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# Aflatoxins exposure: a big economic, environmental and health concern

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## Abstract

Aflatoxin is one of the highly toxic metabolite produced by different species of fungi, growing in susceptible agricultural commodities. These fungi infect many crops, food items dry fruits, milk and milk made products which poses enormous economic losses and health problems worldwide. Aflatoxins are mycotoxins generated by two species of *Aspergillus*, a fungus found, especially hot and humid climates. Among known aflatoxins only six of these AFB1, AFB2, AFG1, AFG2, AFM1, and AFM2 are usually found in staple foods. The most toxic among all types is aflatoxin B1, produced by both *A. flavus* and *A. parasiticus*. Many studies around the world have been conducted to develop methods for AFs detection and quantifications, and to assess the potential health risks of food contamination with AFs in order to reduce the health, environmental and economic burdens. AFs occurrence, toxicology, chemistry, health and environmental hazards as well as its economic burdens, their exposure control and management have been briefly discussed in this article. The available literature proved that local climatic and weather conditions in Jeddah supports the fungal growth, which may infect crops, food items, and milk products ultimately posing enormous economic losses and health problems. So there is big vulnerability of susceptible foods commodities contamination from AFs in the local markets in KSA. Although there are many studies that prove the presence of AFs in food commodities in KSA, yet there is no study to assess the potential risks of dietary exposure of AFs.As aflatoxins are known to be potential carcinogens, so their exposure via food and or feed need to be strictly regulated and controlled which otherwise may result in severe health, environmental and economic risks.

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## Introduction

Aflatoxinis are one of the highly toxic metabolite produced by different species of fungi, growing in susceptible agricultural commodities (EFSA 2012; Farag *et al.*2018). These fungi infect many crops such as, maize, wheat, ricecorn cassava, nuts, peanuts, chilies, soya, cottonseeds, sorghum, rye spices, dry fruits, coca, copra, beans wines, legumes, milk and milk derivatives (Wild and Gon 2010; Kumar *et al.*, 2017).Commodities contamination by Aflatoxins (AFs) poses enormous economic losses and health problems worldwide. The Food and Agricultural Organization (FAO) estimated that every year 25% of world's crops lost due to AFs contamination (Farag *et al.*, 2018; winter and Pereg 2019). Studies recognized that AFs can be hepatotoxic, immunotoxic and mutagenic, hence, the International Agency for Research on Cancer (IARC) classified AFB1 as a group 1 carcinogenic. Moreover, it has been evaluated that in developing countries around 5 billion individuals are at risk because of chronic exposure to aflatoxin as result of ingestion contaminated foods (Farag *et al.*, 2018; winter and Pereg 2019).

Scientists and researchers have since embarked on scientific research on AFs, a result of which has identified 18 types of aflatoxins. The most common of these are AFB1, AFB2, AFG1, and AFG2. According to winter and Pereg (2019), aflatoxins are mainly produced by toxic fungi such as the A. flavus, A. parasiticus, and A. nomiu. Ordinarily, AFs contaminate cereals such as maize, sorghum, rice, dry fruits, and legumes, among others. However, according to Europeon Food Safety Authority (EFSA 2012, 2015), AFs can also contaminate wines, fish, and milk.

Several studies in Saudi Arabia and other countries have investigated the AFs levels in milk of dairy cattle fed on contaminated feed by fungi (Alharbi *et al.*, 2019). Aflatoxin M1 is the most studied mycotoxin in milk and levels exceeding the European Union (EU) maximum level for mycotoxin (0.050 mg/kg) have been found (Flores-Flores, *et al.*, 2015). Recently, milk contamination with AFM1 is recognized in Saudi Arabia (Bokhari, *et al.*, 2017) and other countries such as Egypt, Turkey, Japan, Tanzania, and Kenya (Barug *et al.* 2006).

