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Detrimental Effects of Mycotoxins on Human and Animal Health: a Review

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ABSTRACT

Mycotoxins are natural toxins produced by certain fungi that contaminate various crops and foodstuffs. Mycotoxin contamination is a worldwide problem and leads to numerous negative health effects on humans and animals. Mycotoxins contaminate food crops produced under specific conditions of high relative humidity and temperatures. In the Middle East, climatic conditions enhance mycotoxin growth and prevalence. More than four hundred types of mycotoxins have been found in feed globally. The wide dissemination of mycotoxins in various agricultural commodities, including chicken feed, have raised concerns about their potential presence in chicken products as the main sources of toxins related to human health and economic losses. Findings suggest that mycotoxin contamination in chicken is a global challenge, and continuous monitoring and appropriate management strategies are required to ensure food safety. This review aims to discuss mycotoxin residues in chicken, including their occurrence, toxicological effects, and control strategies.

Introduction

Mycotoxins are natural toxins synthesized by certain fungi that contaminate food commodities. Molds can grow on various crops and foodstuffs, including cereals, grain, spices, nuts, and fruits, often under specific moisture and temperature conditions [1]. Mycotoxins can have a wide range of adverse effects and present a serious threat to the health of human and animals. They have the potential to induce harmful health effects, such as acute poisoning and chronic consequences, like cancer and immunological deficiencies [2].

Mycotoxins are mainly produced as secondary metabolites by mycotoxigenic fungal isolates belonging to the genera *Alternaria*, *Aspergillus*, *Claviceps*, *Fusarium*, *Penicillium*, and *Stachybotrys* and could result from single-species infections or a co-occurrence of species [2]. More than 400 mycotoxins have been recently reported and found in commodities used in food and feed (Table 1).

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Aflatoxins (AFs), fumonisins (FBs), ochratoxins (OTs), trichothecenes (TCs), patulin, and zearalenone (ZEN) are the most prominent compounds linked to marked negative effects on human and animal health, as well as economic problems [3].

Mycotoxin contamination may occur before harvest or during harvesting, handling, or storage due to a lack of standard controls, delayed harvesting time, inadequate storage conditions, temperature, moisture content, and certain biotic conditions [4],[5]. Geographical climate is another factor that promotes the growth of distinct fungi and influences mycotoxin production [6].

Mycotoxin contamination poses a major food safety challenge because mycotoxins are difficult to eliminate during food processing given their resistance to elimination through processes, such as heat, physical, and chemical treatments, throughout all stages of the food chain. Opportunities for mycotoxin transmission to animal-derived products, such as milk, meat, and eggs, are growing, leading to mycotoxin intake by humans [7].

Table (1): Effects of common mycotoxins on human health [28]

Mycotoxin	Fungi producing mycotoxins	Health effects
Aflatoxins	*Aspergillus niger* and *Aspergillus parasiticus*	Hepatotoxicity, immunosuppression
Ochratoxin A	*Aspergillus carbonarius* and *Penicillium verrucosum*	Carcinogenicity, genotoxicity, immunosuppression, nephrotoxicity, induction of upper urinary tract disease
Fumonisins	*Fusarium verticillioides*	Carcinogenicity, hepatotoxicity, nephrotoxicity, immunosuppression
Deoxynival enol	*Fusarium* spp.	Nausea, vomiting, diarrhea, reproductive effects, toxicosis

The presence of mycotoxins in food poses a major threat not only to global food safety but also to global food security due to their negative health and economic consequences. The global prevalence of food crops that are damaged by mycotoxins falls between 60% and 80%, incurring economic losses due to the rejection of exported food products and enormous cost of analysis. Consequently, the control of mycotoxin adulteration is a major goal of the food and agriculture industries [8].

MYCOTOXIN RESIDUES IN CHICKENS

Mycotoxins can affect various crops, including feedstuffs and grains, such as ingredients for poultry feed. They enter the animal production chain when animals consume contaminated feed. The ingestion of mycotoxins by chickens affects their health and productivity and raises concerns about potential human exposure during the consumption of poultry products [9].

Studies have reported the presence of various mycotoxins, such as deoxynivalenol (DON), OTA, AFs, and FBs, in chicken feed [10]. These mycotoxins can be transferred to chicken tissues, including the liver, muscle, kidney, and eggs, through absorption and metabolism in the digestive system. Factors, such as grain quality, storage conditions, and feed processing techniques, contribute to the prevalence of mycotoxin contamination in chickens [11].

