



Heavy metal in the soil-grain-food path: an overview of the role of Mycotoxins in potential hazards associated with animal products

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Abstract

In recent years, the emerging livestock and poultry business has encountered several obstacles in producing healthy and safe products for human consumption while also providing quality and nutritious food for animals. The presence of fungal toxins and fungi in raw materials is the most significant difficulty in supplying food for livestock and poultry, since mycotoxins can reduce output and lower product quality. Also, their residues in the final products (milk, meat, eggs) can transmit their adverse effects to humans. Fungal toxins are produced as a result of the activity of fungi during their growth process, which is called Mycotoxins. Many fungal toxins have been identified to date, including Aflatoxins, Ziralenone, Fumonisin, and Ochratoxins. Aflatoxins contaminate foods, feeds, and other raw materials involved in their production, posing a serious health risk to humans, including carcinogenesis and severe toxicity. Environmental factors affect the production process of Mycotoxins, which depends on the geographical location, agricultural method, sensitivity of agricultural products, etc. Another important point is that some mycotoxins can be used as bioterrorism weapons. Exposure to Mycotoxins can have a wide range of detrimental biological effects, including bleeding, hepatotoxicity, renal toxicity, neurotoxicity, estrogenic, teratogenic, mutagenic, and carcinogenic. Because of the importance of the subject, in the current study, it was tried to review the role of Mycotoxins in potential hazards associated with animal products for humans.

Keywords: livestock; healthy food; fungal toxins; mycotoxins.

Practical Application: The role of Mycotoxins in potential hazards associated with animal products.

1 Introduction

New food safety hazards emerge on a regular basis in today's environment. Food antimicrobial resistance has been challenged by changes in food production, distribution, and consumption, as well as changes in the environment and new and emerging pathogens (Molajou et al., 2021a, b). Increased travel and trade have also increased the likelihood of international pollution (Pouladi et al., 2020). Food safety is increasingly globalizing, and the need to strengthen food safety systems in countries is felt more than ever. Foodborne diseases and incidents of food contamination emphasize the need of ensuring public access to healthy and safe food (Lam et al., 2013; DiPietro et al., 2020).

Safe food does not contain microbial, chemical, or physical contaminants during transport, preparation, and storage and does not cause illness to consumers (Forsythe, 2020; Mitterer-Daltoé et al., 2020). Ensuring that our food is completely healthy and free from microbial, parasitic, and chemical contamination is food safety. The importance of food safety has been highlighted to such an extent that the World Health Organization set its motto in 2015 to promote improved food safety from the farm to the plate (Zhao & Talha, 2021; Chen & Yu, 2021). With the

development of technologies, the consumption of additives, pesticides, antibiotics, and hormones, food production in developing countries has also increased significantly, which has led to undeniable effects on human health and the occurrence of various diseases (Jones & Craddock, 2009).

'Food safety' means ensuring the absence of any microbial, parasitic or chemical contamination in the food consumed by the community, which is of great importance for health (Paparella, 2020). Many believe that food safety around the world is constantly exposed to new threats. Changes in food production, distribution, and consumption, as well as changes in the environment and new pathogens, affect food antimicrobial resistance and affect food safety and health (Wieser et al., 2021). For this reason, it is necessary to strengthen effective monitoring systems for food safety (Jacobsen & Tan, 2021). Consumption of additives, pesticides, antibiotics, and hormones in food production in developing countries has led to significant growth with the development of technology, leading to adverse effects on human health, including liver disease, respiratory diseases,

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congenital anomalies, and cancers in particular (Nabavi et al., 2014; Hartantyo et al., 2020).

Contaminants such as heavy metals such as lead and cadmium enter plants through phosphate fertilizers and industrial effluents, and by feeding livestock with contaminated forage, these contaminants enter the human food cycle through milk. Toxic metals accumulate in organs of the human body, especially the kidneys, resulting in kidney failure. Eating foods contaminated with aflatoxin toxins in products such as wheat and flour, pistachios, peanuts, and milk can also cause liver cancer in humans (Tóth et al., 2016). Obviously, the health of individuals in society is one of the most important areas of dynamism and development in any country. In this regard, providing healthy and safe food is undeniable and vital for maintaining the health of society because unhealthy food will cause irreparable damage to any society (He et al., 2019). The first condition to achieve this importance is the health of food raw materials, especially fruits and vegetables, in different stages of production from farm to fork.

