promoting cancer development [1].

Oxidative Stress and Reactive Oxygen Species (ROS) Generation

Aflatoxins can cause oxidative stress in cells, causing an imbalance between the generation of reactive oxygen species (ROS) and the antioxidant defense mechanisms of the cell. Aflatoxin metabolism by cytochrome P450 enzymes can generate ROS as a byproduct, causing damage to cellular structures such as DNA, lipids, and proteins. Oxidative stress can exacerbate DNA damage, promote inflammation, and contribute to the development of diseases such as cancer and liver damage [19].

SOURCES OF HUMAN EXPOSURE TO AFLATOXIN

Aflatoxin Residues in Animal Product

When contaminated feed is given to farm animals, mainly aflatoxins and ochratoxin A may be found as residues at significant levels in muscles and muscle foods. Additionally, the development of toxic mold during the ripening and aging processes can lead to meat contamination. Even after the animals were exposed to high doses of AFB1, only low levels were discovered in the muscles, frequently below detection limits of the techniques used. Numerous studies on ruminants assessed aflatoxin transfer into lactating cows' milk. However, as with other species, residues can be found in these animals' edible organs like the liver and kidney [10].

According to a report, hams may be processed in a way that facilitates the production of aflatoxin. Therefore, it is crucial to carry out research analyzing the production of AFB1 during the maturation and processing of meat. According to studies, AFB1 contamination of processed meat was rare and the typical toxin level in meat was 10 ng g^{-1} (ppb). It is unclear if AFB1 was created during the processing of meat or if it was already present in muscles at a low level. Mycotoxin may also be present in spices and additives that were added when meat was being processed. Additionally, adding spices could cause a second contamination of the finished product with aflatoxins[4].

Aflatoxin-contaminated milk has historically posed the biggest threat to human health because cows and goats, who produce the majority of drinking milk, are primarily impacted by contaminated forage worldwide. Aflatoxin M1 and M2 are thermo-stable hydroxylated metabolites produced when lactating animals consume contaminated feeds containing aflatoxin. They are named after milk aflatoxins and related to meat aflatoxins as well. AFB1 and AFB2 are metabolized by livestock, and the conversion rate between AFM1 and AFM2 is thought to be 1-3%. Cows can convert AFB1 to AFM1 within 12 to 24 hours of consuming contaminated food. Six hours after consumption, AFM1 residues can be found in milk, and the highest concentrations are attained a few days later. The amount of AFM1 in milk is undetectable after 72 hours [13, 23].

Aflatoxin from Contaminated Grains

Crops can become infected before, during, or after harvest. Aflatoxin pre-harvest infestation of food crops is most common in tree nuts, acha, cottonseed, wheat, peanuts, maize, and other crops. Many other agricultural products, including rice, spices, and coffee, have post-harvest contamination. Inadequate storage of food crops in conditions that promote mould growth, such as warm and humid storage environments, can result in contamination levels that are much higher than those found in the field. Corn and groundnuts are major human exposure sources due to their greater susceptibility to contamination and widespread consumption. Aflatoxin is most commonly found in contaminated grains and thus products [29].

Table no.1. Aflatoxin residues in Contaminated Food Crops in India [16].

Sr. No.	Food Crop	Fungus Species	Type of Mycotoxin	Mycotoxin Concentration (ppb)
1.	Corn	*A. flavus*	AFB1	48–383
2.	Quince	*A. flavus,* *A. parasiticus*	AFB1 AFB2	12.32–241.291 8.231–149.103
3.	Lentil	*A. flavus*	AFB1	3.8–8.6
4.	Black pepper	*A. flavus*	AFB1	39.7–65.9
5.	Coriander	*A. flavus*	AFB1	33.4–67.9
6.	Cumin	*A. flavus*	AFB1	24.9–63.9
7.	Aniseed	*A. flavus*	AFB1	35.3–52.5
8.	Black gram beans	*A. flavus*	AFB1	4.8–15.4

