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Review Article

Public health impacts, animal health risk, and management of mycotoxins contaminating maize (*Zea mays* L.)



Sachin Gahatraj^{a,*} 跑, Kiran Pariyar^b, Santosh Rasaily^c, Jiban Shrestha^d 跑

^a Faculty of Agriculture, Agriculture and Forestry University (AFU), Rampur, Chitwan, Nepal

^b Ministry of Agriculture and Livestock Development (MoALD), Kathmandu, Nepal

^c National Oilseed Research Program, Nepal Agricultural Research Council (NARC), Nawalpur, Sarlahi, Nepal

^d Agriculture Botany Division (ABD), Nepal Agricultural Research Council (NARC), Khumaltar, Lalitpur, Nepal

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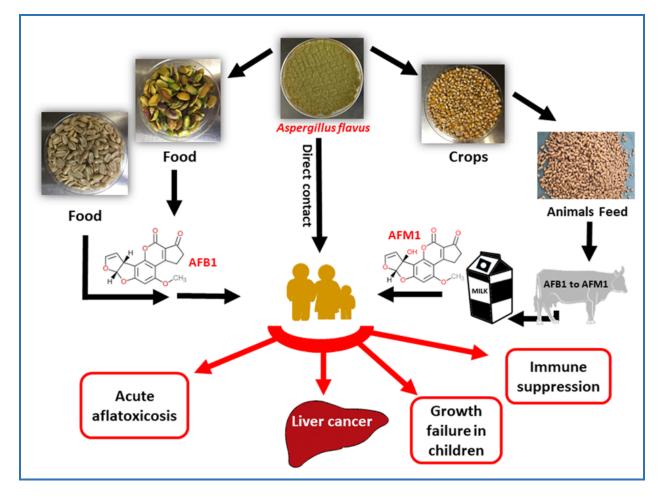
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Mycotoxins Maize Aflatoxins Fumosinin Health

ABSTRACT

Maize is one of the most important agricultural commodities in the world and the third most traded cereal after wheat and rice. Maize contaminated with mycotoxin causes a fundamental problem all over the world. In this study, we assessed the risk of mycotoxin and its management. Mycotoxins are toxic secondary metabolites of fungi that may contaminate the food crops. There are several mycotoxins in crops; however, aflatoxins (produced by Apergillus flavus) and fumonisins (primarily produced by Fusarium verticillioides) are the major concern in maize-based food and feed worldwide. Aflatoxins are hepatotoxic and carcinogenic agents. They are associated with human liver cancer, child growth impairment, and acute toxicoses. Fumosinin may cause esophaseal cancer and neural tube defection in humans, whereas in livestock effects are variable; reproductive disorder, pulmonary edema in swine, leukoencephalomalacia in equines, and reduced feed intake. Management approaches of mycotoxins include cultural and genetic approaches. Cultural practices such as plant quarantine, phytosanitary measures during harvesting and post harvest, and management of insect pest are essential for avoiding contamination of mycotoxin. Development of maize varieties resistant to fungal infection contributes to grow mycotoxins-free maize. Moreover, chemical removal, physical binding or microbial detoxification can be done to avoid mycotoxins contamination. The eating mycotoxins contaminated maize grain was found to be harmful to human and livestock health. Therefore, awareness program on adverse effects of mycotoxins should be provided to public so that the people can be confident that the food they consumed is safe.

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Biographies



Sachin Gahatraj is B.Sc. Ag graduate at Agriculture and Forestry University (AFU), Rampur, Chitwan, Nepal. He is working as Instructor of Plant Science under Government of Nepal. He has done internship (six months) in Prime Minister Agriculture Modernization Project (PM-AMP). He has published four papers in national and international journals. In addition, he has presented papers in 1 national and 4 international conferences.