2 Investigation of possible hazards associated with animal products for humans

Given that the world's population is estimated at 9.1 billion by 2050, the most important challenge facing humans is to change the current agricultural systems to feed this number of hungry people (Molajou et al., 2021a; Afshar et al., 2021).

Excessive population growth and the pattern of industrial activity today, especially since the second half of the present century, have caused environmental pollution, especially heavy metal pollution. Every year, factories, industrial units, and urban centers pollute the environment and agricultural lands by entering their wastewater and effluents into aquatic environments and entering agricultural lands, as well as the use of pesticides and chemical fertilizers. Obviously, there is a significant relationship between the level of heavy metals in the soil and their accumulation in the plant. After accumulating in the green and branched parts of plants or their products, these

metals are consumed by animals and cause serious damage to the health of these organisms. Obviously, the consumption of the products of these animals poses serious risks to the final consumer, namely humans (Jackson, 2009; Hezbullah et al., 2016).

As can be seen in Figure 1, one of the main reasons for human exposure to heavy metals is the soil-grain-food path. Due to the fact that heavy metals are among the most stable and durable compounds in the environment, their gradual entry into the body of living organisms causes the biological accumulation of these metals in the food chain. As a result of this process, the amount of heavy metals in the higher parts of the food chain reaches several times the amount of these elements in water or air, which is a threat to the health of plants and animals that use these foods (Ding et al., 2013; Zhang et al., 2015). By creating various mechanisms, these metals upset the balance in the body of living organisms, especially humans, and cause a wide range of complications and disorders. These complications and disorders are seen in all organs, and various factors, including the type of metal, are involved in them.

Heavy metals such as mercury, lead, cadmium, and arsenic are called xenobiotics (Schröder et al., 2009). This means that these elements are not needed for the body's metabolism, and even small amounts of them are harmful to the body. In fact, heavy metals are no longer expelled from the body after entering the body and are deposited and accumulated in tissues such as fat, muscles, bones, and joints. Eventually, they cause many diseases and complications such as neurological disorders, cancers, abortions, respiratory disorders, liver and kidney, and brain damage, arthritis, hair loss, and osteoporosis (Hou et al., 2020; Qin et al., 2020).

Given this issue and the growing importance of food security in recent years, the attention of the general public and regulatory bodies in the food sector, especially the World Trade Organization, has seriously focused on food safety and quality assessment (Cinar & Onbaşı, 2020). Obviously, the food safety chain in any country must be maintained from the farm to the family table, and in the meantime, the livestock sector plays