Many studies around the world have been conducted to assess the risks of food contamination with AFs in order to reduce the health, environmental and economic burdens. While reviewing literature in Middle East generally and in KSA particularly reveals that collected samples (maize, coffee beans, herbs, cotton seeds, cereals, sorghum, pistachio, peanuts, cashew nuts, milk and milk products) from local markets are found to be contaminated by AFs with levels exceeding the permissible limits (Bokhari, *et al.*, 2017; Farag *et al.*, 2018; Al harbi *et al.*, 2019).

AFs contamination is a worldwide problem which results in the loss of billions of tons of food annually. Human exposure to AFs contaminated foods has also contributed to the loss of many human lives (Shephard, 2003; Strosnider *et al.*, 2006). AF contamination also causes human and animal complications such as hepatotoxicity, immunotoxicity, and teratogenicity (Roze *et al.*, 2013 and Kensler *et al.*, 2011). As well, the WHO has associated AFs exposure to the dietary system with cases of liver cancer in both animals and humans (Hendrickse, 1999).Aflatoxins occurrence, exposure, toxicology, chemistry, health and environmental hazards, economic burdens, and their management have also been briefly discussed in this article.

### *Aflatoxins*

Aflatoxins (AFs) are secondary metabolites generated by fungi that have harmful effects on animals and human, were discovered after the outbreak of 100,000 deaths of turkeys in the United kingdom in 1960s (Cotty and Jaime-Garcia, 2007). Fungi such as *A. flavus, A. parasiticus*, and *A. nomius*, *Aspergillus* as well as *Emericella* spp are the major sources of AFs. These fungi species are found in many foods and feed crops, specially corn, cotton seed, peanuts, and tree nuts (Cotty and Jaime-Garcia, 2007; Kumar *et al.*, 2017). AFs can be classified into hepatotoxins, neurotoxins, immunotoxins, teratogens, mutagens, carcinogens, and allergens (Marasas, 2001; Bhat and Vasanthi, 2003; WHO, 2008). In most cases; the main route for animals and human exposure to AFs is a dietary intake of contaminated food.

*Major types of Aflatoxins*

Based on chromatographic and florescence characteristics, there are more than 20 known types of aflatoxins, nevertheless, the naturally occurring and well-known one types are Aflatoxin $B_1$ Aflatoxin $B_2$, Aflatoxin $G_1$ and Aflatoxin $G_2$. These names were given due to their blue (B) or green (G) fluorescence properties and migration pattern in chromatographic analysis (Wogan and Busby, 1980; Gimeno, 2004; Saleemullah *et al*., 2006; Kumar*et al*., 2017).The level of toxicity associated with aflatoxin varies with the types present, with the order of toxicity being $AFB_1$ > $AFG_1$ > $AFB_2$ > $AFG_2$ (Kumar *et al.* 2017).

*Chemistry of Aflatoxins*

The molecular formulas of the four well known and major AFs as established from elementary analyses and mass spectrometric determinations areas below.

$B_1$: $C_{17} H_{12} O_6$

$B_2$: $C_{17} H_{14} O_6$

$G_1$: $C_{17} H_{12} O_7$

$G_2$: $C_{17} H_{14} O_7$

The Aflatoxin$B_1$is classified as a potential carcinogen since 1987 (IARC 2000). $AFB_1$ is the most common aflatoxinfound in staple foodsand the majour cause of aflatoxicosis in most of the cases. When domestic animals ingested foodstuffs and feeds contaminated by AFB, a biotransformation happens to toxin by liver and converted it into AFM, therefore, AFM1 and AFM2 are hydroxylated forms or metabolic derivate of $AFB_1$ and $AFB_2$ (Dors, 2011)and excreted in milk, urine, tissues and biological fluids of animals (Murphay *et al*, 2006). (Gimeno, 2004; Strosnider et. al., 2006). However, excreting the toxin in milk can be taken up by consumers. Furthermore, it has been reported a linear relationship between the concentrations of $AFB_1$ in contaminated feeds consumed by the animals andconcentration of $AFM_1$ in milk, and about 0.3% to 6.2% of ingested contaminated feeds by $AFB_1$ transformed into $AFM_1$in animal's milk (Bakirci, 2001; Creppy, 2002).