Toxicological effects of mycotoxins on chickens

Mycotoxins affect feed intake, reduce utilization, impair immune responses, and disrupt egg production, as well induce liver and kidney toxicity and increase mortality rates [12].

The severity of the effect of mycotoxins on chickens depends on the type and level of mycotoxin exposure. AFs can cause liver damage, immunosuppression, reduced growth performance, and increased susceptibility to infections [13]. OTA has been associated with renal toxicity and immunosuppression [14]. DON is known for its negative effects on intestinal health, growth performance, and immune functions [15]. ZEN is a *Fusarium* mycotoxin that has estrogenic properties and can cause reproductive issues in domestic animals. It can disrupt reproductive functions and cause estrogenic effects [16]. FUMs may lead to impairments in various organs, including the liver, lungs, and kidneys [17].

Mycotoxins can also result in mild-to-moderate histopathological changes in the liver, intestine, spleen, and kidneys. Chickens fed with DON suffered from severe intestinal and liver lesions [18], whereas those fed with OTA exhibited intestinal morphological changes and thymus histopathological changes [19],[20]. Lesions in the spleens of chickens have been linked to T-2, a potent mycotoxin produced in feedstuffs by several *Fusarium* species [21]. Intestinal damages in chickens have also been reported as a result of FBS exposure. FBs are produced by *Fusarium* and other species and are among the most widespread mycotoxins [22]. Histopathological changes in renal cells have been observed in chickens fed with citrinin [23].

MYCOTOXINS IN CHICKEN FEED

AFs

AFs, which constitute a class of mycotoxins consisting of over 20 members, are primarily synthesized by fungal species belonging to the genus *Aspergillus* (*Aspergillus flavus*, *Aspergillus parasiticus*, *Aspergillus nomius*, and *Aspergillus pseudotamarii*). The most prevalent forms of AFs are AFB1, AFB2, AFG1, and AFG2, with these forms being the most dangerous to humans and livestock (Figure 1) [24], [25].

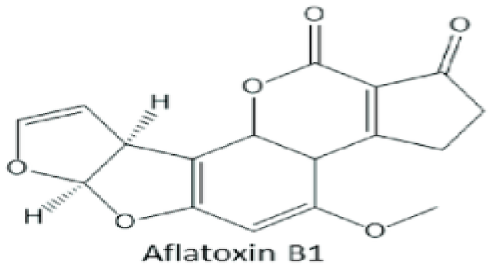


Fig (1): Chemical structure of AF [81]

Various susceptible animals, including chickens, experience adverse toxicological and hepatocarcinogenic effects when exposed to AFs due to their chemical structures. Among all AFs, AFB1 is a highly toxic substance that causes genetic mutations and promotes the development of cancer in a wide range of species. Research has indicated that prolonged exposure to AFB1 can have dire consequences for humans and animals, including diminished immune function, difficulties in absorbing vital nutrients, impaired fertility, and endocrine issues, as well as the potential for birth defects and liver cancer [26].

In poultry, AFs have a range of negative effects, such as weight gain reduction, inefficient feed utilization, decreased egg production and weight, increased fat in the liver, lowered levels of serum protein, diminished pigmentation, liver damage, and weakened immune responses [27],[28]

High levels of AFs in poultry products can lead to considerable toxicity in humans. The East African Community (EAC) has established limits of 20 and 50 μg/kg for AFs and AFB1 in poultry feed, respectively. Levels below EAC limits pose a low risk to human health. However, the high incidence of AFs, combined with the co-occurrence of other mycotoxins, may enhance the likelihood of chronic exposure to AFs, posing a potential health risk [10].

OTs

OTA, the primary OT, has over 20 derivatives and is mainly synthesized by *Aspergillus ochraceus*, *Aspergillus carbonarius*, *Aspergillus niger*, and *Penicillium verrucosum*. It can contaminate crops before harvest and frequently during storage (Figure 2) [29].

