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Review Article

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The Public Health importance of Aflatoxin: A Review

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Abstract

Aflatoxins are naturally secondary metabolites bisfuranocoumarin compounds produced by the fungi. The objective of this paper is to review the public health and economic significance of aflatoxin. Around 25% of the world's crop is affected by mycotoxin, and the vast majority of that is aflatoxin. Aflatoxigenic fungi produce four major toxins: AFG1, AFG2, AFB1, and AFB2 are produced by *Aspergillus parasiticus* and A. *flavus.* For the production of aflatoxins, the molds need some stress factors such as nutritional imbalance, drought, and climate plays a relevant role in fungal development and aflatoxin production in crops in the field and during storage. Aflatoxins are affecting many organs, mainly, the liver is the primary target organ and the disease called aflatoxicosis, causes death, cancer, toxicity, and immune suppression. Various analytical methods employed in analysis of aflatoxins in agricultural food crops and feeds have been explored. Chromatographic methods such as Thin Layer Chromatography High Performance Liquid Chromatography and Enzyme Linked Immunosorbent Assay Detection are considered the gold standard and the most widely used techniques. Agricultural interventions are methods that can be applied either in the field pre-harvest, and post-harvest to reduce aflatoxin levels in food and feed. Physical, chemical and biological methods can be applied and assure the food safety and health concerns of users. Generally these fungal toxins have been shown to cause a variety of toxic and severe health effects in humans and animals thus leading to reduced life expectancy and economic. The effects of aflatoxin on human, animal health, and financial consequences should be made aware to the public is important.

Keywords: Aflatoxicosis; Economic; Public Health; Tumor

1. Introduction

Aflatoxins are a group of mycotoxins produced by certain fungal action during production, harvest, storage, and food processing, and it is considered to be an unavoidable contaminant of foods by the US Food and Drug Administration (FDA) (Wang *et al.*, 2010). It's a common contaminant of foods, particularly in the staple diets of many developing countries. Aflatoxins are naturally secondary metabolites bisfuranocoumarin compounds produced by the fungi *Aspergillus flavus*, *Aspergillus parasiticus*, *Aspergillus nomius* and *Aspergillus tamari* (Uka *et al*., 2020). Aflatoxigenic fungi produce four major toxins AFB1, AFB2 produced by *A. flavus* but AFG1,

AFG2, AFB1, and AFB2 are produced by *A. parasiticus*. The hydroxylated metabolites which is known as AFM1 and AFM2 produced by AFB1 and AFB2, that are of significance as direct contaminants of foods and feeds (Bankole *et al*., 2003)

The multiple staple foods, cash crops such as maize, tree nuts, cassava, millet, peanuts, wheat and a range of spices contaminated by aflatoxins. Aflatoxins have been also detected in eggs, milk, and meat using contaminated feed (Kumar*et al.*, 2017).AFB1 is partially eliminated in the rumen after being consumed by ruminants, but it quickly transforms into AFM1 and AFM2 in the liver after being absorbed. In developing nations, where dairy farmers frequently use various mixed concentrate feeds containing traditional brewery by-products (atela), wheat bran, noug (Guizotia abyssinica) cake, maize grains, and silage to increase production, the risk of human exposure to AFM1 contamination of milk is a major concern. These feeds could become contaminated with AFB1 (Chauhan *et al*., 2018).

Aflatoxins are usually associated with drought stress that often occurs in various crops in the agriculture field before harvest. During the rainy seasons the poor storage conditions can increase the aflatoxins concentration. And these conditions developed chiefly in humid and hot regions where humidity and high temperature are optimal for growth of molds and for production of toxins (Waliyar *et al*., 2015). Several factors provide an ideal environment which promotes the growth of fungi. The principal climatic circumstances such as erratic rainfall, drought, more temperature between 12- 48°C and more humidity (40–89%), provide a suitable environment for the molds growth and aflatoxins production (Battacone*et al*., 2009).

Consumption of aflatoxin contaminated food and feed causes a range of serious health complications in humans and animals, together named as aflatoxicosis (Roze*et al*., 2013). Short term exposure to high doses of aflatoxins results in jaundice, hemorrhage, liver damage and subsequent death and long term exposure to sublethal levels of aflatoxins cause nutritional disorders, immunosuppression, and cancer (Marchese et al., 2018).