*History of Aflatoxins*

Aflatoxins discovery find its roots in 1960s when an outbreak of turkeys disease occurred in England. This disease was named Turkey "X" disease and was eventually attributed toward contaminated Brazilian groundnut import of groundnuts (Richard, 2008). As well as, one of the first outbreaks of aflatoxicosis was reported from western India during 1974 with 106 deaths of indigenous people whose staple food was maize, and the study of the outbreak indicated that the aflatoxins were the major cause of the outbreak. In the same year, the second outbreak was toxic hepatitis outbreak happed and affected human and dogs. In addition, heavy mortality in chicks also reported due to aflatoxicosis in 1982 (Reddy and Raghavender, 2007).

In 2004, WHO investigated and analyzed the outbreak of Jaundice with a high case-fatality rate (125 deaths) which finds its roots into AFs poisoning in Kenya (Ngindu, *et al*., 1982). In USA in 2005, more than 75 dogs died due to consuming pet food contaminated with aflatoxins, and the others (hundreds) experienced severe liver problems (Schmale and Munkvold, 2010). However, within the last decade, a number of important outbreaks of mycotoxicosis have been reported worldwide and these outbreaks emphasize the need for regulation of mycotoxins in food and feed and routine testing of staple food and feed for mycotoxins, especially in developing countries.

*Fungal species and Aflatoxins*

In many developing and under developed countries fungal growth which produce aflatoxins found on crops such as, Mize, wheat, rice, corn cassava, nuts, peanuts, chilies, soya, cottonseeds, sorghum, rye, and spices, also aflatoxin contaminate great variety of foods which are consumed by human; like dry fruits, wines, legumes, farm fish, milk and milk derivates (Gimeno, 2004; Wild and Gon, 2010). Primarily aflatoxins produced by common fungus namely called

Aspergillus and its species, however, the two well defined species are *A. flavus* and *A. parasiticus*, and other species are *A. nomius*, *A. pseudotamarii*, *A. bombycis*, *A. nomius* and *A. australis* (IARC, 2002). Therefore, *A. flavus* and *A. paraciticus* are largely responsible for aflatoxins found on foodstuff in the world wild. As a result *A. flavus* became the most widely reported foodborne fungus and grows optimally at 25°C with a necessary water activity of 0.75, and starts to produce secondary metabolites at 10-12°C. The major hosts of *A. flavus* among food and feed commodities are maize, peanuts and cottonseeds, in most cases the invasion of the plant and seeds or nuts by Aspergillus happened before harvest and because of this high level of aflatoxins produced, which is very hard to eliminate aflatoxins from these products (IARC, 2002).

