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Editorial

The Hazards of Mycotoxins and Key Issues for Future Research

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Contamination of mycotoxins in food and food raw materials poses a serious threat to human and animal health, which has attracted widespread attention. Under normal conditions, the exposure to multiple mycotoxins and the combined exposure of mycotoxins with non-mycotoxin substances can severely challenge established mycotoxin control strategies. In this review, we discuss the potential hazards of mycotoxins, and highlight the importance of studying their molecular mechanisms. In the future, it is imperative to enhance global cooperation and the application and sharing of innovative technologies to improve the detection and control of mycotoxins, thereby ensuring food safety and maintaining human health.

Mycotoxins are secondary metabolites produced by fungi, such as Penicillium, Alternaria, Fusarium, and Aspergillus. They are widely present in food and food-grade raw materials, posing serious threats to human and animal health. To date, around 500 mycotoxins have been reported in the natural environment, including ochratoxins (OTs), zearalenone (ZEN), aflatoxins (AFs), deoxynivalenol (DON), fumonisins (FUMs), tenuazonic acid, patulin, fusarin C, cytochalasins, penicillic acid, T-2 toxin, HT-2 toxin, and citrinin [1]. The Food and Agriculture Organization's assessment indicates that around 25% of the world's food crops were polluted by mycotoxins prior to 1985. Climate change is a key factor influencing mycotoxin contamination. Changes in temperature and moisture due to global climate change directly affect fungal growth and mycotoxin production. For example, *Aspergillus* and *Fusarium* are major mycotoxin-producing fungi, and their contamination levels vary with climatic conditions. This could significantly increase their proportion to roughly 60–80%. There is no denying that this increase is partly attributed to the advancements in analytical techniques [2].

Research has found that contamination by multiple mycotoxins is common in edible and medicinal plants, with seed-type plants being especially susceptible to contamination by *Aspergillus* and *Fusarium* [3]. The presence of these mycotoxins not only impacts food quality but may also lead to serious health risks. It has been reported that mycotoxins are associated with multiple toxic effects, including hepatotoxicity, nephrotoxicity, cardiotoxicity, neurotoxicity, reproductive toxicity, gastrointestinal toxicity, and immunotoxicity [4–7]. Some mycotoxins may cause strong carcinogenicity, such as aflatoxin B1 (AFB1), and it has been classified by the IARC as a group I carcinogen [8]. Clinical epidemiological investigations have revealed that mycotoxin exposure may be directly associated with the occurrence and development of various chronic diseases, such as diabetes, liver cancer, chronic enteritis, and infertility [9–12]. Certain mycotoxins can impair intestinal health by inducing inflammatory responses, immune dysfunction, disrupting the intestinal barrier, triggering oxidative stress, and causing imbalances in gut microbiota [13]. Furthermore, mycotoxin contamination not only affects food safety but also causes significant economic losses [14]. For example, in the United States, the mean annual economic costs of farmer gate cereal crop losses due to AFs, FUMs and trichothecenes, are estimated to be $932 million [15]. Therefore, monitoring mycotoxins and reducing their exposure and contamination in food and food raw materials is crucial for safeguarding human and animal health.

To address this issue, researchers have developed multiple detection methods, such as enzyme-linked immunosorbent assay (ELISA), high-performance liquid chromatography (HPLC), and liquid chromatography-tandem mass spectrometry (LC-MS/MS). They are highly effective, but they are generally confined to laboratory settings [16]. In recent years, some high-throughput analytical methods and new technologies that are rapid, sensitive, portable, and cost-effective have been developed to improve the sensitivity and reliability for the detection of mycotoxins [5,16].

The in-depth study of the mechanisms of the toxic effects of mycotoxins is essential to mitigate their health hazards and for risk assessment. Current data indicate that the toxic mechanisms of mycotoxins are complex, involving various biological processes such as oxidative stress, mitochondrial dysfunction, apoptosis, autophagy, and ferroptosis [17–19]. However, the precise molecular mechanisms by which many mycotoxins induce toxic effects remain unknown. Researchers have found that AFB1 can induce the production of reactive oxygen species (ROS), which results in mitochondrial dysfunction, which promotes inflammatory responses, and facilitates programmed cell death (e.g., pyroptosis, ferroptosis, and apoptosis). These processes have been confirmed to involve multiple signaling pathways, including solute carrier family 7 member 11 (SLC7A11)/glutathione peroxidase 4 (GPX4), nuclear factor erythroid 2-related factor 2 (Nrf2), inositol-requiring enzyme 1 (IRE1)/x-box binding protein 1 (XBP1), toll-like receptor 4 (TLR4), toll-like receptor 2 (TLR2), aryl hydrocarbon receptor (AHR), NOD-like receptor thermal protein domain associated protein 3 (NLRP3), protein kinase A (PKA), Wnt/β-catenin, transforming growth factor-β (TGF-β), protein kinase B (Akt)/mammalian target of rapamycin (mTOR), nuclear factor kappa-B (NF-κB), mitogen-activated protein kinase (MAPK), and myosin light chain kinase (MLCK) pathways [13,20,21]. These findings primarily stem from high-dose exposures, which differ significantly from natural conditions. The interconnected nature of signaling pathways, where factors like massive ROS production cause both direct oxidative damage and broader cascade effects, complicates identifying the primary toxic targets of these mycotoxins. Therefore, we should intensify our research efforts on the molecular mechanisms of mycotoxin toxicity and risk assessment, particularly on the toxic hazards and molecular mechanisms when mycotoxin poisoning occurs under natural conditions.

Mycotoxin contamination in food and raw materials typically involves multiple toxins. Even when individual levels meet regulatory limits, their combined presence can produce significant synergistic or additive toxicity. Studies confirm interactions among regulated mycotoxins (e.g., AFs, FUMs, trichothecenes, and ochratoxins) and emerging types (e.g., beauvericin), as well as between mycotoxins and non-mycotoxin pollutants such as cadmium, where co-exposure with DON demonstrates marked synergistic effects [22–25]. These findings challenge current mycotoxin control standards. Therefore, accurately assessing the combined toxic effects of different mycotoxins and the synergistic effects with currently known pollutants, and more scientifically establishing mycotoxin detection and prevention standards, are essential for maintaining food and public health safety.

In summary, the contamination status of mycotoxins in food-grade raw materials require significant attention. To mitigate mycotoxin contamination in food-grade materials, multifaceted actions, including the improvement of detection technology and storage management, and the innovation in risk assessment are required. A significant gap persists in research and risk assessment of combined mycotoxin/non-mycotoxin contamination exposure, demanding urgent current and future action. It is necessary to strengthen cooperation and the application and sharing of innovative technologies worldwide to enhance the detection and control capabilities of mycotoxins, thereby ensuring food safety and human health.

Author Contributions

Chongshan Dai drafted the original manuscript. Chongshan Dai, Zhihui Hao and Jianzhong Shen review and edited this manuscript. All authors drafted this manuscript and contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

Given his role as Editor Board Member, Chongshan Dai had no involvement in the peer-review of this article and has no access to information regarding its peer-review. Full responsibility for the editorial process for this article was delegated to Corinna Kehrenberg. The authors declare no conflict of interest.

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