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Study of Impact of Mycotoxins on the Human Health

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Abstract

Mycotoxins are secondary metabolites produced by fungi and are capable of causing various diseases in humans and animals. They are naturally occurring chemical substances and are chemically stable which is why they pose a great threat to public health. Accumulation of mycotoxins in the food chain can cause hazardous effects in human. The gut microbiota has a bidirectional relationship with mycotoxin, being the leading cause of the development of mycotoxicosis. These fungal toxins exhibit a number of adverse health effects in animals, even at very low concentrations, and have been associated to cases of acute and chronic poisoning of humans and farm animals since historical times. Preventive measure for controlling contamination should be adopted both before and after harvest. Mycotoxin occurrence cannot be completely avoided, but a number of measures aiming at minimizing mycotoxin levels and mycotoxin exposure can be implemented at multiple points in the food and feed chains.

Keywords: Mycotoxins, Metabolites, Fungi, Microbiota, Food chain, Mycotoxicosis.

INTRODUCTION

Mycotoxins are secondary metabolites produced by filamentous fungi which contaminate a large fraction of the world's food, mainly staple foods such as corn, cereals, groundnuts and tree nuts, besides meat, milk and eggs. This worldwide contamination of foods is an enormous problem to human populations, principally in less industrialized countries and in the rural areas of some developed countries.

Food safety is a priority for humanity. A major menace for food safety is represented by mycotoxins, toxic secondary metabolites produced by molds that infect field crops and which contaminate raw agricultural commodities as well as processed foods and feeds. These fungal toxins exhibit a number of adverse health effects in animals, even at very low concentrations, and have been associated to cases of acute and chronic poisoning of humans and farm animals since historical times. Mycotoxins not only jeopardize the health of consumers and livestock, but they are also a concern for international trading and an important issue for national and international regulatory bodies, which have to cope with the necessity to set limits for mycotoxin content in foods and feeds and harmonize standards throughout the world taking into account both consumers' safety and social and economic impact of regulatory measures.

Mycotoxins are naturally occurring, low molecular weight, chemically stable secondary metabolites produced by fungi like *Aspergillus*, *Fusarium*, *Penicillium* species and are the cause of adverse health effects in humans and animals, leading to mycotoxicosis. They grow on various crops including cereals, nuts, spices and coffee beans, apples under warm and humid conditions. Mycotoxins are exotoxins that are produced when fungal growth ceases due to nutrient limitations and the presence of excess carbon source. Occurrence of mycotoxins in food poses great threat to the consumers and is considered to be one of the major global health issue.

COMMON TYPES OF MYCOTOXINS

There are a number of mycotoxins identified so far, some of them have gained attention due to their

severe health effects and occurrence in food. These includes Aflatoxins, Ochratoxin A and Patulin. Aflatoxins are one of the most deadly mycotoxins produced by *Aspergillus flavus* and *Aspergillus parasiticus*. They affect cereals like sorghum, wheat, rice nuts like almond, pistachio, coconut and spices including turmeric, ginger, pepper, and coriander. They are genotoxic and large doses can damage liver and cause aflatoxicosis [1]. *Aspergillus* and *Penicillium sps* produces Ochtratosin A in cereals, coffee beans, grape juice. One of the most notable effects is kidney damage and also has an effect of fetal immune system. Patulin are commonly found in rotting apples and apple products. In humans it causes vomiting, gastrointestinal diseases, nausea and it also has high potential of being carcinogenic.

IMPACT OF MYCOTOXIN ON HUMAN HEALTH

Mycotoxin has been associated with a variety of acute and chronic human diseases (Table 1). Mycotoxin can occur in food and agricultural products via contamination at any stage of processing, packaging, transport, production and storage [2]. Intake of low levels of mycotoxin over a long period of time causes kidney and liver impairment, whereas exposure to high dose mycotoxin leads to abdominal pain, diarrhea and chronic intoxication. Aflatoxins is amongst one of the potent mycotoxins. It is associated with human diseases including liver cancer, Reye's syndrome, chronic gastritis, Kwashiorkor and respiratory diseases in various parts of the world. *Fusarium* toxins plays a major role in the onset of diseases such as Kashin Beck syndrome, Mseleni joint disease and oesophageal tumours. Contamination of foods and feeds with mycotoxins has been recognized as a matter of global concern since the early 1960s when a severe outbreak in poultry, the Turkey "X" disease, which killed 100,000 turkeys in the UK was discovered to be caused by consumption of mouldy feedstuff contaminated with aflatoxin. However, the association between consumption of mouldy grains and some human and animal diseases has been recognized since historical times [10].