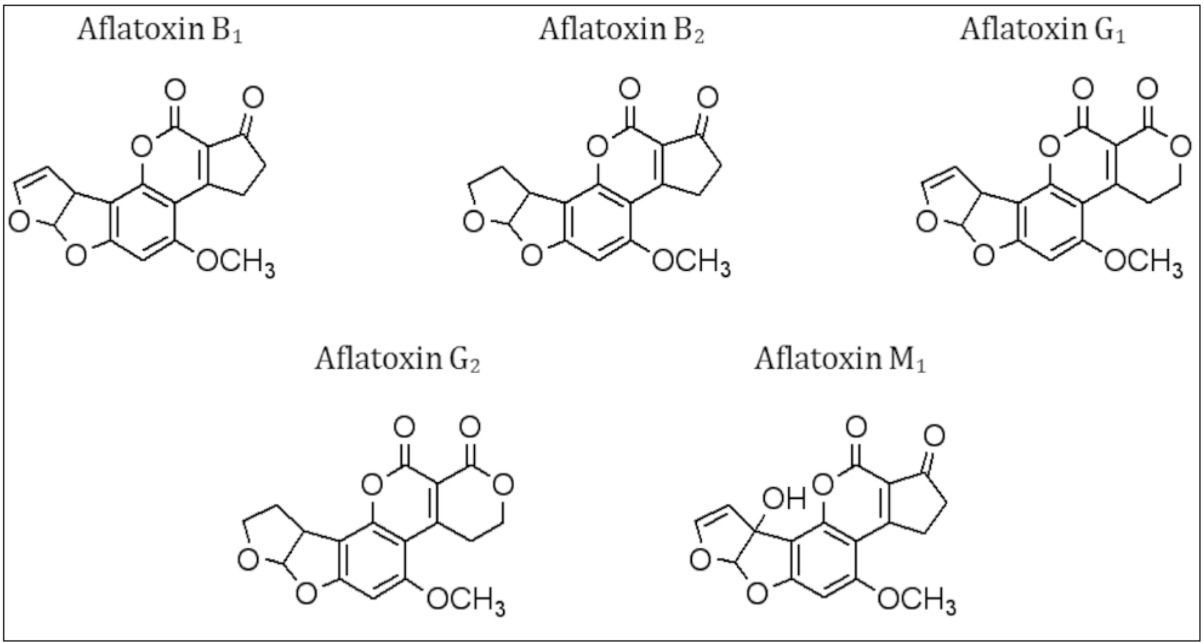


**Fig. 1.** The chemical structure of Aflatoxins.

*Food contamination*

Food contamination refers to the presence of harmful chemical substances and microbiological agents in food which can cause mild to severe illness to consumers, both human and animals. Contaminants are substances not intentionally added to food, it's may be present in food as a result of the various stages, during production, packaging, transporting, handling, processing and also it might result from environmental conditions.

Food spoilage is a disagreeable change in a food's normal state (Virginia Polytechnic Institute, 2012), or when the original nutritional value, texture, and flavor are damaged and the food became harmful and unsuitable to eat, changes can be detected by smell, taste, touch or sight. However, spoilage microorganisms ruin food quality without necessarily contributing to the spread of foodborne illnesses. For instance, yeasts and mold ruin the taste and smell of foodstuffs but they may not necessarily cause illness, (Doyle, 2007).

Food contamination also refers to foods that contain or contaminated by pathogens or its toxins such as bacteria or fungi, that make food unfit for consumption (Koo, 2009). Furthermore, Pathogens have been known to cause foodborne disease without affecting the taste, smell or overall quality of food.

Pathogens provide the greatest concern in food preparation. This is because, under the right conditions, the reproduction and growth can be expeditious. It may also survive under low temperatures and can easily adapt to new developing conditions (EFNRS, 2006).