Kiran Pariyar is working as a Plant Protection Officer at Ministry of Agriculture and Livestock Development, Nepal since 2019 to present. He has worked as Technical Officer at Nepal Agriculture Research Council, under a project named Agriculture and Food Security Project for 14 months (2017-2018). Currently he is working as plant protection officer and has involved for planning and monitoring of the programs that has been conducted at Temperate Horticulture Development Center, Marpha, Mustang. He





has published 4 peer reviewed journal articles, 4 proceeding papers and many other short booklets for farmers' convenience. He is the student of Agronomy and planning to complete MSc. Ag (Agronomy) in March, 2020.

Santosh Rasaily is Agriculture Scientist of NARC working especially in the breeding aspect of Oilseed crops. He had completed his M.Sc.Ag in Genetics and Plant Breeding from Agriculture and Forestry University (AFU), Rampur, Chitwan, Nepal under the Research Grant of ICARDA. He was an executive director in Community Development Advocacy Forum Nepal. He had worked as Research Officer in LIBIRD as well. Similarly, he had also worked as Cluster Agronomist for CIMMYT. He has published 3 papers in national and international journals.

Jiban Shrestha is working as a Scientist (Plant Breeding and Genetics) at Nepal Agricultural Research Council, Nepal since 2010 to present. He has worked as maize breeder at National Maize Research Program, Rampur, Chitwan, Nepal from 2010 to Sept 2017. He has worked as a Coordinator at National Commercial Agriculture Research Program, Pakhribas, Dhankuta, Nepal from Sept. 2017 to Aug. 2018. Now he is working as Scientist at Agriculture Botany Division, Khumaltar, Lalitpur, Nepal. Currently he is working as rice breeder and has involved for evaluation, development and release of normal and hybrid rice varieties. He has published more than 125 peer reviewed journal articles, 12 proceeding papers and 6 books. He has been affiliated to more than 40 journals as editor or reviewer. He has worked as reviewer of 15 international conferences related to agriculture. He has guided 10 agricultural graduate and 4 postgraduate students for their thesis research.

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Introduction

Maize (Zea mays L.) -known as corn- is a major cereal crop which is primarily grown for human food and animal feed through-out the world [1]. It is estimated that global maize consumption will be increased by 16% by 2027 [2]. Agricultural commodities are already contaminated with toxins in field, storage or during processing. Maize is one of the susceptible crops to mycotoxin contamination during production a storage [3]. Maize consumption, by human and livestock, will increase mainly in developing countries where population is burgeoning [4]. Such countries are highly vulnerable to mycotoxins because of lack of knowledge, poor agricultural practices, poor storage conditions, and lack of resistant varieties [3]. There are several toxic fungal metabolites associated with maize. However, few mycotoxins that occur more frequently require most attention. When some fungi grow in crops, they produce toxic substances that remain in the crops posing health risk to consumers. Mycotoxins are secondary metabolites produced by such filamentous fungal species that contaminate staple food crops and feeds-few mycotoxins are aflatoxins, ochratoxins, trichothecenes, zearalenone, fumonisins, tremorgenic toxins, and ergot alkaloid [5]. Among these, aflatoxins (produced by *Apergillus flavus*) and fumonisins (primarily produced by *Fusarium verticillioides* and *F. proliferatum*) are major mycotoxins on maize which are associated with severe health detriments in human, animals, and birds consuming it [4].

Mycotoxins are toxigenic, nephrotoxic, hepatotoxic, carcinogenic, immunosuppressive and mutagenic [6]. FAO has estimated that about 25% of global agricultural food crops are significantly contaminated by mycotoxins 20% of which comes from developing countries [7]. Even low level of toxin in livestock feed primarily cause metabolic disturbances resulting poor productivity. In pig and poultry, poor growth rate, changes in carcass quality, reduced fertility, lower egg production, reduced hatchability of eggs, and immunosupression were observed [8]. Wide range of agricultural commodities is contaminated by mycotoxins produced by several fungi worldwide. These are closely related to human and animal food chain [9]. In recent years, concern toward impacts of mycotoxins

on human and animal health has been increased. However, little is known about health risk of mycotoxins and their management [10].