Various analytical methods employed in analysis of aflatoxins in agricultural food crops and feeds have been explored. While chromatographic methods such as Thin Layer Chromatography High Performance Liquid Chromatography and Enzyme Linked Immunosorbent Assay Detection are considered the gold standard and are thus the most widely used techniques in aflatoxins analysis, they remain largely cumbersome, requiring extensive sample preparations, let alone very expensive equipment. This makes their routine use in analysis confined to laboratories. It is on the account of such limitations that it was necessary to develop more sensitive and better techniques for aflatoxins analyses (Wacoo*et al*., 2014).

Agricultural interventions are methods or technologies that can be applied either in the field (“pre-harvest”) or in drying, storage, and transportation (post-harvest) to reduce aflatoxin levels in food (Wu *et al*., 2010).These toxins cannot be destroyed after contaminations of foods by the usual cooking processes. However these, toxins partially or completely eliminated from food using by physical, chemical and biological methods can be applied and assurance the food safety and health concerns of users (Surai et al., 2010).Therefore, the present topic dedicated on public health and economic significance of aflatoxin.

2. Literature Review

2.1 Etiology of Aflatoxicosis

Around 25% of the world's crop is affected by mycotoxin, and the vast majority of that is aflatoxin. They are regularly found in improperly stored cassava, cottonseed, chili pepper, maize, wheat, millet, peanut, rice, sesame, sunflower seed, and many spices. Aflatoxins are naturally secondary metabolites bisfuranocoumarin compounds produced by the fungi *Aspergillus*

flavus, *Aspergillus parasiticus*, *Aspergillus nomius* and *Aspergillus tamari (*Uka *et al*., 2020).Crops can be contaminated in two phases: *Aspergillus* species infect crops during growth and development. Contamination can build during storage or transport when exposed to warm, humid conditions or severe drought. Animals fed on contaminated feed can pass aflatoxin metabolism products into eggs, milk products, and meat, and thus humans can be exposed (Kumar et al., 2017).

2.2. Types of Aflatoxins

Aflatoxin consists of a group of 20 fungal metabolites. Out of them only B1, B2, G1, G2, M1 and M2 are usually found in foods, where "B" and "G" referring to the blue and green fluorescent colors produced on thin layer chromatography plates under UV light, while the subscript numbers 1 and 2 indicate major and minor compounds, respectively. M1, M2 is the metabolites ofB1, B2 found in human and animal milk. Aflatoxin B1 & B2 are produced by *A.flavus* and *A.parasiticus*. Aflatoxin G1 & G2 are produced by *A.parasiticus* (Bennett *et al*., 2007) and (Wacoo et al., 2014).

2.3. Predisposing Factors

Mycotoxins in feedstuff and finished feed should be monitored from farm-to-fork to assure a safety product for animals and humans. The contamination of animal feedstuff could take place at different stages throughout the entire food chain. The contamination of cereal grains and other agricultural commodities used in animal feed could occur in the field during the pre-harvest phase during harvest, or in processing stages (postharvest). In the pre-harvest period, and potentiated by different factors such as the plant genetics, e.g. the use of corn germplasm not adapted to local conditions (Fountain et al., 2014).

After that, during the growing and harvesting stages, toxin evolution is predisposed by agricultural practices, including the use of fungicides and pesticides, the use of open-pollinated varieties (Warburton et., al 2014), the contact with aflatoxin-producing fungi or its spores, weather conditions and climate during planting and growing and, finally, insect damage. Moisture and temperature play a significant role in fungi growth and the production of aflatoxins. Mycotoxin-producing fungi frequently need higher moisture levels (20.0–25.0 g/100 g) for infection during the pre-harvest phase in the field than fungi that proliferate during storage (13.0–18.0 g/100 g) (Bryden 2011).

It is worth clarifying that the presence of aflatoxin-producing fungi such as *Aspergillus parasiticus* or *Aspergillus flavus* in plants or the field environment does not necessarily imply the contamination of the crops with the toxin. For the production of aflatoxins, the molds need some stress factors such as nutritional imbalance, drought, or water surplus (Tola et. al 2016). Climate plays a relevant role in fungal development and aflatoxin production in crops in the field and during storage (Tola et. al 2016). The substrate or the ingredient that comprises an animal feed is the most important factor in the fungi growth and mycotoxin production mainly due to its nutritional composition (Guerre et al., 2016).