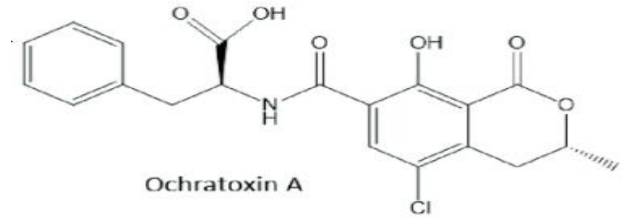


Fig (2): Chemical structure of OTA [81]

OTA was categorized as a group 2B carcinogen by the International Agency for Research on Cancer (IARC), indicating that it is a possible human carcinogen. By contrast, AFB1 is a group 1B carcinogen. Therefore, OTA is less toxic than AF-B [30]. Additionally, OTA has shown various health implications in humans and animals. It has been associated with toxic effects on the nervous system, embryos, liver, and kidneys, as well as harm to the immune and genetic systems in poultry [31]. Balkan endemic nephropathy has been linked to OTA contamination [32]. The consumption of food and chicken feed contaminated with OTA poses potential dangers to poultry and humans due to the carcinogenic effect of this mycotoxin. In chickens, the main effects of consuming feed with OTA include stunted growth, decreased feed efficiency, and heightened water intake, which can negatively affect kidney function. Prolonged exposure to OTA may also lead to liver damage and a high risk of mortality [33].

The level of OTA contamination in feed varies in different regions. An Indonesian study found OTA levels of 20.38 [34], whereas the European Commission established OTA limitations of 0.1 mg/kg in chicken feed [35]. Several reports have shown remarkable effects in chicks fed with 200 μg/kg OTA, resulting in a contamination rate of 41% in chicken meat and 35% in eggs. Further examination revealed that broiler chicks had high OTA concentrations of 0.073 and 1.14 μg/kg in their hearts and kidneys, respectively, accompanied with signs of hepatic necrosis and hemorrhages, as well as renal deterioration and edema [32], [36].

FUMs

FUMs are a class of mycotoxins discovered in the cultures of *Fusarium moniliforme* and *Fusarium verticilliodes.* Over 53 distinct FUMs have been identified. They are classified into four major categories (FA, FB, FC, and FP). FB1, FB2, and FB3 commonly occur together and are the predominant FUMs in food (Figure 3). Among these FUMs, the most dangerous to human and animal health is FB1, which is also the most prevalent and toxic [37].

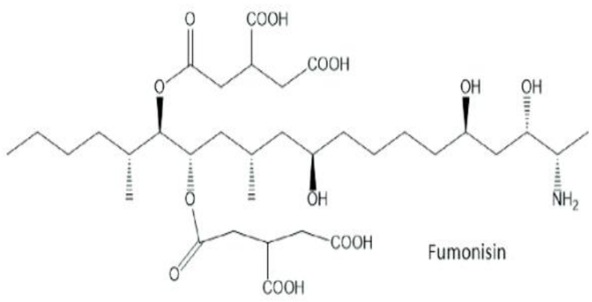


Fig (3): Chemical structure of FUM [81]

Animal feed contaminated with FB1 can pose various forms of physical harm to animals, including pulmonary edema and toxic effects on the intestine, lung, heart, liver, and kidney [38]. Foods containing FB1 can damage myocardial contractility and cause massive blood influx, known as idiopathic congestive cardiopathy, which leads to kidney toxic disease; esophageal cancer; liver failure; and in some cases, hepatic necrosis and hepatocellular carcinoma [39]. Additionally, the administration of excessive levels of FUMs at early stages of pregnancy increase the potential for giving birth to children with brain or spinal cord birth defects [40]. FUMs are the most frequently encountered mycotoxins in livestock feed; they cause decreased body weight gain and liver pathologies, such as necrosis and biliary hyperplasia, in chicks [41].

The European Union (EU) established 20 µg /kg as a safe FUM limit level in poultry feed [42]. FUMs have the potential to cause mycotoxicosis and adverse effects on the gut health and performance of chickens even at concentrations below EU limits [43]. Chicks that were given diets containing 75–400 µg/kg FB1 experienced moderate toxicity. The fast absorption rate of FB1 in the gut may be due to impairments and dysfunctions of the gut barrier caused by oxidative stress and resulting in inflammation [44].

DON

DON is a member of TC mycotoxins, which are produced by fungi of the genera *Fusarium*, *Myrothecium*, *Verticimonosporium*, *Stachybotrys*, *Trichoderma*, *Trichothecium*, *Cephalosporium*, and *Cylindrocarpon*. More than 120 TCs exist. DON is also known as a vomitoxin. The IARC has classified DON as a group 3 human carcinogen. Moreover, DON is the most common mycotoxin (Figure 4) [43].