Public health impacts and animal health risk of mycotoxins

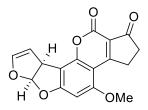
Aflatoxins

Aflatoxins are secondary metabolites pre-eminantly produced by two fungal species : *Aspergillus flavus* and *A. parasiticus* [11]. It might be produced at any stage: during preharvest, harvest, drying or storage. The occurrence and maize damaged by *Aspergillus flavus* was given in Figure 1. Alfatoxins are most acute and chronic toxins of all types of mycotoxins; therefore, the concentration of aflatoxins in agricultural food and feed should be brought under intensive scrutiny [12].



Figure 1. *Aspergillus flavus*. a, Occurrence of *A. flavus* on a maize cob; b, Colonies of *A. flavus* growing on malt extract agar from wheat grain; c-d, *A. flavus* conidial heads [13]

Aflatoxins belongs to a group of difurancoumarins. The structure of aflatoxin was given in Scheme 1. Aflatoxins can bring different unusual modification of animal DNA and protein structure, which ultimately result cancer formation in affected cells. Aflatoxins are economically important among the mycotoxins. Moreover, aflatoxin B1 is the most potential naturally occurring carcinogen, hepatocarcinogenic and hepatotoxic, causing epidemic death of several hundred people in Asia and Africa [13]. Aflatoxin B1 is well known for its nuisance public health impact. It mainly enters into human, showing carcinogenic impacts [14]. Aflatoxins are the major agriculturally important mycotoxins that contaminate food crops. These toxins are associated with human liver cancer, child growth impairment, and acute toxicoses [15]. The outbreak of Aflatoxicosis and human dealth due to this was noticed in India and Kenya (Table 1). Diagramatic presentation of aflatoxin contamination route and detrimental health effects to human was given in Figure 2.



Scheme 1. Strucutre of aflatoxins

Country	No of	Sumptome on signa	Towin	Sourco	Deference
Country	No. of	Symptoms or signs	Toxin	Source	Reference
-	deaths				
India	106	Brief febrile episode, vomiting,	Aflatoxin	Maize	[19]
		anorexia, jaundice, ascites,	B1		
		oedema of legs, massive,			
		gastrointestinal bleeding			
India	97	Fever, vomiting, oedema of feet,	Aflatoxin	Maize	[20]
		jaundice, hepatomegaly, ascites,	B1		
		splenomegaly			
Kenya	12	Brief febrile episode, vomiting,	Aflatoxin	Maize	[21]
		abdominal discomfort, anorexia,	B1		
		jaundice, oedema of legs, ascites,			
		tachycardia, tenderness of liver			
		(rarely enlarged), melaena,			
		gastrointestinal bleeding			

Table 1. Outbreak of aflatoxicosis

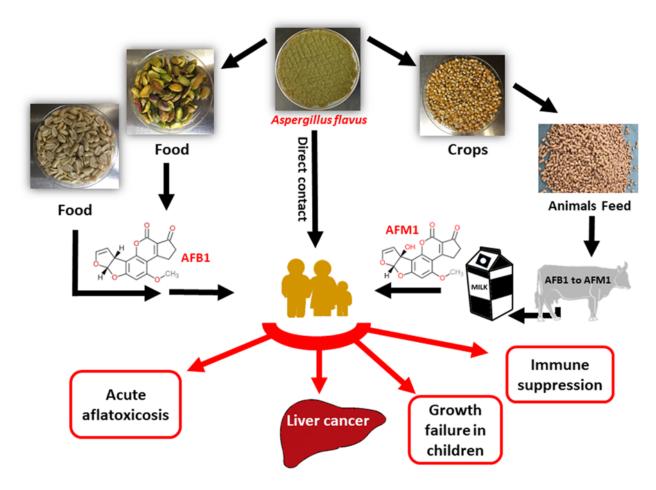


Figure 2. Diagramatic presentation of aflatoxin contamination route and detrimental health effects to human [22]

Hot and humid condition of tropical regions is suitable for growth of mycotoxins producing fungi [16]. Agro-ecosystem is highly vulnerable to climate change since different new disease out-break occurs and that menace our crops either by reducing yield or contaminating with toxins [17]. The pattern of aflatoxins occurrence is liable to climate change, which is happening [12]. Susceptible host crops are sources of aflatoxin that are consumed by animals and/or birds. Ultimately, on consumption of such aflatoxin infected animals or crops, such toxin is biomagnified in human body [18].