The fungi growth in cereals and animal feeds after harvest during transportation or storage are also influenced by the temperature, humidity, water activity, the integrity of the grain, insect damage, and the quantity and type of the mycobiota (Tola et al., 2016). The increase of the humidity in cereals and feeds during transportation and storage could favor an increment of aflatoxin concentration in these products (Kana et. al 2013). Furthermore, the geographic origin, the transportation route, and the area where the feedstuff is stored, and the length of storage together with particular climate conditions will have a significant impact on aflatoxins concentration and animal exposure to this toxin. Due to this, conditions such as geographic region, temperature, humidity, and duration should be taken into account when comparing mycotoxins analysis from raw feed ingredients or in the prediction of aflatoxins contamination in finished feed (Guerre et al., 2016).

Not only cereals perse are necessary components of the animal diets but also the by-products of these grains are commonly used to feed animals (Fafiolu *et al.,* 2015). Mycotoxins are resistant to the majority of food processing techniques. Nevertheless, food processing such as milling, production of ethanol fuels, and beer brewing could affect mycotoxins distribution and concentration (Norgaard et al., 2012).These mycotoxin concentrated fractions are usually employed in animal diets as is the case in rice milling process where several by-products (e.g. rice hulls, rice bran, chipped rice, rice polishings) are used as animal feed ingredient. (Pinotti et., al 2016). We demonstrated that during the production of cheese, the aflatoxins M1 is concentrated in whey which is frequently used to feed young animals or as a feed ingredient by its own right (Chavarría et al., 2017).

2.4. Toxicity

Aflatoxins have been just considered as an important sanitary problem because it has been demonstrated that human exposure to mycotoxins may result from consumption of plant derived foods that are contaminated with toxins and their metabolites (which are present in animal products such as milk, meat, visceral organs and eggs) or exposure to air and dust containing toxins (Jarvis *et al*., 2002). AFB1 is the best studied aflatoxin, is absorbed in the gastrointestinal tract, due to its liposolubility, and low molecular weight, and transported by red blood cells and plasma proteins to the liver**.** In the liver, it is metabolized producing intermediate metabolites that have been related with the toxic and carcinogenic effects of AFs (Marin*et al*., 2012).

Aflatoxin B1 itself is not a potent toxin, and bio activation is needed to exert toxic effects. These reactions are mainly oxidation of AFB1 to hydroxylated metabolites such as aflatoxin M1. Bio activation is required for AFB1to be toxic and this processing predominantly occurs in hepatocytes (Rawal *et al*., 2010). The disease called aflatoxicosis causes acute and chronic presentation in animals and human. Acute aflatoxicosis causes death and chronic aflatoxicosis results in cancer, toxicity, and immune suppression. The liver is the primary target organ. AFB1 is a potent carcinogen (chiu *et al.,* 2018), by bio activation of cytochrome P450 in the liver and AFB1-8, 9-epoxide (AFBO) production. AFBO is needed for carcinogenic and toxic activity (Wu et al., 2009).

Metabolism of AFB1 involves oxidative reactions by members of the CYP450family of isoenzymes. There is a variety of metabolizing enzymes in animal species. In poultry species, CYP2A6, CYP3A37, CYP1A5, and CYP1A1 play a significant role in the biotransformation of AFB1 (Monson et al., 2015).In humans, CYP3A4 in the liver and CYP2A13 in the lung have significant activity in metabolizing AFB1 to AFBO). The rate of AFBO formation and its conjugation with glutathione to reduce the toxicity by glutathione-S-transferase**),** seem to be an important parameter in interspecies and individual differences (Bbosa et al., 2013). AFB1 can cause hepatocellular carcinomas Cytochrome P450 involvement, 1A2 (responsible for AFM1 biosynthesis) and 3A4 result in epoxide formation that leads to non-enzymatic oxidations which turn DNA into a mutagenic prone DNA adduct (encompassing mutations of p53 (activation of ras-proto oncogenes, leading to mutagenicity) Ultimately, the DNA adduct is unstable and suffers renal elimination, for example, through conversion to aflatoxin N-acetyl cysteine (Dohnal et al., 2014).