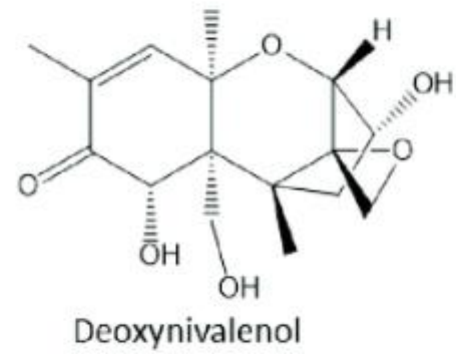


Fig (4): Chemical structure of DON [81]

TCs cause various negative effects on poultry, including oral sores, stunted growth, abnormal feathers, reduced egg laying rates and egg quality, shrinking of the bursa of the fabricius, liver damage due to oxidative stress, disrupted blood clotting, decreased white blood cell count and increased protein in the blood, and immune system suppression [45].

DON is one of the most frequently found mycotoxins in poultry feed due to the high levels of cereals present in chicken diets. The presence of DON in chicken feed can have various effects, including acute infections with high morbidity and mortality rates, chronic diseases, lowered resistance to pathogens, and decreased productivity. Additionally, DON negatively affects the immune response and gut morphology and their functions in chickens [15]. In humans, the consumption of DON can lead to acute temporary symptoms, such as nausea, vomiting, diarrhea, abdominal pain, headache, dizziness, and fever [46].

The UN restricts DON in chicken feed to 5 µg/kg [47]. However, poultry can tolerate 15 µg/kg DON in feed. This high tolerance may be associated with the metabolism of DON, in which native DON is degraded by microbes in the digestive tract and throughout the body into various metabolites [48].

DIAGNOSTIC APPROACHES FOR MYCOTOXICOSIS IN CHICKENS

Mycotoxins in chicken feed ingredients can accumulate in chicken organs or tissues, leading to various pathological conditions and reduced productivity; moreover, they might be passed onto chicken products, exerting adverse effects on human health [49]. Diagnosing mycotoxicosis in chickens is crucial for effective management and ensuring poultry health (Table 2). The diagnosis of mycotoxicosis in chickens include clinical observations, lesion identification, mycotoxin detection, biomarker analysis, histopathology, and toxin quantification [50].

Table (2): Maximum levels of mycotoxins in poultry feed [5]

Mycotoxin guidelines (maximum levels in poultry feed)		
European Food Safety Authority	DON	FUM
Corn and corn by-products	12 ppm	60 ppm
Poultry feed	5ppm	20 ppm

Clinical signs and lesion identification

The initial diagnosis of mycotoxicosis can be based on observing clinical signs and identifying characteristic lesions in infected chickens. These signs can include altered feed consumption, weight loss, reduced growth rates, decreased egg production, and various organ abnormalities. A feed sample should be submitted for analysis together with sick or recently dead poultry. In addition to the feed analysis, a necropsy and relevant diagnostic testing should be conducted if mycotoxicosis is suspected [51].

Detection and quantification of mycotoxins in feed

Samples of feed ingredients should be carefully and properly collected and submitted immediately for the direct detection, analysis, and quantification of mycotoxins by using mycotoxin screening techniques. Liquid chromatography (LC), gas chromatography, LC/mass spectrometry, thin-layer chromatography, high-performance LC, and enzyme-linked immunosorbent assay (ELISA) are commonly employed for mycotoxin analysis. Diagnostic methods allow for the rapid identification of specific mycotoxins and their levels in feed, providing valuable insights into their potential risk levels for chicken health [52]. The presence of mycotoxins can be amplified by taking samples from numerous sites of toxic feed or grain. These samples may be obtained from different locations to improve accuracy.

Biomarker analysis

Biomarker approaches based on the detection and analysis of specific biochemical and molecular markers can indicate mycotoxin exposure or toxic effects in chickens. Biomarkers are indicators involved in oxidative stress, immunological responses, histopathological changes, or alterations in gene expression [53]. Techniques, such as enzyme activity assays; immune-based assays, like ELISA; PCR-based gene expression analysis; or proteomic approaches are used to identify and quantify these biomarkers, aiding in the diagnosis of mycotoxicosis [54],[55]

Histopathological examination

Histopathology is critical for confirming the presence of mycotoxicosis and characterizing its associated lesions. The microscopic examination of stained tissue sections from organs, such as the kidneys, intestines, liver, and respiratory system, allows the identification of characteristic histopathological changes induced by mycotoxins. These changes can include degeneration, necrosis, inflammation, fibrosis, and other structural abnormalities in various organs. Histopathology, when combined with clinical signs and mycotoxin analysis, helps establish a definitive diagnosis [56]–[57].