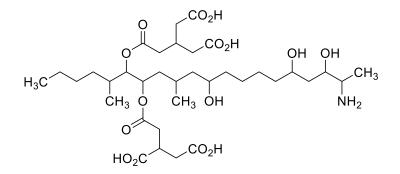
Fumosinins

Fumosinins are produced by *Fusarium verticillioides*, causing 'fusarium ear rot (or pink ear rot)' disease in maize, or grow endophytically in maize kernels and synthesize mycotoxin [23]. *F. verticillioides* are contaminated to healthy crops through either infected silks or seed-to-kernel [24]. It causes economic losses due to yield reduction and poor grain quality. The structure of Fumosinins

was given in Scheme 2. The maize seed and kernel damaged by Fusarium verticillioides was given in Figure 3.

Fumosinin is detrimental to livestock health: reproductive disorder, pulmonary edema in swine, leukoencephalomalacia in equines, and reduced feed intake globally [25]. In addition, fumosinin escalates infection of parasites, bacteria, and viruses in host body of livestock-some examples are salmonellosis in pigs, necrotic enteritis in poultry, swine respiratory disease, coccidiosis in poultry enteric, and septicemia of catfish [26].

In human, fumosinins are associated with esophageal cancer (EC) and neural tube defects (NTDs) [15]. These toxin are able to penetrate intestinal epithelium and reach the systemic compartment that impair immune system [27]. Fumosinin B1 initiates cancer in hepatic cells of mammals by enhancing cancer promoter so called phenobarbital [28].



Scheme 2. Structure of fumisonins B1



Figure 3. *Fusarium verticillioides* damage in maize seed and kernel, (adopted from Dr. Belinda Janse Van Rensburg)

Management approaches of mycotoxins

Preharvest control

The cultural practices include practices to avoid or reduce the contamination in healthy crops from mycotoxins producing fungal strains such as *Apergillus flavus* and *Fusarium verticillioides*. In general, conditions are altered so that fungi could not establish on crops. Some tactics that can be applied at preharvest or standing crops are crop rotation, cropping density, proper irrigation, suitable planting date, and suitable fertilization amount [4]. In additon, few other measures might be pivotal for preharvest mycotoxins management such as plant quarantine, phytosanitary measures, and management of insect pest. It has been found that stress during reproductive growth of maize make crop succeptible to fungal infection which produce mycotoxins and contaminate grains. Such stress might be one or intricate combination of many biotic and abiotic factors: heat stress, drought, insect infestation, plant diseases, weed infestation, and high plant density [29]. Public education and awareness can make people aware of mycotoxins hazards and able to manage it [30]. The water stress combined with fungicide application significantly reduce *Fusarium verticillioides* [31].

Genetic approaches

Several researches have been carried out to develop plant varieties resistant to fungal infection. Eventhough naturally resistant maize genotypes have not been found, aflatoxin resistance has been identified during field testing and maize beeding populations. Host plant resistance to fungal infection through resistant breeding might contribute to grow mycotoxins free maize. Native resistance and transgenic resistance are options that can be utilized for development of fungal tolerance and reduced mycotoxins level [4]. Molecular markers can be employed to speed up breeding for incorporation of chromosomal region with resistance QTL (quatitative trait loci-QTL). Moreover, transgenic maize for insect resistance so called "Bt maize" expresses Bacillus thuringiensis toxins against corn cob borer. Eventually, there is reduction in secondary infection of mycotoxin producing fungi [32]. On top of conventional breeding, marker-assisted selection (MAS) breeding is wide-spread feasible in maize it exploits molecular markers as selection tool in plant breeding. This is based on QTL [33]. Based on ergosterol level, the fungal biomass formed on Bt corn grain was 4-8 times lower than non-transgenic maize. Furthermore, fumosinin B1 concentration on Bt maize grain ranged 0.05-0.3 ppm whereas it was 0.4-9 ppm in non-transgenic maize [34]. Development of host resistance through the addition and/or enhancement of antifungal genes can be achieved by genetic engineering.