Ruminants are more resistant to the mycotoxins than non-ruminants animals because the rumen microbiota is capable of degrading toxins. However, aflatoxins are only partly degraded by ruminal flora resulting in a secondary toxic and carcinogenic metabolite called aflatoxicol. In the case of cattle, sheep, goats, and deer, aflatoxins consumption causes reproductive problems, immune suppression, decrease in milk, beef or wool yield, and reduced feed utilization. Aflatoxins have been shown to reduce feed efficiency in cattle; growth can be altered when ruminants consume contaminated feed for extended periods of time. AFB1 (600 µg kg−1) was shown to depress feed efficiency and rate of gain in steers (Zain et al., 2015).It has been

attributed to compromise ruminal function by reducing cellulose digestion, volatile fatty acids production, and rumen motility (Westlake et al.,1989). Acute exposure to aflatoxins causes in appetence and lethargy (Sulzberger et al., 2017).Aflatoxin levels between 100 and 1 000 µg kg−1 within the diet, cause a decrease in rumen motility, feed efficiency, growth inhibition, and an increase in liver and kidney weight. In lactating dairy cows, researchers report milk production decrease and reduced reproduction efficiency (Gallo et al., 2015).Embryo toxicity has been reported in animals consuming low dietary concentrations of mycotoxins (Zain et al., 2015). In cattle, aflatoxins affect the immune system function by many mechanisms such as inhibition of lymphocyte blastogenesis. AFB1 suppresses mitogen-induced stimulation of peripheral lymphocytes. Chronic exposure can interfere with vaccine-induced immunity (Sulzberger et al., 2017).

Aflatoxins affect the milk quality. Cows metabolize AFB1 to form the monohydroxy derivative, aflatoxin M1 (AFM1), which is secreted into the cow's milk. AFM1 is a potential human carcinogen very resistant to thermal treatments such as pasteurization and freezing. The European Commission Regulation 1881/2006 sets a maximum limit of 0.05 µg kg−1 for AFM1 in raw milk, heat-treated milk, and milk for the manufacture of milk-based products (EC 2006). Nevertheless, higher levels have been found, (Tsakiris et al., 2013).The quality of meat affected by aflatoxin, which mainly affects pH, muscle color, and water-holding capacity (WHC) (Huang et al., 2021).pH is an important factor that determines meat color, tenderness, and WHC, (Wang et al., 2006), pointed out that AFB1 contamination negatively affects meat color.AFB1 can form adducts with DNA, inducing cellular oxidative damage and lipid peroxidation, which may eventually cause a decrease in meat quality (Dohnal et al., 2014). AFB1 exposure significantly increased muscle lightness, while slightly decreased the muscle color, and meat quality was changed after AFB1 exposure. WHC is represented by two indicators: drip loss and cooking loss (Jiang et al., 2017).GenerallyAFB1 impaired meat quality by changing the structure of muscle fibers and meat color and decreasing the muscle water retention capacity (Arshad et al., 2018).

Aflatoxin also can affect laying hens and lead to reduced egg production, poor egg quality and increased mortality of challenged hens. AFB1 adversely influences egg quality by decreasing shell thickness, egg weight and egg energy deposition. The negative impacts of AF on laying hens can be induced when feed contains 1-2 mg/kg (Verma et al., 2007). In addition, AF in laying hen feed can result in an AF residue in the eggs (feed to egg AFB1 transmission ratio was approximately 5000:1); therefore it is very important to control AF concentrations in feeds for laying hens (Oliveira et al., 2000). Consequences of mycotoxin toxicity in other animal do not differ from ruminant animal species. Effects are directly related to losses in production, reduced weight gain, feed conversion, and immune impairment. Kidney, liver, and muscles lesions and residues are found in different species of animal (Anater et al.,2016). The International Cancer Research Institute identifies aflatoxin B1 as a Class 1 carcinogen, resulting in the regulation of this mycotoxin at very low concentrations in traded commodities (20 ppb in grain and 0.5 ppb in milk in the United States; 4 ppb in foods in some European countries (Williams et al., 2004).

2.5. Detection Methods

Various analytical methods employed in analysis of aflatoxins in agricultural food crops and feeds have been explored. While chromatographic methods such as TLC, HPLC,ELISA, Spectroscopic methods andLC-MS are considered the gold standard and are thus the most widely used techniques in aflatoxins analysis, they remain largely cumbersome, requiring extensive sample preparations, let alone very expensive equipment. This makes their routine use in analysis confined to laboratories. It is on the account of such limitations that it was necessary to develop more sensitive and better techniques for aflatoxins analyses (Wacoo et al., 2014).