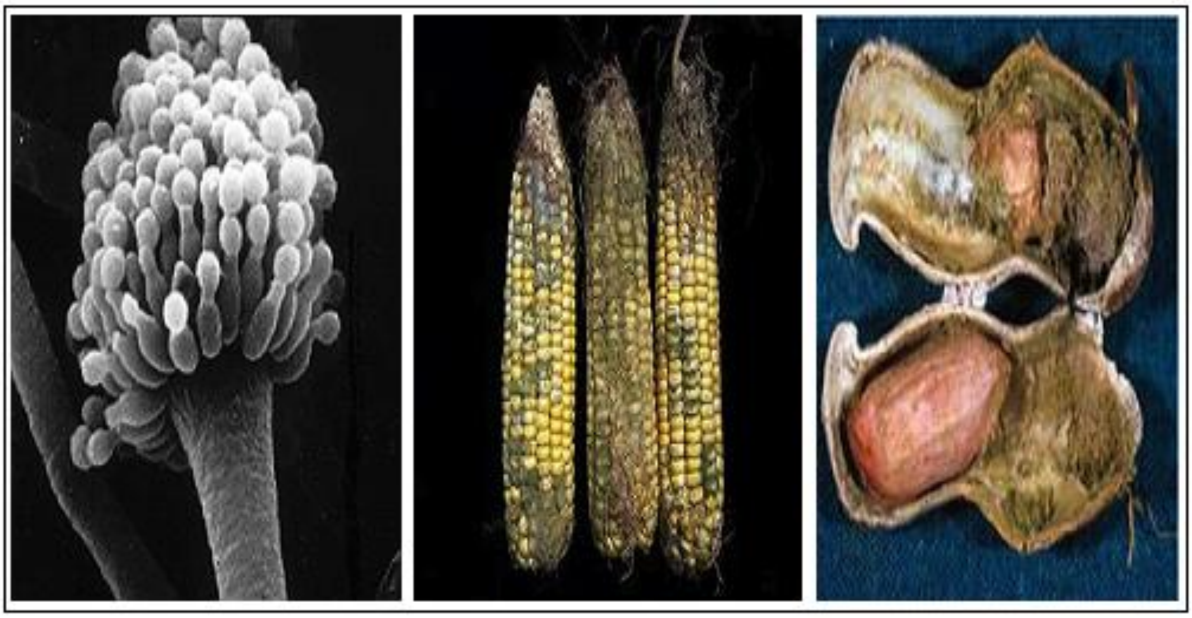

**Fig. 2.** *Aspergillus* and some affected crops.

*Food contaminating agents*

Food contaminating agents include but not limited to bacteria, viruses, parasites, and fungi, and it is important to comprehensively know and understand the different agents of foodborne illnesses. Foodborne pathogens refer to an infectious biological agent that inhabits, creates and contaminates food. In most scenarios, foodborne pathogens also cause food spoilage, (Food Safety, 2010).Fungi cause foodborne illness; fungi are non-motile, single-celled organisms that vary in size from microscopic to larger multi-cellular organisms.

They occur naturally in air, soil, animals, and foods. Like bacteria, fungi can either ruin food or cause disease. They thrive in sweet, acidic foods, cultural commodities that have little water activity. Examples of fungi include yeast, mold, and mushrooms. Molds produce mycotoxins that lead to food contamination. Yeasts are also common food spoilers. They breakdown food and produce carbon dioxide and alcohol as products. As a result of this, the color and smell of food are significantly altered and this affects the quality of food. Fungi can be poisonous. Consumption of certain mushrooms, for instance, has been known to result in tracheal inflammation and blockage, nausea, hallucinations and even diarrhea (MDH, 2010).

*Aflatoxins exposure and their adverse effects*

Food, feed and agricultural commodities contaminated by aflatoxins cause enormous economic and serious human and animal health problems globally. Aflatoxins recognized to be hepatotoxins and carcinogens for human (WHO, 1998). Hence, scientists mentioned that ingestion of aflatoxins contaminated foods by human and animals has significant health effects, because these toxins are nephrotoxic, immunotoxic, teratogenic and mutagenic which are capable of causing acute and chronic effects in human and animals ranging from death to disorder of central nervous, cardiovascular, pulmonary systems and intestinal tract (Bhat and Vasanthi, 2003). The primary disease associated with aflatoxins intake is hepatocellular carcinoma (HCC, or liver cancer) also cause esophageal cancer (Marasas, 2001). According to world Health Organization these diseases is the third leading cause of cancer death globally (WHO, 2008), and every year from 550.000- 600.000 new cases diagnosed, and because of this eighty-three percent of these deaths happened in East Asia and sub-Saharan Africa (Kirk *et al.* 2006).

*Effects on economy*

The incidence and the level of aflatoxins contaminationin commercial food and feeds have been reported and documented very well in almost all regions of the world by scientist and researchers. According to UN (FAO) 25% of world food crops are affected, which results in 1 billion tons of crop losses directly, and the impacts include disease associated with dietary exposure to aflatoxins hence loss of humans and animal's life (WHO, 2008). Also it has been estimated that more than 5 billion people are at risk in developing countries worldwide as a result of such contaminated food consumption (Al harbi *et al.*, 2019). So the economic losses due to AFs are in the form of direct markets losses due to reduced incomes as well as from human and animal's disease burdens. Globally aflatoxins contaminations extend from 35N and 35S latitude, most countries in this area of concern are developing countries which make the situation even worse, as people in such countries commonly rely on highly susceptible crops for their daily diet and income and mostly do not practice proper post-harvest handling, drying, and storage of commodities (Bandyopadhyay and Cotty, 2011). However, high level aflatoxins contaminated foods (higher than the allowable level) either rejected entirely for sale or sold at a lower price for other use, and this transaction can happen at local levels or at the level of trade between countries, causing heavy economic losses in the form of less exports.