Table 1: Toxic Effects of various Mycotoxins on Humans

Mycotoxins	**Fungi**	**Food Contaminated**	**Disease Caused / Toxic Effects**
Aflatoxins	*Aspergillus flavus* *Aspergillus parasiticus*	Corn, Peanuts, Cotton seed, Cereals, Coconut, Oilseed, Figs, Wheat, Rice, Dairy products	Liver tumors in Humans, Hepatotoxicity, Bile duct hyperplasia, hemorrhage in the intestinal tract and kidneys, teratogenicity, Immune suppressive.
Patulin	*Penicillium verrucusum* *Penicillium nordicum* *Penicillium expansum* *Penicillium crustosum* *Penicillium urticae* *Penicillium griseofulvum* *Aspergillus clavatus* *Aspergillus terreus*	Cereal grains, Spices, Cheese, Meat, Plums, Apple, Grapes, Apricot, Olives, Pears, Fruit juices	Nephropathy, Damage in the brain,liver and kidneys of experimental animals, Neurotoxic, Immunotoxic, Genotoxic and terratogenic effects of chronic exposure feed refusal in swine, Reduced weight gain and vomiting, Gastrointestinal problems, Diarrhea. Neural syndrome.
Zearalenone	*Fusarium oxysporum* *Fusarium graminearum* *Fusarium culmorum* *Fusarium equiseti* *Fusarium cerealis*	Wheat, Corn, Hay	Vulvovaginitis, Vaginal prolapse, Rectal prolapse, anestrus and fertility problems, abortion, malformation of testicles and ovaries.
Ochratoxin A (OTA)	*Aspergillus ochraceus* *Aspergillus niger* *Aspergillus carbonarius* *Penicillium nordicum*	Grapes, Raisins, Coffee, Figs, Herbs, Fruits. Wine, Beef	Kidney and Liver damage Loss of appetite Nausea Immune system suppression

SIGNIFICANCE OF MYCOTOXIN IN FOOD INDUSTRY

In addition to risking public health, mycotoxins also generates huge economic loss in food industry. Ergotism is one of the oldest mycotoxin related disease in humans caused by consuming ergot body in rye infected by the fungus *Claviceps sp.* [3]. The first outbreak of mycotoxin occurred in England where almost 100,000 turkeys died due to the consumption of peanut meal imported from Brazil contaminated with aflatoxins [4]. Mycotoxins first affected humans in 1960, and still persists worldwide. It appears in almost all animal feed like wheat bran, maize grain, milk, meat and human food like cereals, nuts and spices. Mycotoxin contamination in food and fodder is becoming a global concern each day. According to reports by Food and Agricultural Organisation (FAO), nearly 25% of world's crops are being affected by

mycotoxin leading to huge economic loss, low product yield, decrease in commercial value of food and loss of human and animal health. Many mycotoxins are known to survive processing into flour and meals and are not easily detectable. Such "hidden" mycotoxin can pose a significant hazard to human health.

ECONOMIC IMPACT OF MYCOTOXINS

Apart from the apparent social implications for public health, the occurrence of mycotoxigenic fungi and mycotoxins in food and feed chains has also major economic impacts to human society. These include (1) reduction of crop output due to plant diseases and from the removal of infected and/or damaged product (sorting), (2) reduced quality and commercial value of produce, (3) reduced animal productivity due to health problems associated with consumption of mycotoxin-contaminated feed, and (4) costs for humans and animals health care [11].The extra production expenses for the control of mycotoxigenic fungi outbreaks, such as the use of selected resistant cultivars and fungicides spraying or for the adoption of specific measures of prevention (e.g., biological control) have also to be taken into account. At post-harvest, the multiple control strategies that have been developed to mitigate the mycotoxin risks in the course of storage, transportation or processing and the cost for the organization and functioning of a surveillance network are all additional burdens for farmers, handlers, processors and, ultimately, for consumers.