Effect of Aflatoxin on Human Health

Reduced appetite, malaise, and a low fever are symptoms of acute high-level aflatoxin exposure; later symptoms, such as vomiting, abdominal pain, and hepatitis, indicate potentially fatal liver failure. The human body suffers hemorrhaging, acute liver damage, edema, and high mortality rates as a result of acute aflatoxicosis caused by extremely high levels of aflatoxin. Chronic low-level aflatoxin exposure, particularly aflatoxin B1, has been linked to hepatocellular carcinoma, or liver cancer, malnutrition, and stunted growth in children. The symptoms of aflatoxicosis are extremely diverse, and the majority go unnoticed due to chronic exposure and cellular changes in multiple organs rather than a single organ[22].According to the Joint FAO/WHO Expert Committee on Food Additives, chronic consumption of staple foods containing at least 1 mg/kg Aflatoxin B1 or exposures ranging from 20 to 120 g/kg body weight per day for 1-3 weeks can result in acute aflatoxicosis [32].

Aflatoxins are being linked to stunting and underweight in children, which can lead to cognitive impairment and increased mortality risks, both of which can lead to lower human capital with long-term economic consequences. This is concerning because children may be exposed to high aflatoxin levels early in life, such as in utero, through breast milk, and through weaning foods commonly used in Africa [2]. Weaning foods are primarily made from maize, but other cereal grains and, in some cases, groundnuts are also used. All of these foods are susceptible to aflatoxin and other mycotoxin contamination. Aflatoxin exposure over time may cause immunosuppression, which may interact with malaria and HIV/AIDS [17].

Exposure to aflatoxin can harm reproductive health in both humans and animals. Chronic exposure to aflatoxins through contaminated food has been linked to a variety of reproductive issues in humans, though the evidence is limited in comparison to its well-established hepatocarcinogenic effects [30].Aflatoxin exposure in males has been linked to decreased sperm count and motility, and it may disrupt males' normal hormonal balance, potentially affecting reproductive function. Aflatoxin exposure in females has been linked to Menstrual Irregularities and adverse pregnancy outcomes such as preterm birth and low birth weight [1]. While studies have suggested possible links between aflatoxin exposure and reproductive health issues, the evidence is not yet conclusive, and more research is needed to establish causality and the mechanisms involved. Overall, aflatoxin exposure can have serious consequences for both human and animal health, necessitating ongoing efforts to monitor and regulate aflatoxin contamination in food and feed to protect public health and livestock welfare.

Methods to Detect Aflatoxin Contamination

The Association of Official Analytical Chemists (AOAC) has published a number of official methods to identify aflatoxin contamination in crop plants [17]. Enzyme-Linked Immunosorbent Assay (ELISA), one of these, is the method that is used the most frequently, followed by a few chromatographic techniques like High-Performance Liquid Chromatography (HPLC), Liquid Chromatography-Mass Spectroscopy (LCMS), and Thin Layer Chromatography (TLC). Wang, Li, et al. in 2017developed a highly specific sandwich ELISA with a minimum detection limit of 1 g/mL for both *A. flavus and A. parasiicus*[31].In food mycology, room temperature phosphorescence (RTP) in aflatoxigenic strains grown on media is commonly used. Aflatoxins immobilized on resin beads have high sensitivity and specificity and can induce RTP in the presence or absence of oxygen and heavy atoms [27]. Furthermore, several biosensors and immunoassays have been developed to detect ultra-trace levels of aflatoxins in food to ensure food safety [17].

Strategies to Control and Detoxify Aflatoxin

Aflatoxin contamination occurs mostly by the atmospheric conditions like, high moisture during harvest, improper drying and storage condition, as these favors the growth of many *Aspergillus* sp. and other fungal species. This can be controlled if the proper care is taken during pre-harvest, post-harvest, storage and transportation of food and feed. Even if these conditions are maintained the chances of contamination cannot be eliminated and hence different strategies are applied to eliminate the aflatoxin contamination. Aflatoxin can be detoxified using physical, chemical, and biological detoxification methods [14]. Physical methods which are used as heating, radiations, and adsorbents. However, physical methods show many disadvantages, e.g., limited applicability, poor detoxification effect. Chemical methods involve treatment with acid, alkali, or oxidizing agent. The use of chemical substances such as chlorine dioxide to disinfect toxins may impair the appearance and taste of food. After chemical treatment, chemical residues in food may be harmful to humans [15].