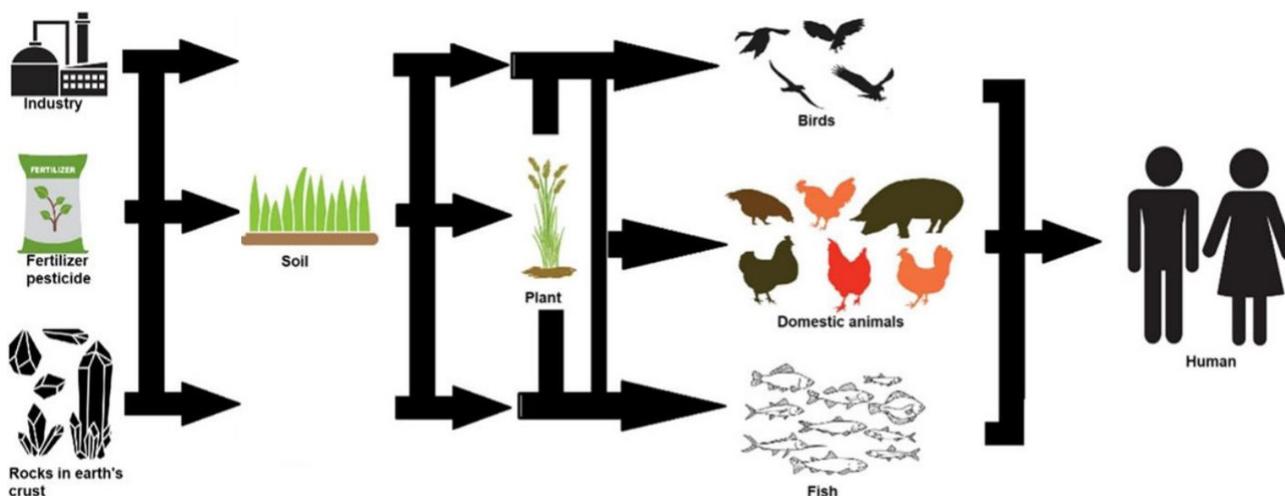


Figure 1. The soil-grain-food path.

an important role in food security as well as the agricultural and economic development of countries. As a global average, livestock products provide about 16% of the dietary calories and have always been an important part of the world's diet. Meat and other animal products provide essential fatty acids, vitamins, and minerals. Therefore, the importance of the livestock industry economically and nutritionally in the world is very high.

Unfortunately, contamination of meat, eggs, milk, and other livestock and poultry products with heavy metals, mycotoxins, drug residues, etc., has caused many concerns in terms of its risks to human health. With this attitude, the study and correct understanding of the causes of contamination in livestock and poultry products and the use of effective measures to reduce the level of these contaminants play an important role in food security and health of the final link in the food chain, namely humans (Raikwar et al., 2008).

In the periodic table, the number of elements with a high atomic weight and metallic properties is referred to as heavy metal. Heavy metals have a very high density (4 to 5 grams per cubic centimeter and even higher), and since different definitions have been given for these elements and different elements have been placed in this category, only the term metals or quasi-metals should be used. Heavy metals in contact with humans can be divided into toxic metals, precious metals, and radioactive metals.

These metals are naturally present in the earth's crust. Despite their low content and low solubility, they are generally separated from the earth's crust by weathering and erosion and enter aquatic and terrestrial ecosystems, known as natural or tectonic contaminants. On the other hand, along with industrial and economic growth and the production of various types of compounds and chemicals that humans have obtained for their well-being using natural resources, it has inadvertently imported substances such as heavy and toxic metals into nature, which poses serious problems and dangers both for the environment and for human beings. Heavy metals can enter the human body, livestock, and poultry in different ways:

- Through direct exposure to heavy metals and polluted environment (polluted air, dirty water, and direct contact with contamination);
- Through contaminated foods.

One of the most important problems caused by the entry of heavy metals into the human body is their inability to metabolize. In fact, heavy metals are no longer excreted from the body after entering the body and are deposited and accumulated in tissues such as adipose tissue, muscles, bones, and joints, which causes many diseases and complications in the body. Heavy metals also replace other salts and minerals needed by the body.

Due to the harmful and adverse effects that heavy metals have on humans and living organisms, it is very important to pay attention to the sources of entry of these metals. The accumulation of heavy metals in the bodies of livestock and poultry and their entry into the human food chain doubles the risks posed by them. With the increase of industrial activities of industry

and the increase of consumption of chemicals, their entry into the water, soil, and air and pollution of the environment have increased the probability of human beings facing the dangers caused by them. One of the things that are gaining global attention today in relation to heavy metals is the contamination of food consumption, including livestock and poultry products. Heavy metals' most important and harmful effects in humans, livestock, and poultry are associated with the metal's arsenic, cadmium, lead, and mercury (Vos et al., 1987).

According to the results of studies on heavy metals and their effects on the human body, these metals can cause many diseases and disorders, including neurological disorders (Parkinson's, Alzheimer's, depression, schizophrenia), various cancers, nutrient deficiency, Hormonal imbalance, miscarriage, respiratory and cardiovascular disorders, liver, kidney and brain damage, allergies and asthma, endocrine disorders, enzyme dysfunction, metabolic changes, infertility, anemia, fatigue, nausea and Vomiting, immune system stimulation, gene damage, skin disorders, osteoporosis and in acute cases death are some of the complications of high levels of heavy metals entering the human body.