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 1ng/g. Similar in many respects with TLC is LC. Usually TLC is used as a preliminary work for optimization of LC separation conditions (Cigic et al., 2009).A Liquid chromatography- mass spectrometry, (LC-MS) is also appropriate for metabolomics because of its good coverage of a wide range of chemicals (Zhou et al., 2012).Hence, LC-MS may be applied in a wide range of sectors including biotechnology, environment monitoring, food processing, and pharmaceutical, agrochemical, and cosmetic industries, (Chaimbault., 2014).

2.5.1. Chromatography

Chromatography is one of the most popular methods to analyze mycotoxins such as Aflatoxins. Gas-chromatography (GC), liquid chromatography (LC), High-performance liquid chromatography (HPLC) and thin layer chromatography (TLC) are the most common techniques of chromatography. Out of these methods, LC and HPLC are the most used. In many cases, they are followed by fluorescence detections stage (Cavaliere et al 2006). LC, TLC and HPLC are the most used quantitative methods in research and routine analysis of aflatoxins (Vosough et al., 2010). These techniques offer excellent sensitivities, but they frequently require skilled operators, extensive sample pretreatment and expensive equipment (Sapsford et al., 2006).

High performance liquid chromatography

HPLC is the most popular method for the analysis of mycotoxins in foods and feeds. Actually, it is quantitative technique that is suited for online cleanup of sample extract and could be combined with different detectors (Li *et al.*, 2006). The mycotoxins extracted from field samples undergo clean up using commercial immunoaffinity columns before their analysis by HPLC. The columns are available for all the important mycotoxins: AFB1, AFB2, AFG1, and AFG2, AFM2, ochratoxin A, T2 Toxin, deoxynivalenol (vomitoxin), citrinin, fumonisins FB1, FB2, FB3, zearalenone, patulin and moniliformin. Multiplex columns are available for AFs, ochratoxin A and zearalenone. The rationale beyond the multiplex columns and for multiplex detection methods is the frequent production of more than one mycotoxin by a single fungus, and the frequent contamination of crops or silage with several species of fungi (Rastogi *et al.*, 2001)**.**

Thin layer chromatography

Thin layer chromatography (TLC), also known as flatbed chromatography or planar chromatography is one of the most widely used separation techniques in aflatoxin B1 analysis. Since 1990, it has been considered the AOAC official method. The TLC method is also used to verify findings by newer, more rapid techniques. The technique is widely used in laboratories throughout the world for food analysis and quality control. Applications of TLC have been reported in areas of food composition, intentional additives, adulterants, contaminants, etc. TLC has been used to analyze agricultural products and plants. It has advantages as, simplicity of operation; availability of many sensitive and selective reagents for detection and confirmation without interference of the mobile phase; ability to repeat detection and quantification; and cost effectiveness analysis, because many samples can be analyzed on a single plate with low solvent usage, and the time that TLC employs to analyze the sample is less that LC method (Sherma., 2000) .Presumptive aflatoxin detection can be performed with thin layer chromatography (TLC) as this method is a simple, robust technique, which is relatively is an inexpensive compared to high performance liquid chromatography methods(Gilbert and Anklam, 2002).

Liquid chromatography-mass spectrometry (LC-MS)

LC–MS technique has become the fastest growing technique available for analysis of mycotoxins. The potential benefits of LC–MS technique for mycotoxin analysis have long been recognized and exploited. Simultaneous determination of multi-mycotoxins can be possible with LC–MS according to the mass to charge ratio (m/z) of analysts, an intrinsic property that provides more specific identification based on molecular weight of the target analyte. The impact of modern LC–MS technique has been signified by the unmatchable sensitivity in quantitation, specificity in identification and number of mycotoxins that could be analyzed in one analysis, (Di Stefano et al., 2012). A modern LC–MS instrument, particularly LC–MS-triple quadrupole (LC– MS-QQQ), has been developed and introduced with increasing sensitivity for quantitative analysis of mycotoxins. Despite high capital costs of LC–MS instruments, many efforts have been exerted to quantitate aflatoxins using this technique (Sforza *et al*., 2006).