However, biological detoxification has high specificity, produces harmless products, and can even completely detoxify toxic products under appropriate conditions. Among them the beneficial bacteria i.e. probiotics can show effective results. Antagonism is the principle mechanism associated with probiotics, can be a useful ability to impair growth or aflatoxin production by aflatoxigenic fungi during storage of food grains or animal feed. Various strains of *Lactobacillaceae and Saccharomyces* can effectively bind aflatoxins through the polysaccharides on the cell wall. Aflatoxin can be degraded by the active substances secreted by microorganisms [11]. Using probiotics for the control of aflatoxin production or

detoxification on grains can also provide an additional probiotic effect on the digestive tract of the consumer [7]. Banwo *et al.,* (2023) studied detoxifying probiotics and evaluated the changes in grain amino acid concentration during the fermentation by probiotics in the presence of either *A. flavus* La 3228 (an aflatoxigenic strain) or *A.flavus*La 3279 (an atoxigenic strain). In this study an increased amino acid concentration was observed in presence of toxigenic *A. flavus* strain compared to control whereas there was no change in amino acid concentration in presence of atoxigenic strain. *Limosilactobacillus fermentum* W310, *Lactiplantibacillus plantarum, Candida tropicalis* MY115, and *Candida tropicalis* YY25 were identified as the potential AFB1 detoxifiers. The study concluded that probiotics were potential aflatoxin detoxifiers but the extent of detoxification was strain and species dependent as well as the amino acid analysis concluded that probiotics did not change the metabolic activity of toxigenic strain [5]. Al-Mamari *et al.,* (2023) stated that *Bacillus subtilis* YGT1 isolated from yoghurt had the ability to degrade aflatoxin B1. In this study, probiotic bacteria were isolated from yoghurt, "*laban"*, "*idli*" batter, among which four isolates showed aflatoxin degradation potential and maximum degradation was observed by yoghurt isolate identified as *Bacillus subtilis* YGT1 by 16*S* rRNA gene sequencing. The AFB1 degradation was confirmed by liquid chromatography/mass spectroscopy analysis. The heated cell free supernatant also showed degradation ability which suggest involvement of bioactive compound in AFB1 degradation. The study concluded that *Bacillus subtilis* YGT1 can be used for the prevention of aflatoxin contamination in food industries [3].

CONCLUSION

In conclusion, aflatoxins are potent toxins with serious consequences for public health. Recognizing their sources, metabolism, toxicity mechanisms, health effects, and potential mitigation strategies is critical in developing effective preventive measures and ensuring the safety of food products for global consumers. To effectively combat aflatoxin contamination and its associated health risks, continued research and collaboration among various stakeholders, including governments, international organizations, and the food industry, are required.