Producing enough food to solve the problem of global hunger is an important issue for developing countries and even developed countries. The Food and Agriculture Organization (FAO) predicts that food production will face problems in this century, given the global food security outlook. Thus, competition over agricultural land and water resources, high energy prices, and climate change indicate that more food must be produced for people worldwide with fewer resources. Sustainable growth in the agricultural sector is a vital factor in feeding the world in the coming decades. As a general conclusion, it can be said that today the contamination of livestock and poultry feed and as a result of their products to heavy metals has caused major concerns because it poses many risks to the health of human communities as end-users of these products. However, contamination with levels above the permissible levels of heavy metals is often not so great that it is immediately dangerous to human health. But since heavy metals are gradually absorbed by the body and their long-term consumption is harmful to health, reducing the level of these metals should be considered a solution. The cooperation of effective regulatory bodies in this field, together with experts and specialists in the livestock and poultry industry, participation in international programs, and using the experiences of successful programs such as the United Nations Environment Program (UNEP), can significantly reduce pollution. The high levels of these metals in livestock and poultry feed and ultimately affect human health.

3 Mycotoxins

The livestock industry plays an important role in the development of the economy and productivity of each country. On a global average, animal products provide about 16% of a person's dietary calories. Meat and other animal products provide an important part of the body's need for protein, essential fatty acids, vitamins, and minerals, so the livestock industry is of great economic and nutritional importance around the world.

In developed countries, meat production had increased from 90 million tons in 1980 to 105 million tons in 2000. In developing countries, meat production increased from 47 million tons to 128 million tons per year during the same period. That means 14% growth in 20 years! In Asia, meat production has almost tripled during this period. During this period, chicken meat production increased from 23 million tons to 57 million tons, milk production from 465 million tons to 567 million tons, and egg production from 27 million tons to 54 million tons. Figure 2 shows the top 20 countries by total meat production from 1961 and 2018. Meat includes cattle, poultry, sheep/mutton, goat, pork, and wild game. By the end of 2018, China's meat production accounts for 1/4 of the entire world. At the same time, there is a significant increase in the trade of raw materials, feed additives, and meat trade (more than doubled). This is where the importance of overseeing agricultural products, raw materials used in animal feed, and humans become clear. It is clear that the continuous cooperation of regulatory bodies, good manufacturing practice (GMP), and the Hazard Analysis Critical Control Point (HACCP) play an important role in reducing the

level of adverse factors (such as pesticides, chemicals, heavy metals, and microbial contamination) in human and animal nutrition (Magan & Olsen, 2004).

Mycotoxins are secondary metabolites produced by a species of filamentous fungus that grows in agricultural products before or after harvest or during transportation or storage (Bhat et al., 2010). According to the World Food Organization, the global distribution and extent of contamination around the world have raised many concerns about these toxins, with more than 25 percent of the world's food contaminated with a variety of toxins. Hence, they are a serious threat to human food security. As can be seen in Figure 3, the various types of mycotoxins have been identified, with different chemical structures and biological activities, some of which may be carcinogenic (e.g., Aflatoxin B1, Ochratoxin A, Fumonisin B1).

Some of these toxins are known as estrogenic mycotoxins (such as Ziralenone); Ziralenone mimics the effects of the hormone estrogen. In low doses, this toxin causes disorders in the maturation of reproductive organs, and in higher doses,