Harvest control

Mycotoxins producing fungi can be transferred from contaminated to healthy maize crops during harvesting and processing-drying and threshing-through instrument used and by the contact of each other. While grains start to dry, field moisture content remains high enough to open avenue for fungal strains producing mycotoxins [4]. Intensive care must be taken while harvesting and handling the grains to avoid breakage: otherwise, injuries might make fungal strains easy to infect [29]. During harvesting of maize grains, care should be taken to avoid injuries to them because injured grains are more susceptible to mycotoxins contamination.

Post harvest control

The post harvest management is to create an environment during storage that avoids growth of mycotoxins producing fungal species or at least curbing the toxins synthesis below safe level. Even if mycotoxins present in food and/or feed, detoxification or decontamination can be employed to reduce toxins absorption in gastrointenstinal tract [7]. Reduction and detoxification of mycotoxins can be done by few practices: physical method (sorting, segregation, floatation, *etc.*); chemical methods (use of calcium hydroxide and ammonia); and microbial method (incorporation of probiotics and/or lactic acid bacteria into diet of human and animals) [30]. On severe infestation of mycotoxins producing fungi, it is wise to dispose maize food or feed with safe measures. Storage temperature is a most important factor for managing mycotoxins production in stored grains, food, and feed. After drying, grains should be cooled and maintained at 1-4 °C storage temperature. During summer, storage temperature can be maintained at 10-15 °C. Insect damage during storage accelerate mycotoxins producing fungal growth; hence, routined observation and treatment should be taken to reduce insect attack as well [4].

There are some approaches for post harvest management of mycotoxins. The physical approach (segregation, sorting, and flotation); cultural (proper plant density, irrigation, insect pest control, management of weeds that harbour such insects, proper handling, proper storage); chemical (use of calcium hydroxide and ammonia); microbial (incorporation of pro-biotics and/or lactic acid bacteria into diet); and genetic (use of local resistance and transgenic crops). Chemo-preventive measures-daily consumption of chlorophyllin or oltipraz and incorporating hydrated sodium calcium alumino-silicates into the diet can decrease effects of aflatoxins. Constant and cost-efficient monitoring and serveillance can reduce risk. Plant quarantine is fundamental to check spread of mycotoxins contamination. The chemical removal, physical binding, or microbial degradation are as options [35]. However, treatment is often expensive, high technology demanding, and even impractical in use. Aflatoxin destruction by ammonia treatment is one of the practical method of chemical removal of mycotoxin [36]. In chemical detoxification, there is often loss of nutritive value and palatability of

food or feed. In sum, the possible management approaches include good agriculture practices such as sanitation, proper storage, and insect pest management. Similarly, other strategies includes decontamination, development of resistant varieties, routine serveillance and awareness campaign [37].

Conclusions

Mycotoxins are chemicals with toxic effects produced in various agricultural crops which are susceptible to mould infestation. Contamination in maize is worldwide challenging problem due to the high economic loss of crop and derimental health impacts to consumers (human, animals, and birds). Numbers of cases of mycotoxins toxicity are reported annually in several cases-many of cases are unreported. People and animals of least and under developed countries are more vulnerable to mycotoxicosis. Therefore, mitigation efforts should be taken promptly. Public education and awareness can play pivotal role as it make people to think about health risks and their management. Awareness of mycotoxin properties, limiting their presence in the environment, preventing exposure above toxic levels will help to maintain both human and animal welfare. Contamination of mycotoxins is unavoidable and dependent upon variety of field and/or storage environmental conditions. Countries should have their own national policies and limits to save public health from contaminating mycotoxins in maize. Integrated mycotoxin management system should be considered and implemented from field to consumers.

Disclosure Statement

No potential conflict of interest was reported by the authors.

Orcid

Sachin Gahatraj 🕩 0000-0002-6294-1733 Jiban Shrestha 🕩 0000-0002-3755-8812

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