REFERENCES

1. Abdeta, D., & Milki, S. (2023). Public health impact of Aflatoxin. *Journal of Bacteriology & Mycology: Open Access*, *11*(1), 34–39. https://doi.org/10.15406/jbmoa.2023.11.00340
2. Anelich, L. E. (2014). Foodborne diseases: Prevalence of foodborne diseases in Africa. In *Elsevier eBooks* (pp. 262–275). https://doi.org/10.1016/b978-0-12-378612-8.00072-x
3. Al-Mamari, A., Al-Sadi, A.M., Al-Harrasi, M. M. A., Sathish Babu, S. P., Al-Mahmooli, I. H. and Velazhahan, R. (2023). Biodegradation of aflatoxin B1 by Bacillus subtilis YGT1 isolated from yoghurt. *International Food Research Journal, 30*(1), 142 – 150
4. Bailly, J., & Guerre, P. (2009). Mycotoxins in meat and processed meat products. In *Springer eBooks* (pp. 83–124). https://doi.org/10.1007/978-0-387-89026-5_4
5. Banwo, K., Adesina, T., Aribisala, O., & Falade, T. D. O. (2023). Detoxification of Aflatoxins in Fermented Cereal Gruel (Ogi) by Probiotic Lactic Acid Bacteria and Yeasts with Differences in Amino Acid Profiles. *Toxins*, *15*(3), 210. https://doi.org/10.3390/toxins15030210
6. Bbosa, G. S., Kitya, D., Lubega, A., Ogwal-Okeng, J., Anokbonggo, W. W., & Kyegombe, D. B. (2013). Review of the biological and health effects of aflatoxins on body organs and body systems. In *InTech eBooks*. https://doi.org/10.5772/51201
7. Da Silva, J. F. M., Peluzio, J. M., Prado, G., Madeira, J. E. G. C., Silva, M. O., Morais, P. B., Rosa, C. A., Pimenta, R. S., & Nicoli, J. R. (2015). Use of probiotics to control aflatoxin production in peanut grains. *The Scientific World Journal*, *2015*, 1–8. https://doi.org/10.1155/2015/959138
8. De Almeida Møller, C. O., Freire, L., Rosim, R. E., Margalho, L. P., Balthazar, C. F., Franco, L. T., De Souza Sant'Ana, A., Corassin, C. H., Rattray, F. P., & De Oliveira, C. a. F. (2021). Effect of Lactic Acid Bacteria Strains on the Growth and Aflatoxin Production Potential of Aspergillus parasiticus, and Their Ability to Bind Aflatoxin B1, Ochratoxin A, and Zearalenone in vitro. *Frontiers in Microbiology*, *12*. https://doi.org/10.3389/fmicb.2021.655386
9. Fanelli, C., & Fabbri, A. A. (1989). Relationship between lipids and aflatoxin biosynthesis. *Mycopathologia*, *107*(2–3), 115–120. https://doi.org/10.1007/bf00707547
10. Feddern, V., Dors, G. C., De C Tavernari, F., Mazzuco, H., Cunha, A., Krabbe, E. L., & Scheuermann, G. N. (2013). Aflatoxins importance on animal nutrition. In *InTech eBooks*. https://doi.org/10.5772/51952
11. Guan, Y., Chen, J., Nepovimova, E., Long, M., Wu, W., & Kuca, K. (2021). Aflatoxin detoxification using microorganisms and enzymes. *Toxins*, *13*(1), 46. https://doi.org/10.3390/toxins13010046
12. Guengerich, F. P. (2001). Common and uncommon cytochrome P450 reactions related to metabolism and chemical toxicity. *Chemical Research in Toxicology*, *14*(6), 611–650. https://doi.org/10.1021/tx0002583
13. Herzallah, S. M. (2009). Determination of aflatoxins in eggs, milk, meat and meat products using HPLC fluorescent and UV detectors. *Food Chemistry*, *114*(3), 1141–1146. https://doi.org/10.1016/j.foodchem.2008.10.077
14. Hosseini, H. (2019). Application of probiotics in aflatoxins Risk reduction in foods: A review. *International Journal of Environmental Sciences & Natural Resources*. https://doi.org/10.19080/ijesnr.2019.22.556087