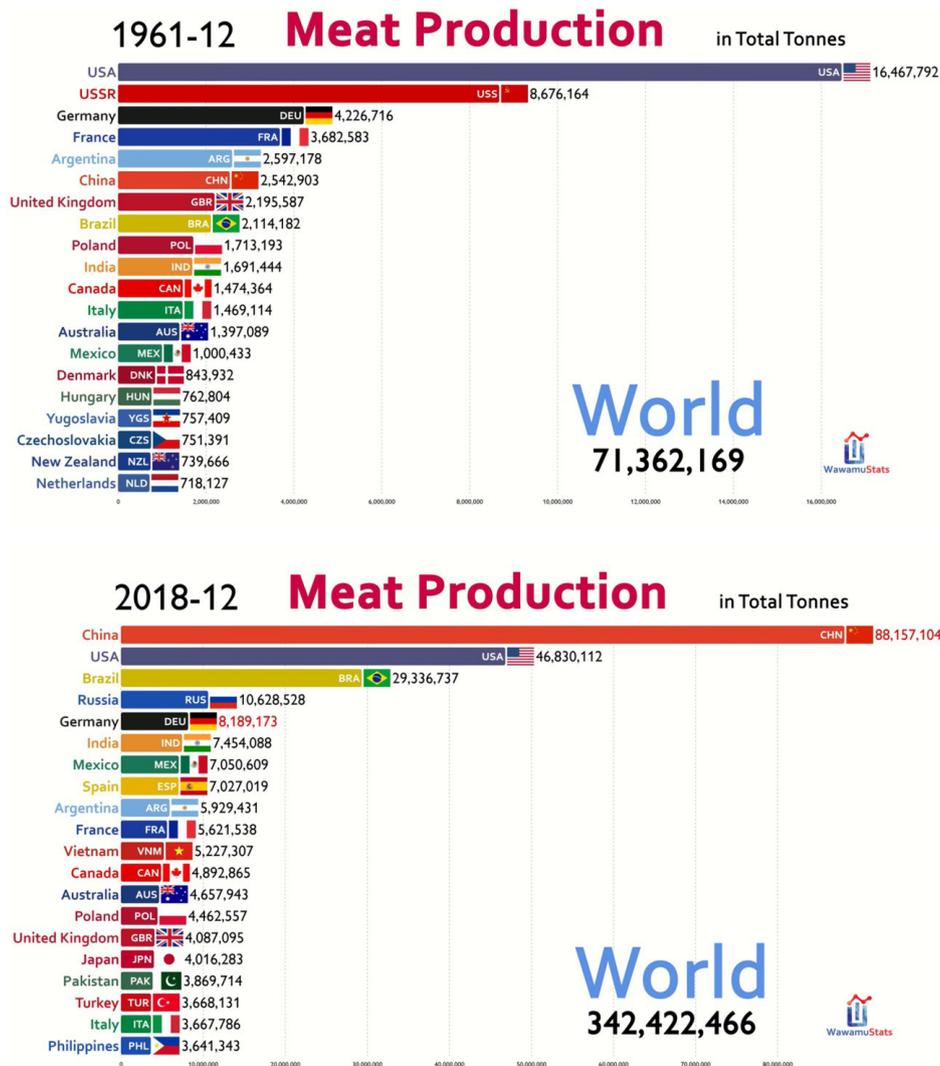


Figure 2. Meat production by country (1961-2018) (Source: Food and Agriculture Organization of the United Nations, 2020).

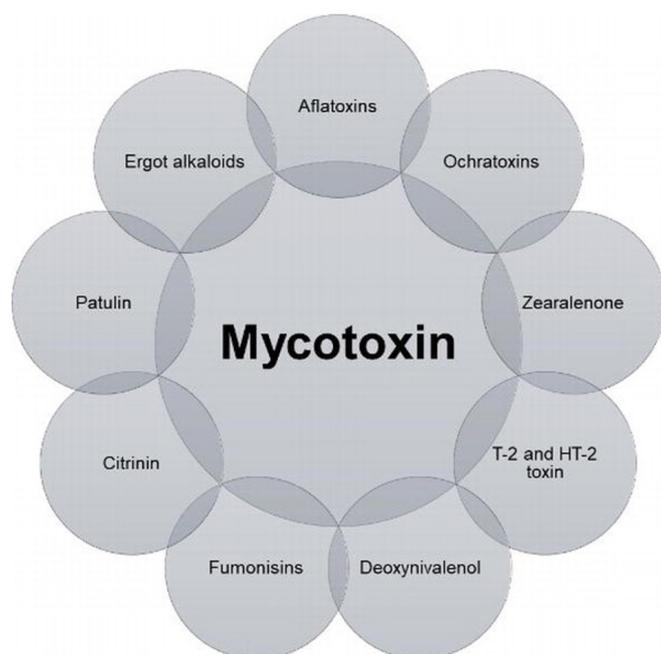


Figure 3. The primary groups of Mycotoxins in various food products.

it causes ovulation disorders, fetal growth disorders, and reproductive disorders, as well as changes in the structure of reproductive organs.