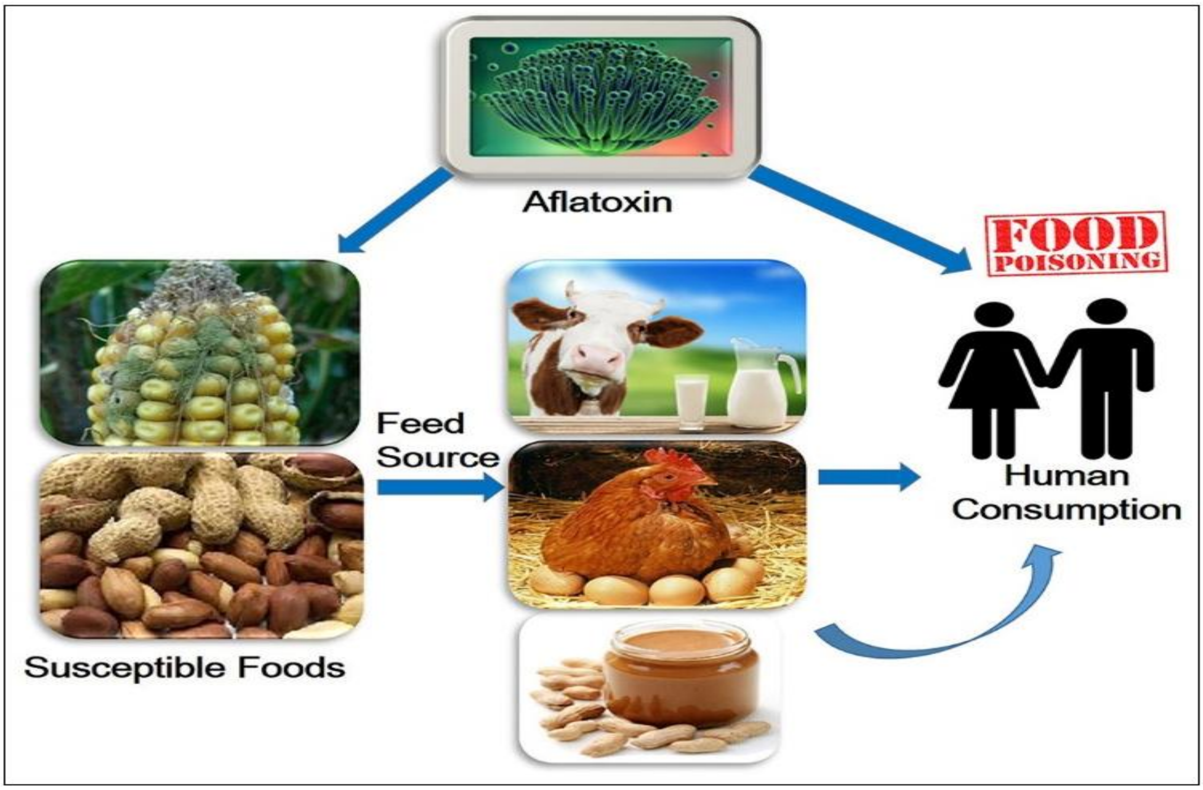


**Fig. 3.** Food, Aflatoxins and humans, an overview (Kumar *et al.*, 2017).

*Effects on livestock*

In animals,aflatoxinslead to pooranimal growth and work as immunesuppressive,scientists reported that $AFB_1$ induce liver and kidney tumors in many animals. Studying experimental animals such as (rats, mice, hamsters, salmon, trout, ducks, tree shrews, woodchucks,and monkeys) with administration of AF($B_1$, $B_2$, $M_1$, $G_1$or $G_2$) showed that aflatoxin was the major cause of cancers in these animals. The individual animal's vulnerability to AFs varies due to factors like age, specie, sex, weather conditionsand nutrition. Furthermore, AFs exposure in animals cause liverdamage, decrease milk and egg and milk production decrease (William *et al.*, 2004; EFSA 2012, 2015; WHO 2008; Zhong *et al.*, 2016)