15. Jalili, M. (2016). A review on aflatoxins reduction in food. *DOAJ (DOAJ: Directory of Open Access Journals)*. https://doaj.org/article/892fb8c24f6d4d7fa76f9c72869456ba
16. Kumar, A., Pathak, H. K., Bhadauria, S., & Sudan, J. (2021). Aflatoxin contamination in food crops: causes, detection, and management: a review. *Food Production, Processing and Nutrition*, *3*(1). https://doi.org/10.1186/s43014-021-00064-y
17. Kumar, P., Mahato, D. K., Kamle, M., Mohanta, T. K., & Kang, S. G. (2017). Aflatoxins: a global concern for food safety, human health and their management. *Frontiers in Microbiology*, *07*. https://doi.org/10.3389/fmicb.2016.02170
18. Liew, W., & Sabran, M. (2018). Mycotoxin: Its impact on gut health and microbiota. *Frontiers in Cellular and Infection Microbiology*, *8*. https://doi.org/10.3389/fcimb.2018.00060
19. Marin, D. E., & Taranu, I. (2012). Overview on aflatoxins and oxidative stress. *Toxin Reviews*, *31*(3–4), 32–43.https://doi.org/10.3109/15569543.2012.730092
20. Mykkänen, H., Zhu, H., Salminen, E., Juvonen, R. O., Ling, W. H., Ma, J., Polychronaki, N., Kemiläinen, H., Mykkänen, O., Salminen, S., & El-Nezami, H. (2005). Fecal and urinary excretion of aflatoxin B1 metabolites (AFQ1, AFM1 and AFB-N7-guanine) in young Chinese males. *International Journal of Cancer*, *115*(6), 879–884. https://doi.org/10.1002/ijc.20951
21. Negash, D. (2018). A review of aflatoxin: occurrence, prevention, and gaps in both food and feed safety. *Journal of Nutritional Health & Food Engineering*, *8*(2). https://doi.org/10.15406/jnhfe.2018.08.00268
22. Nibbelink, S. K. (1986). Aflatoxicosis in food Animals: a Clinical review. *Journal of Chemical Education*, *48*(1), 6.
23. Özdemir, M. (2007). Determination of aflatoxin M1 levels in goat milk consumed in Kilis province. *Ankara Universitesi Veteriner Fakultesi Dergisi*, *50*(1), 1. https://doi.org/10.1501/vetfak_0000000261
24. Payne, G. A., & Brown, M. (1998). GENETICS AND PHYSIOLOGY OF AFLATOXIN BIOSYNTHESIS. *Annual Review of Phytopathology*, *36*(1), 329–362. https://doi.org/10.1146/annurev.phyto.36.1.329
25. Popescu, R. G., Radulescu, A. L., Georgescu, S. E., & Dinischiotu, A. (2022). Aflatoxins in feed: types, metabolism, health consequences in swine and mitigation strategies. *Toxins*, *14*(12), 853. https://doi.org/10.3390/toxins14120853
26. Qureshi, H., Salehiniya, H., Ali, S. A., Anwar, J., Siddiqui, A. A., & Khan, N. A. (2015). Cytotoxic effects of aflatoxin B1 on human brain microvascular endothelial cells of the blood-brain barrier. *Medical Mycology*, *53*(4), 409–416. https://doi.org/10.1093/mmy/myv010
27. Sánchez-Barragán, I., Costa-Fernández, J. M., Sanz-Medel, A., Valledor, M., & Campo, J. (2006). Room-temperature phosphorescence (RTP) for optical sensing. *Trends in Analytical Chemistry*, *25*(10), 958–967. https://doi.org/10.1016/j.trac.2006.07.009
28. Sarma, U. P., Bhetaria, P. J., Devi, P., & Varma, A. (2017). Aflatoxins: Implications on health. *Indian Journal of Clinical Biochemistry*, *32*(2), 124–133. https://doi.org/10.1007/s12291-017-0649-2
29. Tchana, A. N., Moundipa, P. F., & Tchouanguep, F. M. (2010). Aflatoxin contamination in food and body fluids in relation to malnutrition and cancer status in Cameroon. *International Journal of Environmental Research and Public Health*, *7*(1), 178–188. https://doi.org/10.3390/ijerph7010178
30. Verma, R. J. (2004). Aflatoxin cause DNA damage. *International Journal of Human Genetics*, *4*(4), 231–236. https://doi.org/10.1080/09723757.2004.11885899
31. Wang, T., Li, P., Zhang, Q., Zhang, W., Zhang, Z., Wang, T., & He, T. (2017). Determination of Aspergillus pathogens in agricultural products by a specific nanobody-polyclonal antibody sandwich ELISA. *Scientific Reports*, *7*(1). https://doi.org/10.1038/s41598-017-04195-6
32. Yagudayev, E., & Ray, S. D. (2023). Aflatoxin. In *Elsevier eBooks*. https://doi.org/10.1016/b978-0-12-824315-2.00179-2
33. Yu, J. (2012). Current understanding on aflatoxin biosynthesis and future perspective in reducing aflatoxin contamination. *Toxins*, *4*(11), 1024–1057. https://doi.org/10.3390/toxins4111024
34. Yu, J., Mohawed, S., Bhatnagar, D., & Cleveland, T. E. (2003). Substrate-induced lipase gene expression and aflatoxin production in Aspergillus parasiticus and Aspergillus flavus. *Journal of Applied Microbiology*, *95*(6), 1334–1342. https://doi.org/10.1046/j.1365-2672.2003.02096.x

CITATION OF THIS ARTICLE

Yeole R. B., Bhutada S. A. and Dahikar S. B.: Aflatoxin Toxicology: Unraveling the Comprehensive Overview of a Potent Mycotoxin. Bull. Env. Pharmacol. Life Sci., Spl Issue [2]: 2023: 202-208.