Different types of mycotoxins (neurotoxic, nephrotoxic, dermonecrotic, and immunosuppressants) have been identified in more information. The effects of mycotoxins on laboratory animals have been studied, and in addition, the effects of the presence of a combination of mycotoxins on human health have not yet been properly identified. Mycotoxins are commonly found in agricultural products such as corn, sorghum seeds, barley, wheat, rice flour, cottonseed meal, peanuts, and other grains, and most are relatively stable compounds (DeVries et al., 2002).

Contamination of feed with mycotoxins is one of the main problems in animal nutrition. Mycotoxins produce mold on nutrients, damaging vital organs and causing numerous side effects in living organisms. On the other hand, it is not easy to remove contaminants from contaminated foods. The harmful effects of mycotoxins on animal health are widespread. Meanwhile, the economic effects of declining productivity in animals, increasing the incidence of disease due to reduced immune system strength, damage to vital organs, and reduced reproductive capacity are far more harmful than death from poisoning by these toxins.

Food contamination with mycotoxins is a global food security problem, as the harms of these toxins lead to livestock and agricultural products and endanger public health by entering human food through the consumption of animal products. The mechanism of action of dangers caused by mycotoxins in the human body is very complex. Mycotoxins cause liver and kidney tissue damage, neurological complications, immune dysfunction, and carcinogenesis. These toxins can even cause embryonic abnormalities by altering the structure of nucleic acids in the structure of DNA.

Aflatoxins are one of the most important types of mycotoxins found in nature. Aflatoxins are currently of interest for their high toxicity, which mainly affects crops such as corn and cereals. Of all the fungal species, *Aspergillus* is the most contaminated in food and generally grows in oxygen-rich and carbon-rich environments. However, some species of *Aspergillus* can survive in environments with very low nutrients and humidity. In addition to causing great economic losses, these toxins may enter the human food chain through the consumption of contaminated animal products, causing damage to liver cells and increasing the risk of cancer. Exposure to high doses of aflatoxins poses a serious risk to human health. In 1988, the International Cancer Research Organization classified aflatoxins as one of the leading causes of cancer in humans.

Even at low levels, Aflatoxins can reduce immune function, reproductive disorders, tumors, fetal mortality, and congenital anomalies. Therefore, many countries have developed special monitoring programs to measure and determine the permissible limits of these toxins in food (Ayofemi Olalekan Adeyeye, 2020).

Humans are exposed to the dangers of mycotoxins through the consumption of contaminated foods caused by the growth of fungi. Concentrations of mycotoxins or their metabolites in human food are usually much lower than their levels in animal feed. Therefore, the probability of severe poisoning in humans is low. However, in animal products, the residues of carcinogenic mycotoxins, such as aflatoxins B1 and M1, and ochratoxin A, pose a serious threat to human health, and their levels must be monitored and controlled. Nervous system disorders, gastrointestinal dysfunction, and weakened immune system are among the long-term side effects of mycotoxins.

4 Investigating ways to deal with the effects of fungal toxins

The following methods have been suggested to neutralize or reduce the amount of aflatoxin toxin;

- A- Physical methods, including physical separation, heating, etc;
- B- Chemical methods, including separation by solvents, microbes, and yeasts (organic and inorganic adsorbents).

Research shows that adding some nutrients to the diet reduces the effects of mycotoxins, which are called toxin binders. One of the available methods is the use of inorganic adsorbents in the diet of animals, which binds to the aflatoxin molecules, immobilizes them, and prevents their absorption in the body. The use of materials such as aluminum silicates, bentonite is effective in neutralizing toxins. Organic matter is called mannan oligosaccharide, which plays an important role in neutralizing mycotoxins.