2.5.2. Enzyme Linked Immunosorbent Assay Detection

The ELISA technique is currently used in the detection of aflatoxins in agricultural products and a number of commercially available ELISA kits based on a competitive immunoassay format are widely used (Huybrechts., 2011). Most of the kits use horseradish peroxidase (HRP) and alkaline phosphatase (AP) enzymes as labels in analysis of aflatoxins (Ostadrahimi *et al.,* 2014). The producers of the tests have considered the different regulatory limits of different regions. A substantial part of agricultural raw materials can be analyzed with the ELISA technique, according to the guidance provided by the producer, without the application of particular cleaning steps. ELISA analysis of more complicated sample types, like compound feed, however, may provide inaccurate results. In order to avoid this situation, it is recommended to consult the producer of the tests concerning the sample to be analyzed. Alternatively, the process is recommended to be individually validated for the matrices to be tested. However, if the measurement of a complex matrix is needed, which is not on the list of substances validated by the producers, or if the aim is to confirm the result of a rapid test, the sample has to be analyzed with reference methods (Andreasson et al., 2015).

An improved version of ELISA is (Tumor Specific Antigen) TSA-ELISA, where the intensity of the sign generated by ELISA can be increased several folds by the addition of tyramide (Zhang *et al*., 2018). The ELISA method offers a number of advantages: (a) it is possible to perform the test on a 96-well assay platform, which means that a large number of samples can be analyzed simultaneously (b) ELISA kits are cheap and easy to use and do not require extensive sample cleanup and (c) there are no inherent health hazards associated with enzyme labels as there are for isotopes. However, the ELISA technique requires multiple washing steps, which may at times prove not only laborious but also time consuming (Huybrechts, 2011).

2.5.3. Spectroscopic methods

Fluorescence Spectrophotometry. Absorption in the ultraviolet-visible region is very important procedure for unraveling the molecular structures of materials. However, for some molecules, the process of absorption is followed by emission of light of different wavelengths. In other words, such molecules are said to fluoresce. Fluorescence is very important in the characterization and analysis of molecules that emit energy at specific wavelengths and has been used to analyze aflatoxins in grains and raw peanut.The fluorometric method can quantify aflatoxin from 5 to 5000ppb within less than 5 minutes. However, for better analysis of aflatoxins using fluorometry, derivatization may be required to improve the fluorescence of aflatoxins(Babu., 2010).

2.6. Detoxification Methods

The increasing number of reports on the presence of aflatoxins in food and feedstuffs dictates the need for decontamination procedures; such procedures should not only reduce the mycotoxin content to “safe “levels below regulatory limits but should also have the following characteristics: easy to use, inexpensive and free of the potential for forming compounds that are still toxic or compromising the national value of the treated commodity (Mendez *et al.*, 2004). Although numerous detoxification methods have been tested, only some of them seem to be able to fulfill the efficacy, safety, safeguarding measures of nutritional elements and costs requisites of a detoxification process. These methods can be divided into three subcategories, which are physical, chemical and biological techniques (Bozoglu and Tokusoglu, 2011).

Physically, aflatoxin contaminated seeds can be removed by handpicking or photoelectric detecting machines, but this is labor intensive and expensive. Heating and cooking under pressure can destroy nearly 70% aflatoxin. Dry roasting can reduce about 50-70% of aflatoxin and sunlight drying of aflatoxin contaminated feed could reduce the toxin level by more than 70% (Gowda et al., 2013).In recent times, ionizing irradiation (viz. electron beam, gamma and ultraviolet rays) and nonionizing irradiation (viz. infrared waves, radio waves, visible light waves and microwaves) has been employed extensively for the degradation of aflatoxin present in the food and feed. Electron beam irradiation (EBI) technology has great potential for aflatoxin degradation. EBI technology offers the advantage of high effectiveness, low equipment cost, dosage control, short processing time, low heat generation, few variables and in-line processing (Kim et al., 2014).

Gamma (γ) rays have been the most preferred radiation source for the food owing to its high penetrability and reactivity. Treatment of food by gamma rays has no toxicological or microbiological hazards (Farkas et al., 2011).

Additionally, γ irradiation results in the interaction of high energy of γ rays with the water present in the food products. This produces highly reactive free radicals such as superoxide radical ($O2•−$), hydrogen (H•) radical and hydroxyl ion ($OH−$) that in turn destroy aflatoxins and also attack DNA pathogenic microbes (Silva Aquino 2012).Ultraviolet (UV) irradiation is also highly cost effective and eco-friendly (Gayan et al., 2014). Treatment of food products with moderate doses of UV rays has no negative impact on its sensory and physicochemical properties (Delorme et al., 2020).