Estimations of the costs of mycotoxins are not available for all the world regions. In the USA, the total cost has been estimated 0.5–1.5 billion USD per year; Council for Agricultural Science and Technology CAST (2003) reports a yearly cost of 0.9 billion for crop losses of corn, wheat, and peanuts plus an additional 0.5 billion for regulatory enforcement, testing, and quality control measures. In developing countries, it is likely that losses exceed those in the USA. For instance, in three Asian countries (Indonesia, Philippines, and Thailand) annual losses were estimated at 0.9 billion USD for aflatoxins only [11]. Even if prevention measures are enforced, sometimes these are not effective enough to avoid the occurrence of mycotoxins at levels close or above the maximum allowable levels for food, resulting in low quality and reduced price of the produce or, in the worst scenarios, in rejection of lots or diversion towards alternative and low revenue uses, such as feed production or conversion to bioethanol. Many staple agricultural commodities such as wheat, rice, barley, corn, sorghum, soybeans, groundnuts and oilseeds are at high risk of mycotoxin contamination. For this reason, regulations on allowable levels of mycotoxins in staple food have been set and are strictly enforced by most countries. However, standards vary greatly among countries, particularly between developed and developing countries, and this difference may cause major trade issues in the globalized market. For some developing countries, where agricultural commodities account for a large part of the total national export, the economic impact of rejection of mycotoxin-contaminated products, as for both lost trade and additional costs for inspection, disposal and compensation in the case of claims, is considerable [12]. While the human health losses from adverse effects of mycotoxins are primarily relevant to the social impact of mycotoxins, they have also economic impacts that can be evaluated by the tools of health economics. This cost can be calculated in two ways. The first is cost of illness, which is mainly relevant to developed countries because a large portion of the cost is health-care related. The second is disability-adjusted life years, which is applicable to both developed and developing countries.

MYCOTOXIN AND GUT HEALTH

The role of mycotoxin towards gut health and microbiota has been comprehensively discussed. Existence of a bi directional relationship is noted between mycotoxins and gut microbes, whereby they are involved in the development of mycotoxicosis. It is well established that healthy gut microbiota plays a significant role in the overall health of an individual. A person with healthy and balanced gut microbiota has the capability to eliminate mycotoxicosis naturally from the host. Till date there are various approaches to maintain a healthy gut microbiota, apart from several other benefits it also protects the host from the toxicity of mycotoxins [5]. The gastrointestinal tract is responsible for food ingestion, digestion, elimination of waste products and nutrient absorption. The GI tract acts as a filter against harmful mycotoxins. When a person intakes contaminated food, mycotoxins can alter normal intestinal morphology and functions, thus, leading to change in the diversity of gut microbiota [13-15].

CONCERNS OF MYCOTOXINS IN FOOD CHAIN

Mycotoxins become visible in the food chain due to mould infection in crops before or after harvest. Manifestation of mycotoxins can occur directly due to consumption of infected food or indirectly by animals that are fed contaminated feed. Consumption of food products contaminated with mycotoxins can lead to acute illness or can cause cancer and immune deficiency. They have a significant impact on human health as well as cost of food production. Extensive mycotoxin contamination is an area of great concern as it represents hazard for food safety. Globally, 30 to 90% of food and feed samples are contaminated leading to detrimental health effects. High levels of aflatoxin on the food chain has been associated with liver cancer in humans. The concentration of mycotoxins varies with food processing. For example, processed cereals and grains have been reported to possess great amount of mycotoxin in them. According to a survey, the highest concentration of zearalenone contamination occurred in

North and South America, Central Europe, Africa and Southeast Asia. This confirms the contamination is strongly dependent upon regional climatic conditions such as excessive moisture, temperature, humidity, drought, insect damage and agricultural practises [6, 13]. Mycotoxins enter food supply via direct contamination from mould growth on the food consumed. It can also affect indirectly by the use of contaminated ingredients in processed food (Fig 1). It can also occur due to consumption of animal products, such as milk which might contain mycotoxin residue caused by using mouldy feed to the milk producing animal.