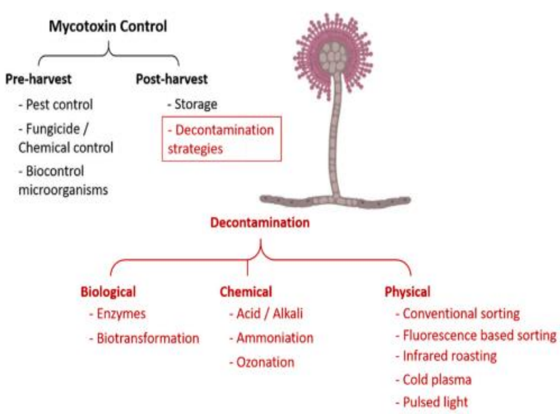
STRATEGIES FOR THE PREVENTION OF MYCOTOXIN CONTAMINATION

Several approaches are being used to reduce toxicity and improve the safety of food products. The strategies for mycotoxin control can be divided into pre- and postharvest techniques depending on their timing. Preharvest methods, which include preventing fungal infections in the field rather than in subsequent stages, are preferred for controlling mycotoxins. Postharvest methods include physical, mechanical, chemical, and biological control strategies [58].

Preharvest Strategies

Mechanical control

This method entails the ongoing monitoring of mycotoxins in agricultural crops and general products, as well as the prevention of mold and fungal growth on crops and foodstuffs. It is the best approach to prevent the detrimental effects of mycotoxins on animals and human health (Figure 5) [59]. Implementing good agricultural practices, such as utilizing resilient cultivars, treating seeds with disinfectants, insecticides, practicing crop rotation, and employing appropriate fungicides and herbicides, is vital to achieve these goals. Products of natural plant origins are also used [60]. Antagonistic beneficial bacteria and fungi are biological control products that are used in agricultural practice. The mechanical sorting of products contaminated with mycotoxins from clean products is crucial to ensure the production of food free from mycotoxins [61]. The best way to control mycotoxins is to prevent contamination in the field. However, this approach may not always be possible. As a result, postharvest strategies are designed to reduce fungal contamination and subsequently the mycotoxin levels in agricultural products during storage, processing, and transport. These strategies include applying chemical and natural agents and irradiation, as well as improving drying and storage processes [62].



Fig(5): Pre- and postharvest prevention and decontaminations processes for mycotoxin control [80]

Postharvest Strategies

Physical control

Physical control includes various physical techniques, like washing, sieving, sorting, irradiation, and heating, as well the application of mycotoxin binders to minimize mycotoxin content in food products. The initial steps involved in mycotoxin control are washing and sorting [63]. Washing has been proven to reduce the levels of different mycotoxins in grains. Given their low density, mycotoxin-contaminated fractions float and can be easily disposed of [64]. However, this approach might be ineffective especially when applied in controlling widespread mycotoxin contamination [65]. Another suggested technique is subjecting the mycotoxin-contaminated food to temperatures of 150 °C or higher; this method has been proven to decrease the levels of mycotoxins, such as AFs, FUMs, DON, and ZEN [66]. While thermal techniques can help mitigate mycotoxins, they alone are insufficient for completely eliminating these contaminants due to the inherent thermal stability of most mycotoxins [67]. Another potential physical method for controlling mycotoxins is the addition of mycotoxin binders to contaminated foods. These binders attach to mycotoxin molecules, creating a complex that hinders their absorption in the gut. Aluminosilicate, activated charcoal, zeolites, cholestyramines, and clays are among the most often utilized adsorbents [68]. Although this technique shows rapid and efficient adsorption rates for different mycotoxins in vitro, some adsorbents still have weak adsorption and specificity for particular mycotoxins, restricting their applications. Additionally, these binders may inadvertently bind to food micronutrients, reducing their bioavailability [69], [70].