Biologically, which are based on the action of microorganisms on mycotoxins and their mechanism of action is based on competition by nutrients and space, interactions, and antibiosis, among others (Fazeli *et al*., 2009). Biological control of mycotoxin is a promising approach for reducing both pre and post-harvest mycotoxin contamination in food crops (Velazhahan *et al.*, 2010). Different organisms, including bacteria specially, probiotics and dairy strains of lactic acid bacteria, yeasts strains of *Saccharomyces cerevisiae* and non-toxigenic Aspergillus fungi, have been tested for their ability in the control of AFs contamination (Yin *et al*., 2008).

Chemically, there is no reliable method for feed decontamination from aflatoxin; various workers have screened a large number of chemicals viz. benzoic acid, propionic acid, copper sulfate, synthetic zeolites, citric acid etc. these chemicals have shown the reduction of aflatoxin in vitro (Safara *et al*., 2010)

2.7. Public Health Significance and Economic Impacts

Aflatoxins have economic and health importance because of their ability to contaminate human food and animal feeds, in particular cereals, nuts and oilseeds. The toxins have adverse effects on plants, animals and humans. They are responsible for damaging up to 25% of the world’s food crops, resulting in large economic losses in developed countries and human and animal disease in under-developed countries (Abbas *et*

al., 2005). The toll of the effects on human health includes the cost of mortality, the cost of productive capacity lost when people die prematurely, the cost of morbidity, losses resulting from hospitalization and the cost of healthcare services, both public and private. There is intangible cost of pain, suffering, anxiety and reduction of the quality of life (Bhat *et al*., 2003).

2.7.1. Public health significance

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 (Arapceska *et al*.,2015). Over 5 billion people in developing countries worldwide are estimated to be at risk of chronic exposure to aflatoxins through contaminated foods. Aflatoxins are naturally occurring contaminants of food according to Guo (Gou et al., 2000).

Animals and humans are exposed to aflatoxins through consumption of contaminated products such as dairy products (e.g. milk, cheese, and yogurt (Prandini *et al.*, 2009). Aflatoxin is both a food safety and public health issue because of its toxicity. When it is consumed, it can exert toxicity by altering intestinal integrity or control the expression of cytokines which can result in stunted growth in children and immune suppression. In the liver, aflatoxin may be transformed by certain p450 enzyme to its DNA reactiveformAflatoxin-8-9-epoxide which binds to liver proteins and lead to their failure, resulting in acute aflatoxicosis or it may bind to DNA, contributing to aflatoxin induced hepatocellular carcinoma (liver cancer). (Ogodo and Ugbogu 2016).

2.7.2. Economic impacts

The magnitude of the economic impacts of the health consequences associated with consumption of aflatoxin contaminated food in developing countries is not known due to a lack of good data. According to them, the quantification of economic losses and estimation of the effects of aflatoxin on health will encourage Health Ministries to enforce standards and provide crucial advocacy to benefit the rural poor, such as improving their level of education about aflatoxin exposure (Wu *et al*., 2011). The economic impact of aflatoxins derives 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 (Bennett *et al.*, 2015).The chronic and acute exposures of cattle to aflatoxin cause significant economic loss. In addition to financial losses and economic damage to agricultural and animal husbandry, losses due to aflatoxin contamination of foods include major pharmaceutical and health costs to treat food poisoning. Consumption of aflatoxin contaminated feed reduces productivity of livestock (Gizachew et al., 2016).

2.8. Control and Prevention

Elicits for action could also be based upon other factors which indicate or influence aflatoxin contamination, such as reporting of death among livestock or domestic animals which are often given lower quality grain. Modeling of aflatoxin contamination based on weather conditions from planting to post-harvest could also serve as a trigger (Campa *et al.*, 2005).To minimize risks associated with unavoidable exposure to AFs, regulation and monitoring measures must be supported by in field (preharvest) and storage (postharvest) interventions which may be applied to minimize AF contamination. AFM1 is excreted in milk of dairy animals following metabolism of AFB1 ingested with feed. Contamination of milk may, thus, be reduced either directly, decreasing AFM1 content of contaminated milk, or

indirectly, decreasing AFB1 contamination in feed of dairy animals (Jard et al., 2011).