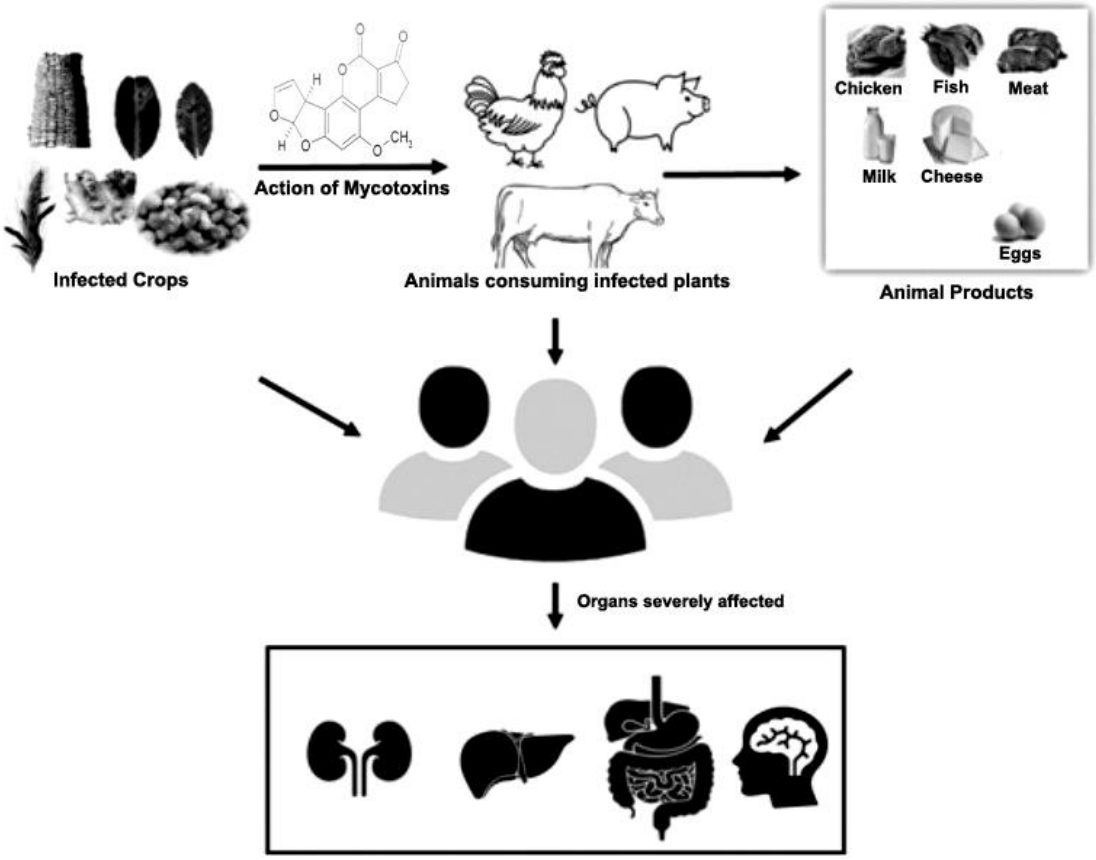

Fig 1: Effect of Mycotoxin on Human Health

ROLE IN BIOTERRORISM

The abuse of mycotoxins as a biological weapon is not only theory based as there are evidence to prove the use of aflatoxins as a part of Iraqi biowarfare programme during the 1980's. It is preferred over other chemical warfare agents as there are no real time detection or any alarming signs of fire, blast and they are highly stable capable of causing potent acute toxicity. Some researchers say mycotoxins are impractical biological weapon, as large amount of pure mycotoxin is required to be effective [7]. On the contrary, fungal weapon do not require any elaborate facilities for its growth, purification of toxins or any trained personnel. Poisoning of crops in field via mycotoxins would be ineffective, therefore it's dispersion in a public places might be a method of choice for bioterrorism attacks, as the entire population would be exposed.

PREVENTION OF MYCOTOXIN CONTAMINATION

There have been several attempts to minimise mycotoxin contamination, such as changes in plant breeding, detoxification and good agricultural practices. Varieties of rye, wheat and millet are cultivated that are resistant to mycotoxins. Other approaches such as avoiding water stress, minimising insect infestation are seen to be effective. Appropriate drying techniques, maintaining proper storage and not exposing nuts and cereals to moisture can decrease contamination, especially in peanuts [8]. Many countries have introduced legislation concerning mycotoxins like aflatoxin, ergot alkaloids, and ochratoxins [9]. Continuous surveillance and monitoring of human population for diseases related to mycotoxins have been carried in various parts of the world to ensure food free from naturally occurring contaminants.

CONCLUSION

Mycotoxins are poisonous, naturally occurring chemical compounds produced by fungi under favourable conditions. Almost 25% of the world's crops are contaminated by molds and fungal growth. Their toxicity not only leads to adverse animal and human health affects but also cause major environmental changes. Although, the extent of its toxicity depends upon several factors like period of exposure, type of mycotoxin, nutritional value, still it's harmful effects cannot be overlooked. Control of contamination by mycotoxin should be one of the foremost approaches in order to maintain public health and improve economic condition of the countries.

Conflict of Interest: Authors declare that they have no conflict of interest.

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