*Effects on humans*

Humans are exposed to AFs by consuming foods contaminated with products of fungal growth because fungal growth is not easy to be prevented infood (William *et al.*, 2004). Theaflatoxicoses evidence in human has been reported from many parts of the world such as Kenya, India, Taiwan, Uganda, and many others. For example, by eating contaminated corn, 104 people were died in India from a total of 400 people, in Kenya high consumption of aflatoxin contaminated food killed 12 people, also in southeast Asia, 19 patients became jaundice and sick within hours of eating rice and pasta, of the 19 patients 17 presented hepatitis symptoms, 7 presented renal failure and 14 died because of liver failure (Hendrickse, 1999). In developing countries estimate that 5 billion people are at risk of uncontrolled exposure to aflatoxins or poorly controlled exposure to aflatoxins, and this is because of security blankets in crops at pre-harvest and post-harvest level are not as strict as in developed countries. However high levels of AFs in blood may depress immune system and children stunting growth. In most of the cases aflatoxicosissyndromes varies from abdominal pain, convulsions, pulmonary edema, coma and evendeath (Shephard, 2003; William *et al.*, 2004). As mentioned earlier human and animals exposed to aflatoxins through their diets and they may experience acute or chronic aflatoxicosis because of ingestion of foodstuff and feeds contaminated by aflatoxins(Gong *et al.*, 2003; Xiaoxia *et al.*, 2015;).

*Aflatoxins detection*

Because aflatoxins have adverse effects on human and animals health and also causes series economic losses when tons of foods and crops have to be discarded or destroyed as a result of contamination. And for insuring food safety, maximum levels for AFTs has been set in food and feeds by national and international organizations and countless approaches have been developed for the determination of AF concentrations in food and feed commodities.

For that, a number of analytical methods have been developed such as chromatography, immunoassay and, and other rapid screening kits available (EFSA 2012, 2015).

*Chromatography*

Chromatographyis one of the popular methods for quantifying aflatoxin. With the beginning of aflatoxin analysis and detection, Gas chromatography (GC) was repeatedly used for detection and quantification of compounds. Later on some new techniques were developed using chromatography-based technique for aflatoxins detection, namely, Liquid chromatography LC, High performance liquid chromatography HPLC, and thin layer chromatography TLC (Stroka *et al.*, 2000; Bacaloni *et al.*, 2008) the one nowadays is most commonly used especially for aflatoxins detection. Moreover, there are combination of methods with pre-process techniques can detect the concentration of aflatoxins in a solution a perfect way, for instance immune affinity column sample clean-up followed by a normal or reverse phase of HPLC separation with fluorometric detection and mostly sued for quantitative determination because of the characteristics of specificity, high sensitivity and simplicity of performance (Muscarell *et al.*, 2007).

*Immunoassay*

This is an immunochemical technique for aflatoxins detection based on antibody-antigen reaction (Lee *et al.*, 2004), because different kinds of aflatoxins molecules can be considered as an antigen so that it's probable to detect them by developing antibodies against the compounds. Majority of immunological techniques are based on enzyme-linked immunosorbent assay (ELISA) the technique which has good sensitivity, speed, and simplicity. As well some other qualitative and semi-quantitative lateral flow immunoassays (LFIAs) applied for aflatoxins detection in foods and feed and milk (Ho and Wauchop, 2002; Anfossi *et al.*, 2011, salter *et al.*, 2006).

*Biosensors and other methods*

Biosensor is another method to improve the weaknesses of previously mentioned methods; it is multidisciplinary tools with vast potential in detection and quantification of aflatoxin. This technique has all kinds of biosensors that base their performance on different physical or biochemical rules, for example optical, optoelectronic, electrochemical, piezoelectric, DNA and combined. Therefore these devices have an enormous impact on healthcare, food management, and agronomical economy (Nayak *et al.*, 2009).