The presence and growth of Aspergillus on pre-harvested crops is dependent on the environment. Agricultural practices including proper irrigation and pest management can reduce aflatoxin contamination. Pre-harvest interventions include choosing crops with resistance to drought, disease, and pests and choosing strains of that crop which are genetically more resistant to the growth of the fungus and the production of aflatoxins (Dowd et al. 2003). Elimination of inoculum sources such as infected debris from the previous harvest may prevent infection of the crop (Olanya et al., 1997). A biopesticide, consisting of a non-aflatoxigenic strain of Aspergillus, may competitively exclude toxic strains from infecting the crop (Dowd et al., 2003). During post-harvest, before storage, crops should be properly dried to prevent the development of aflatoxins. Sorting and disposing of visibly moldy or damaged kernels before storage has proven to be an effective method for reducing, but not eliminating, the development of aflatoxins (Fandohan et al., 2005). During storage, moisture, insect, and rodent control can prevent damage to the crop and reduce aflatoxin development (Hell et al., 2000).This study illustrates that simple and inexpensive post-harvest methods can have a significant impact. Feeds have to be kept hygienically and prevent molds formation by using available methods that are accessible for them in their environment aware extension workers and owners of livestock on impact of aflatoxin in feeds: implications to livestock and human health (Saini and Kaur, 2012).

Reduction through food processing procedures: Sorting can remove a major part of aflatoxin contaminated units, but levels in contaminated commodities may also be reduced through food processing procedures that may involve processes such as washing, wet and dry milling, grain cleaning, dehulling, roasting, baking, frying, nixtamalization and extrusion cooking (Gashaw, 2016).However, the chemical reaction may involve temporary inactivation of aflatoxins, a process that may reverse in the gastric acid of the stomach.These methods do not always transfer well to other communities due to lack of acceptance (Fandohan et al., 2005.

Control strategies for reducing aflatoxins, including enterosorption and chemoprotection, attempt to reduce the effects of aflatoxin exposure or the bioavailable portion of aflatoxins in food. Enterosorption is the use of clay, such as NovaSil, with a high affinity for aflatoxins (Wang et al., 2005). Clay has been used as an anti-caking additive in animal feed and has been shown to protect animals from ingested aflatoxins. Chemoprotection is the use of chemical (e.g. Oltipraz, Chlorophylin) or dietary intervention (e.g., broccoli sprouts, green-tea) to alter the susceptibility of humans to carcinogens and has been considered as a strategy to reduce the risk of HCC in populations with high exposures to aflatoxins (Kensler et al., 2004). Control AF concentrations in feeds, animal and poultry, reduce the toxin in the product of animals (Oliveira et al., 2000). Sulforaphane increasing pathways leading to aflatoxin detoxification in humans, the practicality of using a drug-based method for prevention in developing countries is limited. Fortunately, oltipraz is not the only agent that affects enzyme changes through the Nrf2-Keap1 pathway. Many foods have high levels of these enzyme inducers (Fahey, and Kensler, 2007).A beverage formed from hot water infusions of 3-day-old broccoli sprouts, containing defined concentrations of glucosinolates as a stable precursor of the anticarcinogen sulforaphane, was evaluated for its ability to alter the disposition of aflatoxin (Kensler et al., 2005). Sulforaphane has been extensively examined for its chemo preventive properties and is a potent activator of the Nrf2-Keap1 pathway, leading to increased expression of carcinogen-detoxifying enzymes (Dinkova et al., 2007).

3. Conclusion

Generally aflatoxins are a group of mycotoxins that are typically produced by specific fungi; their occurrence is influenced by specific environmental factors. Hence, the level of

contamination will vary depending on geographic location, agricultural and agronomic practices, and the susceptibility of commodities to fungal invasion during pre-harvest, storage, and or processing periods. Flavonoids and the associated health disorders in humans and animals (such as immune suppression, cancer, and teratogenicity, among others) have been acknowledged as a significant health and economic problem that necessitates measures to reduce exposure by using proper agricultural practices, product storage, and control of the products intended for human or animal consumption. Widespread screening of foods and feeds that may be contaminated with aflatoxin has resulted from its high toxicity and carcinogenicity as well as its capacity to produce a variety of clinical diseases. The storing of foods in a dry and hygienic place to stop the growth of mold, choosing crop varieties that are resistant to illness, pests, and drought and The public awareness about aflatoxin impact on human, animal health and its financial consequences are better to avoid the problem.

Conflict of Interest

No Conflict of Interest between all Authors.

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