Contamination of raw foods (cereals and fodder) by fungi and fungal toxins is inevitable. One of the most common ways to minimize the problems caused by fungi is to add compounds to the diet that can stop the fungi from multiplying and stopping their activity. Such food additives absorb fungal toxins in the gastrointestinal tract and prevent their transfer to the blood

and then to body tissues. Due to the extremely wide and diverse chemical structure of fungal toxins, each of the antifungal compounds can specifically absorb specific mycotoxins and cannot Aluminosilicates, for example, are known to absorb aflatoxins but have no effect on the uptake of other fungal toxins. On the other hand, Fungal-contaminated feed usually contains a variety of fungal toxins, which indicates the need for a multifunctional adsorbent.

It should be noted that the active and effective substance of organic adsorbents is the glucomannan modified cell wall of *Saccharomyces cerevisiae*. Other studies had shown that when the toxic alkaloid ergot in sorghum was added to the diet of broilers, weight gain was severely affected and slowed compared to the healthy diet group. Addition of modified glucomannan organic adsorbents to a diet containing fungal toxin-maintained growth and feed conversion ratio at each diet level. It can be said that the ability to absorb organic adsorbents is superior to bentonite, zeolite, and aluminosilicate compounds.

As we know, fungal toxins can be absorbed by several different mechanisms. One of these mechanisms is the combination with toxins by having special capacities that result in the non-displacement of toxins in the gastrointestinal tract and reduce their bioavailability. But this mechanism alone is not effective against the toxins Ziralenone, Fumonisin, and Ochratoxins.

Another mechanism is the biological deformation of toxins that are resistant to adsorption, by which all the above toxins are absorbed. In general, the chemical composition and physical nature of the cell wall of *Saccharomyces cerevisiae* in organic adsorbents, in addition to the activation process performed on them, have created numerous areas on their surface for the physical adsorption of toxic fungal molecules. Also, the mineral compounds in these products are able to cause ionic changes in the structure of toxins, which makes them more efficient.

5 Conclusions

As mentioned, fungal toxins are produced from different species of fungi during the process of growth or storage. As a result of consuming these substances in animals, symptoms such as anorexia, weight loss, lack of proper weight gain, reduced production, weakened immune system, diarrhea, etc., occur. In addition to these issues, fungal toxins cause huge economic losses to production units and threaten global food security. In 1960, more than 100,000 turkeys died in the UK from an unknown disease. After research and studies, it was discovered that the disease was transmitted to poultry as a result of the consumption of Brazilian peanuts and led to many losses in turkeys, perch, and quails. After conducting many experiments, it was found that the feeds in question were contaminated with a fungal toxin, which led to casualties.

According to the FAO, millions of tons of food are lost each year as a result of fungal contamination. Mycotoxin's contamination is caused by the use of contaminated food in eggs and meat products. Mycotoxins contaminate around a quarter of the world's food and feed production, causing major economic losses and harming human and animal health, productivity, livelihood, family security, and income. Agricultural commodities

are frequently contaminated by mycotoxins as a consequence of a cumulative process that begins before harvest and continues through the whole food production chain. Sensitivity to Mycotoxins also shows a species difference that varies with sex, age, and nutrition. Younger animals are generally more sensitive to this toxin. Because of the importance of the subject, in the current study, it was tried to review the role of Mycotoxins in potential hazards associated with animal products for humans.

Given that mycotoxins are a serious threat to the health of human communities worldwide, monitoring the growth of mycotoxins is important both in the health and economy of the agricultural and livestock industries and in human health and food security. In order to produce healthy and safe food, pathogens must be evaluated and controlled from the beginning of the food production cycle, from the time of planting, during the process of harvesting, processing, storage, use in animal feed, and then entering the market. Meanwhile, continuous monitoring of raw materials used in animal feed as the most important link in the supply chain of protein consumed by humans is of particular importance. Today, advances in laboratory methods have made it possible to accurately measure these materials. Also, the use of pesticide sorbents, observance of principles and methods of monitoring the quality of animal feed, and proper and principled management during the breeding period are very effective in managing the risks of mycotoxins and producing healthy food. Effective control of mycotoxins and safe food production requires cooperation between all sectors of the food production chain, especially effective regulatory bodies in this field and experts in the food, agriculture, and animal husbandry industries.

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