Chemical control

Chemical treatments are another effective choice for mycotoxin elimination. In acidification, poultry feed is soaked in acidic solutions, such as hydrochloric acid, which has shown high efficacy in reducing the toxicity from contaminated commodities [71]. Ammoniation involves the degradation of mycotoxins by ammonia to reduce their levels to undetectable levels and inhibits fungal growth. However, this hydrolytic process can be reversed [72]. Ozonation is a unique chemical technique that can be used to prevent mycotoxin contamination in stored grains. The use of ozone in gas and liquid forms has been reported to be a safe and efficient method for the detoxification of various mycotoxins in food stuffs [73]. Upon using ozone to detoxify DON, the toxicity of DON remarkably reduced without leaving any residues [74].

Biological control

Biological approaches include oxidation, hydrolysis, glycosylation, or acetylation, in which mycotoxins are converted into metabolites that are either nontoxic or have reduced toxicity by the use of living microorganisms or the enzymes that they produce [75].

These microorganisms have been isolated from the environment and microbial flora of the mammalian gastrointestinal tract and have demonstrated efficacy against various mycotoxins [76]. The bacterial strain *Eubacterium* BBSH 797 remarkably reduced the negative consequences of DON and T-2 toxin in chickens [77]. Furthermore, a wide range of other microorganisms, including *Saccharomyces cerevisiae* and *Brevibacterium linens*, and enzymes, such as carboxypeptidase A, can prevent fungal growth and mycotoxin production [78]. Moreover, certain fungal species, such as *Aspergillus* and *Penicillium*, are particularly effective in detoxifying mycotoxins in chickens [79].

CONCLUSION

The symptoms of mycotoxin exposure seen in experimental research are typically induced by quantities frequently found in farm feed used for chicken production. Mycotoxins, which can change into forms that are more harmful than their precursors, may be connected to these symptoms. These concealed toxins can avoid detection through traditional means and exert detrimental effects on chickens, such as impaired growth and feed efficiency, immunological suppression, and organ damage. The application of efficient mitigating techniques, including enhanced feed quality control, mycotoxin-binding agents, and toxin deactivation technologies, is essential to protect the health and productivity of chickens. Cooperation among researchers, regulatory agencies, and poultry producers is important to address the above challenges and advance the development of reliable detection techniques and detoxification technologies suited to the particular requirements of the poultry business. The poultry industry can well protect animal health, guarantee product safety, and uphold high standards of food security for customers by overcoming these obstacles. Continuous monitoring and effective management strategies have been a must for controlling food contamination and ensuring food safety. Further studies are required to develop novel and cost-effective approaches to minimize the effect of mycotoxin residues in chicken on poultry products.

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السموم الفطرية وتأثيرها الضار على صحة الإنسان والحيوان: مراجعة

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الخلاصة:

السموم الفطرية هي سموم طبيعية تنتجها فطريات معينة تلوث مجموعة متنوعة من المحاصيل والمواد الغذائية المختلفة. يعد تلوث بالسموم الفطرية مشكلة عالمية تؤدي إلى العديد من التأثيرات الصحية السلبية على كل من البشر، الحيوانات ومحاصيل الغذاء في ظل ظروف مناخية معينة من الرطوبة النسبية ودرجات الحرارة العالية، تتوفر الظروف المناخية في الشرق الأوسط، مما يعزز نمو السموم الفطرية وانتشارها في هذه المنطقة.

فقد تم العثور على أكثر من أربعمائة نوع من السموم الفطرية في الأعلاف على مستوى العالم. أثار انتشار السموم الفطرية في مختلف السلع الزراعية، بما في ذلك علف الدجاج، مخاوف بشأن وجودها المحتمل في منتجات الدجاج كمصدر رئيسي للسموم المتعلقة بصحة الإنسان والخسائر الاقتصادية.

تشير النتائج إلى أن تلوث الدجاج بالسموم الفطرية يمثل تحديًا عالميًا، ويتطلب الأمر مراقبة مستمرة واستراتيجيات إدارة مناسبة لضمان سلامة الغذاء. تهدف هذه المراجعة إلى مناقشة بقايا السموم الفطرية في الدجاج، بما في ذلك حدوثها وتأثيراتها السمية واستراتيجيات المكافحة.

الكلمات المفتاحية: الأفلاتوكسينات؛ سلامة الغذاء؛ الفومونيزينات؛ الميكوتوكسينات؛ الأوكراتوكسين أ؛ التريكوثيسين