*Aflatoxins exposure control*

Regulations and limitations: Because of economic and health problems caused by contaminated commodities, regulations are made on basis of aflatoxins toxic effects, and these hazards are evaluated by Joint Expert Committee on Food Additives of WHO. Yet around 100 countries established regulations on aflatoxin to sustain human and animal's health. European food safety authority established regulation about the level of aflatoxin; hence the total aflatoxins in nuts should not exceed 4µg/kg, in the USA, action level of total aflatoxin in all foods except milk is 20µg/kg, in Brazil the maximum level does not exceed 20 µg/kg in all food commodities (Bennett and Klich 2003; Cornell University, 2009). Hence, around 100 countries established regulations on aflatoxin to sustain human and animal health and surly the global economic, by monitoring and analyzing commodities and crops that vulnerable to aflatoxin contamination, usually mass food shipment tend to be highly homogenous in their distribution so it is necessary to ensure that an adequate sampling plan is used to monitor imported materials. For that, a number of analytical methods have been developed such as TLC, ELISA and HPLC and other rapid screening kits available.

Even where good manufacturing practices have been followed, food and feed contaminations with aflatoxins are unavoidable; hence, the Food and Drugs Administration (FDA) established specific guideline on aflatoxins' acceptable level in human food and animal feed. What is more, it is very difficult to estimate the concentration of aflatoxin in a largenumber of materials due to the variability of testing procedures, hence we cannot 100% estimate the concentration of aflatoxins in materials (Cornell University, 2009). Estimates of "safe doses" are usually stated as a "tolerable daily intake". For example, in the United States, the FDA guideline is 20 ppb total aflatoxin in food designed for human consumption and 100 ppb is the limit for breeding cattle and mature poultry (Bennett and Klich, 2003). The European Union sets limits for AFB1and for total AFs as 2-12 µg/kg and 4-15 µg/kg respectively.

*Good agricultural practices (GAPs)*

In order to eliminate aflatoxins contamination the most important part is by following the good agricultural practices, and it can be achieved by preventing the contamination of crops in the field, while harvesting, during transportation and storage, or detection and subsequent removal of contaminating agents from food supply chain (Razzaghi *et al.* 2014). Some pre harvesting GAPs are but not limited to land preparation, removal of crop waste, fertilizers application, and rotation of crop and their varieties, fungal, insects and pests control, Control of fungal infection, drought stress management,. While the important post harvesting GAPs for aflatoxins exposure control include moist level control during handling and storage, maturity stage harvesting, harvesting at safe moisture level and crops drying immediately after harvesting.

And during food processing, separation of contaminated material physically can be an effective manner of reducing aflatoxin level, for instance; sorting color changed peanuts remove the moldy ones, also density segregation, mechanical separation and the removal of fines and screenings from grain and nut shipments are very effective measures for processed food contamination management(Food Safety Watch, 2013).

## Conclusion

Globally, AFs contamination is big problem, the factors playing important role are high temperatures, humidity, and unsafe supply chain and transportation andbad storage conditions. In this article we discuss aflatoxins occurrence, contaminating factors, toxicity, agriculture, livestock, health and overall economic burdens. Aflatoxins control and management strategies like pre and post harvesting good agriculture practices, strict rules regulations and their enforcement mechanism were also briefly discussed. AFs are a very toxic group of mycotoxins and cause developmental and immune system suppression, cancer and death, and due to their high toxicity and carcinogenic potential, they are of high concern for the safety of food. As it's evident from local climatic and weather conditions in Kingdom of Saudi Arabia (KSA) that these factors are common in KSA. So there is big vulnerability of susceptible foods commodities contamination from AFs. Although there are many studies that prove the presence of AFs in food commodities in KSA, yet there is no study to assess the potential risks of dietary exposure of AFs. Hence, contamination of crops and direct human exposure from aflatoxins cause a significant economic loss for marketers, processors and producers of susceptible food crops.Aflatoxin risk assessment is necessary as it provides information on the potential risks of AF-exposure to animal and human health. Prospective studies need to be planned to assess the AFs health, environmental and economic risks in Saudi Arabia and in Jeddah particularly.

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